

# PERIOPERATIVE MANAGEMENT OF PATIENTS UNDERGOING LIVER RESECTION

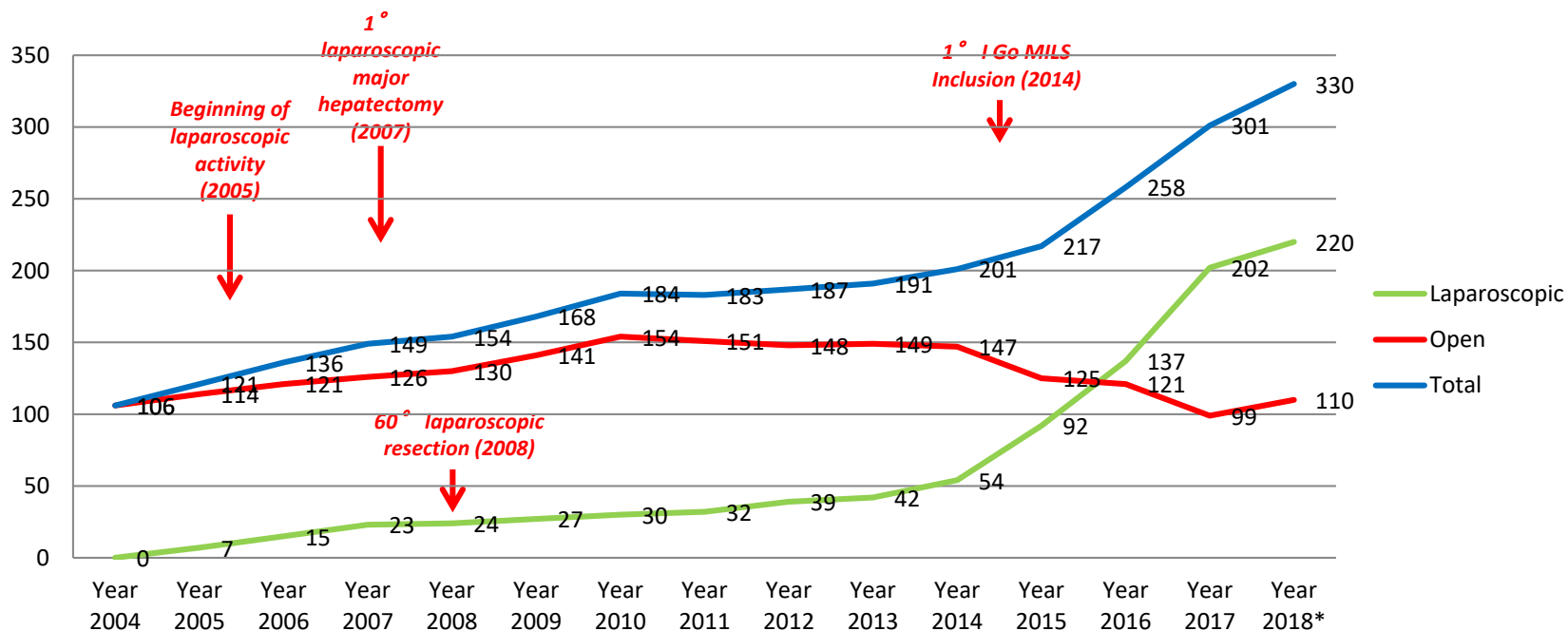
Francesca Ratti

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Milano

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## Liver resection activity – Hepatobiliary Surgery Division San Raffaele Hospital, Milano (2004-2018)



**2005:** Ratio  
MILS/Whole  
series  
**5.8%**

**2010:**  
MILS/Whole  
series  
**16.3%**

**2016:**  
MILS/Whole  
series  
**53.1%**

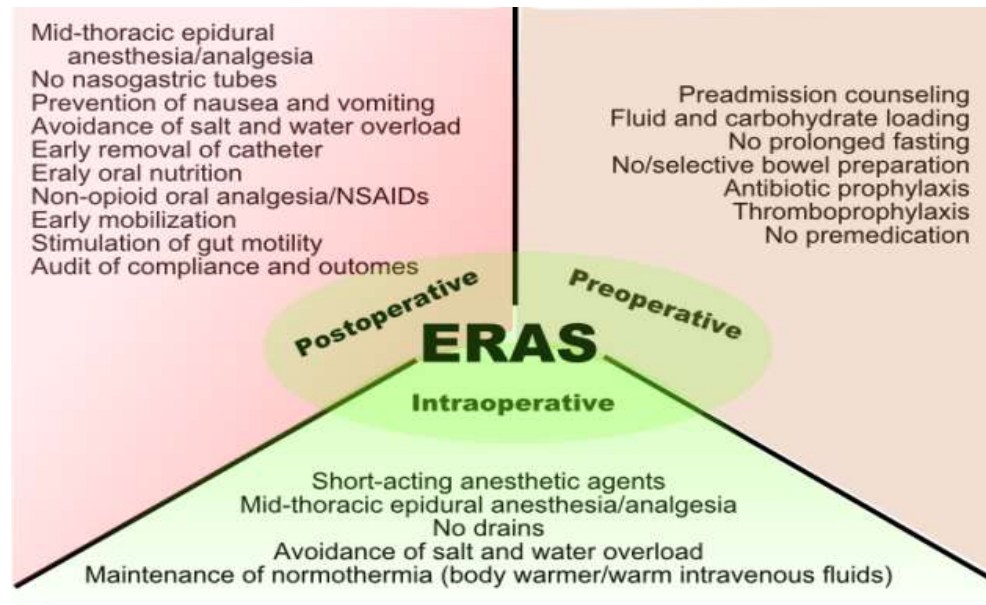
**2018:**  
MILS/Whole  
series  
**71.1%**

*Development of «minimally invasive techniques»*



*Effort to implement  
«minimally invasive perioperative management»*

**Perioperative management has been optimized to improve surgical outcome**



*“The establishment and adoption of evidence-based practice guidelines improves surgical outcomes”*

First do it better, than do it quicker

Henrik Kehlet

## Effect of ERAS in liver surgery

Original article

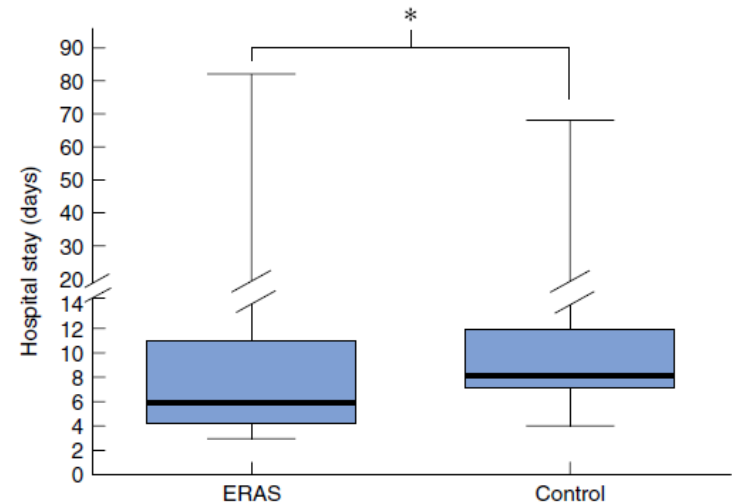
Br J Surg, 2008

### Initial experience with a multimodal enhanced recovery programme in patients undergoing liver resection

R. M. van Dam<sup>1</sup>, P. O. Hendry<sup>3</sup>, M. M. E. Coolsen<sup>1</sup>, M. H. A. Bemelmans<sup>1</sup>, K. Lassen<sup>4,5</sup>, A. Revhaug<sup>4,5</sup>, K. C. H. Fearon<sup>3</sup>, O. J. Garden<sup>1</sup> and C. H. C. Dejong<sup>1,2</sup>, on behalf of the Enhanced Recovery After Surgery (ERAS) Group

*In patients treated according to ERAS protocol*

- ✓ Faster functional recovery
- ✓ Shorter length of stay



ORIGINAL ARTICLE

HPB, 2009

### The effect of a multimodal fast-track programme on outcomes in laparoscopic liver surgery: a multicentre pilot study

Jan H. Stoot<sup>1</sup>, Ronald M. van Dam<sup>1</sup>, Olivier R. Busch<sup>2</sup>, Richard van Hillegersberg<sup>2</sup>, Marieke De Boer<sup>4</sup>, Steven W.M. Olde Damink<sup>1,3</sup>, Marc H. Bemelmans<sup>1</sup> & Cornelis H.C. Dejong<sup>1,3</sup> on behalf of the Enhanced Recovery After Surgery (ERAS) Group

*“A multimodal enhanced recovery programme in laparoscopic liver surgery is feasible, safe and may lead to accelerated functional recovery and reductions in LOS»*

	Group 1 ERAS programme (n = 13)	Group 2 Traditional care (n = 13)	P-value
Primary outcome			
Total LOS, days*	5.0 (3–10)	7.0 (3–12)	0.305 <sup>†</sup>
Secondary outcomes			
Functional recovery, days*	3 (1–7)	5 (2–8)	0.044 <sup>†</sup>
Complications, n (grade)	2 (I)	2 (I)	1.0
Conversions, n	2	2	1.0
Blood loss, ml*	50 (50–200)	250 (50–800)	0.002 <sup>†</sup>
Operation time, min*	118 (85–192)	180 (51–340)	0.293 <sup>†</sup>

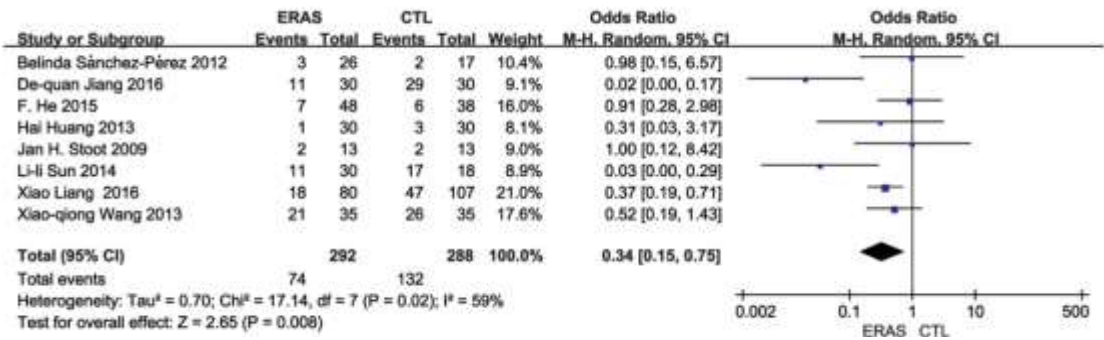
Enhanced recovery after surgery programs versus traditional perioperative care in laparoscopic hepatectomy: A meta-analysis

Rui Yang a,1, Wan Tao b,1, Yang-yang Chen c, Bing-hong Zhang b, Jun-ming Tang a, Sen Zhong a,\*, Xian-xiang Chen a,\*\*

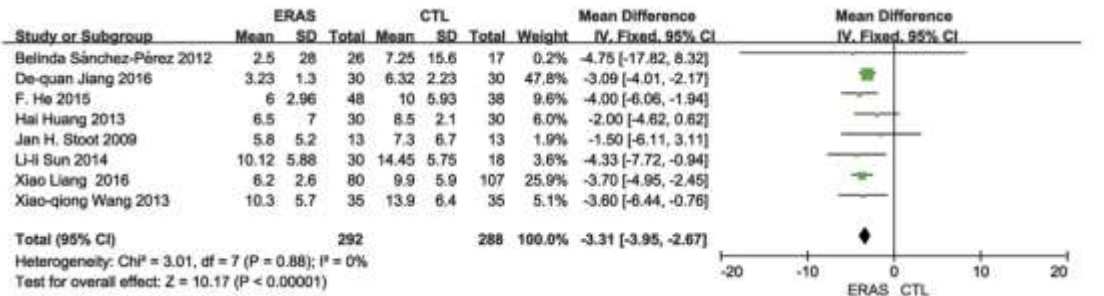
Int J Surg, 2016

550 patients from 8 RCTs or CCTs

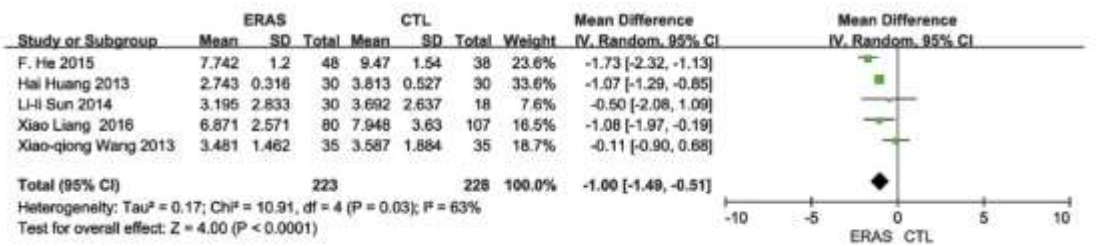
Complications



Hospital stay



Costs



Support ERAS

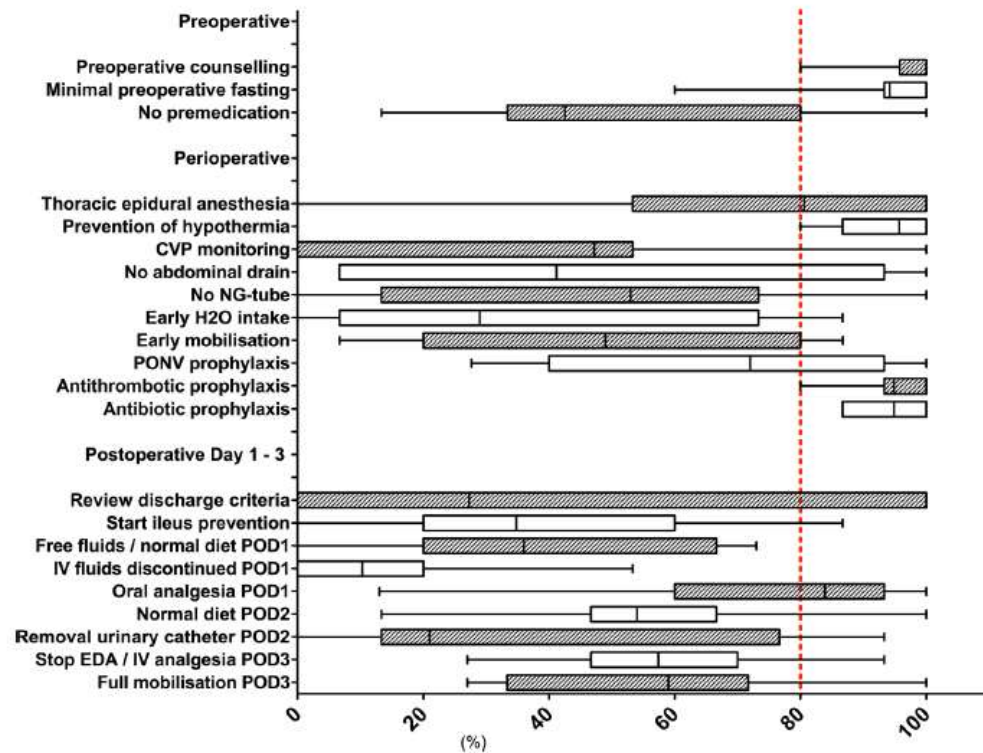




## Is Current Perioperative Practice in Hepatic Surgery Based on Enhanced Recovery After Surgery (ERAS) Principles?

E. M. Wong-Lun-Hing · R. M. van Dam · L. A. Heijnen · O. R. C. Busch ·  
T. Terkivatan · R. van Hillegersberg · G. D. Slooter · J. Klaase · J. H. W. de Wilt ·  
K. Bosscha · U. P. Neumann · B. Topal · L. A. Aldrighetti · C. H. C. Dejong

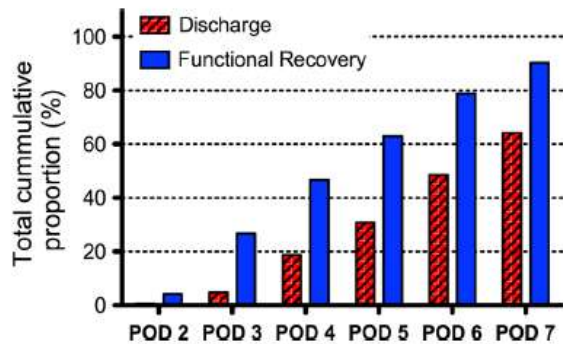
*“Perioperative care among centers that perform liver resections varied substantially and elements of enhanced recovery programs had already been implemented as part of daily surgical practice. This may standardize care and improve recovery after liver surgery”.*



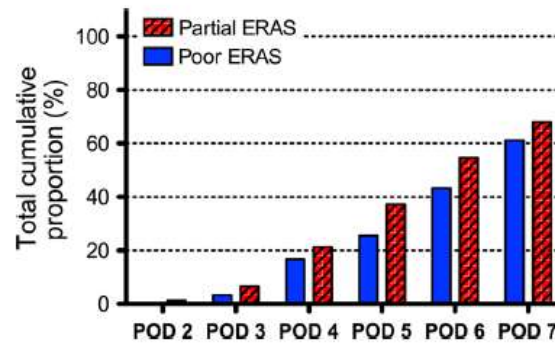


## Is Current Perioperative Practice in Hepatic Surgery Based on Enhanced Recovery After Surgery (ERAS) Principles?

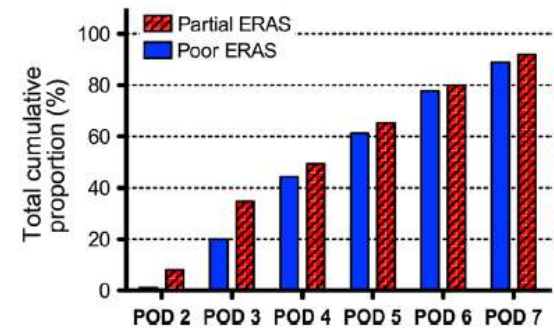
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*Discrepancy between functional recovery and discharge*



*Faster discharge in centers with more extensive adoption of ERAS protocol*



*Faster functional recovery in centers with more extensive adoption of ERAS protocol*



SCIENTIFIC REVIEW

## Guidelines for Perioperative Care for Liver Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations

Emmanuel Melloul<sup>1,2</sup> · Martin Hübner<sup>1</sup> · Michael Scott<sup>3</sup> · Chris Snowden<sup>4,5</sup> · James Prentis<sup>6</sup> · Cornelis H. C. Dejong<sup>7</sup> · O. James Garden<sup>8</sup> · Olivier Farges<sup>9</sup> · Norihiro Kokudo<sup>10</sup> · Jean-Nicolas Vauthey<sup>11</sup> · Pierre-Alain Clavien<sup>12</sup> · Nicolas Demartines<sup>1</sup>

**Table 2** RCTs dedicated to liver surgery selected in the systematic review with the level of evidence

Author	Year	Jadad score	Level evidence	Studied items	Morbidity	LOS
Lassen	2008	6	1	Postoperative artificial nutrition	No difference	No difference
Darouiche	2010	4	1	Skin preparation	Preoperative cleansing with chlorhexidine is superior to povidone-iodine for preventing SSI	Not assessed
Hayashi	2011	7	1	Perioperative steroids administration	Positive impact on liver function. No difference in complications	No difference
Wong	2007	5	2	Preventing intraoperative hypothermia	Perioperative warming reduce blood loss and complications	No difference
Okabayashi	2009	3	2	Postoperative glycaemic control	Intensive insulin therapy using a closed-loop system lower SSI	Decreased
Pessaux	2007	5	2	Prophylactic Nasogastric intubation (NGT)	NGT has no advantage. NGT increased the risk of pulmonary complications	No difference
Igami	2011	4	2	Prevention of delayed gastric emptying (DGE)	DGE reduced with omental flap on the cut surface after left-sided hepatectomy	Not assessed
Yoshida	2005	3	2	Prevention of delayed gastric emptying (DGE)	DGE reduced with omental flap on the cut surface after left-sided hepatectomy	Not assessed
Hendry	2010	2	2	Use of postoperative laxatives	Earlier passage of first stool, no change in morbidity	Decreased
Jones	2013	7	1	Goal-directed fluid therapy	Decreased	Decreased

LOS length of hospital stay

# Italian Perioperative Program



Italian Perioperative Program



## Protocollo resezioni epatiche

Versione: Novembre 2014

### Team Coordinator:

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Principale chirurgo Epato biliare Ospedale San Raffaele Milano

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OSPEDALE SAN RAFFAELE  
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Unità Operativa Complessa  
CHIRURGIA EPATO-BILIARE e WEEK SURGERY  
Direttore Prof. Giacobbe Failli  
Unità Funzionale CHIRURGIA EPATO-BILIARE  
Responsabile Dott. Luca Aldighetti

## LA RESEZIONE EPATICA: INFORMAZIONI PER IL PAZIENTE

La resezione epatica è un intervento chirurgico che consiste nell'asportazione di una porzione di fegato affetta da patologia. L'intensità e il tipo di intervento epatico viene definito sulla base dell'estensione del lesione che deriva dalla modalità della sua estensione oncologica.

### LEZIONI IN ANATOMIA DEL FEGATO

Il fegato è un organo muscoloso situato nella parte superiore destra dell'addome, dove il condotto che porta addensato da alcuni legamenti ad esempio per la maggior parte lo spazio di Wirsung del condotto cistico dritto. Nella superficie superiore del fegato è ben visibile il legamento falciforme che si inserisce longitudinalmente dividendo il fegato in un lobo anatomico destro (a piccole lesioni) ed un lobo anatomico sinistro. Nella base del fegato si trova visibile la cava inferiore che è situata in un "V" del lobo epatico destro. Attraverso il peduncolo epatico avviene l'ingresso del fegato (in epatica) in strutture principali: l'arteria epatica, che fornisce sangue ossigenato al fegato; la vena porta che trasporta sangue che proviene dall'intestino, dalla milza e dal pancreas; la via biliare (compresa del coledoc e del dotto epatico) che trasporta la bile prodotta dal fegato per poi essere nell'intestino dove svolgerà le sue funzioni digestive.



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## ANESTESIA E ANALGESIA POST-OPERATORIA NELLA CHIRURGIA EPATO-BILIARE

U.O. di Anestesia Generale  
Direttore Prof. Luigi Barilli

### Caratteristiche Paziente

questo piccolo brochure informativo ha lo scopo di volerla spiegare, nel migliore modo possibile, le tecniche di anestesia ed analgesia (assenza del dolore) e sui vari tempi.

Questo ospedale, ha organizzato il TEAM EPATO-BILIARE a cui Lei si è rivolto, ha speso l'idea di un lavoro d'équipe (Chirurgo, Anestesia ed Infermiere) hanno sviluppato una competenza specifica negli interventi su fegato e vie biliari a condizionali (prevedibili), volto a migliorare ed a ottimizzare l'esito clinico durante il suo ricovero in ospedale, nell'ambito di un programma vero con l'adesione ERAS (Enhanced Recovery After Surgery, cioè "rapido recupero dopo la chirurgia").

A questo scopo, al posto di renderle più agevole la fase postoperatoria e legato al suo preparazione ottimale e di una attenta gestione intraoperatoria.

Il nostro Anestesia sarà al suo fianco durante questo percorso cercando di rendere il periodo postoperatorio meno doloroso possibile. Si accende di dolore il meglio delle attuali tecniche (vitali) con più rapidità ed agilità. Perché il nostro scopo è quello di raggiungere un trattamento analgesico combinato "a misura" per Lei, in accordo con la tipologia di intervento scelta dal Chirurgo.

L'intervento chirurgico necessita di un'anestesia GENERALE, che prevede la perdita di coscienza, la intubazione (è il bloccamento di tutti i suoi riflessi per rendere possibile l'intervento) e di una adeguata somministrazione del dolore. Al fine di garantire un'ottimale recupero del dolore, soprattutto nei primi giorni dopo l'intervento chirurgico, l'anestesia in sala operatoria associata, all'anestesia generale, una tecnica di analgesia postoperatoria, utilizzando un blocco nervoso centrale o periferico (adesso sarà possibile).

La tecnica di analgesia postoperatoria, associata all'anestesia generale, nella chirurgia epato-biliare sono le seguenti:

1. Analgesia EPIDURALE: è una tecnica, prima di iniziare l'anestesia generale, con paziente sedato, viene inserito un piccolo catetere peridurale nella colonna a livello lombare, previa anestesia locale. La tecnica non è dolorosa, ma bisogna semplicemente puntare il catetere in un punto preciso (posizione) con cautela. Attraverso questo catetere verrà somministrata un farmaco analgesico locale, in questo modo la trasmissione del dolore da parte delle fibre nervose contenute nella spazio peridurale che innervano la zona dell'intervento chirurgico verrà bloccata dall'anestesia locale.



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## ***Inclusion criteria***

- ✓ All the patients undergoing liver resection, irrespectively of both the extension of the resection (major or minor) and the approach (laparoscopic or open) are treated according to ERAS protocol
- ✓ All the patients requiring liver surgery in association with procedures including common bile duct resection (e.g. biliary-enteric anastomosis) or colorectal resections (e.g. patients undergoing combined resection of colorectal cancer with synchronous liver metastases) are treated according to ERAS protocol





## ***a. Preoperative step (outpatient)***

### **1. Surgical evaluation**

- Indication to surgery
- Transfusion Risk Score evaluation and, if necessary, activation of «anaemia protocol»
- Evaluation of nutritional status by the means of MUST index (Malnutritional Universal Screening Tool).
- Navigator Nurse (NaNu) takes charge of the patient

\* If nutritional status is not adequate (weight loss of 10-15% in the last 6 months, BMI<18.5, serum albumin <30) the intake of oral supplements (immunonutrition) is recommended 5-7 days before surgery. In case of severe malnutrition, enteral nutrition supplement is considered





### ***a. Preoperative step (outpatient)***

#### 2. Meeting with Navigator Nurse (within the week following surgical evaluation)

- Nurse Counselling for the patient
- Nurse Counselling for the caregiver
- Evaluation of motility and self-care autonomy by administration of a specific questionnaire
  - If necessary, a preoperative/postoperative physiotherapy support is required
- Evaluation of the psychological status (together with Clinical Psychologists)

3. Preoperative meeting with the hepatobiliary team (surgeon, anaesthesiologist), which will take place in the hospital 2-4 weeks before surgery.





### ***a. Preoperative step (inpatient)***

- ✓ No bowel preparation (unless the patient refers no canalization in the 3 days before surgery)
- ✓ Routine blood tests, typing of blood group. Blood units are required to be available during surgery (According to Transfusion Risk Score – TRS)
- ✓ Depilation
- ✓ Dinner and intake of 2 packages (400 ml) of PREOP (12,5 gr of maltodextrin/100 ml of drink). No intake of solid food for 6 hours and no intake of liquids for 2 hours before surgery
- ✓ No anaesthetic premedication
- ✓ Antibiotic therapy is started if a biliary drainage is in place







## ***b. Intraoperative step***

- Liver resections are performed under general anaesthesia, with the association, if possible, of a locoregional analgesia technique, to obtain an adequate control of postoperative pain.
- Management protocols (especially in terms of analgesia) can be classified according to the planned resection :

### *Tailored standardization*

MAJOR OPEN  
LIVER RESECTIONS  
(  $\geq 3$  hepatic  
segments)

MINOR OPEN  
LIVER RESECTIONS  
(  $\leq 3$  hepatic  
segments)

LAPAROSCOPIC  
LIVER RESECTIONS





**b. Intraoperative step**

	Minor Open	Major Open	Laparoscopic	Perihilar
<b>CVC</b>	No	No	No	No
<b>Vigileo</b>	Yes	Yes	Yes	Yes)
<b>Anaesthesia</b>	Gen + Peri or Gen + Spin (ev. TAP)	Gen + PVB	Gen + Spin (ev. TAP) or Gen + ESP	Gen + PVB
<b>Paracetamol</b>	1g x 3	1g x 3	1g x 3	1g x 3
<b>Tapentadol</b>	NO	As rescue	50 mg x 2	No
<b>NSAID</b>	Ketorolac 30 mg ab (max 90 mg die) as rescue	Ketorolac 30 mg ab (max 90 mg die) as rescue	Ketorolac 30 mg ab (max 90 mg die) as rescue	Ketorolac 30 mg ab (max 90 mg die) as rescue

A nutritional digiunostomy is considered whenever a patient requiring a major or extended resection has a significant risk of postoperative liver failure



# Intraoperative monitoring of stroke volume variation versus central venous pressure in laparoscopic liver surgery: a randomized prospective comparative trial

Francesca Ratti<sup>1</sup>, Federica Cipriani<sup>1</sup>, Raffaella Reineke<sup>2</sup>, Marco Catena<sup>1</sup>, Michele Paganelli<sup>1</sup>, Laura Comotti<sup>2</sup>, Luigi Beretta<sup>2</sup> & Luca Aldrighetti<sup>1</sup>

<sup>1</sup>Division of Hepatobiliary Surgery, and <sup>2</sup>Department of Anaesthesiology and Intensive Care, IRCCS San Raffaele Hospital, Milano, Italy

	SVV group (n = 45)	CVP group (n = 45)	p
Conversion, n (%)	3 (6.7)	8 (17.8)	0.02
Reason for conversion, n (%)			
Haemorrhage	0 (0)	4 (8.9)	0.05
Oncologic inadequacy	1 (2.2)	2 (4.4)	ns
Anaesthesiological problems	0 (0)	1 (2.2)	ns
Damage to the liver	1 (2.2)	0 (0)	ns
Inadequate biliostasis	1 (2.2)	0 (0)	ns

	SVV group (n = 45)	CVP group (n = 45)	p	
Pringle manoeuvre, n (%)				
	Not performed	19 (42.2)	24 (53.3)	
	Performed	26 (57.8)	21 (46.7)	
Length of surgery (min)	Mean ± SD	220 ± 50	210 ± 60	ns
Blood Loss (mL)	Mean ± SD	150 ± 100	300 ± 250	0.04
Associated procedures, n (%)				
	None	39 (86.7)	41 (91.1)	
	Colecistectomy	6 (13.3)	4 (8.9)	
Surgical margin, n (%)				
	R0	44 (97.8)	45 (100)	
	R1	1 (2.2)	0 (0)	
Surgical margin (mm)	Mean ± SD	8 ± 4	9 ± 6	ns
Intraoperative blood transfusions, n (%)				
	No	43 (95.6)	43 (95.6)	
	Yes	2 (4.4)	2 (4.4)	
Total blood transfusions, n (%)				
	No	43 (95.6)	41 (91.1)	
	Yes	2 (4.4)	4 (8.9)	
Morbidity, n (%)		5 (11.1)	6 (13.3)	ns
Grade of complications, n (%)				
Minor	I grade	1 (2.2)	1 (2.2)	ns
	II grade	2 (4.4)	3 (6.7)	ns
Major	IIIa grade	1 (2.2)	1 (2.2)	ns
Mortality, n (%)				
		0 (0)	0 (0)	ns
Functional recovery (days)	Median (range)	3 (1–6)	3 (1–7)	ns
Length of stay (days)	Median (range)	4 (2–10)	5 (3–13)	ns





## ***b. Intraoperative step***

- Antibiotic prophylaxis (1° generation cefalosporin) and single dose of methylprednisolon according to body weight
- Active warming-up of the patient
- Nasogastric/orogastric tube removed at the end of the procedure
- Monitoring of the volemic status by minimally invasive techniques (EV1000: Stroke Volume Variation, Stroke Volume, Cardiac Output, Oxygen Delivery)
- Liver transection is performed within hypovolemic status (SVV between 15 and 20%): normal volemia is restored at the end of the procedure. Cristaloids infusion 3-4 mL/kg/h
- No abdominal drainage, unless specific contraindications
  - Unsatisfactory biliostasis/haemostasis at the end of procedure
  - Redo surgery
  - Resections of areas not easily accessible by percutaneous drainage
  - Patients requiring biliary enteric anastomosis or colorectal anastomosis
  - Patients with biliary enteric anastomosis (risk of intrahepatic abscesses)
- No ICU

# EUROPEAN GUIDELINES for anaesthesiological management



## Evidence-based, perioperative Goal-Directed Therapy (GDT) protocols.

Several single centre randomized controlled trials, meta-analysis and quality improvement programs have shown that perioperative GDT decreases postoperative complications and hospital length of stay when compared to standard fluid management.<sup>1-5</sup>

This summary describes the three main perioperative GDT strategies which have been successfully used to decrease postoperative morbidity and length of stay:

- Stroke Volume (SV) optimization with fluid
- Oxygen Delivery Index ( $iDO_2$ ) optimization with fluid and inotropes
- Pulse Pressure Variation (PPV) or Stroke Volume Variation (SVV) optimization with fluid

This summary does not recommend the use of any specific medical device, and the choice of the treatment protocol is left at the discretion of the anesthesiologist in charge.



### c. Postoperative step

- ✓ Antithrombotic profilaxis: from the night of surgery, according to institutional protocols (contraindications: < 6 h from surgery; PLT<50.000; INR>1,8; resection of more than 70% of the liver parenchyma)
- ✓ Ev fluids and other therapies: crystalloids 10 ml/kg/die ev. In case of hypotension, use of inotrope or vasopressor drugs is allowed. Diuretic stimulation if diuresis under 30-40 ml/h. In all the patients use of PPI is recommended, as well as ondansetron 4 mg ev to treat PONV.
- ✓ Nutrition: when awake, the patient can take liquids. Oral diet is allowed is the patient is back in the ward before 2 p.m.
- ✓ Analgesia
- ✓ No antibiotic prophylaxis (unless the patient has a biliary drainage or a biliary enteric anastomosis)





### c. Postoperative step

#### First POD

- Ev fluids and other therapies: crystalloids 10 ml/kg/die ev. In case of hypotension, use of inotrope or vasopressor drugs is allowed. Diuretic stimulation if diuresis under 30-40 ml/h. In all the patients use of PPI is recommended, as well as ondansetron 4 mg ev to treat PONV.
- Enteral feeding: allowed if the patient tolerates it
- Early mobilization: at least 4 hours seat
- Pain control: as in POD 0

#### Second POD

- Ev fluids and other therapies: Ev fluids discontinuation, removal of catheter for diuresis and CVC (in patients who have it). In all the patients use of PPI is recommended. Contraindications for fluids discontinuation: no normovolemic status, no adequate oral liquids intake, increased transaminases (>1000 AST or ALT), perihilar tumors
- Enteral feeding: the patient drinks at least 1500 mL of fluids and have normal oral diet
- Early mobilization: at least 6 hours seat . Deambulation
- Pain control





### c. Postoperative step

#### Third POD

- Enteral feeding: the patient drinks at least 1500 mL of fluids and have normal oral diet
- Early mobilization: Deambulation
- Discharge criteria evaluation

#### Forth POD

- Enteral feeding: the patient drinks at least 1500 mL of fluids and have normal oral diet
- Early mobilization: Deambulation
- Pain control: with oral analgesics only
- If all discharge criteria are met and the patient agrees, he/she can be discharged







## **Discharge criteria**

**Adequate oral feeding**

**Adequate pain control with oral analgesics**

**Normal deambulation and self-care autonomy**

**No complications**

**Patient agreement**



# OSR hyper-ERAS PROTOCOL



## Inclusion criteria

### *Surgery (only laparoscopic):*

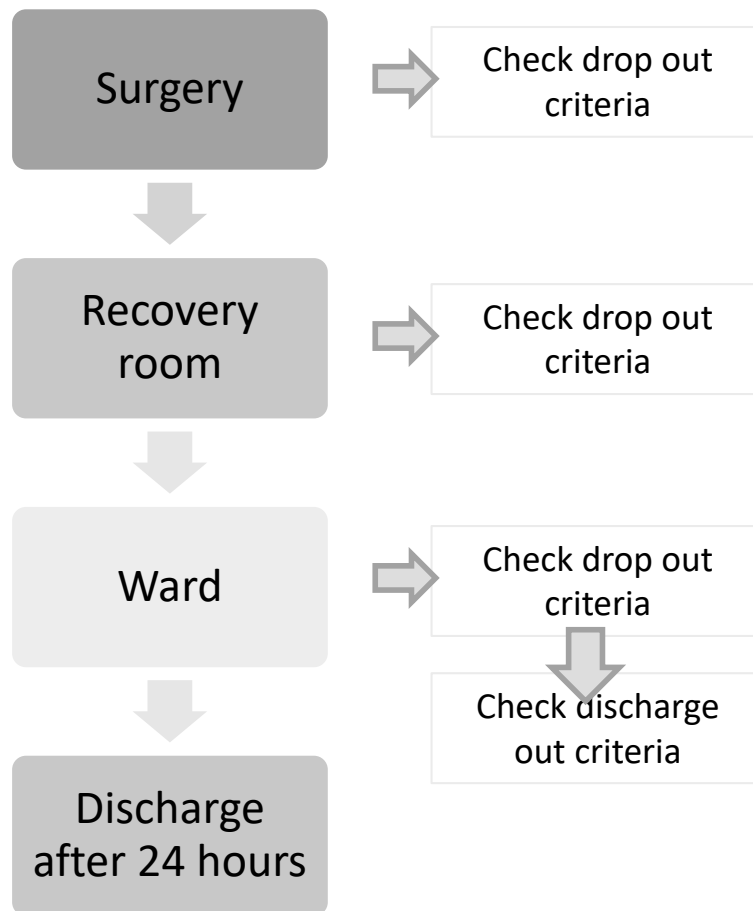
- Cysts unroofing
- Minor resections (<3 segments)
- Lesions in “laparoscopic” segments
- First resection (redo excluded)

### **Patient**

- Age < 75 years
- ASA I and II
- Adequate nutritional status
- Transfusion Risk Score = 0 or 1

### **Environment**

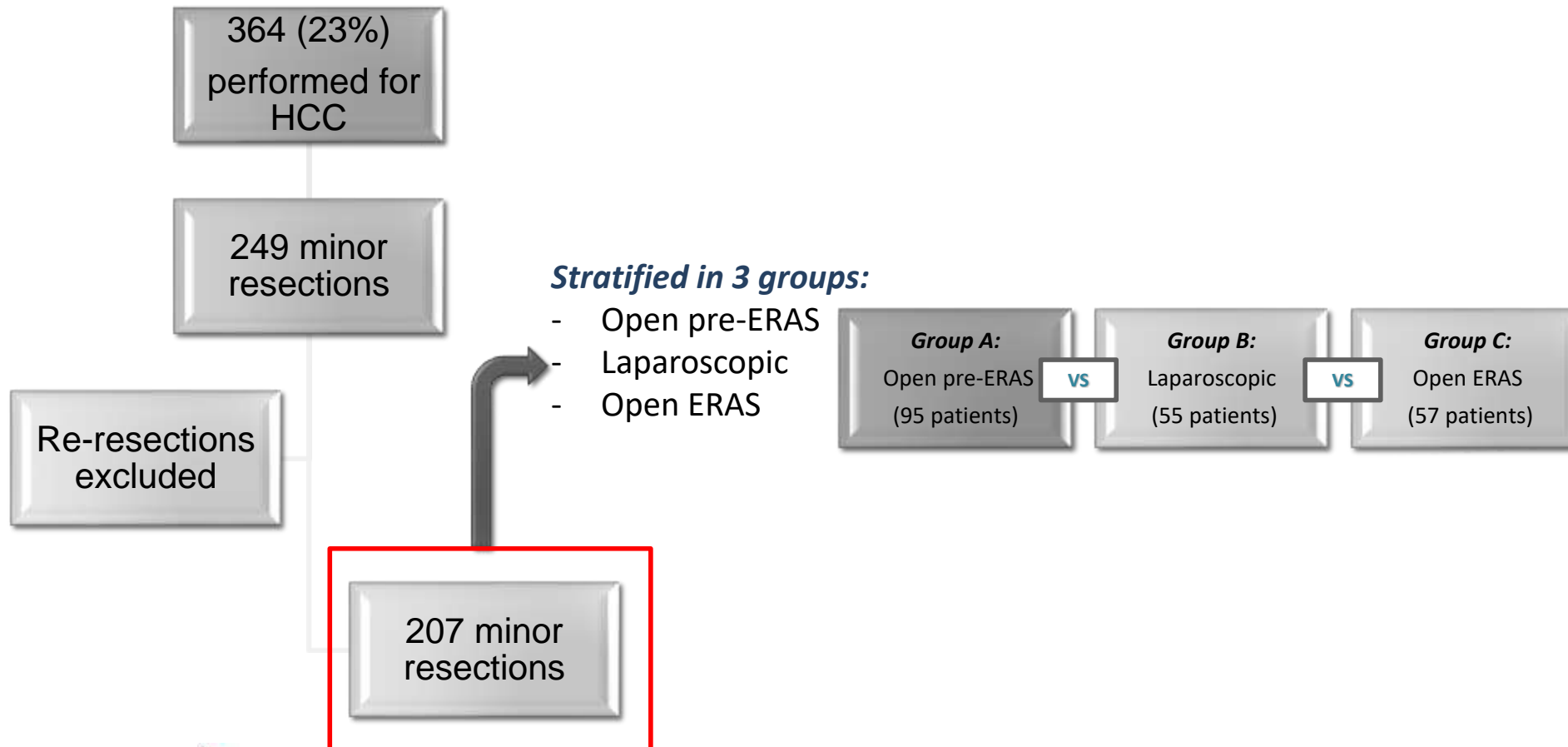
- Presence of the caregiver
- Less than 30' far from OSR
- Adequate level of comprehension

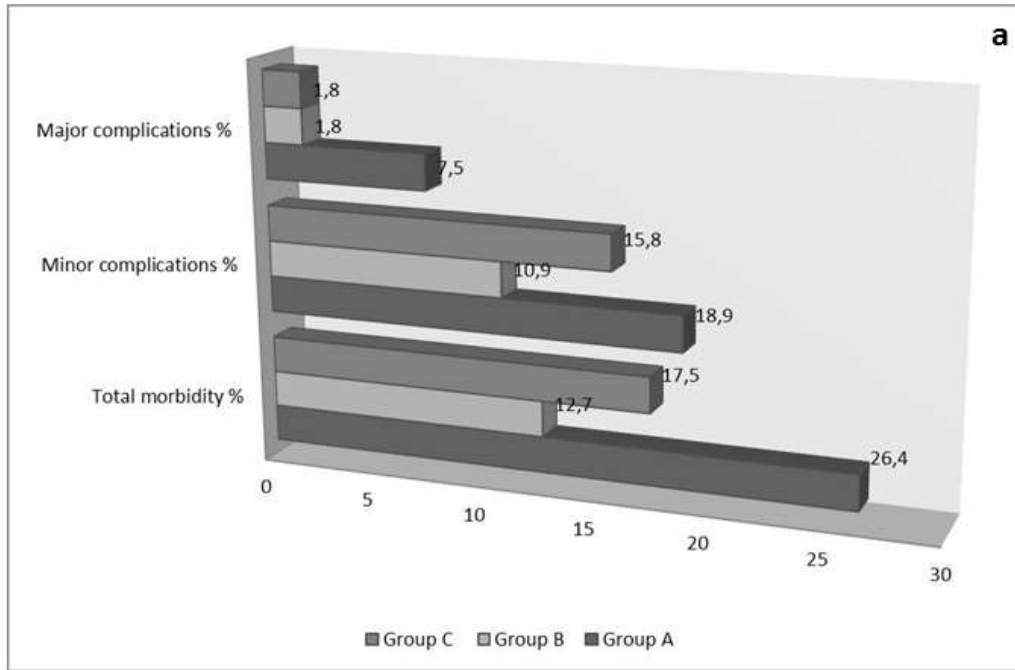


Impact of ERAS approach and minimally-invasive techniques on outcome of patients undergoing liver surgery for hepatocellular carcinoma

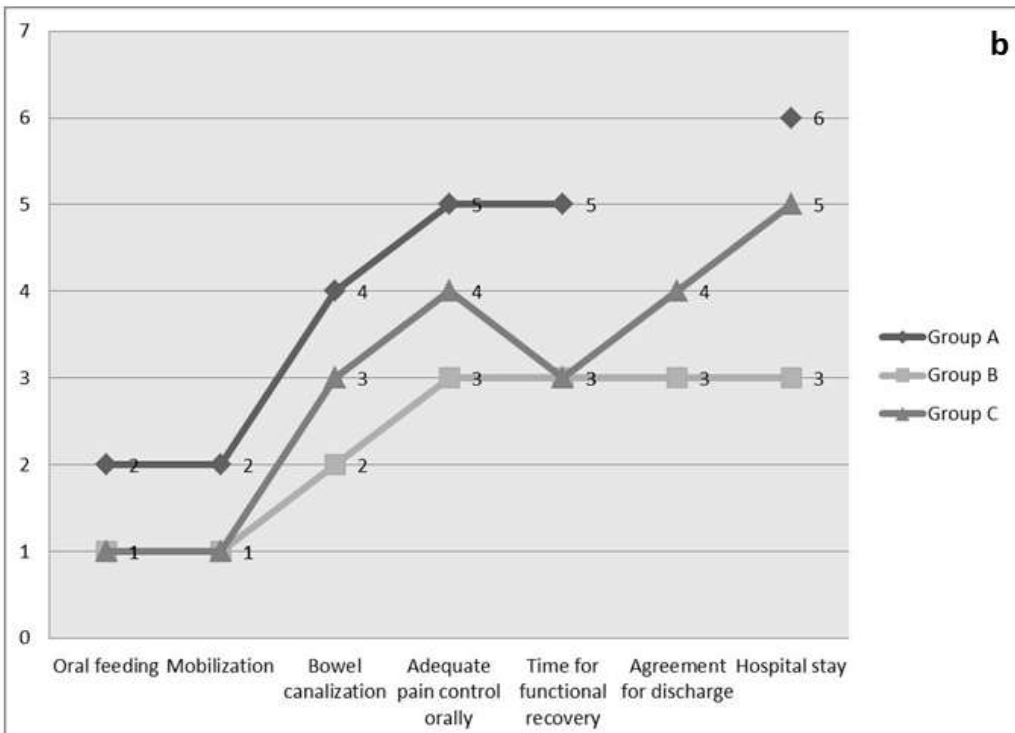
Francesca Ratti<sup>a,c</sup>, Federica Cipriani<sup>a</sup>, Raffaella Reineke<sup>b</sup>, Marco Catena<sup>a</sup>, Laura Comotti<sup>b</sup>, Luigi Beretta<sup>b</sup>, Luca Aldrighetti<sup>a</sup>

From January to May 2014, 1583 hepatic resections were performed at the Hepatobiliary Surgery Division of San Raffaele Hospital, Milano





***Outcome of patients  
undergoing liver resection  
for HCC at OSR***



- ✓ Gruppo A: Resections Open pre-ERAS
- ✓ Gruppo B: Resections LPS
- ✓ Gruppo C: Resections Open ERAS

The clinical and biological impacts of the implementation of fast-track perioperative programs in complex liver resections: A propensity score-based analysis between the open and laparoscopic approaches

Ratti F, Cipriani F, Reineke R, Comotti L, Paganelli M, Catena M, Beretta L, Aldrighetti L.

*Laparoscopy is the natural field for a wide implementation of ERAS protocols themselves.*

Variable, n(%)	LPS Group (n=102)	Open Group (n=102)	P
Preoperative counselling	85 (83.3)	79 (77.4)	NS
Minimal preoperative fastening	100 (98)	98 (96.1)	NS
No bowel preparation	99 (97.1)	98 (96.1)	NS
Preop drink intake	94 (92.2)	93 (91.2)	NS
No premedication	99 (97.1)	94 (92.2)	NS
<b>Thoracic epidural anesthesia</b>	67 (65.7)	83 (81.4)	0.043
<b>Avoidance of morphin</b>	97 (95.1)	89 (87.2)	0.044
Prevention of hypothermia	102 (100)	102 (100)	NS
SVV monitoring	84 (82.4)	77 (75.5)	0.048
No abdominal drain	65 (63.7)	61 (59.8)	NS
No NG tube	102 (100)	102 (100)	NS
Early liquid intake (POD 0-1)	102 (100)	100 (98)	NS
<b>Early mobilization (POD 0-1)</b>	98 (96.1)	89 (87.2)	0.033
PONV prophylaxis	94 (92.2)	98 (96.1)	NS
Antithrombotic prophylaxis	96 (94.1)	94 (92.2)	NS
Antibiotic prophylaxis	102 (100)	102 (100)	NS
I/R injury prevention	99 (97.1)	98 (96.1)	NS
Review discharge criteria	102 (100)	102 (100)	NS
<b>Ileus prevention</b>	51 (50)	60 (58.8)	0.049
<b>Free fluids/normal diet POD1</b>	75 (73.5)	55 (53.9)	0.028
<b>IN fluids discontinued POD2</b>	69 (67.6)	41 (40.2)	0.019
<b>Oral analgesia POD2</b>	71 (69.6)	21 (20.6)	0.001
Normal diet POD2	100 (98)	95 (93.1)	NS
<b>Removal urinary catheter POD2</b>	85 (83.3)	63 (61.8)	0.027
<b>Full mobilization POD3</b>	102 (100)	90 (88.2)	0.029
<b>Discharge POD3-4</b>	76 (74.5)	50 (49)	0.015

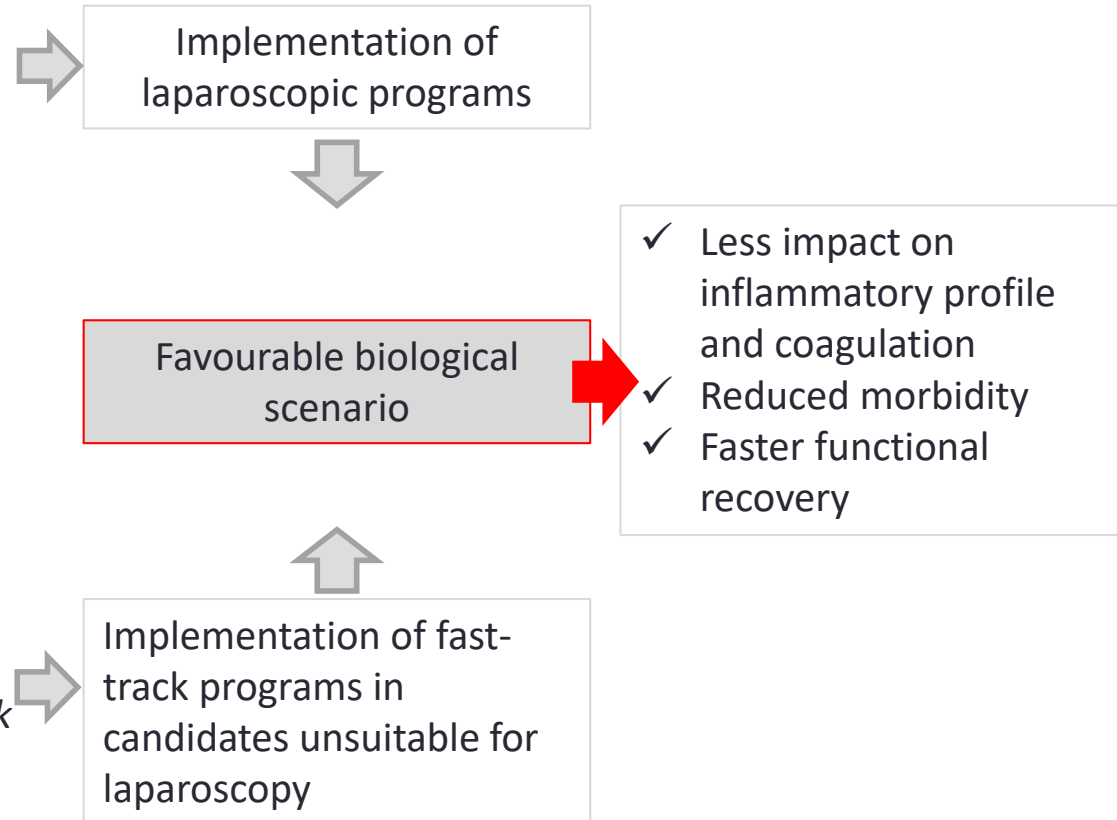
*83.3% of patients in the LPS and 77.4% in the Open group respected more than 20 ERAS items*

Surgery 2018



### **LPS approach**

*Mini-invasiveness*  
*Easy application of FAST track*



### **Open approach**

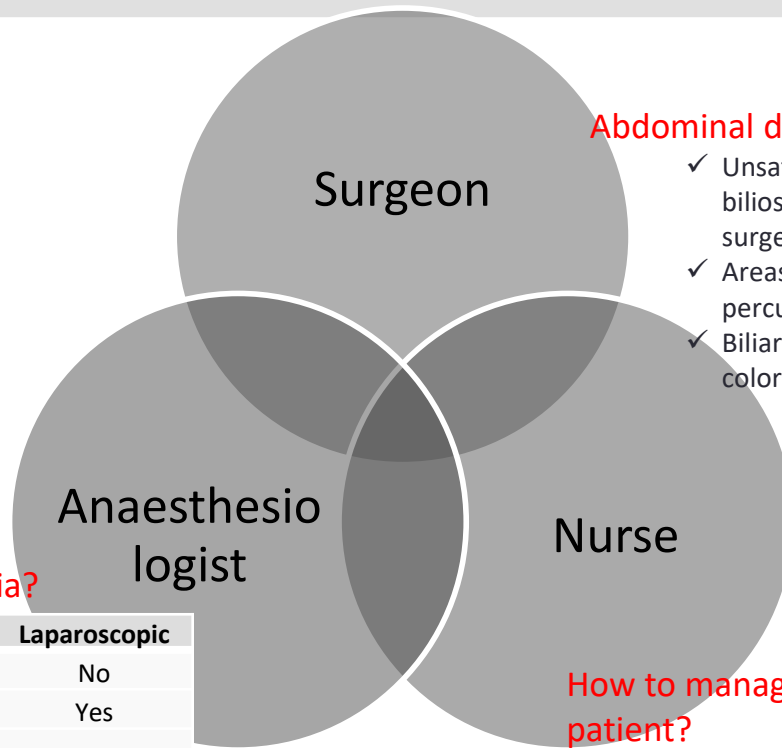
*«Maxi»-invasiveness*  
*«Hard» application of FAST track*



# How to implement ERAS programs?



## 1 Team building (specific skills for specific issues)



### Abdominal drainage, when?

- ✓ Unsatisfactory biliostasis/haemostasis      Redo surgery
- ✓ Areas not easily accessible by percutaneous drainage
- ✓ Biliary enteric anastomosis or colorectal anastomosis

### How to manage pain and volemia?

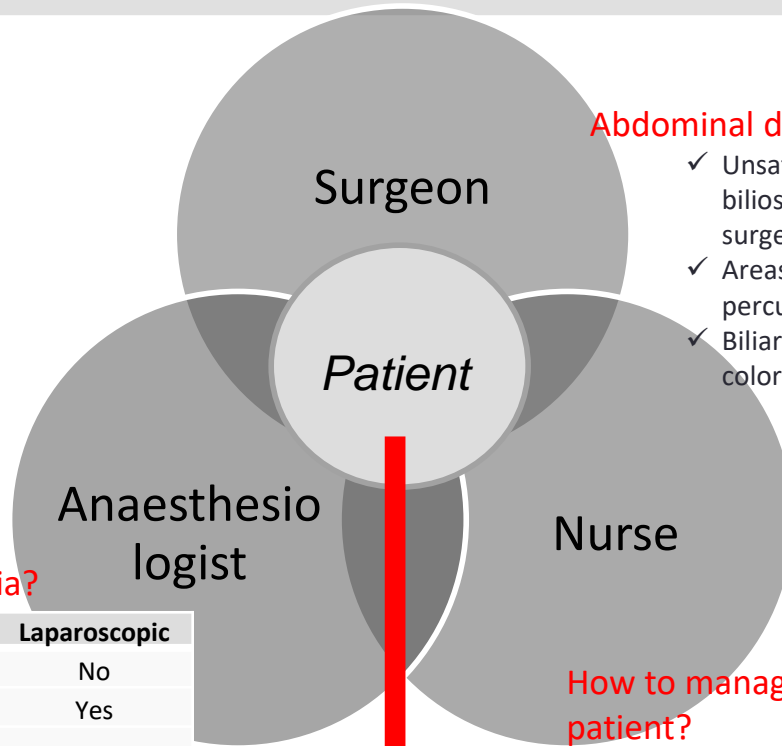
### How to manage the contact with the patient?

	Minor Open	Major Open	Laparoscopic
<b>CVC</b>	No	No	No
<b>Vigileo</b>	Yes	Yes	Yes
<b>Anaesthesia</b>	Gen + Peri or Gen + Spin	Gen + PVT	Gen + Spin
<b>Paracetamol</b>	1g x 3	1g x 3	1g x 3
<b>Tapentadol</b>	50 mg x 2 (if spinal)	No	50 mg x 2
<b>NSAID</b>	Ketorolac 30 mg ab	Ketorolac 30 mg ab	Ketorolac 30 mg ab

# How to implement ERAS programs?



## 1 Team building (specific skills for specific issues)



Abdominal drainage, when?

- ✓ Unsatisfactory biliostasis/haemostasis Redo surgery
- ✓ Areas not easily accessible by percutaneous drainage
- ✓ Biliary enteric anastomosis or colorectal anastomosis

How to manage pain and volemia?

How to manage the contact with the patient?

Compliance

	Minor Open	Major Open	Laparoscopic
<b>CVC</b>	No	No	No
<b>Vigileo</b>	Yes	Yes	Yes
<b>Anaesthesia</b>	Gen + Peri or Gen + Spin	Gen + PVT	Gen + Spin
<b>Paracetamol</b>	1g x 3	1g x 3	1g x 3
<b>Tapentadol</b>	50 mg x 2 (if spinal)	No	50 mg x 2
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# How to implement ERAS programs?



1

Team building (specific skills for specific issues)

2

Prospective development of the protocol (periodic internal discussion)

2011

- **Version 1.0**
- Protocol developed from international trials
- Surgeon + anaesthesiologist

2014

- **Version 2.0**
- Protocol revised according to team experience
- Surgeon + anaesthesiologist + nurse

2016

- **Version 3.0**
- Protocol revised according to team experience, prospective data and guidelines
- Involved physiotherapists and psychologists

2019

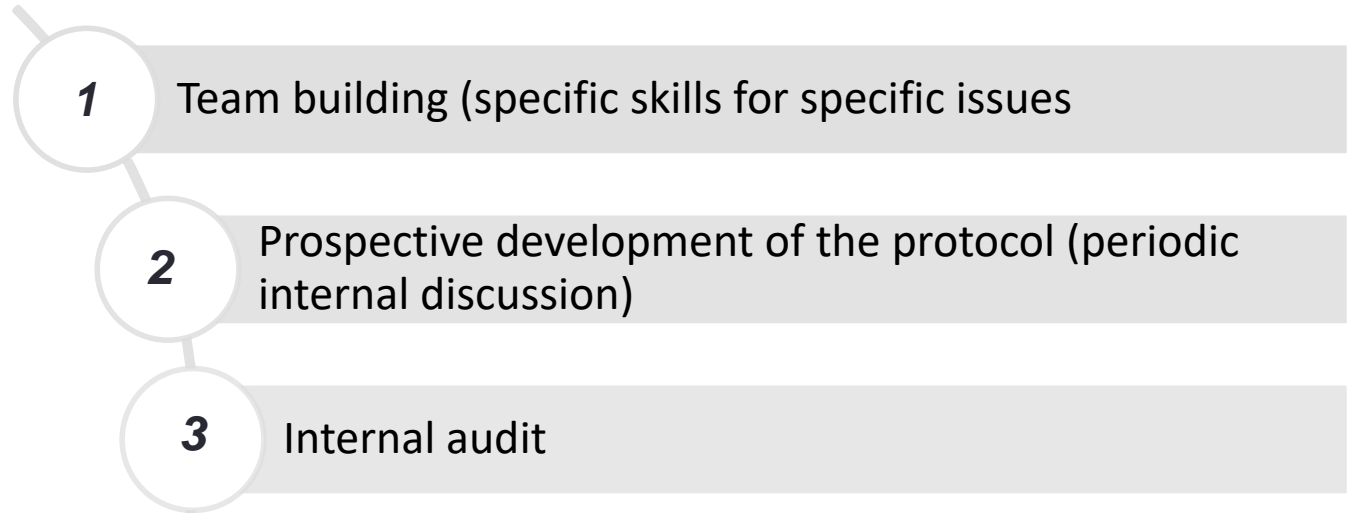
- Version 4.0
- Navigator nurse implementation
- Steroids adjusted on patient weight
- Preoperative FKT



2018

- **Version Hyper**
- Selected patients

## *How to implement ERAS programs?*



## How to implement ERAS programs?



1

Team building (specific skills for specific issues)

2

Prospective development of the protocol (periodic internal discussion)

3

Internal audit

4

International multi-institutional trials

Randomized clinical trial

**Randomized clinical trial of open *versus* laparoscopic left lateral hepatic sectionectomy within an enhanced recovery after surgery programme (ORANGE II study)**

E. M. Wong-Lun-Hing<sup>1,2</sup>, R. M. van Dam<sup>1,13</sup>, G. J. P. van Breukelen<sup>3,4</sup>, P. J. Tanis<sup>6</sup>, F. Ratti<sup>14</sup>, R. van Hillegersberg<sup>7</sup>, G. D. Slooter<sup>8</sup>, J. H. W. de Wilt<sup>9</sup>, M. S. L. Liem<sup>10</sup>, M. T. de Boer<sup>11</sup>, J. M. Klaase<sup>12</sup>, U. P. Neumann<sup>1,13</sup>, L. A. Aldrighetti<sup>14</sup> and C. H. C. Dejong<sup>1,2,5,13</sup>, on behalf of the ORANGE II Collaborative Group\*



## Specific effect of ERAS: PROCEDURES (Left lateral sectionectomy)

Randomized clinical trial

### Randomized clinical trial of open *versus* laparoscopic left lateral hepatic sectionectomy within an enhanced recovery after surgery programme (ORANGE II study)

Br J Surg 2016

E. M. Wong-Lun-Hing<sup>1,2</sup>, R. M. van Dam<sup>1,13</sup>, G. J. P. van Breukelen<sup>3,4</sup>, P. J. Tanis<sup>6</sup>, F. Ratti<sup>14</sup>, R. van Hillegersberg<sup>7</sup>, G. D. Slooter<sup>8</sup>, J. H. W. de Wilt<sup>9</sup>, M. S. L. Liem<sup>10</sup>, M. T. de Boer<sup>11</sup>, J. M. Klaase<sup>12</sup>, U. P. Neumann<sup>1,13</sup>, L. A. Aldrighetti<sup>14</sup> and C. H. C. Dejong<sup>1,2,5,13</sup>, on behalf of the ORANGE II Collaborative Group\*

	RCT			Registry		
	OLLS (n= 11)	LLLS (n= 13)	P‡	ONR (n= 13)	LNR (n= 54)	P‡
Functional recovery (days)	3 (3–5)	3 (3–3)	0.284	3 (3–3)	3 (3–4)	0.529
Adequate pain control with oral analgesia only	3 (2–3)	3 (2–3)	0.539	3 (3–4)	2 (2–3)	0.017
Independent mobility or preoperative level	3 (3–4)	3 (2–3)	0.071	3 (3–4)	3 (2–3)	0.240
No intravenous fluid	2.5 (2–3)¶	2 (1–3)¶	0.273	2 (1–4)	2 (1–2)	0.308
Tolerance of solid food	1 (1–1)	1 (1–1)	0.738	2 (1–2)	1 (1–1)	0.002
Normal or decreasing serum bilirubin level	2.5 (1–3)	1 (1–3)	0.232	0 (0–1)	1 (0–2)	0.161
Postoperative milestones (days)						
Free oral fluids	0 (0–1)	0 (0–0)	0.563	1 (0–1)	1 (0–1)	0.202
Removal of indwelling urinary catheter	3 (2–3)	2.5 (1–3)	0.140	3 (3–6)	2 (1–3)	0.031
First flatus	1 (1–2)	1 (1–2)	0.446	2 (1–3)	2 (1–2)	0.076
First stool	3 (2–4)¶	2 (2–3)¶	0.307	3 (3–4)¶	2 (2–3)¶	0.138
LOS (days)	4.5 (4–6)	4 (3–5)	0.049	5 (4–7)	4 (3–5)	0.064
Difference (LOS – functional recovery) (days)	1 (0–3)	1 (1–2)	0.832	2 (1–3)	1 (0–2)	0.042
Delay in discharge*†	8 of 10 (80)	9 (69)	1.000§	11 (85)	23 (43)	0.090§
Reasons for delay in discharge*						
Logistical	2 of 10 (20)	5 (38)		6 (46)	11 (20)	
Medical	3 of 10 (30)	1 (8)		2 (15)	5 (9)	
Patient preference	2 of 10 (20)	2 (15)		0 (0)	2 (4)	
Unknown	1 of 10 (10)	1 (8)		3 (23)	15 (28)	



## Specific effect of ERAS: PROCEDURES (Major resections)

### ORANGE II PLUS Trial

An international multicentre randomised controlled trial of open versus laparoscopic hemihepatectomy within an ERAS programme

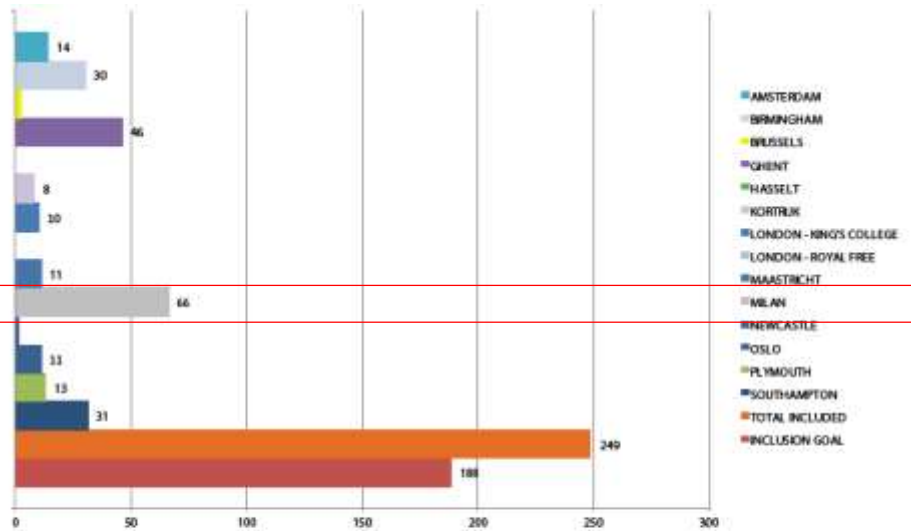


Figure 3 - trial accrual per centre.

Milan, Ghent, Southampton and Birmingham are responsible for the majority of the inclusions.

1. Milan - 66 randomisations
2. Ghent - 46 randomisations
3. Southampton - 31 randomisations
4. Birmingham - 30 randomisations



Centres started



15

Patients included in RCT



249/250

## How to implement ERAS programs?

