

World Journal of *Gastroenterology*

World J Gastroenterol 2019 February 28; 25(8): 888-1036



REVIEW

- 888 Current and future pharmacological therapies for managing cirrhosis and its complications
Kockerling D, Nathwani R, Forlano R, Manousou P, Mullish BH, Dhar A

MINIREVIEWS

- 909 Outcomes of per oral endoscopic pyloromyotomy in gastroparesis worldwide
Mekaroonkamol P, Shah R, Cai Q

ORIGINAL ARTICLE**Basic Study**

- 923 Dbx2 exhibits a tumor-promoting function in hepatocellular carcinoma cell lines *via* regulating Shh-Gli1 signaling
Hu YT, Li BF, Zhang PJ, Wu D, Li YY, Li ZW, Shen L, Dong B, Gao J, Zhu X
- 941 Dynamic changes of key metabolites during liver fibrosis in rats
Yu J, He JQ, Chen DY, Pan QL, Yang JF, Cao HC, Li LJ
- 955 Procyanidin B2 protects against diet-induced obesity and non-alcoholic fatty liver disease *via* the modulation of the gut microbiota in rabbits
Xing YW, Lei GT, Wu QH, Jiang Y, Huang MX

Case Control Study

- 967 Triggers of histologically suspected drug-induced colitis
Brechmann T, Günther K, Neid M, Schmiegel W, Tannapfel A

Retrospective Study

- 980 Women on the liver transplantation waitlist are at increased risk of hospitalization compared to men
Rubin JB, Sinclair M, Rahimi RS, Tapper EB, Lai JC
- 989 Two-year delay in ulcerative colitis diagnosis is associated with anti-tumor necrosis factor alpha use
Kang HS, Koo JS, Lee KM, Kim DB, Lee JM, Kim YJ, Yoon H, Jang HJ
- 1002 Big-data analysis: A clinical pathway on endoscopic retrograde cholangiopancreatography for common bile duct stones
Zhang W, Wang BY, Du XY, Fang WW, Wu H, Wang L, Zhuge YZ, Zou XP

Observational Study

- 1012 Lethal-7-related polymorphisms are associated with susceptibility to and prognosis of gastric cancer
Jia ZF, Cao DH, Wu YH, Jin MS, Pan YC, Cao XY, Jiang J

EVIDENCE-BASED MEDICINE

- 1024** Establishing a model to measure and predict the quality of gastrointestinal endoscopy
Wang LW, Lin H, Xin L, Qian W, Wang TJ, Zhang JZ, Meng QQ, Tian B, Ma XD, Li ZS

CASE REPORT

- 1031** Crohn's-like acute severe colitis associated with Hermansky-Pudlak syndrome: A case report
Girot P, Le Berre C, De Maissin A, Freyssinet M, Trang-Poisson C, Bourreille A

ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Yoshihiro Ikura, DSc, MD, Chief Doctor, Professor, Department of Pathology, Takatsuki General Hospital, Takatsuki 569-1192, Osaka, Japan

AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. The *WJG* Editorial Board consists of 642 experts in gastroenterology and hepatology from 59 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, etc. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

INDEXING/ABSTRACTING

The *WJG* is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, Scopus and Directory of Open Access Journals. The 2018 edition of Journal Citation Report® cites the 2017 impact factor for *WJG* as 3.300 (5-year impact factor: 3.387), ranking *WJG* as 35th among 80 journals in gastroenterology and hepatology (quartile in category Q2).

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Shu-Yu Yin* Proofing Editorial Office Director: *Ze-Mao Gong*

NAME OF JOURNAL <i>World Journal of Gastroenterology</i>
ISSN ISSN 1007-9327 (print) ISSN 2219-2840 (online)
LAUNCH DATE October 1, 1995
FREQUENCY Weekly
EDITORS-IN-CHIEF Subrata Ghosh, Andrzej S Tarnawski
EDITORIAL BOARD MEMBERS http://www.wjgnet.com/1007-9327/editorialboard.htm
EDITORIAL OFFICE Ze-Mao Gong, Director
PUBLICATION DATE February 28, 2019

COPYRIGHT © 2019 Baishideng Publishing Group Inc
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 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

Big-data analysis: A clinical pathway on endoscopic retrograde cholangiopancreatography for common bile duct stones

Wei Zhang, Bing-Yi Wang, Xiao-Yan Du, Wei-Wei Fang, Han Wu, Lei Wang, Yu-Zheng Zhuge, Xiao-Ping Zou

ORCID number: Wei Zhang (0000-0003-0318-0773); Bing-Yi Wang (0000-0002-3713-0488); Xiao-Yan Du (0000-0003-4605-0313); Wei-Wei Fang (0000-0003-0453-4133); Han Wu (0000-0002-8040-6419); Lei Wang (0000-0003-0178-5930); Yu-Zheng Zhuge (0000-0002-0649-4457); Xiao-Ping Zou (0000-0002-7274-3626).

Author contributions: Zhang W and Zou XP designed the research; Zhang W, Wang BY, Du XY, Fang WW, Wu H, Wang L, and Zhuge YZ performed the research; Du XY, Fang WW, Wu H, and Wang L analyzed the data; Zhang W, Wang BY, and Zhuge YZ wrote the paper; all authors read and approved the final manuscript.

Institutional review board

statement: The study was reviewed and approved by the Ethics Committee of The Affiliated Drum Tower Hospital of Nanjing University Medical School.

Informed consent statement:

Patients were not required to give informed written consent prior to the study because the analysis retrospectively used their clinical data.

Conflict-of-interest statement: The authors have no conflict of interests to declare.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0)

Wei Zhang, Han Wu, Lei Wang, Yu-Zheng Zhuge, Xiao-Ping Zou, Department of Gastroenterology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing 210008, Jiangsu Province, China

Bing-Yi Wang, Xiao-Yan Du, Wei-Wei Fang, Medical Division, Yidu Cloud (Beijing) Technology Co., Ltd. Beijing 100101, China

Corresponding author: Xiao-Ping Zou, PhD, Professor, Department of Gastroenterology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, No. 321, Zhongshan Road, Nanjing 210008, Jiangsu Province, China. zouxp@nju.edu.cn

Telephone: +86-13770771661

Fax: +86-25-83106666

Abstract**BACKGROUND**

A clinical pathway (CP) is a standardized approach for disease management. However, big data-based evidence is rarely involved in CP for related common bile duct (CBD) stones, *let alone* outcome comparisons before and after CP implementation.

AIM

To investigate the value of CP implementation in patients with CBD stones undergoing endoscopic retrograde cholangiopancreatography (ERCP).

METHODS

This retrospective study was conducted at Nanjing Drum Tower Hospital in patients with CBD stones undergoing ERCP from January 2007 to December 2017. The data and outcomes were compared by using univariate and multivariable regression/linear models between the patients who received conventional care (non-pathway group, $n = 467$) and CP care (pathway group, $n = 2196$).

RESULTS

At baseline, the main differences observed between the two groups were the percentage of patients with multiple stones ($P < 0.001$) and incidence of cholangitis complication ($P < 0.05$). The percentage of antibiotic use and complications in the CP group were significantly less than those in the non-pathway group [adjusted odds ratio (OR) = 0.72, 95% confidence interval (CI): 0.55-0.93, $P = 0.012$, adjusted OR = 0.44, 95% CI: 0.33-0.59, $P < 0.001$, respectively]. Patients spent lower costs on hospitalization, operation, nursing, medication, and

license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See:

<http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Received: December 6, 2018

Peer-review started: December 6, 2018

First decision: January 6, 2019

Revised: January 11, 2019

Accepted: January 18, 2019

Article in press: January 18, 2019

Published online: February 28, 2019

medical consumable materials ($P < 0.001$ for all), and even experienced shorter length of hospital stay (LOHS) ($P < 0.001$) after the CP implementation. No significant differences in clinical outcomes, readmission rate, or secondary surgery rate were presented between the patients in the non-pathway and CP groups.

CONCLUSION

Implementing a CP for patients with CBD stones is a safe mode to reduce the LOHS, hospital costs, antibiotic use, and complication rate.

Key words: Common bile duct stones; Endoscopic retrograde cholangiopancreatography; Clinical pathway; Outcomes; Costs

©The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We utilized a big-data process and application platform for exploring the value of clinical pathway (CP) implementation in patients with common bile duct stones undergoing endoscopic retrograde cholangiopancreatography. Univariate and multivariable regression/linear models were developed to compare the outcomes between the patients in the non-pathway and CP groups. Our findings demonstrated that a CP is a safe mode to reduce the length of hospital stay, hospital costs, antibiotic use, and complication rate. The present study provides big-data evidence for clinical standardization of CPs.

Citation: Zhang W, Wang BY, Du XY, Fang WW, Wu H, Wang L, Zhuge YZ, Zou XP. Big-data analysis: A clinical pathway on endoscopic retrograde cholangiopancreatography for common bile duct stones. *World J Gastroenterol* 2019; 25(8): 1002-1011

URL: <https://www.wjgnet.com/1007-9327/full/v25/i8/1002.htm>

DOI: <https://dx.doi.org/10.3748/wjg.v25.i8.1002>

INTRODUCTION

Gallstone disease is one of the most frequent biliary diseases leading to hospitalization and imposing a significant financial burden. The worldwide prevalence of gallstones presents a rising tendency due to the change of dietary structure and routine living customs in recent years^[1,2]. Of the patients who suffered from gallstones, approximately 10%-15% were found to have synchronous common bile duct (CBD) stones^[3,4]. The clinical manifestations of CBD stones are varied from biliary colic to a combination of complications, such as acute pancreatitis or cholangitis; sometimes, CBD stones even may be asymptomatic^[5]. Treatment and management of CBD stones have changed considerably during the last three decades. With the popularization of minimally invasive surgery in clinical practice, endoscopic retrograde cholangiopancreatography (ERCP) is currently recognized as a standard therapy for patients with CBD stones^[6,7]. Despite this, a risk of complications after ERCP cannot be avoided, and it is even associated with increased morbidity and mortality^[8]. In addition, there is evidence showing that in some patients with gallstones received ERCP and routine care at first admission, re-admission and longer preoperative stay were caused^[9]. Due to the growing complexity of CBD stone treatments and care, it is crucial to develop a standardized multidisciplinary approach to avoid chaotic management of this disease.

A clinical pathway (CP) is an advanced medical diagnosis, treatment, and management mode, which may optimize medical treatment by facilitating clinical assessments, improving utilization efficiency of medical sources, and reducing economical expenses^[10-12]. Nowadays, a CP is thought to be an effective tool to be explicit about the sequencing, timing and provision of interventions in clinical practice and can guide physicians and nursing staff in providing evidence-based results^[13,14]. Moreover, analysis of evaluating indexes (including clinical outcome, efficiency indicators, financial indicators, and antibiotic use indicators) can guarantee the effectiveness of the CP implementation and optimization^[15,16]. One study has demonstrated that a CP presents sustainable effects in gallstone-related care, resulting in shorter length of hospital stay (LOHS) and lower hospital expenses^[9]. In addition, several studies conducted in other surgical domains also presented similar results^[17-19].

However, implementation of the CP in China is in its start-up stage, especially in the field of hepatobiliary surgery. The status and value of the CP in the management of patients with CBD stones after ERCP remain to be explored. Given this concern, a retrospective study based on a big-data, intelligence database platform was launched. The aim of the present study was to analyze the impact of a CP on LOHS, readmission, treatment outcomes, hospital costs, and postoperative complication rate in patients with CBD stones undergoing ERCP.

MATERIALS AND METHODS

Study patients and data collection

This is a retrospective study of patients with CBD stones who received ERCP at Nanjing Drum Tower Hospital (Nanjing, Jiangsu Province, China) between January 2007 and December 2017. This study was approved by Ethics Committee of the Affiliated Drum Tower Hospital of Nanjing University Medical School (201817001), and informed consent was obtained from all subjects.

All patients aged above 18 years old without previous ERCP history were included in this study. The exclusion criteria were: (1) Patients with previous or present hepatolithiasis; (2) patients with severe liver diseases, cardio-pulmonary or renal inadequacy; (3) patients with severe hematologic diseases and concomitant obvious coagulopathy; (4) patients with combined gallbladder, CBD, duodenal papillary neoplasm, or congenital choledochal cyst; (5) patients who underwent Billroth I and II gastrectomy or gastrojejunostomy; and (6) pregnant patients. Subjects who met criteria for this study were extracted automatically from a big-data, intelligence database platform (Yidu Cloud Technology Co. Ltd., Beijing, China) by setting the inclusion and exclusion criteria. The study population consisted of two groups which accepted conventional care (non-pathway group) and a CP (CP group), respectively.

Demographic and clinical characteristics of subjects were obtained from electronic medical records. Outcomes of pathway complementation were compared between the two groups in LOHS (total and preoperative LOHS), readmission rate (a second hospital admission within 30 d due to CBD stones and postoperative complications), treatment outcomes, hospital charges (also including medication, operation, perioperative examinations, nursing and medical consumable materials charges), antibiotic use, secondary surgery rate, and postoperative complications.

CP

A set of sophisticated CPs for patients with CBD stones was implemented at this hospital in 2012. Development and optimization of the CP involved a multidisciplinary team under the instruction of relevant guidelines, including attending surgeons and residents, an anesthesiologist, a head of pharmacy faculty, and representatives from nursing and rehabilitation department. The training of the CP was performed before implementation to relevant personnel. Pathway I was designed for patients with expected LOHS less than 5-10 d, while pathway II was used for LOHS of 7-10 d. These CPs were explicit about the sequence of strategies for diagnosis, treatment, medication, routine care, and assessment. The pathway I is shown as an example in Appendix 1.

Statistical analysis

All statistical analyses were conducted using SAS, version 9.4 (SAS Institute, Cary, NC, United States). Data following a normal distribution are presented by mean \pm standard deviation (mean \pm SD), and otherwise are presented as median (interquartile range). Differences between the two groups were compared using Wilcoxon signed-rank test (continuous variables) or chi-squared test (categorical variables). In addition, univariable logistic regression models were used to determine whether odds of outcomes differed between the groups. We also utilized multivariable logistic (linear) regression models for evaluating the effect of pathway complementation on each outcome by controlling age, gender, smoking and drinking habits, the number of stones, and white blood cell (WBC) count at hospital admission. A *P*-value < 0.05 was considered statistically significant.

RESULTS

Two thousand six hundred and sixty-three eligible patients were included finally, of whom 467 were in the non-pathway group and 2196 in the clinical-pathway group (Figure 1). Table 1 shows the comparison of demographic and clinical characteristics

between the patients who received routine care and CP care. There were no differences between the two groups in terms of age, gender, insured status, health behaviors, or maximum diameter of stones. The percentage of patients with multiple stones was found to be significantly different between the two groups ($P < 0.001$). The number of patients suffering from comorbidities was similar, although the percentage of patients with cholangitis was higher in the non-pathway group ($P = 0.041$). Although WBC counts in both groups were within the normal range, there was a significantly higher WBC count among the patients in the non-pathway group ($P = 0.005$).

Table 2 presents the outcomes of efficiency, treatment, hospital costs, and antibiotic use following the CP implementation. The median total LOHS was 8 (range, 6-11) d in the non-pathway group, while it was one day shorter (7, 5-9) in the CP group ($P < 0.001$). The pre-operative LOHS was found to be similar between the two groups. There were no significant changes with respect to the treatment outcomes (recovered, improved, not improved, and died) in both groups, and even no patients died in our study. Thirty-four (7.28%) patients in the non-pathway group required readmission to hospital, while readmission rate (173, 7.88%) was increased after pathway complementation, although this difference was not statistically significant ($P = 0.661$). A considerably decreasing trend in the costs was observed among patients with the CP implementation, including hospitalization, medication, operation, nursing, materials, and preoperative examination ($P < 0.001$). In addition, implementation of the CP was associated with a reduced proportion of antibiotic use ($P < 0.001$). The median time of antibiotic use [11 (7.0-17.0) d] in the CP group was one day shorter than that before the CP complementation [12 (8.0-18.5) d] ($P = 0.004$). For patients in the CP group, secondary procedure occurred more frequently, although this difference was not statistically significant (16.94 vs 14.78%, $P = 0.253$).

The postoperative complication rates are compared in **Table 3**. About 26.77% of patients with routine care had at least one complication, while the incidence of complications dropped to 14.39% after the CP complementation ($P < 0.001$). The incidence rates of acute pancreatitis and liver abscess were considerably lower in patients after CP implementation, with significant differences between the two groups ($P < 0.001$).

The effect of the CP complementation on each outcome was also assessed by univariate and multivariate logistic regression through controlling age, gender, smoking and drinking habits, the number of stones, and WBC count at hospital admission (Tables 4 and 5). After adjusting for differences between the two groups, antibiotic use and postoperative complications were less in patients with the CP complementation [odds ratio (OR) = 0.72, 95% confidence interval (CI) 0.55-0.93, $P = 0.012$; and OR = 0.44, 95% CI 0.33-0.59, $P < 0.001$, respectively]. The costs of hospitalization, operation, nursing, medication, and materials ($P < 0.001$ for all) and LOHS ($P < 0.001$) decreased significantly after implementation of the CP.

DISCUSSION

Despite wide adoption of CPs throughout different departments currently, their evaluation and optimization remain doubtful^[20]. The purpose of this study was to compare the indicators of CP implementation in five domains (clinical outcome, efficiency indicators, financial indicators, and antibiotic use indicators) for patients with CBD stones undergoing ERCP. Our results confirmed that pathway implementation in CBD stones was associated with reduced total LOHS, costs, antibiotic use, antibiotic use duration, and complication rate. More importantly, the decrease has not been achieved at the expense of increased readmission rate or mortality.

With the development of endoscopic technique, ERCP is considered a preferred therapeutic method in management of CBD stones. However, it can be still challenging in some cases, such as high total hospital expenses and high risk of post-ERCP complications^[21,22]. CP, one of the main modes to standardize treatment and care, is increasingly adopted by hospitals to strive to better outcomes and lower costs. However, the definition of CP has not yet been fully elucidated in clinical practice, and the impact of pathway complementation is varied by different factors and conditions^[23,24]. Findings of our study are consistent with those obtained by Kristin *et al* who demonstrated a considerable reduction in terms of costs and LOHS in patients with complicated gallstone disease after the CP implementation^[9]. More recent studies showed similar improvements in other specialties of diseases, such as acute pancreatitis^[25], breast cancer^[15], and chronic obstructive pulmonary disease^[26]. However, pre-operative length of stay showed no distinct disparity in our study, and

Table 1 Demographic and clinical characteristics of patients

Characteristic	Non-pathway group (n = 467)	Cinical pathway group (n = 2196)	P value
Age, yr (median, range)	64 (52-75)	63 (51-75)	0.405
Female, n (%)	235 (50.32)	1093 (49.77)	0.829
Medical insurance, n (%)	217 (46.47)	945 (43.03)	0.174
Health behavior, n (%)			
Smoking	57 (12.21)	260 (11.84)	0.825
Alcohol use	36 (7.71)	164 (7.47)	0.858
Comorbidity, n (%)			
Hypertension	155 (33.19)	703 (32.01)	0.621
Diabetes	68 (14.56)	292 (13.30)	0.468
COPD	11 (2.36)	54 (2.46)	0.895
Myocardial infarction	0	6 (0.27)	0.258
Cholangitis	74 (15.85)	271 (12.34)	0.041 ^a
Cholecystolithiasis	188 (40.26)	780 (35.52)	0.053
JPD	1 (0.21)	10 (0.46)	0.460
CBD stone number ≥ 5, n (%)	201 (43.04)	1173 (53.42)	< 0.001 ^a
Maximum diameter of stones, cm (median, range)	0.8 (0.6-1.2)	0.9 (0.6-1.2)	0.949
Laboratory test (median, range)			
Temperature (°C), n = 359/2113	36.5 (36.3-36.8)	36.5 (36.3-36.8)	0.855
WBC count, n = 370/1451	6.0 (4.7-9.2)	5.7 (4.6-7.6)	0.005 ^a
Direct bilirubin level, n = 363/1439	12.2 (5.6-44.2)	10.7 (4.8-37.2)	0.210
Total bilirubin level, n = 363/1439	22.6 (12.7-57.6)	21.2 (12.5-51.9)	0.628
AST, n = 363/1440	47.9 (22.8-104.5)	45.4 (23.5-104.8)	0.842
GGT, n = 363/1439	257.4 (115.3-492.4)	265.1 (109.9-519.4)	0.918
ALP, n = 363/1439	161.7 (99.9-283.3)	154.9 (97.4-259.3)	0.536
ALT, n = 364/1443	85.1 (29.6-203.2)	89.0 (32.0-206.9)	0.946
Cr, n = 361/1431	62.0 (52.0-74.0)	62.0 (2.0-73.0)	0.966

^aP < 0.05 was considered statistically significant.

COPD: Chronic obstructive pulmonary disease; JPD: Juxtapapillary duodenal diverticulum; CBD stones: Common bile duct stones; WBC: White blood cell; AST: Aspartate transaminase; GGT: Gamma-glutamyl transpeptidase; ALP: Alkaline phosphatase; Cr: Creatinine.

the implementation of pathway might have greater impact on postoperative hospital stay. Similar to our results in terms of antibiotic use, Dona *et al*^[27] reported that there was a reduction of antibiotic prescriptions in patients with community-acquired pneumonia after introducing a CP. Our study provided further evidence that the CP implementation can also significantly reduce the duration of antibiotic use and three-line antibiotic prescriptions. Thus, it is possible to conclude that a marked reduction of costs appears to be associated with several factors, such as effective pre-operative examination and rational use of medications and materials. Moreover, CP seems to be one of key approaches to maximize cost-effectiveness, while without sacrificing good treatment outcomes^[28]. The most common causes of dropout from CP were postoperative complications that needed additional treatment. The findings of the present study demonstrated that rates of complications were lower in patients operated upon admission who implemented the CP compared to patients receiving routine care. There have been multiple previous publications in various domains which have demonstrated the lower incidence of complications following critical pathways^[29-31]. However, critical factors may have affected outcomes, such as patients' characteristics, living habits, disease features, and individual laboratory measurements. Thus, these factors did not affect the findings that CP use achieved a significantly shorter LOHS, lower costs, and reduced complications after adjustments.

Large-scale populations with gallstones and data process and application platform utilization are the main strengths in the present study. Furthermore, the findings were demonstrated by adjusting the potential confounders. However, this study was limited by its single-center retrospective design, indicating that further multiple-center trials with larger variable are in need to confirm the results.

In conclusion, findings of our study have demonstrated that patients with CBD stones who accepted the CP appear to be significantly lower in the LOHS, the costs,

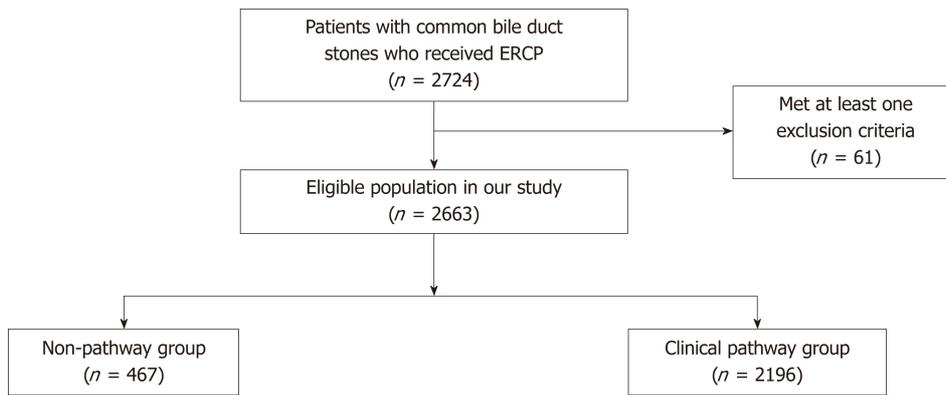


Figure 1 Flow diagram of study population.

the rate of antibiotic use, and the incidence of complications. Our study provides further evidence of CP use in Chinese patients and also standardizes gallstone management and treatment.

Table 2 Comparison of length of hospital stay, clinical outcomes, hospital charges, and drug use between the non-pathway and clinical pathway groups

Characteristic	Non-pathway group (n = 467)	Cinical pathway group (n = 2196)	P value
Length of total hospital stay (median, range)	8 (6-11)	7 (5-9)	< 0.001 ^a
Pre-operative length of stay	2 (1-4)	2 (1-3)	0.451
Readmission, n (%)	34 (7.28)	173 (7.88)	0.661
Clinical outcomes, n (%)			0.115
Recovered	223 (47.75)	1146 (52.19)	
Improved	236 (50.54)	1028 (46.81)	
Not improved	8 (1.71)	22 (1)	
Died	0	0	
Charges of hospitalization (CNY), (median, range) n = 467/2183	21508.3 (17150.6-30045.8)	18362.9 (15665.8-22895.2)	< 0.001 ^a
Charges of medication, n = 459/2153	6620.6 (3429.4-12239.7)	4900.6 (3172.4-8186.0)	< 0.001 ^a
Charges of operation, n = 458/2151	5741.0 (4519.2-7324.0)	5455.2 (2670.0-6964.0)	< 0.001 ^a
Charges of nursing, n = 454/2133	188.0 (115.0-288.0)	120.0 (74.0-211.0)	< 0.001 ^a
Charges of materials, n = 409/1540	7916.4 (6696.0-10552.6)	6985.5 (6135.1-8224.7)	< 0.001 ^a
Charges of examination, n = 459/2153	2698.0 (2224.5-3799.5)	2463.5 (2134.5-3105.5)	< 0.001 ^a
Antibiotic use, n (%)	260/430 (60.47)	832/1737 (47.90)	< 0.001 ^a
Antibiotic usage duration (d) (median, range), n = 260/832	12 (8.0-18.5)	11 (7.0-17.0)	0.004 ^a
Three line antibiotic use, n (%)	51/430 (11.86)	149/1737 (8.58)	0.035 ^a
Secondary surgery, n (%)	69 (14.78)	372 (16.94)	0.253

^aP < 0.05 was considered statistically significant.**Table 3 Comparison of postoperative complication rates between the non-pathway and clinical pathway groups**

Characteristic	Non-pathway group (n = 467)	Cinical pathway group (n = 2196)	P value
Total, n (%)	125 (26.77)	316 (14.39)	< 0.001 ^a
Acute pancreatitis	113 (24.20)	298 (13.57)	< 0.001 ^a
Gallbladder perforation	1 (0.21)	1 (0.05)	0.227
Gastrointestinal hemorrhage	0	2 (0.09)	0.514
Biliary tract infection	2 (0.43)	4 (0.18)	0.308
Liver abscess	10 (2.14)	11 (0.50)	< 0.001 ^a

^aP < 0.05 was considered statistically significant.**Table 4 Univariate logistic regression analysis of outcomes**

Characteristic	Non-pathway group (n = 467)	Cinical pathway group (n = 2196)	OR (95%CI)	P value
Length of total hospital stay (median, range)	8 (6-11)	7 (5-9)		< 0.001 ^a
Pre-operative length of stay	2 (1-4)	2 (1-3)		0.078
Readmission, n (%)	34 (7.28)	173 (7.88)	1.09 (0.74, 1.60)	0.661
Clinical outcomes, n (%)			1.21 (0.99, 1.47)	0.064
Charges of hospitalization (CNY) (median, range)	21508.3 (17150.6-30045.8)	18362.9 (15665.8-22895.2)		< 0.001 ^a
Medication	6620.6 (3429.4-12239.7)	4900.6 (3172.4-8186.0)		< 0.001 ^a
Operating	5741.0 (4519.2-7324.0)	5455.2 (2670.0-6964.0)		< 0.001 ^a
Nursing	188.0 (115.0-288.0)	120.0 (74.0-211.0)		< 0.001 ^a
Materials	7916.4 (6696.0-10552.6)	6985.5 (6135.1-8224.7)		< 0.001 ^a
Examination	2698.0 (2224.5-3799.5)	2463.5 (2134.5-3105.5)		< 0.001 ^a
Antibiotic use, n (%)	260/430 (60.47)	832/1737(47.90)	0.60 (0.49, 0.75)	< 0.001 ^a
Antibiotic usage duration (d) (median, range)	12 (8.0-18.5)	11 (7.0-17.0)		0.310

Three line antibiotic use, <i>n</i> (%)	51/430 (11.86)	149/1437 (8.58)	0.69	0.036 ^a
Secondary surgery, <i>n</i> (%)	69 (14.78)	372 (16.94)	1.18	0.254
Complications	125 (26.77)	316 (14.39)	0.46 (0.36, 0.58)	< 0.001 ^a

^a*P* < 0.05 was considered statistically significant. OR: Odds ratio; CI: Confidence interval.

Table 5 Multivariate logistic and linear regression analysis of outcomes

Characteristic	Adjusted OR (95%CI) or coefficients	<i>P</i> value
Length of total hospital stay	-1.71 (-2.30, -1.12) ¹	< 0.001 ^a
Hospitalization costs	-5572.26 (-6931.48, -4213.03) ¹	< 0.001 ^a
Medication costs	-2760.03 (-3738.96, -1781.11) ¹	< 0.001 ^a
Operating costs	-382.08 (-635.30, -128.85) ¹	< 0.001 ^a
Nursing costs	-138.25 (-195.83, -80.66) ¹	< 0.001 ^a
Materials costs	-1688.35 (-2049.61, -1327.10) ¹	< 0.001 ^a
Examination costs	-138.25 (-195.83, -80.66) ¹	< 0.001 ^a
Three line antibiotic use	0.89 (0.60, 1.31)	0.546
Antibiotic use, <i>n</i> (%)	0.72 (0.55, 0.93)	0.012 ^a
Complications	0.44 (0.33, 0.59)	< 0.001 ^a

¹Coefficients.

^a*P* < 0.05 was considered statistically significant, adjusted for age, gender, smoking, alcohol use, the number of stones, and white blood cell count at hospital admission.

OR: Odds ratio; CI: Confidence interval.

ARTICLE HIGHLIGHTS

Research background

Endoscopic retrograde cholangiopancreatography (ERCP) is widely recognized as a standard endoscopic technique for patients with common bile duct (CBD) stones. However, ERCP is associated with significant morbidity, mortality, and longer preoperative stay. A clinical pathway (CP) is an advanced methodology that provides a sequence of diagnosis, treatment, and management. Although CP implementation could optimize medical treatment and improve efficiency of medical sources utilization, CP implementation for CBD stones has not been fully promoted at present.

Research motivation

Current situation and value of the CP in management of CBD stones receiving ERCP still need to be explored. With the arrival of the era of big-data, we utilized a big-data process and application platform to provide a solid data base and scientific evidence for the establishment of the CP.

Research objectives

The objective of this study was to compare length of hospital stay (LOHS), costs, clinical outcomes, antibiotic use, and postoperative complication rate before and after implementing a CP for patients with CBD stones undergoing ERCP.

Research methods

Patients with CBD stones from Nanjing Drum Tower Hospital between January 2007 and December 2017 were identified from a big-data, intelligence database platform (Yidu Cloud Technology Ltd., Beijing, China). The enrolled population consisted of two groups which accepted conventional care (non-pathway group, *n* = 467) and the CP (CP group, *n* = 2196), respectively. Univariate and multivariable regression/linear models were utilized to compare the medical records and outcomes.

Research results

The percentage of antibiotic use and complications in the CP group were significantly less than those in the non-pathway group [adjusted odds ratio (OR) = 0.72, 95% confidence interval (CI) 0.55-0.93, *P* = 0.012, adjusted OR = 0.44, 95%CI 0.33-0.59, *P* < 0.001, respectively]. Patients experienced lower costs in hospitalization, operation, nursing, medication, and materials (*P* < 0.001 for all), and even shorter LOHS (*P* < 0.001) after implementation of the CP. No significant differences in clinical outcomes, readmission rate, or secondary surgery rate were presented between the patients in non-pathway and CP groups.

Research conclusion

In conclusion, implementation of the CP for patients with CBD stones undergoing ERCP significantly reduced LOHS, the costs, the rate of antibiotic use, and the incidence of complications without increasing readmission rates. A CP is confirmed to be an effective mode which is explicit about the sequencing, timing, and provision of interventions in the field of CBD stones. Meanwhile, our study provides further big-data evidence of a multidisciplinary CP in Chinese patients.

Research perspectives

Despite that this is the rare big-data evidence of a CP in Chinese patients with CBD stones, further multiple-center studies with larger variable are essential to strengthen the results.

ACKNOWLEDGEMENTS

We sincerely appreciate Yidu Cloud (Beijing) Technology Co. Ltd., China for providing technical support in extracting data by using the big-data intelligence platform.

REFERENCES

- 1 **Acalovschi M.** Gallstones in patients with liver cirrhosis: Incidence, etiology, clinical and therapeutical aspects. *World J Gastroenterol* 2014; **20**: 7277-7285 [PMID: 24966598 DOI: 10.3748/wjg.v20.i23.7277]
- 2 **Zhu Q,** Sun X, Ji X, Zhu L, Xu J, Wang C, Zhang C, Xue F, Liu Y. The association between gallstones and metabolic syndrome in urban Han Chinese: A longitudinal cohort study. *Sci Rep* 2016; **6**: 29937 [PMID: 27443986 DOI: 10.1038/srep29937]
- 3 **Anand G,** Patel YA, Yeh HC, Khashab MA, Lennon AM, Shin EJ, Canto MI, Okolo PI, Kalloo AN, Singh VK. Factors and Outcomes Associated with MRCP Use prior to ERCP in Patients at High Risk for Choledocholithiasis. *Can J Gastroenterol Hepatol* 2016; **2016**: 5132052 [PMID: 27446845 DOI: 10.1155/2016/5132052]
- 4 **Tazuma S.** Gallstone disease: Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). *Best Pract Res Clin Gastroenterol* 2006; **20**: 1075-1083 [PMID: 17127189 DOI: 10.1016/j.bpg.2006.05.009]
- 5 **Aslan F,** Arabul M, Celik M, Alper E, Unsal B. The effect of biliary stenting on difficult common bile duct stones. *Prz Gastroenterol* 2014; **9**: 109-115 [PMID: 25061492 DOI: 10.5114/pg.2014.42507]
- 6 **Kenny R,** Richardson J, McGlone ER, Reddy M, Khan OA. Laparoscopic common bile duct exploration versus pre or post-operative ERCP for common bile duct stones in patients undergoing cholecystectomy: Is there any difference? *Int J Surg* 2014; **12**: 989-993 [PMID: 24998206 DOI: 10.1016/j.ijssu.2014.06.013]
- 7 **Bray MS,** Borgert AJ, Folkers ME, Kothari SN. Outcome and management of endoscopic retrograde cholangiopancreatography perforations: A community perspective. *Am J Surg* 2017; **214**: 69-73 [PMID: 28173939 DOI: 10.1016/j.amjsurg.2017.01.034]
- 8 **Morris S,** Gurusamy KS, Sheringham J, Davidson BR. Cost-effectiveness analysis of endoscopic ultrasound versus magnetic resonance cholangiopancreatography in patients with suspected common bile duct stones. *PLoS One* 2015; **10**: e0121699 [PMID: 25799113 DOI: 10.1371/journal.pone.0121699]
- 9 **Sheffield KM,** Ramos KE, Djukom CD, Jimenez CJ, Mileski WJ, Kimbrough TD, Townsend CM, Riall TS. Implementation of a critical pathway for complicated gallstone disease: Translation of population-based data into clinical practice. *J Am Coll Surg* 2011; **212**: 835-843 [PMID: 21398156 DOI: 10.1016/j.jamcollsurg.2010.12.047]
- 10 **Elliott MJ,** Gil S, Hemmelgarn BR, Manns BJ, Tonelli M, Jun M, Donald M. A scoping review of adult chronic kidney disease clinical pathways for primary care. *Nephrol Dial Transplant* 2017; **32**: 838-846 [PMID: 27257274 DOI: 10.1093/ndt/gfw208]
- 11 **De Luca A,** Toni D, Lauria L, Sacchetti ML, Giorgi Rossi P, Ferri M, Puca E, Prencipe M, Guasticchi G; IMPLimentazione Percorso Clinico Assistenziale Ictus Acuto (IMPLICIA) Study Group. An emergency clinical pathway for stroke patients--results of a cluster randomised trial (isrctn41456865). *BMC Health Serv Res* 2009; **9**: 14 [PMID: 19159477 DOI: 10.1186/1472-6963-9-14]
- 12 **Schuur JD,** Baugh CW, Hess EP, Hilton JA, Pines JM, Asplin BR. Critical pathways for post-emergency outpatient diagnosis and treatment: Tools to improve the value of emergency care. *Acad Emerg Med* 2011; **18**: e52-e63 [PMID: 21676050 DOI: 10.1111/j.1553-2712.2011.01096.x]
- 13 **Bradywood A,** Farrokhi F, Williams B, Kowalczyk M, Blackmore CC. Reduction of Inpatient Hospital Length of Stay in Lumbar Fusion Patients With Implementation of an Evidence-Based Clinical Care Pathway. *Spine (Phila Pa 1976)* 2017; **42**: 169-176 [PMID: 27213939 DOI: 10.1097/BRS.0000000000001703]
- 14 **El Baz N,** Middel B, van Dijk JP, Oosterhof A, Boonstra PW, Reijneveld SA. Are the outcomes of clinical pathways evidence-based? A critical appraisal of clinical pathway evaluation research. *J Eval Clin Pract* 2007; **13**: 920-929 [PMID: 18070263 DOI: 10.1111/j.1365-2753.2006.00774.x]
- 15 **van Dam PA,** Verheyden G, Sugihara A, Trinh XB, Van Der Mussele H, Wuyts H, Verkinderen L, Hauspy J, Vermeulen P, Dirix L. A dynamic clinical pathway for the treatment of patients with early breast cancer is a tool for better cancer care: Implementation and prospective analysis between 2002-2010. *World J Surg Oncol* 2013; **11**: 70 [PMID: 23497270 DOI: 10.1186/1477-7819-11-70]
- 16 **de Vries M,** van Weert JC, Jansen J, Lemmens VE, Maas HA. Step by step development of clinical care pathways for older cancer patients: Necessary or desirable? *Eur J Cancer* 2007; **43**: 2170-2178 [PMID: 17870519 DOI: 10.1016/j.ejca.2007.08.004]
- 17 **Shin KC,** Lee HS, Park JM, Joo HC, Ko YG, Park I, Kim MJ. Outcomes before and after the Implementation of a Critical Pathway for Patients with Acute Aortic Disease. *Yonsei Med J* 2016; **57**: 626-634 [PMID: 26996561 DOI: 10.3349/ymj.2016.57.3.626]
- 18 **Thursky K,** Lingaratnam S, Jayarajan J, Haeusler GM, Teh B, Tew M, Venn G, Hiong A, Brown C,

- Leung V, Worth LJ, Dalziel K, Slavin MA. Implementation of a whole of hospital sepsis clinical pathway in a cancer hospital: Impact on sepsis management, outcomes and costs. *BMJ Open Qual* 2018; **7**: e000355 [PMID: 30019016 DOI: 10.1136/bmjopen-2018-000355]
- 19 **van der Kolk M**, van den Boogaard M, Ter Brugge-Speelman C, Hol J, Noyez L, van Laarhoven K, van der Hoeven H, Pickkers P. Development and implementation of a clinical pathway for cardiac surgery in the intensive care unit: Effects on protocol adherence. *J Eval Clin Pract* 2017; **23**: 1289-1298 [PMID: 28719134 DOI: 10.1111/jep.12778]
- 20 **Dong W**, Huang Z. A Method to Evaluate Critical Factors for Successful Implementation of Clinical Pathways. *Appl Clin Inform* 2015; **6**: 650-668 [PMID: 26763576 DOI: 10.4338/ACI-2015-05-RA-0054]
- 21 **Dasari BV**, Tan CJ, Gurusamy KS, Martin DJ, Kirk G, McKie L, Diamond T, Taylor MA. Surgical versus endoscopic treatment of bile duct stones. *Cochrane Database Syst Rev* 2013; CD003327 [PMID: 23999986 DOI: 10.1002/14651858.CD003327.pub3]
- 22 **Platt TE**, Smith K, Sinha S, Nixon M, Srinivas G, Johnson N, Andrews S. Laparoscopic common bile duct exploration; a preferential pathway for elderly patients. *Ann Med Surg (Lond)* 2018; **30**: 13-17 [PMID: 29946453 DOI: 10.1016/j.amsu.2018.03.044]
- 23 **Lion KC**, Wright DR, Spencer S, Zhou C, Del Beccaro M, Mangione-Smith R. Standardized Clinical Pathways for Hospitalized Children and Outcomes. *Pediatrics* 2016; **137**: pii: e20151202 [PMID: 27002007 DOI: 10.1542/peds.2015-1202]
- 24 **Singh SB**, Shelton AU, Greenberg B, Starner TD. Implementation of cystic fibrosis clinical pathways improved physician adherence to care guidelines. *Pediatr Pulmonol* 2017; **52**: 175-181 [PMID: 27797455 DOI: 10.1002/ppul.23635]
- 25 **Vujasinovic M**, Makuc J, Tepes B, Marolt A, Kikec Z, Robac N. Impact of a clinical pathway on treatment outcome in patients with acute pancreatitis. *World J Gastroenterol* 2015; **21**: 9150-9155 [PMID: 26290642 DOI: 10.3748/wjg.v21.i30.9150]
- 26 **Nishimura K**, Yasui M, Nishimura T, Oga T. Clinical pathway for acute exacerbations of chronic obstructive pulmonary disease: Method development and five years of experience. *Int J Chron Obstruct Pulmon Dis* 2011; **6**: 365-372 [PMID: 21760723 DOI: 10.2147/COPD.S20423]
- 27 **Donà D**, Zingarella S, Gastaldi A, Lundin R, Perilongo G, Frigo AC, Hamdy RF, Zaoutis T, Da Dalt L, Giaquinto C. Effects of clinical pathway implementation on antibiotic prescriptions for pediatric community-acquired pneumonia. *PLoS One* 2018; **13**: e0193581 [PMID: 29489898 DOI: 10.1371/journal.pone.0193581]
- 28 **Kim HE**, Kim YH, Song KB, Chung YS, Hwang S, Lee YJ, Park KM, Kim SC. Impact of critical pathway implementation on hospital stay and costs in patients undergoing pancreaticoduodenectomy. *Korean J Hepatobiliary Pancreat Surg* 2014; **18**: 14-20 [PMID: 26155241 DOI: 10.14701/kjhbps.2014.18.1.14]
- 29 **Husni ME**, Losina E, Fossel AH, Solomon DH, Mahomed NN, Katz JN. Decreasing medical complications for total knee arthroplasty: Effect of critical pathways on outcomes. *BMC Musculoskelet Disord* 2010; **11**: 160 [PMID: 20630086 DOI: 10.1186/1471-2474-11-160]
- 30 **Burgers PT**, Van Lieshout EM, Verhelst J, Dawson I, de Rijke PA. Implementing a clinical pathway for hip fractures; effects on hospital length of stay and complication rates in five hundred and twenty six patients. *Int Orthop* 2014; **38**: 1045-1050 [PMID: 24337751 DOI: 10.1007/s00264-013-2218-5]
- 31 **Walters DM**, McGarey P, LaPar DJ, Strong A, Good E, Adams RB, Bauer TW. A 6-day clinical pathway after a pancreaticoduodenectomy is feasible, safe and efficient. *HPB (Oxford)* 2013; **15**: 668-673 [PMID: 23458383 DOI: 10.1111/hpb.12016]

P- Reviewer: Gonzalez-Ojeda AG, Hauser G, Senturk H
S- Editor: Yan JP **L- Editor:** Wang TQ **E- Editor:** Yin SY





Published By Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

