

Cost-benefit analysis of enhanced recovery after hepatectomy in Chinese Han population

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Abstract

Background: Enhanced recovery after surgery (ERAS) programs have been proved effective for enhancing the clinical healing rate and reducing hospitalization cost in most countries of the world. It's a multi-model approach that designed to optimize perioperative pathway, attenuate the surgical stress response, and decrease postoperative complications.

Objective: The economic benefit from the application of ERAS to colorectal surgery has been demonstrated in China. However, such economic benefit of ERAS programs for hepatectomy hasn't been clarified yet. This study was carried out to explore the clinical efficacy and cost effectiveness of ERAS in Chinese Han population after hepatectomy.

Methods: ERAS program was implemented in our department for hepatectomy in December 2016. In total, 79 consecutive patients after hepatectomy were chosen as ERAS group (ERAS protocol) in coming half year while 121 consecutive patients after hepatectomy were chosen as Pre-ERAS group (traditional protocol) in past half year. The operation time, intraoperative blood loss, length of hospital stay (LOS), complication, readmission, and hospitalization cost of 2 groups were compared.

Results: The LOS of ERAS group was 5.81 ± 1.79 days, significantly shorter than that of Pre-ERAS group (8.06 ± 3.40 d) ($P = .000$). The operation time was 168.03 ± 46.20 minutes for ERAS group and 175.41 ± 64.64 minutes for Pre-ERAS group respectively ($P = .417$). The intraoperative blood loss was 166.58 ± 194.13 mL (ERAS group) and 205.45 ± 279.63 mL (Pre-ERAS group) ($P = .293$). It should be noted that the hospitalization cost of ERAS group was 51556.18 ± 8926.05 Yuan (7835.05 ± 1355.45 US dollars), significantly less than that of Pre-ERAS group 60554.66 ± 15615.31 Yuan (9202.56 ± 2371.24 US dollars) ($P = .000$). The application of ERAS effectively saved 8998.48 Yuan (1367.51 US dollars) for each patient.

Conclusions: ERAS implementation for hepatectomy surgery is safe and feasible for Chinese Han population. It eventually enhanced the clinical healing rate. The benefits from such programs include a reduction of the LOS, complication, and readmission rates. So each patient has access to better medical service. It effectively relieved the financial burden of patients. The benefits from such programs include a reduction of the hospitalization cost, especially in medication cost. So each patient can afford the diseases.

Abbreviations: ASA = American Society of Anesthesiologists, BMI = body mass index, CT = computed tomography, ECG = electrocardiogram, ERAS = enhanced recovery after surgery, ICER = incremental cost-effectiveness ratio, ICU = intensive care unit, LOS = length of hospital stay.

Keywords: benefits, Chinese Han population, enhanced recovery after surgery, hepatectomy, hospitalization cost

1. Introduction

Enhanced recovery after surgery (ERAS) is a clinical-based multi-model care pathway widely used in the world. It has been proved effective in reducing the length of hospital stay (LOS) and the incidence of complication and promoting patients rehabilitation after surgery.^[1] In recent years, ERAS has been gradually applied to various types of clinical surgeries, especially colorectal surgery.^[2,3]

ERAS program is an integrative and multidisciplinary innovation, in which traditional clinical pathway is changed.^[4] ERAS aims to reduce trauma and stress response of patients to promote recovery via multi-model, multi-channel, and integrative approaches ahead, during and after operation.^[5] Its main strategy is to optimize the perioperative treatment through surgery, anesthesia, nursing, and other multi-disciplinary cooperation.^[6] The most important perioperative measures include 5 entries: multi-model analgesic regimen to avoid or reduce the use of opioid analgesics; avoidance or reduction in using nasogastric tube; early postoperative bed activity; early recovery of oral intake and drinking water; avoidance of too much or too little intravenous infusion.^[7,8]

To date, the study on the application of ERAS to hepatectomy is very rare. To empirical knowing, the incidence of complication after hepatectomy is high (15%–48%), and the LOS in hospital is long.^[9] These problems can be solved by ERAS application. Thus, it is highly appreciated. So far, ERAS program has been proved cost-effective for colorectal surgery in China.^[10] The main purpose of this study was to assess the primary clinical efficacy and cost-effectiveness of ERAS after hepatectomy for Chinese Han population.

Editor: Weina Chen.

The authors declare no conflicts of interest.

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Medicine (2018) 97:34(e11957)

Received: 21 February 2018 / Accepted: 27 July 2018

<http://dx.doi.org/10.1097/MD.00000000000011957>

Table 1
Changes in perioperative care.

	ERAS	Pre-ERAS
Preoperative		
Counseling and education	Physicians and nurses	General notice
Fasting	Clear fluids allowed until 2 hours before surgery, solids until 6 hours before surgery	Clear fluids allowed until 8 hours before surgery, solids until 12 hours before surgery
Bowel preparation	No routine bowel preparation	Normal bowel preparation
Balanced intravenous fluids	Control infusion volume (Limited to 2000 mL/d or less)	None
Intraoperative		
Drain tube (placed)	No routine use	Routine use
Urinary catheter	Placed after anesthesia, removed after surgery	Placed on the day before surgery, removed on 2 to 5 days after surgery
Anesthesia	Epidural anesthesia	Intravenous anesthesia
Hypothermia preparation	Pay attention to insulation (mild intraperitoneal rinse)	None
Postoperative		
Analgesia	Intravenous controlled analgesia (PCIA)	Opioid analgesics
Drain tube (removed)	Removed on 2 to 3 days after surgery	Removed, drainage <30 mL
Nutrition	Drinking water on the first day after surgery, liquid diet gradually change to a normal diet	Drinking water after the exhaust of the anus, and gradually change to a normal diet
Mobilization	Require the patient to take the initiative, get out of bed the next day	None

ERAS = enhanced recovery after surgery.

2. Methods

ERAS has been tentatively applied after hepatectomy in the Affiliated Hospital of Qingdao University in December, 2016, where ERAS protocol has been explored in gastrointestinal surgery in 2011 with a wealth of experience. We followed the protocols including counseling and education (physicians and nurses), fasting (provision of oral nutrition), no routine bowel preparation, balanced intravenous fluids, no routine use drain tube, epidural anesthesia, intraoperative warm-air body heating, multi-model anesthesia, normal diet, and more mobilization out of bed (Table 1). Our ERAS teams have hepatectomy surgeries based on ERAS guidelines published by Chinese surgical experts and European ERAS association.^[11] This study was a retrospective survey, and the data were collected from previous medical records and did not involve patient consent. It was approved by the ethics committee of The Affiliated Hospital of Qingdao University.

2.1. Patient grouping

A total of 200 patients with primary hepatocellular carcinoma (HCC) who received hepatectomy from July 2016 to June 2017 participated in this study. All patients were given detailed information after admission and voluntarily participated in the study with full knowledge. All patients were divided into 2 groups by establishing 2 retrospective queues based on the beginning of ERAS: Pre-ERAS, 121 consecutive patients without experiencing ERAS for hepatectomy from July to Dec 2016; ERAS, remaining 79 consecutive patients who received ERAS for hepatectomy from Jan to Jul 2017.

2.2. Perioperative parameters

Perioperative parameters of the measurement involved three parts, including preoperative, intraoperative, and postoperative. The emphasis was focused on postoperative parameters relating to the LOS, complication, and readmission. The LOS was calculated according to the time from the first operation to

discharge. Complication was graded to minor, major and mortal according to the Dindo–Clavien classification.^[12] The readmission was the rate of second hospital admission after 30 days.^[13,14] The basic demographic and clinical differences were also measured.

2.3. Cost analysis

A comprehensive analysis of patients' real costs was performed with the method early described by Joliat et al.^[15] Cost, specifically of the intraoperative and pre/postoperative, was compared based on the information obtained from hospital information system. Intraoperative cost mainly included the expense for disposable material, anesthesia and operating room use. Preoperative and postoperative cost covered the expense in intensive care unit (ICU), medical care, nursing care, medication, blood, laboratory, radiology, inspection, pathology, and housing among others.^[16] The details of the cost were shown in Table 2.

Table 2
Contents of cost.

Cost	Contents
ICU care	Mainly referred to ICU nursing
Physiotherapy	Covered the expense in physical therapy and rehabilitation
Laboratory	Covered the expense in diagnostic test
Radiology	Covered the expense in x-ray, CT, and ultrasonic inspections.
Inspection	Mainly referred to vital capacity tests, ECG monitoring among others
Pathology	All examination expense during the pathological diagnosis
Housing	Mostly determined by the length of hospital stay and the diagnostic fee
Administration	None
Others	Mainly referred to the heating expense in winter

CT = computed tomography, ECG = electrocardiogram, ICU = intensive care unit.

Table 3
Patient demographics and surgical characteristics.

	Pre-ERAS group (n = 121)	ERAS group (n = 79)	Test value	P
Sex	85/36	52/27	$\chi^2=0.378$.540
Age	56.92 ± 10.89	55.47 ± 11.26	$t=-1.018$.775
BMI	24.67 ± 2.88	24.57 ± 3.69	$t=-0.277$.070
Smoker			$\chi^2=0.714$.700
Yes	53	30		
Stopped because of surgery	8	4		
No or unknown	60	45		
Drinker			$\chi^2=6.201$.045
Yes	38	16		
Stopped because of surgery	10	3		
No or unknown	73	60		
Diabetes	14	7	$\chi^2=0.397$.641
Chemo therapy	0	0		
ASA grade			$\chi^2=2.280$.320
I	0	1		
II	88	53		
III	33	25		
IV	0	0		
Main procedure			$\chi^2=7.549$.673
Partial hepatectomy	108	65		
Left-sided hepatectomy	8	5		
Right hepatectomy	5	7		
Middle hepatectomy	0	2		
Caudate hepatectomy	0	0		

ASA=American Society of Anesthesiologists, BMI=body mass index, ERAS=enhanced recovery after surgery.

2.4. Cost-minimization analysis

Cost-minimization analysis was carried out, aiming to assess the cost saving per patient. The saving was measured by subtracting the ERAS cost from the pre-ERAS cost. The cost-minimization was realized by taking the minimum among all programs.^[17,18]

2.5. Cost-effectiveness analysis

Average cost-effectiveness ratio, that is, the cost of producing one effect each. This present analysis was obtained by calculating the average cost per patient to the overall cure rate ratio. We calculated and compared using C/E.

Incremental cost-effectiveness ratio, that is, the ERAS group and pre-ERAS group were compared, the ratio of cost change to effectiveness change when taking different treatments. We calculated and compared using incremental cost-effectiveness ratio (ICER).

$$\text{ICER} = (C1 - C2)/(E1 - E2) = \Delta C/\Delta E$$

2.6. Statistical analysis

Either T or Mann-Whitney U test was used for continuous variables, χ^2 test was used for discrete variables and Wilcoxon rank sum test was used to non-normal distribution data. Statistical analysis was performed using SPSS 21.0 (IBM, Armonk, NY).

3. Results

A total of 200 patients with hepatectomy have participated this program at the Affiliated Hospital of Qingdao University, 121 in the pre-ERAS group and 79 were in the ERAS group. All patients

were treated by the same group of physicians. Demographics and surgical characteristics of the 2 groups were shown in Table 3.

3.1. Perioperative outcome

The number of laparoscopic surgery was 54 for pre-ERAS group and 39 for ERAS group, and no significant difference existed between 2 groups ($P=.737$). Pre-ERAS group were similar to ERAS group in the mean operation time and the mean anesthesia time. The mean operation time was 175 minutes versus 168 minutes (pre-ERAS vs ERAS; $P=.417$). Similarly, the mean anesthesia time was 234 minutes versus 220 minutes (pre-ERAS vs ERAS; $P=.176$). The blood loss was 205 mL for Pre-ERAS and 167 mL for ERAS group, similar with each other ($P=.293$).

The mean postoperative LOS was significantly longer in pre-ERAS group than in ERAS group (8.06 vs 5.81 d, $P=.000$), whereas the ICU stay of ERAS group was similar to that of pre-ERAS group (1.78 vs 1.93 d; $P=.429$). The complication rate was significantly different between 2 groups, 15 cases in pre-ERAS group, including 6 cases of bile leakage, 1 case of ascites, 3 cases of incision infection and 1 case of hepatic failure, and 4 cases in ERAS group, 2 cases of bile leakage, 1 case of ascites, 1 case of hepatic failure. Pre-ERAS group were also significantly different from ERAS group in complication ($P=.040$) and readmission ($P=.033$) (Table 4).

3.2. Cost analysis

Based on ERAS, the mean cost was 51556.18 Yuan (7835.05 US dollars) per patient, lower than 60554.66 Yuan (9202.56 US dollars) ($P=.000$) of pre-ERAS. The preoperative and postoperative cost of ERAS was 27566.79 Yuan (4190.50 US dollars), also lower than that of pre-ERAS 35315.83 Yuan (5368.45 US dollars) ($P=.000$). There was significant difference between

Table 4

Perioperative outcome.

	Pre-ERAS group (n = 121)	ERAS group (n = 79)	Test value	P
Type of surgery			$\chi^2=0.611^a$.737
Open surgery	67	40		
Laparoscopic surgery	54	39		
Duration of operation, min	175.41 ± 64.64	168.03 ± 46.20	$t=-0.814$.417
Duration of anesthesia, min	234.34 ± 79.29	220.25 ± 49.60	$t=-1.358$.176
Intraoperative blood loss	205.45 ± 279.63	166.58 ± 194.13	$t=-1.055$.293
Length of ICU stay, d	1.93 ± 1.29	1.78 ± 1.22	$t=-0.793$.429
Length of hospital stay, d	8.06 ± 3.40	5.81 ± 1.79	$t=-5.425$.000
Complications	15	4		.040
Bile leakage	6	2		
Plenty of ascites	1	1		
Pleural effusion	4	0		
Incision infection	3	0		
Intestinal obstruction	0	0		
Hepatic failure	1	1		
Readmission	5	1		.033
Mortality rate	0	0		

ERAS=enhanced recovery after surgery, ICU=intensive care unit.

2 groups in nursing care, medication, laboratory, pathology, and housing costs ($P < .05$). The lower cost of ERAS group indicated that the implementation of ERAS protocol efficiently reduced the costs in treatment, drug, laboratory, and inspection among others (Table 5).

3.3. Cost-minimization analysis

The difference of mean total cost per patient between ERAS and pre-ERAS groups was 8998.48 Yuan (1367.51 US dollars), demonstrating that the application of ERAS efficiently reduced patients' hospitalization cost and saved 8998.48 Yuan (1367.51 US dollars) for each patient (Table 6).

3.4. Cost-effectiveness analysis

We assessed the impact of ERAS on patients' health services utilization within 30 days of discharge by comparing pre-ERAS

groups and ERAS groups using the data from the inpatient department of hospital. The cure rate is the number of cures per 100 patients treated by the doctor. It can also be defined as the probability that a disease can be cured. It was showed that the cure rate of patients with hepatectomy was significantly increased after the implementation of ERAS. (82.64% vs 91.14%) (Table 7).

$$\text{Cure rate} = \frac{\text{cured(patients)}}{\text{Treated(patients)}}$$

Cost-effectiveness analysis was necessary to further evaluate the advantages and disadvantages of the 2 surgical regimens. The results showed that the cost-effectiveness ratio (C/E) of the pre-ERAS group is 73.31 thousand Yuan (11.19 thousand US dollars) and that of the ERAS group is 56.59 thousand Yuan (8.64 thousand US dollars) (Table 8).

In incremental analysis that allows all variables to vary simultaneously, we analyzed 2 scenarios: incremental cost;

Table 5

Mean cost per patient for ERAS and Pre-ERAS groups.

	Cost per Patient (Yuan)		Difference	P
	ERAS group	Pre-ERAS group		
Total intraoperative	23989.39	25238.83	-1249.44	.074
Disposable materials	15381.67 (2500.66, 30853.51)	16746.63 (878.6, 44092.5)	-1364.96	.266
Anesthesia and operating room	8607.72 (3143, 18390)	8492.20 (90, 18493)	115.52	.533
Total preoperative and postoperative	27566.79	35315.83	-7749.04	.000
ICU care	265.17 (0, 751.59)	281.89 (0, 1235.43)	-16.72	.575
Medical care	3353.97 (1060.8, 6608.07)	3650.14 (158.75, 7918.07)	-296.17	.143
Nursing care	848.99 (60, 1691)	1116.96 (370, 3433)	-267.97	.000
Medication	13222.02 (4298.98, 31383.51)	17328.29 (3937.75, 110766.79)	-4106.27	.004
Blood	162.29 (0, 6314)	201.18 (0, 3969)	-38.89	.700
Laboratory	4644.99 (2253.6, 9345)	6480.79 (2652.2, 60396.2)	-1835.8	.003
Radiology	2339.02 (180, 7384)	2758.78 (237.03, 9594)	-419.76	.072
Inspection	525.67 (103.1, 1623.36)	678.87 (0, 9907)	-153.2	.230
Pathology	1395 (0, 3370)	1863.93 (0, 4540)	-468.93	.000
Housing	771.13 (244, 1367)	913.81 (360, 2071)	-142.68	.001
Others	38.54 (4, 76)	41.19 (0, 112)	-2.65	.487
Total	51556.18 (34352.29, 69571.47)	60554.66 (31403.47, 106634.05)	-8998.48	.000

Table 6
Cost-minimization analysis.

	Cost per patient (Yuan)		Difference (ERAS-pre-ERAS)
	ERAS	Pre-ERAS	
Intraoperative costs	23989.39	25238.83	-1249.44
Preoperative and postoperative costs	27566.79	35315.83	-7749.04
Total costs	51556.18	60554.66	-8998.48

incremental effectiveness. Table 9 showed the cure rate increased by 1% and cost reduced by 1058 Yuan with the implementation of ERAS.

We estimated health care costs/savings associated with effectiveness calculated in the first step for the pre-ERAS and ERAS patients using a economic methodology model-ling technique (Figs. 1 and 2). In Figure 1, the Y axis represents the effectiveness, which indicates an effect (cure rate) of 0.826 in pre-ERAS and 0.911 in ERAS; in Figure 2, the Y axis represents the cost, which indicates a cost of 60.55 thousand Yuan in pre-ERAS and 51.56 thousand Yuan in ERAS. It can be seen that the cost-effectiveness of ERAS is significantly better than that of the pre-ERAS group.

4. Discussion

China has the heaviest population of patients with liver disease in the world, and a large number of patients with liver cancer. There were about 700,000 cases of new liver cancer around the world each year, of which more than one half occurred in China. However, the benefits of introducing the ERAS program for Chinese Han patients with hepatectomy were not clear.

Our study showed that the Los of ERAS group is 5.81 days, which is shorter than the LOS in Pre-ERAS group (8.06 d). This finding was consistent with the study of Dai Shida et al.^[19] As reported, the median LOS of the ERAS group (7 vs 10 d) was shorter with a 3-day reduction for colorectal cancer. In terms of the return on investment, the application of ERAS in hepatectomy would save 8998.48 Yuan (1367.51 US dollars) per patient in return, which was consistent with the results of six controlled trials, a meta-analysis wrote by Mariëlle.^[20]

In our study, different cost was observed between the pre-ERAS and ERAS groups, in which some items cost had risen and the other had fallen. The biggest saving was in medication, especially after the application of ERAS to hepatectomy. The difference between use and not use was statistically significant ($P=.004$). The reduction in medication cost was due to a reduction in drug use, which was attributed to the combination of the standard clinical pathway and the standard nursing care in the ERAS program.^[21,22] In addition, the application of ERAS was helpful for reducing postoperative complications.^[23] So there were a fewer and fewer patients taking drugs to cure postoperative complications. These findings were consistent

Table 7
Comparison of 2 groups cure rate.

	Treated	Cured	Cure Rate (%)
Pre-ERAS	121	100	82.64
ERAS	72	79	91.14

Table 8
Cost-effectiveness ratio.

	Cost (thousand Yuan)	Effectiveness	Cost-effectiveness	Advantage
Pre-ERAS	60.55	0.826	73.31	
ERAS	51.56	0.911	56.59	✓

with professor Joliat’s research: less postoperative medication was used related to ERAS.^[15] All of these results support the conclusion that ERAS can lead to a reduction in medication cost.

The second statistically significant gain in ERAS group was the reduction in laboratory cost ($P=.003$). The number of laboratory diagnostic items reduced, which could be due to the reduced postoperative complications, the standardized clinical pathway, the postoperative nursing care, and the combination of all measures in ERAS.^[24–26] However, our findings suggested that anesthesia and operating room cost was similar in 2 groups. According to the previous studies, anesthesia and operating room cost was responsible for the second main absolute gain (£ 2045) in the ERAS group, which was in line with Labgaa’s results.^[27] Our study showed that ERAS played an important role in decreasing the economic burden on patients, and many item costs had fallen significantly, including nursing care, medication, laboratory, pathology, and housing.

However, anesthesia and operating room costs rose in ERAS group. The anesthesia methods were different between ERAS group and pre-ERAS group: epidural anesthesia in ERAS is better than intravenous anesthesia in pre-ERAS for patients. The cost of anesthesia consists of basic anesthesia costs and anesthetic drug costs. The basic anesthesia costs were essentially the same in both groups, while the cost of anesthetic drugs was relatively high in ERAS group. There was no significant difference in operating time between the 2 groups during the operation.

Regarding to the composition of the cost, we found that the disposable materials cost and the medication cost were the largest proportion. According to the foreign studies, however, these 2 costs accounted for a small proportion.^[10] This is probably due to the fact that the former was mainly depended on imports. On the contrary, the proportion of ICU care cost, medical care cost, and nursing care cost were lower in China. Different countries have different medical habits and environment. The charges of medical work mainly base on the patient’s conditions.^[28,29] At present, all these costs are constantly adjusted, so that it really reflects the medical value in China.

Previous studies showed that systematic evaluation of ERAS was safe and feasible, it benefited patients mainly in a shorter Los and relatively lower cost.^[30] A study by Bernard et al^[31] found that gynecologic tumor surgery significantly reduced the Los (5 vs 7 d, $P<.001$). This result supported the view that ERAS program could achieve clinical promotion.^[32] The average LOS in Chinese Han patients with colorectal surgery could be reduced

Table 9
Incremental cost-effectiveness ratio.

	Effectiveness	Cost (thousand Yuan)	Incremental Effectiveness	Incremental Cost	ICER
Pre-ERAS	0.826	60.55	0.085	8.99	-105.8
ERAS	0.911	51.56	-	-	

ERAS=enhanced recovery after surgery, ICER=incremental cost-effectiveness ratio.

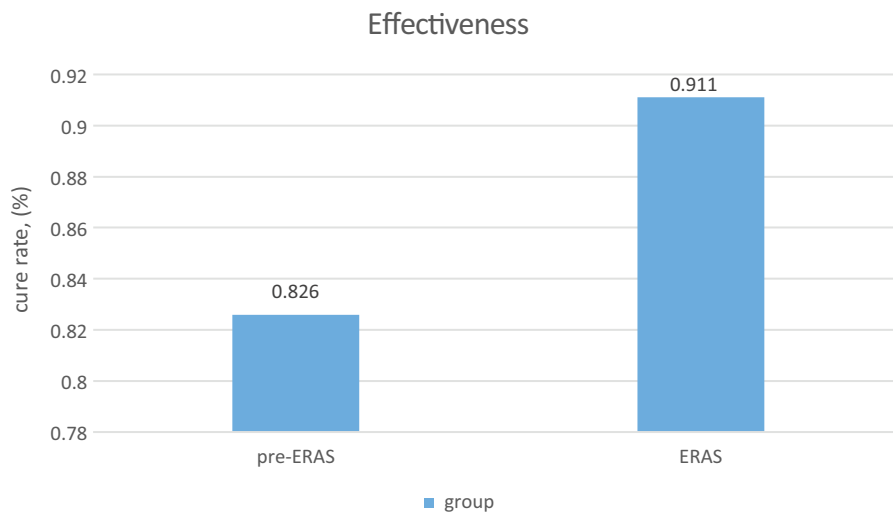


Figure 1. Effectiveness-analysis.

by 2.5 days and the risk of postoperative complications was reduced by 47%, which were found in a study by Danlong Feng. A fewer patients were readmitted to the hospital for treatment, and none of the patients died in our study.

Recent systematic reviews on ERAS showed that it was cost-effective. In terms of Nguyen’s study, he referred that every \$ 1 spent in ERAS would bring \$ 3.8 (range, \$ 2.4–\$ 5.1) in return.^[33] Nevertheless, our present study suggests a detailed analysis of the actual cost of ERAS in liver surgery. Therefore, ERAS program should be gradually extended from tertiary hospitals to secondary hospitals in China in order to solve China’s medical problems, “proper health care is difficult to get” and “proper health care is expensive.”

However, this study also has some limitations. We only focused on the implementation of ERAS in the Affiliated Hospital of Qingdao University and the sample may not be broadly representative. More studies on the use of ERAS in hepatectomy are needed, especially randomized prospective studies.

5. Conclusion

This study demonstrated that the initial phase of the ERAS implementation program for hepatectomy surgery in the Affiliated Hospital of Qingdao University was safe and effective for Chinese Han population. It eventually enhanced the clinical healing rate. The benefits from such programs including a reduction of the LOS, complications, and readmission rates. So each patient has access to better medical service. It effectively relieved the financial burden of patients. The benefits from such programs including a reduction of the hospitalization cost, especially in medication cost. So each patient can afford diseases. Cost savings was different between our present study and other studies from foreign countries on ERAS applications. It’s mainly due to different medical habits and environment in different countries. The total savings or return on investment may be more substantial when ERAS is spread to other clinical departments. However, this study also has some limitations. We only focused on the implementation of ERAS in the Affiliated Hospital of

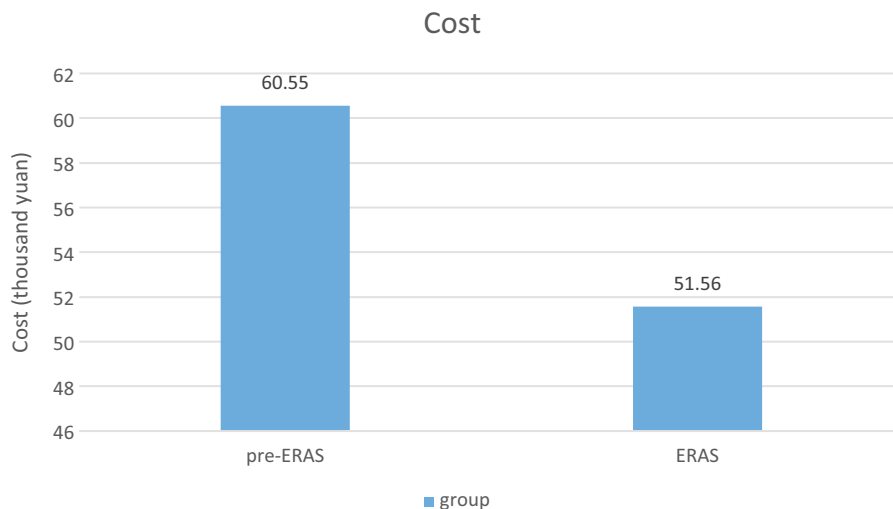


Figure 2. Cost-analysis.

Qingdao University and the sample may not be broadly representative.

Acknowledgments

We would like to thank all the ERAS team of our institution for the daily clinical and research work. We are grateful to Meng Zhou who gathered patient data and to Dan Liu who helped in the completion of the ERAS liver database. Professor Gao of the accounting department is also acknowledged for providing us with all the real costs and financial data.

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