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ORIGINAL RESEARCH

Effectiveness of a Clinical Pathway for Hepatic Cystic Echinococcosis Surgery in Kashi Prefecture, Northwestern China: A Propensity Score Matching Analysis

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ABSTRACT

Introduction: Surgical treatment for hepatic cystic ehinococcosis (CE) is not standardized in Kashi Prefecture. Previous evidence identified effectiveness of a clinical pathway in the field of liver surgery. However, proof of a clinical pathway program, especially for CE patients, is lacking. This study aimed to assess the validity of a clinical pathway for hepatic CE surgery performed on patients from Kashi Prefecture.

Methods: A clinical pathway was developed and implemented by a multidisciplinary team for patients undergoing hepatic CE surgery. Two groups were formed from patients undergoing hepatic CE surgery during a defined period before and after implementing a clinical pathway. Additionally, a propensity score matching analysis was performed.

Results: In the overall analysis (n = 258) as well as the matched analysis (n = 166), after implementing the clinical pathway, hospital stay was significantly reduced from 13 to 10 days and from 14 to 10 days, respectively ($P < 0.05$). Postoperative morbidity did not increase. Cost analysis showed a significant decrease in median costs of medication and nursing in favor of the clinical pathway (medication: 5400 CNY vs. 6400 CNY, P = 0.038; nursing: 3200 CNY vs. 4100 CNY, P = 0.02).

Conclusion: Implementing the clinical pathway for hepatic CE surgery is feasible and safe. The clinical pathway achieved significant reduction of hospital stay without compromising postoperative morbidity. Costs of medication and nursing are significantly reduced. The clinical pathway program is valid and propagable to a certain extent, especially in remote, poor-resourced medical centers in endemic areas.

Keywords: Clinical pathway; Cystic echinococcosis; Surgery

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Key Summary Points

Why carry out this study?

Cystic echinococcosis (CE) remains a continuous threat but standardized treatment is lacking in Kashi Prefecture.

Clinical pathway has shown effectiveness for liver surgery, but investigations into its impact on CE surgery are lacking.

This is the first report showing efficacy of the clinical pathway for hepatic CE surgery.

What was learned from the study?

Implementing the clinical pathway reduces hospital stay and some of the costs without increasing postoperative morbidity.

This process is valid and extendable, especially for remote, poor-resourced medical centers in endemic areas.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.14653095.

INTRODUCTION

Cystic ehinococcosis (CE), also named hydatid cyst, is a zoonotic tapeworm disease caused by *Echinococcus granulosus*, occurring when intermediate hosts accidentally ingest tapeworm eggs. Liver is targeted in 70% of the cases. Although presenting slow growth and a benign nature, it may cause lethal disability or serious complications [1, 2]. Among different surgical methods, the open procedure is widely accepted and preferred by the surgeons in poorly resourced areas compared to laparoscopic surgery and percutaneous puncture technique. Kashi district is located at the northwestern border of China, Middle Asia, and is an endemic region for CE but lacks medical resources and advanced techniques. The therapeutic method is not standardized among the different centers, and life-threatening issues exist such as misdiagnosis, inappropriate surgical process, inadequate medical therapy and lack of follow-up. The clinical pathway (CP)—a multidisciplinary program aiming at obtaining an optimal clinical result—meets the need in the current situation by improving diagnostics and treatment in Kashi. After numerous studies suggested CP implementation is safe and feasible in colorectal, pancreatic and gastric surgery [3, 4], CP implementation for liver resection in cases of non-parasitic disease has also been proved effective in the literature, and most of the clinical pathways were designed based on principles of enhanced recovery after surgery (ERAS) [5–7].

Hence, we designed this study to analyze the efficacy of a CP program developed specifically for hepatic CE patients (CP group) undergoing surgery, considering hospital stay, costs and postoperative morbidity as outcomes compared to traditional management (TM group). The aim of this study is to reach a standard, suitable protocol for local surgeons by offering detailed optimal sequencing and timing of interventions.

METHODS

Study Design

During the period of January 2017 and October 2020, a total of 258 patients who underwent CE surgery at the hepatobiliary surgical unit of the First People's Hospital of Kashi Prefecture were enrolled in this study. It is the largest hospital situated in a 4 million population area and covers 70% of all CE surgeries here. The CP was implemented in July 2019 for hepatic CE patients, and a prospective clinical database was built for the CP group. Patients treated before applying CP (TM group) were retrospectively

Table 1 Summary of the clinical pathway protocol and differences from traditional management

	Clinical pathway	Traditional method
Pre-OP	Diagnose primarily with ultrasound or CT scan	
Outpatient	Surgical assessment, admit those who meet surgical indication	
OP prep	**Patients receive a CP process brochure, sign consent, added to WeChat CP contact list**	
Days 1–2	Regular blood tests, abdominal contrast CT, chest x-ray, ECG, (MRCP if needed)	
	Surgeon checks the patient. Cardiologist, respiratory or required physician consultation	
	CP routines explained orally plus **daily protocol WeChat notification**	No WeChat notification
1 day	Carbohydrate-rich drinks (400–500 ml), skin preparation	
Before OP	Free movement	
Day of OP	Carbohydrate drinks until 2 h before surgery, **gastric tube after anesthesia**	Gastric tube before anesthesia
	Before the end of surgery: remove gastric tube and urinary catheter; for ASA $\geq$ 3 or with dysuria, keep catheter	Routinely keep tube and catheter till POD 1
Post-OP	Routinely back to surgical unit after surgery	
Day 0	Intravenous fluid, continuous oxygen and monitor	
	Analgesics: self-controlled i.v. pump 48 h + i.v. paracetamol	
	After 6 h: sips of water, carbohydrate drinks up to 200 ml	No oral feeding
	After 6 h: sitting and standing, encouraging patients with small incisions to get out of bed	No mobilization encouraged
POD 1	**Light liquid diet 500–800 ml,** continuous intravenous fluid	Sips of liquid drink
	Blood test, drainage biliary test, monitor off, oxygen off	
	Out of bed ≥ twice/24 h, sitting ≥ 2 h/24 h	Not specified
POD 2	Light diet 800–1200 ml, reduction of intravenous fluid	
	Out of bed mobilization ≥ 4 times/24 h, sitting ≥ 6 h/24 h	Not specified
	Wound care, continuous oral + i.v. paracetamol or NSAIDs	
	Regular abdominal and surgical site ultrasound, **drainage removal**	Drainage removal from POD 3
POD 3	Light diet 1500 ml, no intravenous fluid	
	Free mobilization, $\leq$ 4 h lying 8 a.m.–9 p.m.	
	Blood test	
	Consider discharging patients with satisfactory recovery	Routinely discharged from POD4
POD 4	Regular diet, free movement	

Table 1 continued

	Clinical pathway	Traditional method
	Wound care, oral NSAIDs	
	Discharge	
POD 5–7	Complicated cases: blood test, drainage biliary test, ultrasound, discharge	
Follow-up	**WeChat video call visit** weekly for 1st month	No video chat visit and nursing
	WeChat video call, continuous nursing for patients discharged with drainage	
	Visit surgeon months 1, 3, 6; ultrasound test 6th month	
	Guide oral albendazole and monthly liver enzyme test	

Main differences between the two protocols are in bold print
CT computed tomography, *ECG* electrocardiograph, *MRCP* magnetic resonance cholangiopancreatography, *i.v.* intravenous, *NSAID* nonsteroidal anti-inflammatory drug, *OP* operation. *POD* postoperative day

analyzed via data extracted from the Hospital Information System. Patients selected for surgery were assessed using the American Society of Anesthesiologists (ASA) score for risks and comorbidity. Postoperative complications were recorded according to the Clavien-Dindo classification [8]. The laparoscopic procedure was excluded from analysis because our department first introduced it for hepatic CE after the CP implementation and it was not performed in the TM group. Other exclusion criteria were as follows: patients undergoing venous or biliary tract reconstruction, hepaticojejunostomy or bile duct drainage due to jaundice or intraoperatively confirmed bile leakage; patients simultaneously receiving extra-hepatic hydatid cyst surgery; patients receiving percutaneous puncture aspiration. The same surgical team, led by the chief surgeon, conducted all the surgeries. The presented study received approval from the Ethics Committee of the First People's Hospital of Kashi Prefecture (KDYY-202066) and conformed to the Helsinki Declaration of 1964 (as revised in 2013) concerning human and animal rights. Written consent was required for the clinical pathway group. All data were collected anonymously with personal identification deleted, so written informed consent for the traditional management group was waived by the Ethics Commission as this was a retrospective observational analysis.

Clinical Pathway for Hepatic Cystic Echinococcosis

Surgeons, anesthesiologists, intensive care specialists, nurses, pharmacologists and physical therapists were involved in the development of the CP protocol. We studied related literature on the clinical pathway for liver resection [7, 9] and then confirmed the process according to the reality of the medical situation for CE patients in Kashi (Table 1). Two months before introducing CP, related medical staff were invited to a group chat organized for this program via the WeChat platform, a social network app widely used in China, to be informed about the CP protocol details and online meetings.

Multiple therapeutic options are possible for hepatic CE, including surgery, percutaneous puncture, anti-parasitic drug treatment and a "watch-and-wait" approach, centering on cyst type according to the World Health Organization (WHO) ultrasound classification [1], cyst size and location. Since the disease presents cancer-like features which are prone to recurrence, a radical procedure, total cystectomy of the entire cyst without opening it, is

Table 2 Clinical characteristics of patients before and after propensity score matching

	Before matching			After matching		
	CP n = 92	TM n = 166	P-value	CP n = 83	TM n = 83	P-value
Sex, n (%)			0.795			0.534
Male	50 (54.3)	93 (56.0)		46 (55.4)	42 (50.6)	
Female	42 (45.7)	73 (44.0)		37 (44.6)	41 (49.4)	
Age [years, median (IQR)]	51 (25–62)	48 (24–66)	0.751	50 (23–59)	51 (22–62)	0.792
ASA score, n (%)			0.042*			0.866
1–2	64 (69.6)	134 (80.7)		58 (69.9)	57 (68.7)	
3	28 (30.4)	32 (19.3)		25 (30.1)	26 (31.3)	
WHO type, n (%)			0.715			0.369
CE1	38 (41.3)	76 (43.2)		37 (44.6)	34 (41.0)	
CE2	31 (33.7)	51 (29.0)		26 (31.3)	21 (25.3)	
CE3	23 (25.0)	49 (27.8)		20 (24.1)	28 (33.7)	
Location, n (%)			0.034*			0.930
Right posterior	29 (31.5)	44 (26.5)		27 (32.5)	29 (34.9)	
Right anterior	34 (37.0)	43 (25.9)		30 (34.9)	28 (33.7)	
Left median	17 (18.5)	33 (19.9)		15 (18.1)	13 (12)	
Left lateral	12 (13.0)	46 (27.7)		11 (14.5)	13 (19.3)	
Cyst diameter, n (%)			0.585			1.000
$<$ 10 cm	67 (72.8)	126 (75.9)		61 (73.5)	61 (73.5)	
$\geq$ 10 cm	25 (27.2)	40 (24.1)		22 (26.5)	22 (26.5)	
Surgery type, n (%)			0.027*			1.000
Total cystectomy	71 (77.2)	106 (63.9)		64 (74.7)	64 (74.7)	
Sub-total cystectomy	21 (22.8)	60 (36.1)		19 (25.3)	19 (25.3)	
OP time [min, mean (SD)]	236.3 ± 56.2	197.6 ± 47.7	0.047*	218.7 ± 59.1	195.5 ± 43.9	0.154
Incision, n (%)			0.010*			0.724
$\geq$ 10 cm	66 (71.2)	92 (55.4)		63 (75.9)	61 (73.5)	
$<$ 10 cm	26 (28.8)	74 (44.6)		20 (24.1)	22 (26.5)	

IQR interquartile range, *ASA* American Society of Anesthesiologists, *WHO* World Health Organization, *OP* operation, *SD* standard deviations
*Statistically significant

Table 3 Comparison of main outcomes before and after propensity score matching

	Before matching			After matching		
	CP n = 92	TM n = 166	P-value	CP n = 83	TM n = 83	P-value
Hospital stay (days)						
Overall [median (IQR)]	10 (7–13)	13 (7–16)	0.048*	10 (7–13)	14 (8–16)	0.041*
Post-OP [median (IQR)]	5 (3–10)	7 (5–12)	0.026*	5 (3–10)	8 (5–13)	0.023*
Cost (*10^3CNY)						
Overall [median (IQR)]	34.2 (18.0–53.9)	42.1 (20.7–57.6)	0.257	37.9 (24.5–51.1)	42.2 (29.0–55.1)	0.270
Surgery [median (IQR)]	6.5 (5.5–7.9)	6.6 (5.7–8.2)	0.310	6.6 (5.7–8.2)	7.3 (6.3–8.0)	0.639
Medication [median (IQR)]	5.6 (2.8–7.3)	6.7 (3.6–9.5)	0.143	5.4 (3.7 –7.4)	6.4 (4.2–8.9)	0.038*
Nursing [median (IQR)]	3.3 (2.8–6.5)	4.0 (2.8–5.1)	0.274	3.2 (2.5–4.9)	4.1 (3.2–6.4)	0.020*
Complication, n (%)			0.998			0.527
Without	71 (77.2)	128 (77.1)		65 (78.3)	64 (77.1)	
Clavien-Dindo I–II	17 (18.5)	31 (18.7)		15 (18.1)	18 (21.7)	
Clavien-Dindo ≥ IIIa	4 (4.3)	7 (4.2)		3 (3.6)	1 (1.2)	

IQR interquartile range, *OP* operation
*Statistically significant

recommended for hepatic CE. In these cases, perioperative anti-parasitic drugs are not required. If the lesion resection is too risky because of the location, such as segment I, perihilar, or involves vital vessels that should be preserved, surgeons may choose a safer conservative procedure, sub-total cystectomy, which will open the cyst cavity intraoperatively. Perioperative anti-parasitic drug (albendazole) was required 2 weeks before to at least 6 months after surgery for sub-total cystectomy [10].

Baseline characteristics and perioperative results of all patients were compared between the two groups (Tables 2 and 3). Feasibility of CP was assessed through several main modifications in the protocol (Table 4). We also performed propensity score matching (PSM) analysis to obtain more accurate results. Matching subjects were selected from variables, which may have affected surgical difficulty and discharge variance according to clinical experience. The primary endpoint of this study was hospitalization period, the secondary endpoint was treatment costs, and the tertiary endpoint included side effects of the surgery.

Preoperative Protocols

The insurance is valid only for hospital-admitted patients, so the patients were only examined by ultrasound or upper abdominal CT scan at the outpatient clinic and were admitted if they met the surgical indication. When a preoperative anti-parasitic drug was necessary, the patient was admitted after 2 weeks of oral albendazole treatment. Once in the surgical ward, patients were educated about the details of the CP protocol and signed the consent. We also established a CP contact list on the WeChat platform for patients to notify them about daily arrangements. The protocol is described in Table 1; focal differences between CP and TM are shown in bold print. Essential blood tests

Table 4 Feasibility analysis of several main modifications of the clinical pathway protocol

	Overall $n = 258$		CP $n = 92$		TM $n = 166$		
	n	%	*n*	%	*n*	%	*P*-value
Remove gastric tube under anesthesia	136	52.7	79	85.9	57	34.3	< 0.001*
Re-insert gastric tube after removal	10	3.9	5	5.4	5	3.0	0.334
Remove urine catheter under anesthesia	90	58.1	58	63.0	32	19.3	< 0.001*
Re-insert urine catheter after removal	6	2.3	2	2.2	4	2.4	0.904
Remove drainage POD 2	96	37.2	45	48.9	51	30.7	0.004*
Abdominal abscess after drainage removal	15	5.8	6	6.5	9	5.4	0.718

POD postoperative day
*Statistically significant

and vital organ function assessment for surgical preparation took 2–3 days.

Operative Protocols

Patients were positioned either in supine position or with 15–30° right-side elevation. All patients underwent the same general anesthetic protocol, which was induced by continuous isoflurane inhalation. Remifentanil, a potent ultrashort-acting synthetic opioid, was used as analgesic. The patient was maintained with desflurane, sufentanil and rocuronium bromide, based on body mass, heart rate and blood pressure stability. A nano-gastric tube and urinary catheter were inserted after anesthesia.

A subcostal incision was chosen and extended to the midline or to the left if necessary. The incision is considered large when longer than 10 cm, which changes the postoperative mobilization schedule (Table 1). After adhesion between the cysts and the neighboring organs was lysed and full access to the hydatid cysts was achieved, the peritoneal cavity was isolated by gauze soaked in 10% hypertonic saline prior to dissecting the hydatid cyst to prevent implantation from potential cyst content spillage during resection. According to the location, size and type of the lesion, total cystectomy was the preferred and recommended procedure according to expert consensus [10, 11]. In this procedure, the cyst was entirely removed surgically, strictly following the principles of liver resection without opening the cyst content. Nutrient vessels of the cyst and confirmed biliary leakage were sutured with 5/0 Prolene. Harmonic ACE (Ethicon Endo-Surgery) was used to resect the cyst for most patients. Pringle maneuver was applied to control bleeding in some cases, with clamping and unclamping times of 10 min and 5 min, and lower central venous pressure was controlled to 2–4 mmHg during parenchymal dissection to control intraoperative bleeding.

For sub-total cystectomy, injection of a protoscolecide into the cyst for parasite inactivation is an integral part of the surgical technique [12, 13]. In brief, the cyst was punctured and pressure relieved by suctioning of the hydatid fluid with a needle connected to negative pressure. Then, 20% hypertonic saline solution was injected into the cystic cavity; after a 10-min interval, the cystic contents were evacuated. After three repetitions of this injection-aspiration procedure, cystic contents were totally removed through small fenestration. After that, the cystic wall was removed as much as possible

along the edge of the liver. Intra-cystic biliary leakage was sutured with 3-0 or 4-0 Prolene.

A drainage tube was placed routinely. When the surgery ended, the nasogastric tube was removed before transferring the patient to the recovery ward. Urinary amount was recorded and the catheter was removed before leaving the postoperative recovery unit. Patients were routinely sent back to the surgical ward; only a few patients needed a transition to the intensive care unit (ICU).

Postoperative Protocol

Patients were monitored overnight after returning to the surgical ward and given 2–4 l/min oxygen by nasal catheter for 12 h. Oral sips of water or carbohydrate-rich drinks were allowed after 6 h, up to 200 ml on the day of surgery and 500–800 ml on the first postoperative day. Patients with smaller incisions were advised to sit and stand/walk after 8 h; a detailed mobilization protocol was developed for each postoperative day. An analgesic program was developed in stages for different time points. The patient-controlled intravenous analgesic pump, which is attached to all the patients on the recovery ward, contains parecoxib sodium 1 mg/ml with 48 h of dose. The pump infuses continuously with a speed of 2 ml/h, and a 0.5-ml bolus is injected if the patient-controlled button is pressed when there is a spike in pain. Analgesic pump was removed after 48 h; then, the pathway was switched to enteral analgesics: diclofenac 50 mg at a maximum dose of 150 mg per day, tramadol 50 mg at a maximum dose of 300 mg per day. Intravenous fluid administration was restricted from the surgery process to subsequent therapy. It was continuously reduced each day to a full stop at postoperative 48 or 72 h, except for required situations. Postoperative albendazole was administered only for patients who underwent sub-total cystectomy from postoperative day 1. All drainage (nasogastric tube, urinary catheter, abdominal drainage) removal was specified at an earlier time compared to pre-pathway treatment. Discharge was arranged from postoperative day 3, considering complications, ASA score, peritoneal drainage and pain tolerance. When a biliary leakage continued > 2 weeks, the patient could be discharged with abdominal drainage, and WeChat video call visiting and nursing were arranged regularly. The patients were seen at an outpatient clinic for removal of stitches; subsequent follow-up was scheduled at 2 and 4 weeks and 3 and 6 months. Patients who were ordered to take albendazole had liver enzymes tested monthly and consulted a specialist. Detailed information of the CP protocol is shown in Table 1.

Statistical Analysis

Propensity score matching (PSM) analysis was applied to reduce the bias of original data [14]. We performed PSM analysis via logistic regression to estimate a propensity score for each patient. The following covariates were entered in the model: ASA score, surgery type, cyst location and cyst diameter. We matched 83 patients in the CP group with 83 patients in the TM group using the 1:1 optimal matching algorithm without replacement (caliper = 0.2). For all patients and matched patients, continuous variables between the two groups were compared using Student's *t*-test or the Mann-Whitney *U*-test; binary and ordinal categorical variables were compared using the chi-square test and Kruskal-Wallis test, respectively. All statistical analyses were performed using SPSS 24.0 (IBM, Armonk, NY, USA) and PSM for SPSS, version 3.04. For all statistical tests, $P < 0.05$ was considered statistically significant. All *P* value calculations were two-sided tests.

RESULTS

Baseline Characteristics of Patients Before and After PSM

The left half of Table 2 shows an overview of the clinical and operative features of the patients in the two groups. A total of 258 patients were included for analysis; 92 (50 males, 42 females) recovered according to the CP process and 166 of them (93 males, 73 females) were treated with traditional management. Baseline characteristics were similar in both groups with

median age of 51 (25–62) and 48 (24–66) years in the CP and TM group, respectively. Regarding ASA score, 134 of 162 (80.7%) patients in TM group has a lower score (1 or 2), which is significantly more compared to CP group (64/92, 69.6%, $P = 0.042$). Locations of the cysts were unevenly distributed between groups ($P = 0.034$). WHO type and diameter of the cysts showed no significant differences between groups. CP group, which reported a higher proportion of total cystectomy, also reported significantly longer operation times and larger incisions ($P < 0.05$).

Analysis after PSM, shown on the right side of the Table 2, showed that 83 patients (46 males, 37 females) from the CP group were matched with 83 patients (42 males, 41 females) from the TM group, with median age of 50 (23–59) and 51 (22–62) years, respectively. Perioperative characteristics are similar between groups. After matching, in both groups, 19 patients underwent sub-total cystectomy and 64 patients underwent total cystectomy ($P = 1.0$). Other matching covariates such as ASA score and cyst location were distributed without significant differences between groups ($P > 0.05$). Moreover, there was no significant difference between groups when comparing operative duration ($P = 0.154$) and incision length ($P = 0.724$).

Endpoint Analysis Before and After PSM

Table 3 shows the main outcomes of this study through original and matched data. Before matching, overall and postoperative median hospitalization periods in CP group were shortened by 3 and 2 days, respectively, compared to TM group; after matching, this shortening was by 4 and 3 days, respectively. For cost analysis, before PSM, it showed a reduction in CP group regarding overall hospital charge and cost for surgery, medications and nursing, but no significant difference between the two groups was evident. After matching, significant reduction in CP group was found compared to TM group in costs of medication ($P = 0.038$) and nursing ($P = 0.020$). There was no postoperative mortality in either group. Comparison of complications revealed no significant differences between groups with either original data or matched data when assessed in subgroups using Clavien-Dindo classification.

We also performed an analysis of feasibility and safety on several main modifications of the CP protocol, which is shown in Table 4. Significantly more patients (79 of 92, 85.9%) in CP group had gastric tube removed under anesthesia, which was routinely removed the next morning in most patients in TM group ($P < 0.001$). Among overall patients, re-insertion of gastric tubes occurred in five patients in each group, which was not significantly different. Same results were observed when removing urinary catheter under anesthesia. Forty-five of 92 patients in CP group had abdominal drainage removed at postoperative day 2, which was significantly more compared to 55 of 166 patients in TM group ($P = 0.04$). Furthermore, abdominal abscess after removal of drainage occurred in six and nine patients in the two groups respectively without statistically significant differences ($P = 0.718$).

DISCUSSION

In this study, we developed a clinical pathway concerning improvements of therapy and its time points and analyzed its feasibility and efficacy especially for hepatic CE patients from Kashi Prefecture. To our knowledge, this is the first study discussing the effectiveness of CP for hepatic CE patients. As a cosmopolitan disease, CE continues to be a significant public health issue, with western China being the area of highest endemicity, and Kashi district is one of the high burden areas of northwestern China. Our study proved that CP implementation significantly reduced the hospitalization period and costs of medication and nursing without compromising postoperative morbidity and mortality. Several important improvements which could substantially relieve the pain and improve patient's experience did not increase postoperative complications.

Prior studies on clinical pathway have noted the crucial impact of surgical approach and ASA score on discharge variance. Several studies

reported significant reduction of hospital stay with laparoscopic surgery versus an open procedure, for both CE [15] and other hepatic diseases [16]. Because laparoscopic hepatic CE surgery was adopted in our center after CP implementation, we excluded the laparoscopic approach from analysis. Our study assessed concurrent morbidities using ASA score, which is believed to affect recovery from abdominal surgery. In a clinical pathway program for gastrectomy, Nakagawa and colleagues reported ASA and postoperative morbidity were the risk factors for discharge variance [17]. Since ASA scores were significantly different between groups in our data, we performed the PSM process to reduce bias. Results in the current study are in line with the meta-analysis of Wang et al., in which a total of 19 studies were identified: 4 randomized controlled trials and 15 non-randomized controlled trials. Their study found that the clinical pathway could reduce hospital stay and costs for open surgery without increasing mortality or readmission rate [18]. Another meta-analysis from Ahmed et al. reported similar results [19].

A substantial result in our data is the significantly longer operation time in CP group. One of the reasons that could explain this data skew is: there were significantly more right posterior and left lateral located cysts in CP and TM group, respectively, being difficult to access and dissect in the former while having easy exposure and resection in the latter. In other words, more complicated cases were accumulated in CP group. Lesion size is another objective cystic characteristic impacting the difficulty level of surgery. Furthermore, a subjective strategy chosen by surgeons which puts remarkable weight on the difficulty of the operation is surgery type, total or sub-total cystectomy. The former requires resection of the entire adventitial layer (sub-adventitial resection), which is a fibrous barrier from the host defense [20]. The laminated layer and germinal layer, which are suggested not to be exposed intraoperatively, are the contagious parasitic component wrapped by an adventitial layer [10]. Since total cystectomy is risky for large and deeply located cases, surgeons from less-skilled and poorly resourced remote areas might prefer the latter procedure. Our center has begun to focus on adherence to recommendations and expert consensus in recent years; consequently, radical resection formed a significantly higher proportion in CP group than TM group (77.2% vs. 63.9%, $P = 0.027$). Based on the skewed data with more deeply located cases and radical resections in CP group, we performed PSM with surgery type, cyst location and size. Interestingly, non-matching parameters such as operative time and incision length were also normalized between groups after PSM. Very little was found in the literature on the question of whether incision length correlates with postoperative pain, early mobilization and hospital stay. Since small incision laparoscopic surgery reduces the hospitalization period, results will be more accurate after eliminating this difference between groups.

Existing research has reached little agreement on whether CP implementation for liver surgery reduces postoperative complications and morbidity. Two randomized controlled trials on liver resection reported significantly lower complication rates of CP procedures based on ERAS principles compared to the non-pathway group, with complication rates of 22% vs. 44%, $P = 0.002$, and 30% vs. 46%, $P = 0.03$, respectively [21, 22]. The findings of the current study indicate that postoperative complications do not alter after introducing CP, with overall complication rates of 22.8% vs. 22.9%, $P = 0.998$, and 21.7% vs. 22.9%, $P = 0.527$, respectively, before and after PSM. No mortality was reported in the present study. These results are in accord with recent studies indicating no statistical significance of morbidity and mortality after liver resection [6, 16, 23].

After taking more aggressive interventions such as removing the nasogastric tube and catheter and abdominal drainage in advance, the results showing that postoperative complications did not increase are favorable. Previous studies have demonstrated that there were no differences in overall morbidity, incidence of pulmonary complications, postoperative vomiting and postoperative duration of hospital stay between patients keeping gastric tubes or having them removed immediately after surgery [24]. Gastric tube removal was postponed when

nurses and young doctors were subjectively concerned about the discomfort of repositioning the tube for an awake patient. Our result proves that this concern is not necessary for hepatic CE surgery. In CP group, we removed the catheter before leaving the postoperative recovery unit except for patients with ASA 3 or with dysuria, which helped to relieve catheter-related discomfort and pain. Encouragingly, patients seldom suffered re-positioning after removal of these insertions; results showed no statistical significance between groups. This could prevent dramatic, intolerable pain for the patients caused by the gastric tube and urinary catheter. In the present study, we tried to remove abdominal drainage on the postoperative day 2 for suitable patients, and significantly more patients in CP group achieved this (48.9% vs. 30.7%, $P = 0.004$).

Concerning cost analysis, in our overall data, introduction of a clinical pathway reduced median total hospital costs from 42,100 (20,700–57,600) CNY to 34,200 (18,000–53,900) CNY, but this result was not statistically significant. Data before PSM showed no significant differences in any subgroup analyses. After PSM, overall cost and operation charges were still similar between groups ($P > 0.05$). However, median costs of medication and nursing were significantly lower in CP group. This could be explained by the fact that components of the CP program focus on the sequencing and timing of interventions and bring few changes to the surgical process. Furthermore, costs of medications and nursing compose only a small proportion of overall costs; consequently, their reduction contributed little to the overall costs. There is no convincing evidence of cost-effectiveness of implementation of a clinical pathway for liver surgery, and none of it targets hepatic CE patients. He et al. conducted a randomized trial of laparoscopic hepatectomy comparing the traditional management and clinical pathway, and a significant reduction in hospital costs was reported ($P = 0.03$) in the clinical pathway group, without details of the cost reduction in their literature [23]. Two studies from Ovaere et al. and Joliat et al. yielded a decrease in overall costs in favor of the clinical pathway without significant differences [9, 25], but a significant decrease of postoperative costs was achieved in the study of Ovaere et al. Although only cost-effectiveness of medication and nursing could be demonstrated in the present study, these findings still add weight to the argument that costs can be reduced after implementation of a clinical pathway for hepatic CE surgery.

Study Limitation

The main limitation of this study is its observational design with two groups of patients from different periods, and the study was limited by all the characteristics of retrospective analyses. This is a single institutional work with all procedures led by a chief surgeon, which is another limitation. This is partially corrected by the matched analysis with even distribution of baseline and clinical characteristics between groups. Despite these limitations, our results can be considered a real-word reflection of the clinical pathway practiced for hepatic CE surgery.

CONCLUSION

Based on the reality of the lack of standardized treatment for hepatic CE patients in Kashi Prefecture, our study established a cost-effective and easily performed clinical pathway program for caregivers. This study has shown that implementing the clinical pathway reduces hospital stay and some of the costs without increasing the postoperative morbidity. This program is valid and propagable to a certain extent, especially for remote, poor-resourced medical centers in an endemic area. Further investigation of the clinical pathway for hepatic CE is needed. Especially, large randomized controlled trials which give sufficient attention to standardizing the surgical process could provide more definitive evidence.

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Compliance with Ethical Guidelines. The presented study received approval from the Ethics Committee of the First People's Hospital of Kashi Prefecture (KDYY-202066) and conformed with the Helsinki Declaration of 1964 (as revised in 2013) concerning human and animal rights. Written consent was required for the clinical pathway group. All data were collected anonymously with personal identification deleted, so written informed consent for the traditional management group was waived by the Ethics Commission as this was a retrospective observational analysis.

Data Availability. The datasets generated during the current study are available from the corresponding author on reasonable request.

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