

## RESEARCH ARTICLE

# Impact of a Clinical Pathway on Hospital Costs, Length of Stay and Early Outcomes after Hepatectomy for Hepatocellular Carcinoma

Liang Zhu<sup>1,2&</sup>, Jun Li<sup>3&\*</sup>, Xiao-Kang Li<sup>4&</sup>, Jun-Qiang Feng<sup>5&</sup>, Jian-Min Gao<sup>1\*</sup>

## Abstract

**Background:** A clinical pathway (CP) can standardize and improve perioperative care for a number of interventions. In hepatic surgery, however, pertinent evidence is very limited. This study was conducted to implement a CP for hepatocellular carcinoma (HCC) patients undergoing hepatectomy, and to evaluate its effects on hospital costs, length of hospital stay (LOHS) and early clinical outcomes. **Materials and Methods:** Medical records for HCC patients undergoing hepatectomy were retrospectively reviewed before implementation of a CP (the non-CP group) from March 2012 to August 2012. This information was compared with the data collected prospectively from patients after implementation of the CP (the CP group) between September 2012 and April 2013. Hospital costs, LOHS and early clinical outcomes were evaluated and compared between groups. **Results:** There were no significant differences in terms of patient clinical characteristics between the two groups. For clinical outcome measures, no significant differences were found in postoperative complications, mortality and readmission rate. The hospital costs were significantly reduced from 24,844 RMB in the non-CP group to 19,761 RMB in the CP group ( $p < 0.01$ ). In addition, patients of the CP group also had shorter LOHS compared with the non-CP group (8.3 versus 12.3 days,  $p < 0.001$ ). **Conclusions:** The CP proved to be an effective approach to minimize hospital costs and LOHS with hepatectomy for HCC without compromising patient care.

**Keywords:** Clinical pathway - hepatectomy - hepatocellular carcinoma - hospital costs - length of hospital stay

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## Introduction

Hepatocellular carcinoma (HCC) is the fifth most frequent cancer and the third most common cause of cancer-related mortality in the world (Jemal et al., 2011). In the Asia-Pacific region, HCC is also one of the important health problems, being very burdensome and highly lethal (Bridges et al., 2011). Currently, it has been widely accepted that hepatectomy achieves the best outcomes in well-selected candidates, and is still considered as one of the potentially curative treatments for HCC, especially under the circumstance of lack of donors for liver transplantation (Galuppo et al., 2013; Tang et al., 2014). Although hepatectomy is a cost-effective treatment both from the clinical and patients' perspectives, it still represents a significant cost due to its high risk of postoperative morbidity and mortality. Those could also be a critical issue in healthcare systems because of the gradual decline in available funds for public healthcare.

Clinical pathway (CP) is the management plans that delineate specific clinical care goals for patients and

provide the sequence and timing of actions necessary to achieve these goals with optimal efficiency (Pearson et al., 1995). Although CPs had been used since the 1980s, there is increasing debate about what they are and how they affect patients' care and outcomes. As a consequence, their use is still jeopardized in high volume and costly care like HCC. Evidence is needed to support public health decision makers in their understanding the real impact of this methodology (Panella et al., 2008; Barbieri et al., 2009).

To date, studies have found that CP can decrease hospital costs and length of hospital stay (LOHS) for some surgical procedures, such as gastric (Seo et al., 2012), colorectal (Feroci et al., 2013), orthopedic (Ayalon et al., 2011), thoracoscopic (Schwarzbach et al., 2010), and urologic procedures (Nagata et al., 2007). However, data are sparse on the implementation of it in hepatectomy. This study represents an attempt to examine whether application of a CP for HCC patients undergoing hepatectomy could help decrease hospital costs and LOHS without increasing complications, mortality and readmission rate.

<sup>1</sup>School of Public Policy and Administration, Xi'an Jiaotong University, <sup>2</sup>Department of Medical Education, the Fourth Military Medical University, <sup>3</sup>Department of Burns and Cutaneous Surgery, Xijing Hospital, <sup>4</sup>Department of Teaching and Medical Administration, Xijing Hospital, <sup>5</sup>Department of Teaching and Medical Administration, Tangdu Hospital, the Fourth Military Medical University, Xi'an, China <sup>&</sup>Equal contributors \*For correspondence: xjburns@163.com

## Materials and Methods

The study was carried out at a general hospital located with a high-volume hepatic surgery unit in the city of Xi'an. As one of the largest hospitals in the western area of China, it is equipped with 3213 beds, and serves as facilities for teaching and research purposes of the Fourth Military Medical University. The study was approved by the Human Research Ethics Committees of the Fourth Military Medical University.

Based on various international treatments and nursing recommendations as well as on available evidence from literature, the specific CP was designed to standardize the treatment processes of hepatectomy for HCC patients, with the emphases on decreasing hospital costs and LOHS. A multidisciplinary team comprising surgeons, nurses, pharmacists, wound care specialists and operating room personnel was assembled to develop the CP. All aspects of patient care were analyzed and were outlined, which included the preoperative evaluation, education for postoperative care, earlier oral feeding, earlier discontinuation of intravenous fluid, early ambulation, and the postoperative discharge day. An abbreviated version of the CP used is shown in Table 1.

The study included patients who underwent elective hepatectomy with histologically proven and diagnosed HCC at our institution from March 2012 to April 2013. The non-CP group comprised patients from March 2012 to August 2012, who were treated according to the traditional pathway prior used in our department (n=68). The CP group consisted of patients operated between September 2012 (when the CP was implemented) and April 2013 (n=65).

Clinical characteristics of the patients included age, gender, preoperative co-morbidities (such as hypertension, diabetes), preoperative Child-Pugh score of liver, location of the tumor (left lobe, right lobe and others such as caudate lobe or multiple lobes), tumor size, surgical procedures defined according to the Brisbane 2000 terminology (non-anatomical resection, segmentectomy, and so on), and blood transfusion in the operation. All the operations were performed by the same veteran surgeons in both groups. Outcome quality was measured through postoperative complications, mortality (in-hospital death or death occurring within 30 days of discharge) and readmission rate (a second hospital admission within 30 days as a result of complications). Complications were classified as general (such as wound infection, pneumonia, and urinary tract infection) and surgical complications (such as intra-abdominal hemorrhage, bile leak, and intra-abdominal abscess).

The data of hospital costs related to hospitalization were obtained from the computer database of department of medical information. Hospital costs per case were defined as the total expenditures that a patient paid to the hospital during the period from admission to hospital discharge. These charges included the costs of perioperative examinations, operation, anesthesia, blood transfusion, medication, bed, and nursing. Hospital stay was recorded as total, preoperative and postoperative LOHS. Preoperative LOHS was determined by calculating

**Table 1. Abbreviated Version of CP for Hepatectomy**

Time	Activity
Preoperative	-Education for postoperative care -Preoperative tests -Preoperative medication management -No bowel preparation
Day of surgery	-General anesthesia -Routine drainage of the peritoneal cavity -No routine nasogastric drainage -Postoperative analgesia -Monitoring of patient without sending routinely to the intensive care unit
1st postoperative day	-Initiation of feeds/diet -Out of bed ambulation (<1h a day) -Chest and limb physiotherapy
2nd postoperative day	-Reduction of intravenous fluids -Out of bed ambulation (<2h a day) -Chest and limb physiotherapy -Education in wound care
3rd postoperative day	-Cessation of postoperative analgesia -Reduction of intravenous fluids -Out of bed ambulation (<4h a day) -Chest and limb physiotherapy -Removal of peritoneal drainage device
4nd postoperative day	-Stop intravenous fluids -Necessary oral medication -Out of bed ambulation (<6h a day) -Assessment of postoperative morbidity
5nd postoperative day	-Normal oral intake -Out of bed ambulation (<8h a day) -Wound care
6nd postoperative day	-Discharge education -Outpatient follow-up instruction -Discharge home

the difference in calendar days between the day of admission and operation. Postoperative LOHS was the days between the operation and discharge.

### Statistical analysis

Continuous variables are expressed as median (range). Descriptive statistics were used to summarize the demographic and clinical data. Complications, mortality, readmission rate were analyzed by using the Fisher's exact test. Hospital costs and LOHS were compared by the Mann-Whitney U test. Data analyses were performed by using SPSS 16.0 for Windows (SPSS, Chicago, IL, USA). Statistical significance was defined as  $p < 0.05$  using two-sided probability.

## Results

Clinical data were recorded and compared in Table 2 between the two groups. No differences in age or gender were observed. In addition, there were also similar with respect to preoperative co-morbidities, Child-Pugh score, tumor location, tumor size, surgical procedure, and blood transfusion.

The different parameters of outcome quality were showed and compared in Table 3. There were no statistically significant differences between the two groups with respect to postoperative complications (35.3% versus 39.7%,  $p=0.7430$ ). The most common complications were similar in the two groups, which included general complications (wound infection, pneumonia, and urinary tract infection) and surgical complications (bile leak, intra-

**Table 2. Clinical Data of Patients**

Factors	CP (n=65)	non-CP (n=68)	P value
Age(years).median (range)	53(32-71)	52(30-73)	0.5632 <sup>†</sup>
Gender, n (%)			
Male	40(61.5)	46(67.6)	0.4613 <sup>§</sup>
Female	25(38.5)	22(32.3)	
Co-morbidity, n (%)			
Yes	32(49.2)	36(52.9)	0.6687 <sup>§</sup>
No	33(50.7)	32(47.0)	
Child-Pugh score, n (%)			
A(5-6)	49(75.3)	51(75.0)	0.7693 <sup>‡</sup>
B(7-9)	13(20.0)	15(22.0)	
C(10-15)	3 (4.6)	2 (2.9)	
Tumor location, n (%)			
Left lobe	27(41.5)	32(47.1)	0.3367 <sup>‡</sup>
Right lobe	23(35.4)	27(39.7)	
Others	15(23.1)	9 (13.2)	
Tumor size (cm), median(range)	5.2(2.0-7.1)	5.0 (2.4-6.9)	0.6537 <sup>†</sup>
Surgical procedure, n (%)			
Non-anatomical resection	10(15.3)	9(13.2)	0.6223 <sup>‡</sup>
Segmentectomy	11(16.9)	9(13.2)	
Bisegmentectomy	19(29.2)	21(30.8)	
Hemihepatectomy	10(15.3)	13(19.1)	
Extended hemihepatectomy	15(23.0)	16(23.5)	
Blood transfusion, n (%)			
Yes	28(43.1)	38(55.8)	0.1398 <sup>§</sup>
No	37(56.9)	30(44.1)	

<sup>†</sup>Mann-Whitney U-test; <sup>‡</sup>Pearson Chi-Square test; <sup>§</sup>Fisher's Exact test, Significant level  $p<0.05$

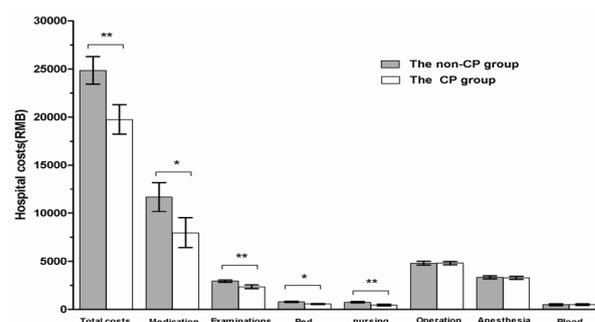
**Table 3. Comparison of Postoperative Outcomes**

Factors	CP (n=65)	non-CP (n=68)	P value <sup>‡</sup>
Total complications, n (%)	23 (35.3)	27 (39.7)	0.7430
General	17 (26.1)	18 (26.4)	0.8504
Surgical	6 (9.2)	9 (13.2)	0.5924
Mortality, n (%)	1 (1.5)	1 (1.4)	1.0000
Readmission, n (%)	3 (4.6)	5 (7.3)	0.7200

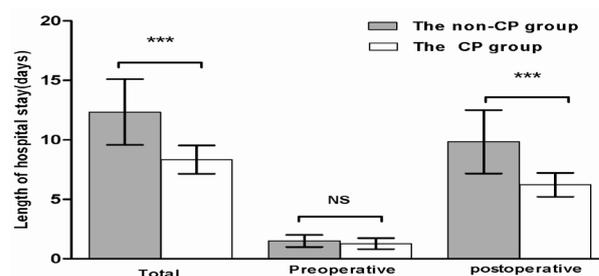
<sup>‡</sup>Fisher's Exact test, Significant level  $p<0.05$

abdominal abscess, and intra-abdominal hemorrhage). For general complications, patients were all cured by conservatively treatment, such as wound care and antibiotics. Two patients in the CP group and three patients in the non-CP group developed postoperative bile leak and required insertion of an intra-abdominal drain. One patient in the CP group and two patients in the non-CP group had a percutaneous drainage because of an intra-abdominal abscess. In addition, three patients in the CP group and four patients in the non-CP group showed intra-abdominal hemorrhage and required reoperation for hemostasis.

The differences of the mortality were also not significant between groups (1.5% versus 1.4%,  $p=1.000$ ). Each group had one postoperative death, respectively. In the CP group, a patient died on postoperative day 5 due to rapidly progressing septic shock. While in the non-CP group, a patient died on postoperative day 4 without the cause of death being fully clarified. As for readmission rate, it was 4.6% in the CP group and 7.3% in the non-CP group, but the difference was not statistically significant ( $p=0.7200$ ). Three patients were readmitted in the CP group, two for wound infection and one for intra-abdominal abscess. In the non-CP group, five patients were readmitted, two for bile leak, two for wound infection,



**Figure 1. Comparison of Hospital Costs (RMB) between Two Groups.** (\* $p<0.05$ , \*\* $p<0.01$ , Mann-Whitney U test)



**Figure 2. Comparison of Length of Hospital Stay between Two Groups.** (\*\*\*) $p<0.001$ , NS= No Significance, Mann-Whitney U test)

and one for intra-abdominal abscess. In summary, by comparison the parameters of outcome quality, it can be concluded that the CP has no apparently negative impact on patient care.

Data concerning hospital costs are presented in Figure 1. The total hospital costs decreased significantly in the CP group than that in the non-CP group by implementation of the CP (19,761 versus 24,844 RMB,  $p<0.01$ ). For the purpose of more detailed analysis, hospital costs were divided into seven categories. Among them, four items decrease significantly in the CP group as compared with the non-CP group, which included medication (7,980 versus 11,681 RMB,  $p<0.05$ ), perioperative examinations (2,350 versus 2,948 RMB,  $p<0.01$ ), bed (560 versus 816 RMB,  $p<0.05$ ) and nursing (441 versus 756 RMB,  $p<0.01$ ). There were no differences in operation ( $p=1.0000$ ), anesthesia ( $p=0.7533$ ), and blood transfusion ( $p=0.8413$ ). The LOHS is presented in Figure 2. Implementation of the pathway resulted in a significantly decrease of total LOHS in the CP group than that in the non-CP group (8.3 versus 12.3 days,  $p<0.001$ ). This outcome mainly resulted from the reduction of postoperative LOHS. Because in the CP group, postoperative LOHS was 6.2 days, which is significantly shorter than 9.8 days in the non-CP group ( $p<0.001$ ). However, there were no statistically significant differences with respect to preoperative LOHS (1.2 versus 1.5 days,  $p=0.1836$ ).

## Discussion

The development of CP, which provides a standardized routine with high standard of care for patient and ensures cost containment, is an important trend in medicine.

This study describes the implementation of a CP and its effectiveness on the management of hepatectomy for HCC. We have confirmed that the use of the CP has significantly decreased hospital costs and LOHS of the patients. More importantly, the decrease has not been achieved at the expense of increased postoperative complications, mortality and readmission rate.

In China, the medical expenditures still remain a severe barrier for many common people, and there are still a lot of patients who cannot afford the treatment of cancer-related operations (Zhu et al., 2011). For this reason, one of the most important aims of the CP in this study concerns the reduction of hospital costs. The significant decrease in hospital costs of hepatectomy seems largely due to the decrease of medication which constitutes the majority of total hospital expenditures. In fact, high medication, which may commonly represent 43.9 percent of expenditure per inpatient episode, is a common phenomenon in different Chinese hospitals. A lot of factors appear to have contributed to increasing hospital medication expenditures in China, including irrational use of drugs, inter-hospital differences, and possibly the social or insurance characteristics of a hospital's patient population (Long et al., 2013). In this study, the CP provides a standardized proposal for perioperative drug use, which means that doctors cannot use unnecessary drugs optionally. As a result, the interventions lead to effective control of medication and finally reduce the total hospital costs. In the CP group, the total hospital costs reduction amounts to 19,761 RMB per patient and in the non-CP group 24,844 RMB per patient. Every year in China, there are 350,000 new liver cancer patients, about 20% of whom need operations. Assuming treatment of all patients according to the CP, and an annual number of 70,000 hepatectomy for HCC, approximately 360 million RMB could be saved per year.

Another paramount part of cost saving may be achieved through a significant reduction in LOHS. LOHS can be considered as an important marker of medical resource consumption. Longer LOHS among the inpatients may suggest that they receive more inpatient care (Hsia et al., 2003). Limiting LOHS after surgery benefits not only the patients but also the hospital management in terms of cost effectiveness. Many studies have found that LOHS is highly correlated to hospitals' total costs and constitutes the main component of costs of cancer treatments (Penel et al., 2008). The use of CPs can decrease LOHS and cost of several common surgical procedures, including appendectomy for acute appendicitis (Takegami et al., 2003), endocrine surgery (Kulkarni et al., 2011), and pulmonary lobectomy (Schwarzbach et al., 2010). In this study, both the postoperative hospital stay and total hospital stay after pathway implementation are found to be significantly shorter than those of the non-CP group. The mean LOHS for hepatectomy in our study is 8.3 days in the CP group, which is similar to that in a recent single-centre study in China (Lin et al., 2011). Recently, it was evident that perioperative comprehensive supportive care interventions, including health education, psychological support and stress management, were associated with a shorter LOHS in patients with esophageal carcinoma

(Zhang et al., 2013). Similarly, in this study, multiple factors may contribute to the reduction of LOHS, including preoperative education of hospital health-care, earlier mobilization and resumption to regular diet, and earlier discontinuation of intravenous fluid.

In our view, the benefits of clinical pathway include not only the reduction in costs and hospital stay but also the promotion of patient and family collaboration by providing detailed information on the treatment process. Besides, it can also influence better training of professionals, facilitating teamwork, and improving the satisfaction of care team members via multidisciplinary communication (Deneckere et al., 2012). However, CP should be constantly monitored and revised to ensure that they remain effective and relevant and that they are operated in the way they have been designed to. Until now, the short-term benefits of CP have been widely reported in various operations, but the impact of it on the long-term outcomes of cancer surgery is still not clear. Recently, a fast-track surgery pathway was used to help patients getting better sooner after colorectal cancer surgery (Lohsirawat, 2014). Emerging evidence indicated that the application of the fast-track pathway in colon cancer surgery effectively inhibited release of post-operative inflammatory mediators, with a reduction in perioperative stress and a preservation of post-operative immune system (Wang et al., 2012), which was related to better anti-tumor activity and may increase survival (Karanika et al., 2013). Theoretically, CP might be of oncological benefit in cancer patients because it could maintain integrity of immune system and increase feasibility of postoperative chemotherapy. However, there are still no reports examining the long-term results of the application of CP in HCC surgery. Thus, the investigation of oncological outcomes of CP in HCC surgery should be proceeded.

Some limitations must be considered in this study. First, the number of subjects in both groups is relatively modest, and the study population is still relatively small. A larger sample size might reveal meaningful differences in certain outcomes such as readmission rates. Another limitation is the reliance on data from a single hospital in China. The single-center design can limit the generalization of the results, indicating that further trials with larger samples and variable measurements are in need to confirm the present findings.

In summary, the results of the current study support the implementation of a clinical pathway for hepatectomy of HCC which dramatically reduces costs and resources utilization without any apparent detrimental effect on quality of patient care. This study will also provide a basis for a larger, prospective, randomized, multi-institutional collaborative investigation to confirm or refute these initial observations.

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