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Enhanced recovery care versus traditional care after laparoscopic liver resections: a randomized controlled trial

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China Map



**Hangzhou ,ZheJiang
G20 summit ,2016**

History of Sir Run Run Shaw Hospital



- Opened on May 2, 1994
- Donated by Hong Kong *Philanthropist*
Sir Run Run Shaw
- Co-Funded by Zhejiang Provincial
Government

Introduction of the SRRSH



- The first JCI hospital in China
- 32 clinical specialties, 2400 hospital beds.
- Specialty: Minimally invasive treatment and laparoscopic technique.

Our surgery department:

laparoscopic liver resections

ALPPS, laparoscopic Pancreatoduodenectomy ...

key lab of laparoscopic technique of Zhejiang Province



Outpatient Lobby

Campus



Health Promotion Center



Enhanced Recovery After Surgery (ERAS)

First proposed by Professor *Henrik Kehlet* in 1997

Multimodal approach to control postoperative pathophysiology and rehabilitation

H. KEHLET

Summary

Major surgery is still associated with undesirable sequelae such as pain, cardiopulmonary, infective and thromboembolic complications, cerebral dysfunction, nausea and gastrointestinal paralysis, fatigue and prolonged convalescence. The key pathogenic factor in postoperative morbidity, excluding failures of surgical and anaesthetic technique, is the surgical stress response with subsequent increased demands on organ function. These changes in organ function are thought to be mediated by trauma-induced endocrine metabolic changes and activation of several biological cascade systems (cytokines, complement, arachidonic acid metabolites, nitric oxide, free oxygen radicals, etc). To understand postoperative morbidity it is therefore necessary to understand the pathophysiological role of the various components of the surgical stress response and to determine if modification of such responses may improve surgical outcome. While no single technique or drug regimen has been shown to eliminate postoperative morbidity and mortality, multimodal interventions may lead to a major reduction in the undesirable sequelae of surgical injury with improved recovery and reduction in postoperative morbidity and overall costs. (Br. J. Anaesth. 1997; 78: 606-617).

Key words

Surgery, stress response, Pain, postoperative.

trauma-induced endocrine metabolic activation of several biological cascade systems (cytokines, complement, arachidonic acid metabolites, nitric oxide, free oxygen radicals, etc). Although these responses have to confer an advantage for survival, they are amplified and prolonged, also leading to a loss of body cell mass and physiological reserve. The key question in our view is whether or not a modification of these responses may improve surgical outcome. Additionally, if such a modification is controlled, one may ask if patients can undergo major surgery on an ambulatory basis.

This article reviews current approaches to controlling postoperative dysfunction, surgical stress and pain. It discusses how multimodal interventions may lead to a reduction in the undesirable sequelae of surgical injury with accelerated recovery and reduction in postoperative morbidity and overall costs. The discussion will focus on elective surgery and multiple organ failure, reviewed elsewhere.²



Multimodal interventions may lead to a major reduction in the undesirable sequelae of surgical injury with improved recovery and reduction in postoperative morbidity and overall costs.



Pro Henrik Kehlet



Concept of ERAS



Combination of various evidence-based techniques reduces the stress response and organ dysfunction and therefore greatly shorten the time required for full recovery.

Wilmore DW, Kehlet H. Management of patients in fast track surgery. BMJ 2001

Practice of H-ERAS in SRRSH



ERAS-MDT for laparoscopic liver resection



- Surgeon
- Nurse
- Anesthetist
- APS team (Acute pain service)
- Respiratory therapist
- Nutritionist
- Rehabilitation physician
- Psychiatrist



A retrospective study in SRRSH



2014.6-2015.7 187 patients of laparoscopic liver resection were included.

Traditional group: 107; ERAS group: 80

A retrospective study in SRRSH

Medicine®

OBSERVATIONAL STUDY

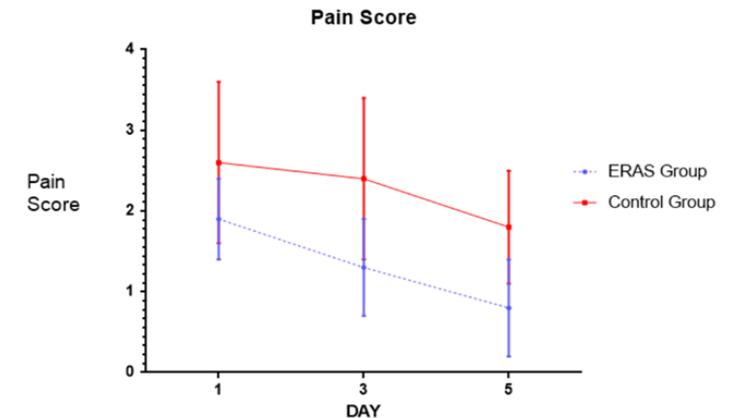
OPEN

Enhanced Recovery Program Versus Traditional Care in Laparoscopic Hepatectomy

Xiao Liang, MD, Hanning Ying, MM, Hongwei Wang, MD, Hongxia Xu, BN, Hong Yu, MD, Liuxin Cai, MD, Yifan Wang, PhD, Yifan Tong, MM, Lin Ji, MM, Raojun Luo, MM, and Xiu-Jun Cai, MD, PhD

Postoperative hospital stay (day) *	6.2±2.6	9.9±5.9	< 0.001
Function recovery days*	5.0±2.3	8.5±4.4	< 0.001
Readmission(< 30 days)	3	5	0.60
Cost (RMB) *	45201.3±16916.6	52287.3±23878.8	0.02

*Values are median (interquartile range) and †mean(s.d.). CRP: C reactive protein.



The pain score of the control group (the red line) was higher than the ERAS group (the blue line). The pain score was significantly different between two groups on day 1, day 3 and day 5 (all $p < 0.001$).

RCT in SRRSH



The RCT of ERAS in laparoscopic liver resections was performed 2015.8 to 2016.8

ClinicalTrials.gov

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Trial record **1 of 1** for: [Enhanced Recovery After Surgery Protocol Versus Traditional Care in Laparoscopic](#)

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Enhanced Recovery After Surgery Protocol Versus Traditional Care in Laparoscopic Hepatectomy

This study is currently recruiting participants. (see [Contacts and Locations](#))

Verified August 2015 by Sir Run Run Shaw Hospital

Sponsor:

Sir Run Run Shaw Hospital

Information provided by (Responsible Party):

Xiujun Cai, Sir Run Run Shaw Hospital

ClinicalTrials.gov Identifier:

NCT02533193

First received: August 11, 2015

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[History of Changes](#)

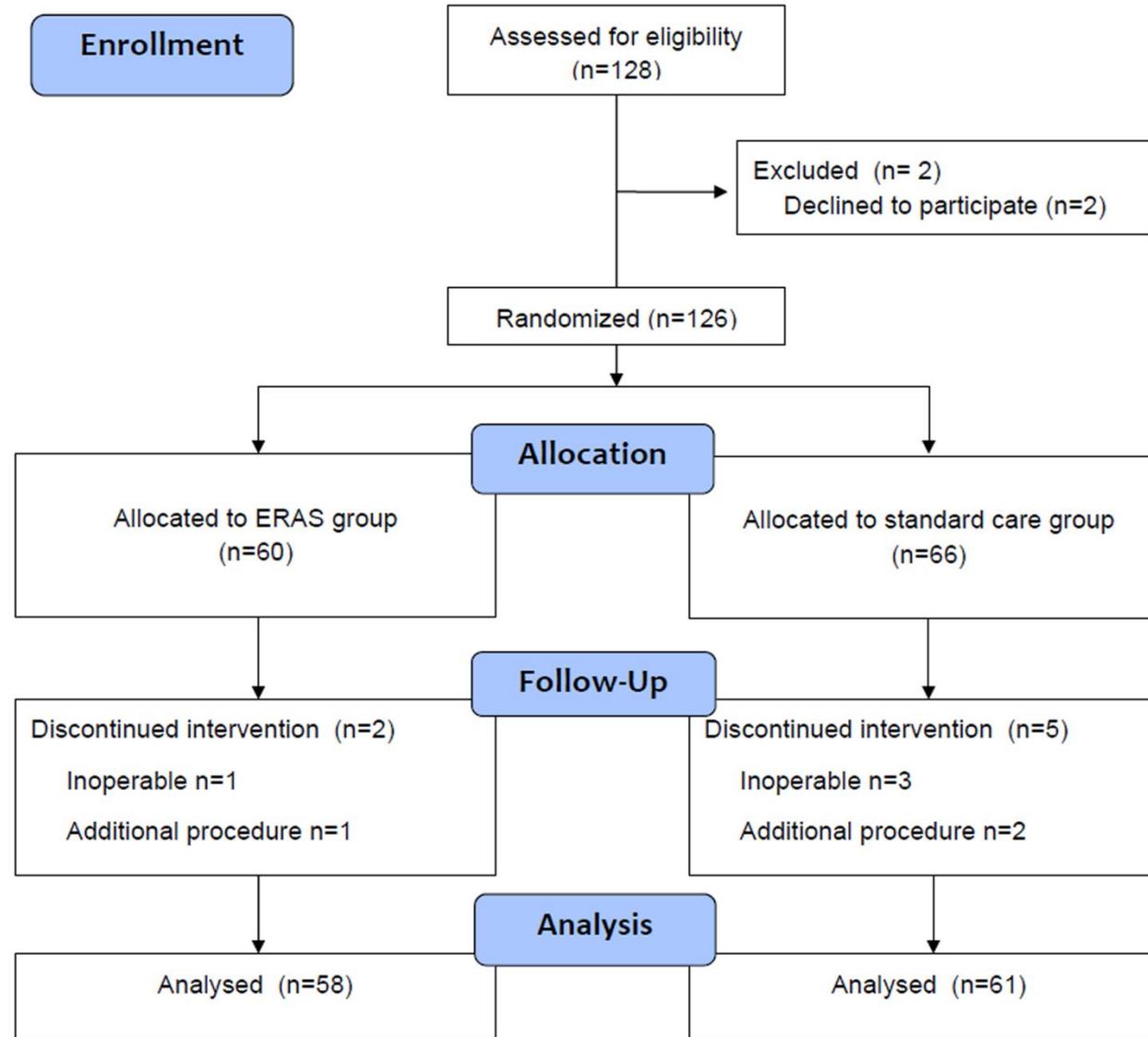


Fig. 1 CONSORT diagram for the trial. ERAS, enhanced recovery after surgery

Patients were randomly divided into two groups

- **Group**

ERAS group: 58 patients who received ERAS program

Standard care group: 61 patients who received standard care

- **Outcomes**

Primary outcome was length of hospital stay (LOS) after surgery.

Second outcomes included hospital costs, postoperative complications and 30-readmissions.

Summary of ERAS program

Before surgery

1. Perioperative education, including mobilization and dietary goals
2. No routine bowel preparation
3. Oral nutrition

Day of surgery

1. Carbohydrate drinks until 2 h before surgery (400ml)
2. Combined tracheal intubation
+ general anesthesia local anesthesia (0.2%ropivacaine)
3. No nasogastric tube or removed as early as possible
4. Less abdominal drain used

POD 0

1. Drink water 6h after surgery
2. Restricted intravenous fluid 2000-2500ml
3. APS ward round
4. Multimodal analgesia: 40 mg ParecoxibNa (Dynastat) i.v. per 12 hours and 50mg-100mg Tramadol twice a day by oral. PCIA used if necessary.

POD 1

1. Oral nutritional supplements (Liquid) or semi-liquid diet
2. Mobilization twice daily
3. Urinary catheter removed
4. Reduce intravenous fluid

POD 2

1. Oral semi-liquid diet
2. Stop maintenance intravenous fluid
3. Mobilization four times daily
4. Remove CVC
5. Remove abdominal drainage tube

POD 3

1. Stop intravenous anesthetics and use oral Tramadol or Celecoxib
2. Normal mobilization
3. Normal diet
4. Check the discharge criteria

POD 4 - home

1. Continue the events as day 3
2. Check the discharge criteria
3. Education for discharge and recovery plan at home

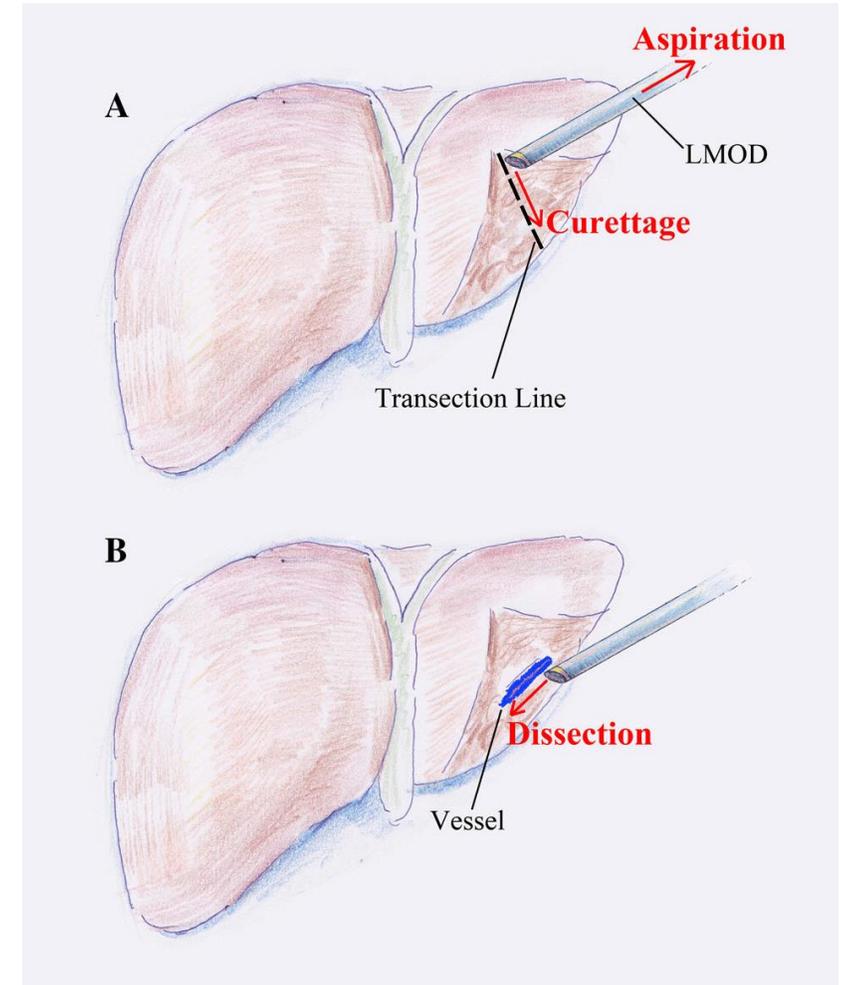
Surgical technique for liver transection and dissection

- laparoscopic Peng's multifunctional operative dissector (LPMOD)
 - >2 mm would be dissected and be further clipped or ligated
 - < 2 mm would be directly divided and sealed by electric coagulation.
 - >10 mm, laparoscopic linear staples would be adopted to seal and transect them.

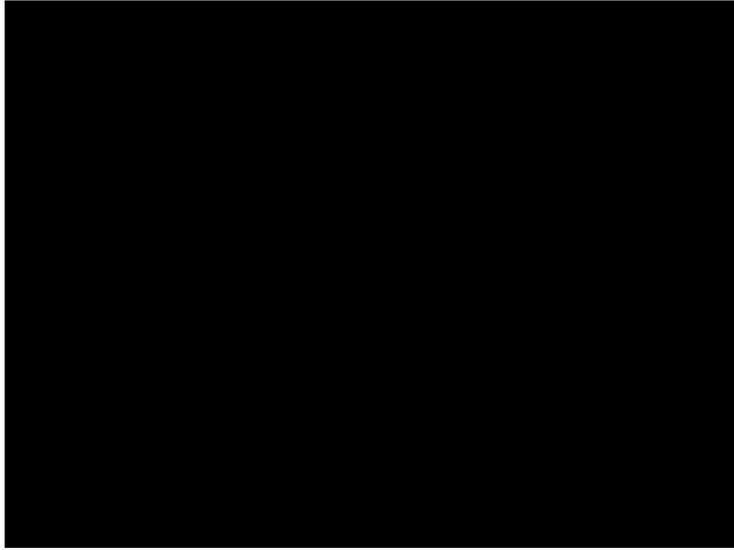


LPMOD: laparoscopic Peng's multifunctional operative dissector

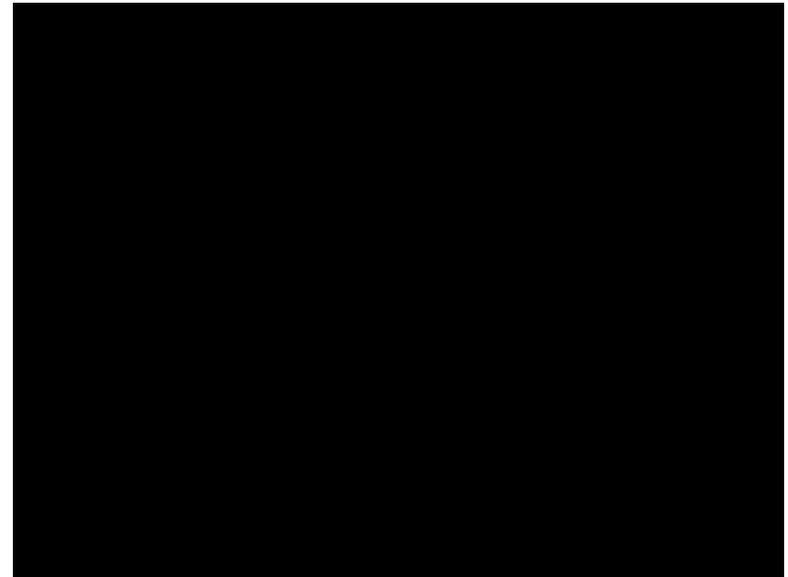
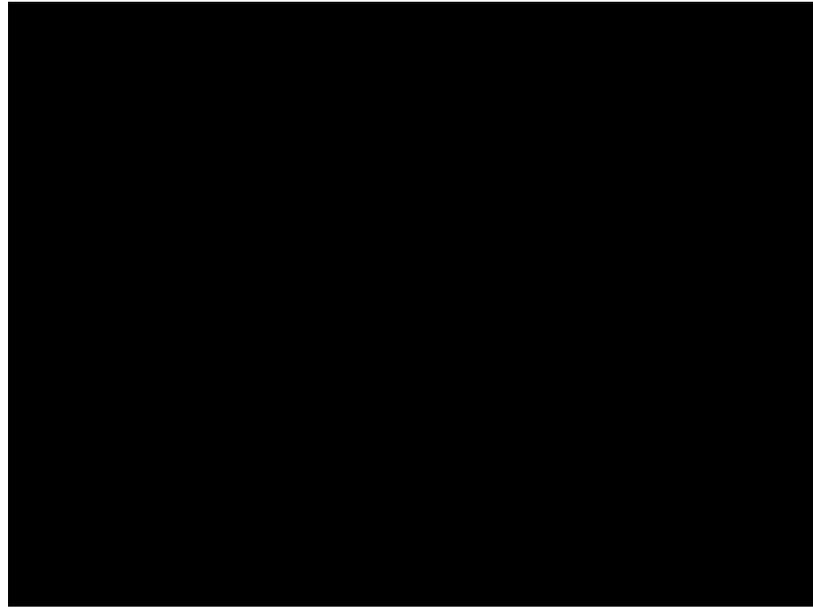
- Special instrument for laparoscopic liver transection.
- Based on the Peng's multifunctional operative dissector (PMOD).
- Extended the length of the stalk of PMOD and modified the aspiration system to fit the laparoscopic situation.
- Used for blunt dissection, electric coagulation, cutting and aspiration and can bluntly dissect intrahepatic ducts and vessels.
- all the functions can be executed at the same time.



Surgical technique for liver transection and dissection



Simple pringle



Results: short hospital stay and less cost

Operative details and outcomes

	ERAS (n=58)	Traditional care (n=61)	P
Conversion to laparotomy	2 (3.4)	3 (4.9)	1.000 [‡]
Operative time (min)**	165 (55-445)	180 (60-450)	0.060 [†]
Blood loss (ml)**	150 (50-800)	200 (10-2000)	0.070 [†]
Blood transfusion (No. of patients)	6 (10.3)	12 (19.7)	0.156 [§]
Blood plasma only	2	3	
Multiple blood components	4	9	
Nasogastric tube (No. of patients)	0 (0)	12 (19.7)	<0.001 [‡]
Duration of first flatus(h) **	38 (17-59)	64 (44-84)	<0.001 [†]
Duration of urinary drainage (days)**	1 (0-3)	2 (1-9)	<0.001 [†]
Length of hospital stay (days) **	5 (1-24)	8 (6-11)	<0.001 [†]
Hospital costs (¥)*	45413.1±18168.9	55794.1±22218.4	0.006 [†]
Readmission rates (<30 days)	4 (6.9)	5 (8.2)	1.000 [‡]

Results: less complications of GRADE I

Complications of patients

	ERAS (n=58)	Traditional care (n=61)	P
Patients with complications	21 (36.2)	34 (55.7)	0.033[§]
GRADE I	18 (31.0)	32 (52.5)	0.018[§]
Ascites (Diuretics/electrolytes)	9 (15.5)	16 (26.2)	0.152 [§]
Wound infection	1 (1.7)	1 (1.6)	
Nausea/Vomiting	6 (10.3)	15 (24.6)	0.042[§]
Others	2 (3.4)	0 (0)	
GRADE II	9 (15.5)	16 (26.2)	0.152[§]
Liver failure	6 (10.3)	8 (13.1)	0.639 [§]
Pneumonia	0 (0)	3 (4.9)	
Intestinal obstruction	0 (0)	1 (1.6)	
Sepsis	2 (6.1)	2 (3.3)	
Others	1 (1.7)	2 (3.3)	
GRADE IIIa	5 (8.6)	9 (14.8)	0.299[†]
Bile leak	2 (3.4)	3 (4.9)	
Abdominal abscess	1 (1.7)	2 (3.3)	
Pleural effusion	2 (3.4)	4 (6.6)	
GRADE IIIb	0 (0)	1 (1.6)	
Hemorrhage and reoperation	0 (0)	1 (1.6)	
GRADE IV a	1 (1.7)	1 (1.6)	
Respiratory failure (Pulmonary embolism)	0 (0)	1 (1.6)	
Liver failure requiring ICU management	1 (1.7)	0 (0)	
GRADE IV b	0 (0)	1 (1.6)	
GRADE V	0	0	

Results: less pain

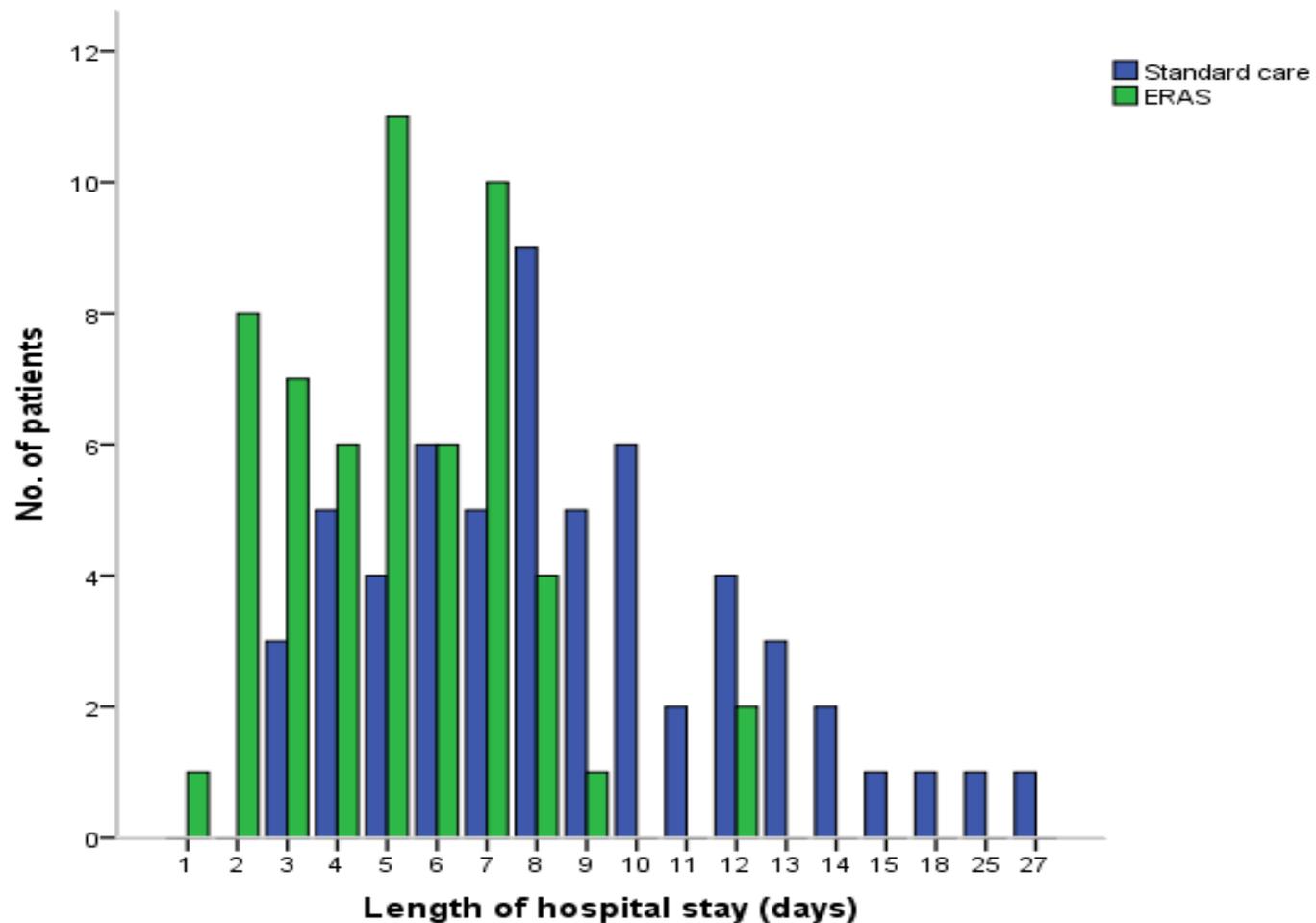


VAS of pain score

	ERAS (n=58)	Traditional care (n=61)	P
POD1 (No. of patients)	58	61	
VAS Score*	2.5 (1.0)	3.1 (1.2)	0.010 [†]
No. of patients (VAS ≥ 4)	11 (19.0)	24 (39.3)	0.017 [§]
POD3 (No. of patients)	50	61	
VAS Score*	2.2 (0.9)	2.5 (0.9)	0.036 [†]
No. of patients (VAS ≥ 4)	4 (8)	11 (18.0)	0.166 [‡]
POD5 (No. of patients)	37	53	
VAS Score*	1.9 (0.9)	2.1 (1.0)	0.237 [†]
No. of patients (VAS ≥ 4)	2 (5.4)	5 (9.4)	0.696 [‡]

Results

Postoperative length of hospital stay



Discussion: perioperative of education

1. Perioperative education and evaluation play an important role in ERAS program.

Patients and their families were given more detailed explanation of ERAS interventions and the technique of laparoscopic liver resection.

Nurse navigators were set up to contribute to the delivery of patient-centered care by guiding patients and families.



Discussion: Multimodal approach to PONV



2. Multimodal approach to PONV was used in ERAS group based on our protocol of PONV.

PONV is considered to be common after major surgery.

Laparoscopic approach is associated with a higher incidence of PONV.

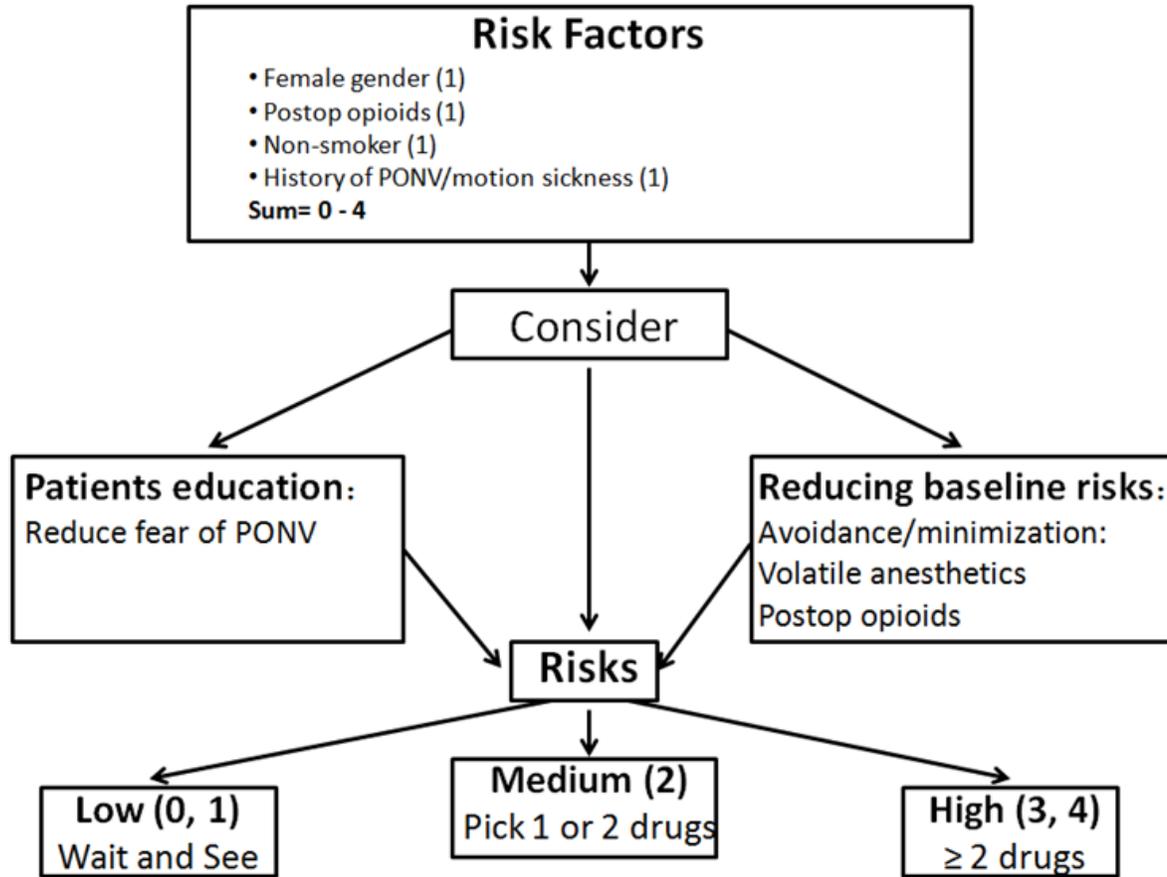
According to the strong recommendations from ERAS guidelines for liver surgery on PONV, a multimodal approach is useful, and patients should receive PONV prophylaxis with 2 antiemetic drugs.

	ERAS (n=58)	Traditional care (n=61)	P
Patients with complications	21 (36.2)	34 (55.7)	0.033 [§]
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Wound infection	1 (1.7)	1 (1.6)	
Nausea/Vomiting	6 (10.3)	15 (24.6)	0.042 [§]
Others	2 (3.4)	0 (0)	

1. Gan, T.J., et al., Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*, 2014. 118(1): p. 85-113.

2. Jones, C., et al., Randomized clinical trial on enhanced recovery versus standard care following open liver resection. *BRITISH JOURNAL OF SURGERY*, 2013. 100(8): p. 1015-1024.

The management of PONV in SRRSH



A. The management of PONV in Sir Run Run Shaw Hospital.

B. The choice of drugs for PONV

Dopamine 2 (D2) Receptor antagonists	Metoclopramide	10mg, q12h, iv	Medium Risk	High Risk
5HT3 antagonists	Ondansetron	4-8mg, q4-6h, iv		
	Tropisetron	2mg, qd, iv		
Glucocorticoid	Dexamethasone	5-10mg, qd, iv		
	Methylprednisolone	40-80mg, qd, iv		
Butyrophenones	Droperidol	0.625-1.25mg		

Discussion: pain control



3. Pain control in laparoscopic liver resection

- Multimodal analgesia (MMA) currently is considered as the main analgesic selection.
- Pre-operation: 1) analgesic strategy made by MDT and 2) education for reducing fear of pain
- Intra-operation: 1) 0.75% ropivacaine for local anesthesia around the trocar incision.
2) Wound infusion catheter was used if the incision was large.
3) Transversus abdominis plane (TAP) and patient controlled analgesia (PCA) were used according to patient will and clinical need.
- Post-operation: 1) ParecoxibNa (Dynastat) per 12 hours and Tramadol 50mg-100mg twice a day by oral were used after surgery.
2) Acute pain service (APS) visited patients once a day to evaluate the effect of pain control and adjust analgesic strategy.

Discussion: pain control



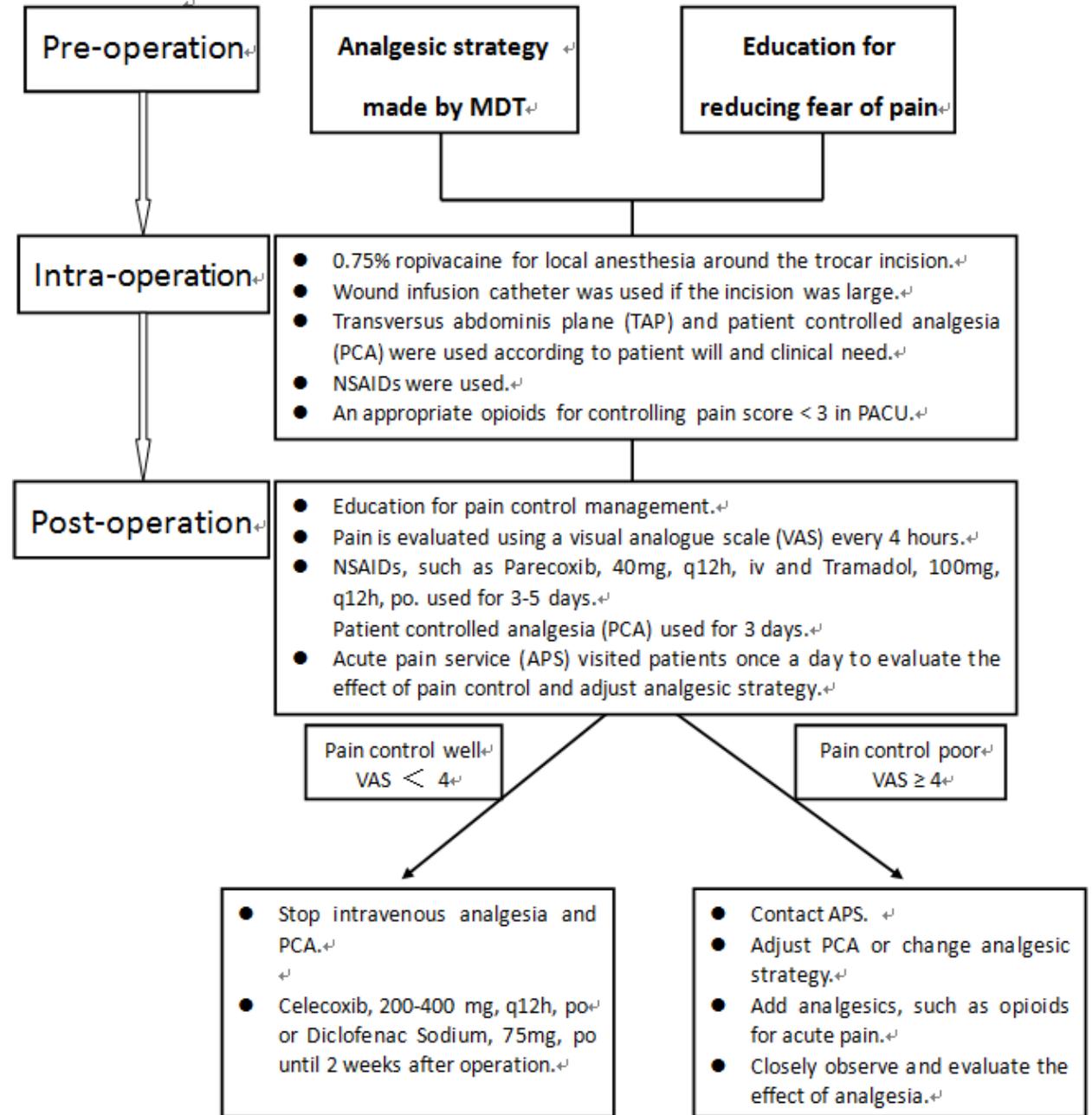
No Patient controlled epidural analgesia (PCEA) was used in laparoscopic liver resection

1. The result showed that pain is controlled well in ERAS group by multimodal analgesia without epidural anesthesia.
2. Epidural analgesia would increase risks of complications with prolonging the prothrombin time after liver resections.
3. **Most importantly**, laparoscopic liver resection has small incisions and less injury. Patients suffer from less pain by minimally invasive operation.
4. More studies about the value of epidural anesthesia are needed.

1. Melloul, E., et al., Guidelines for Perioperative Care for Liver Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations. World J Surg, 2016. 40(10): p. 2425-40.

2. Sakowska, M., et al., A Change in Practice from Epidural to Intrathecal Morphine Analgesia for Hepato-Pancreato-Biliary Surgery. WORLD JOURNAL OF SURGERY, 2009. 33(9): p. 1802-1808.

The protocol of pain control management in ERAS group



Discussion: no routine surgical drainage?



4. No routine surgical drainage ?

- Kyoden et al. showed that prophylactic drainage could reduced the frequency of subphrenic abscess and biliary fistula or biloma formation.
 - 3 RCTs on liver resection only, with low sample size, suggested omit routine prophylactic drainage.
 - **It remains uncertain for liver resection.**
In China, many patients with liver cirrhosis have severe ascites and liver failure.
High risk of complications, such as bleeding, bile leakage, and ascites.
- Surgical drainage should be used based on clinical need.**

Discussion: compliance is important

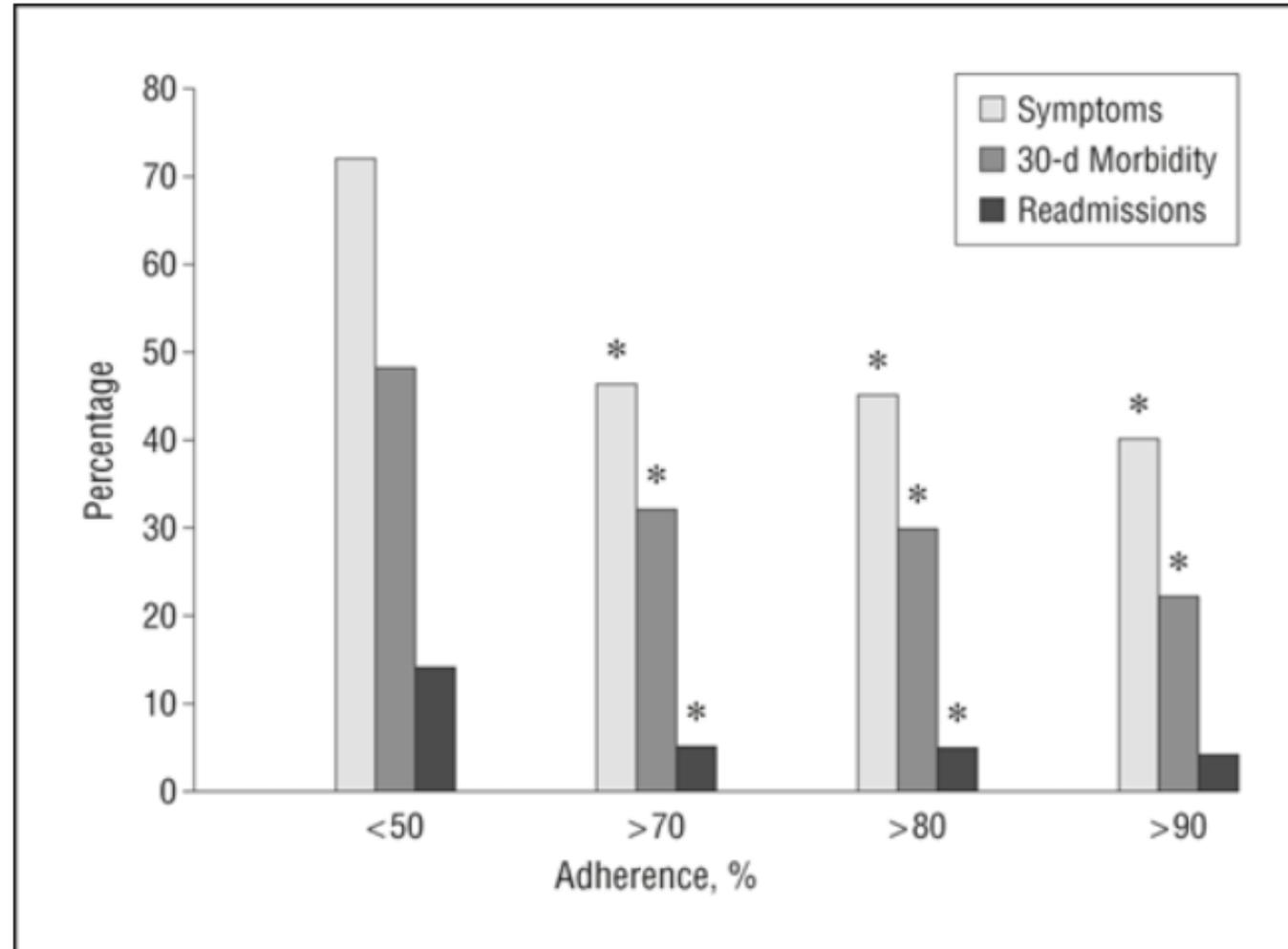


5. Compliance

- Previous studies have shown that high compliance may improve outcome.
- Auditing compliance has been an important element in ERAS implementation.
- Strict adherence to the protocol is a key for the success of ERAS.

	ERAS (n=58)	
	Element present	No. who followed element
Preop. information, education, counselling and daily goals	Yes	58
Preop. nutrition	Yes	58
Avoid oral bowel preparation	Yes	58
Preop. fasting and carbohydrate drink up to 2 h before surgery	Yes	58
Pre-anesthetic medication (avoid long-acting anxiolytics)	Yes	58
Prophylaxis against thromboembolism	Yes	58
Antimicrobial prophylaxis and skin preparation	Yes	58
Minimally invasive approach	Yes	56
Postop. nausea and vomiting – multimodal approach	Yes	58
Avoid nasogastric tube	Yes	58
Prevent intraop. hypothermia	Yes	58
Periop. fluid management (goal-directed fluid therapy)	Yes	58
Avoid routine surgical drainage or remove early (less than 3 days)	Yes	50
Urinary drainage: 1–2 days only	Yes	56
Postop. analgesia – multimodal analgesia (avoid opiates)	Yes	58
Postop. nutritional and early oral intake	Yes	58
Postop. glucose control	Yes	58
Avoid stimulation of bowel movement	Yes	58
Early mobilization	Yes	58
Audit	Yes	58

High compliance improve outcomes



Gustafsson, U.O., et al., - Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. - Arch Surg. 2011 May;146(5):571-7.

Conclusion



- ERAS protocol is **feasible and safe** for laparoscopic liver resection.
- Patients in ERAS group have **less pain, complications and short hospital stay**.

Grazie

спасибо

Dziękuję

ধন্যবাদ

Thank you

Gracias

متشكرين

Дзякую вам

Takki

谢谢

ありがとう

Merci

Ευχαριστώ

شكر

ขอบคุณ

תודה רבה

Mwita ova

Təşəkkür edirəm

شكر

감사합니다

多謝

մերսի

Danke