

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

Published online: 10 December 2013 © Société Internationale de Chirurgie 2013

## Abstract

*Background* The worldwide introduction of multimodal enhanced recovery programs has also changed perioperative care in patients who undergo liver resection. This study was performed to assess current perioperative practice in liver surgery in 11 European HPB centers and compare it to enhanced recovery after surgery (ERAS) principles.

*Methods* In each unit, 15 consecutive patients (N = 165) who underwent hepatectomy between 2010 and 2012 were retrospectively analyzed. Compliance was classified as

Presented at the 10th World Congress of the International Hepato-Pancreato-Biliary Association, Paris, France, 1–5 July 2012.

E. M. Wong-Lun-Hing (⊠) · R. M. van Dam · L. A. Heijnen · U. P. Neumann · C. H. C. Dejong Department of Surgery, Maastricht University Medical Center, PO Box 616, 6200 MD Maastricht, The Netherlands e-mail: e.wong@maastrichtuniversity.nl

R. M. van Dam  $\cdot$  U. P. Neumann  $\cdot$  C. H. C. Dejong Department of Surgery, University Hospital Aachen, Aachen, Germany

O. R. C. Busch Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands

# T. Terkivatan

Department of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

R. van Hillegersberg Department of Surgery, University Medical Center Utrecht, Utrecht, The Netherlands

#### G. D. Slooter

Department of Surgery, Maxima Medical Center, Veldhoven, The Netherlands

"full," "partial," or "poor" whenever  $\geq 80$ ,  $\geq 50$ , or <50 % of the 22 ERAS protocol core items were met. The primary study end point was overall compliance with the ERAS core program per unit and per perioperative phase. *Results* Most patients were operated on for malignancy (91 %) and 56 % were minor hepatectomies. The median number of implemented ERAS core items was 9 (range = 7–12) across all centers. Compliance was partial in the preoperative (median 2 of 3 items, range = 1–3) and perioperative phases (median 5 of 10 items, range: 4–7). Median postoperative compliance was poor (median 2 of 9 items, range = 0–4). A statistically significant difference was observed between median length of stay and median time to recovery (7 vs. 5 days, P < 0.001).

J. Klaase

Department of Surgery, Medical Spectrum Twente, Enschede, The Netherlands

J. H. W. de Wilt Department of Surgery, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

K. Bosscha Department of Surgery, Jeroen Bosch Hospital, Den Bosch, The Netherlands

B. Topal Department of Surgery, University Hospital Leuven, Louvain, Belgium

L. A. Aldrighetti Department of Surgery, San Raffaele Hospital, Milan, Italy

C. H. C. Dejong Nutrim School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, The Netherlands *Conclusion* Perioperative care among centers that perform liver resections varied substantially. In current HPB surgical practice, some elements of the ERAS program, e.g., preoperative counselling and minimal fasting, have already been implemented. Elements in the perioperative phase (avoidance of drains and nasogastric tube) and postoperative phase (early resumption of oral intake, early mobilization, and use of recovery criteria) should be further optimized.

#### Introduction

A multimodal enhanced-recovery perioperative care program for elective abdominal surgery was introduced by Kehlet et al. [1] at the end of the last century. The enhanced-recovery concept combines several evidencebased aspects of perioperative care into a structured care pathway, thereby enabling accelerated postoperative recovery and potentially reducing postoperative morbidity. Within the surgical community, several groups, such as the international enhanced recovery after surgery (ERAS) collaboration, have embraced and studied the enhancedrecovery concept. This led to the successful introduction of a new standard in perioperative care for colorectal surgery patients [2]. In recent years the same principles have also been applied in the perioperative care of liver surgery patients, and a few studies have shown that the program is feasible, safe, and effective for resection of hepatic tumors [3-10].

Actual data on the status of current practice and whether multimodal clinical pathways in liver surgery have been implemented are scarce. Over time, several elements of the ERAS concept have probably been introduced without implementation of a fully formal enhanced-recovery program. A recent survey in the international HPB community showed marginal implementation of ERAS protocols worldwide [11]. Based on the successful introduction and implementation of ERAS programs in various fields of surgery [12–17] and promising results in hepatic surgery, further dissemination of the ERAS concept within the liver surgical field seems desirable. First, to accelerate recovery and reduce length of hospital stay, it is necessary to aim for uniform and evidence-based perioperative management. Moreover, a structured and detailed program with welldefined recovery and discharge criteria can improve comparability of clinical outcomes in clinical audits and future clinical trials. Finally, it is likely that implementation will have a synergetic effect with minimally invasive surgery, as shown in colorectal surgery [18].

It has been suggested that implementation of a structured enhanced-recovery program in liver surgery is hard to achieve since multidisciplinary involvement is essential [19]. However, surgical practice has changed over the years and many ERAS elements may have already been introduced in current practice. Therefore, following an initial electronic survey [11], the aim of this study was to more accurately evaluate current perioperative care by assessing to what extent the different elements of an ERAS program have been implemented in liver surgery in a group of expert HPB units in Europe.

# Methods

### Study design

A retrospective analysis of prospectively collected data was conducted to assess current perioperative practice in patients undergoing liver surgery in a number of expert HPB centers in Europe. Fifteen consecutive patients per center were assessed. All available medical records (patient and nursing charts, surgery and anesthesia reports) for the different elements in the pre-, intra-, and postoperative phases of admission were reviewed and evaluated using a detailed baseline checklist that consisted of the previously described ERAS elements [4]. This checklist (see the Appendix) was further developed and adjusted by two hepatic surgeons (RMvD, CHCD) and two researchers (EMWLH, LH). Primary study endpoints were overall compliance with the ERAS core program per unit and per element. Secondary endpoints were day of discharge and time to functional recovery (FR).

## ERAS elements and compliance

The program's core elements are displayed in Table 1 and are grouped as pre-, peri- (day of surgery), and postoperative elements. If an element in the checklist was marked as "yes," the hospital was able to apply the ERAS element for a particular patient. Details explaining (non)compliance were also added to the "Comments" section of the checklist. Compliance was defined as the degree to which individual units or elements were in accordance with the ERAS program. Units were classified as "fully," "partially," or "poorly" compliant whenever  $\geq 80$ ,  $\geq 50$ , or <50 %, respectively, of the assessed 22 ERAS core items were met. Per individual element, an 80 % cutoff value was set to qualify a unit as "compliant." In addition, time to FR was assessed with predefined and previously described criteria [4, 5] (Table 2).

#### Study population

Liver units with a declared interest to participate in a random controlled trial (RCT) on laparoscopic liver

#### Table 1 ERAS core protocol elements

<ul> <li>Preoperative</li> <li>Preoperative counseling</li> <li>Minimal preoperative fasting (solid food up to 6 h + clear fluids up to 2 h) + carbohydrate loading</li> <li>No anxiolytic premedication</li> <li>Perioperative</li> <li>Thoracic epidural analgesia</li> <li>Prevention of hypothermia</li> <li>CVP monitoring (CVP &lt;5 mmHg)</li> <li>No routine drainage of the peritoneal cavity</li> <li>No standard nasogastric drainage</li> <li>Start intake of water and free fluids</li> <li>Early mobilization</li> <li>Postoperative nausea and vomiting (PONV) prophylaxis</li> <li>Antibiotic prophylaxis</li> <li>Postoperative days 1–3</li> <li>Daily review of discharge criteria</li> <li>Ileus prevention (MgO/Macrogol/Lactulose)</li> <li>Free fluids/normal diet POD 1</li> <li>Intravenous fluids discontinued POD 1</li> <li>Oral analgesia POD 1</li> <li>Normal diet POD 2</li> <li>Removal of urinary catheter POD 2</li> <li>Stop epidural/intravenous analgesia POD 3</li> <li>Full mobilization POD 3</li> </ul>	
Minimal preoperative fasting (solid food up to 6 h + clear fluids up to 2 h) + carbohydrate loading No anxiolytic premedication Perioperative Thoracic epidural analgesia Prevention of hypothermia CVP monitoring (CVP <5 mmHg) No routine drainage of the peritoneal cavity No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antibiotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Preoperative
up to 2 h) + carbohydrate loading No anxiolytic premedication Perioperative Thoracic epidural analgesia Prevention of hypothermia CVP monitoring (CVP <5 mmHg) No routine drainage of the peritoneal cavity No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antibiotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Preoperative counseling
Perioperative Thoracic epidural analgesia Prevention of hypothermia CVP monitoring (CVP <5 mmHg) No routine drainage of the peritoneal cavity No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	
Thoracic epidural analgesia Prevention of hypothermia CVP monitoring (CVP <5 mmHg) No routine drainage of the peritoneal cavity No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	No anxiolytic premedication
Prevention of hypothermia CVP monitoring (CVP <5 mmHg) No routine drainage of the peritoneal cavity No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antibiotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Perioperative
CVP monitoring (CVP <5 mmHg) No routine drainage of the peritoneal cavity No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Thoracic epidural analgesia
No routine drainage of the peritoneal cavity No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Prevention of hypothermia
No standard nasogastric drainage Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	CVP monitoring (CVP <5 mmHg)
Start intake of water and free fluids Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	No routine drainage of the peritoneal cavity
Early mobilization Postoperative nausea and vomiting (PONV) prophylaxis Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	No standard nasogastric drainage
Postoperative nausea and vomiting (PONV) prophylaxis Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Start intake of water and free fluids
Antithrombotic prophylaxis Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Early mobilization
Antibiotic prophylaxis Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Postoperative nausea and vomiting (PONV) prophylaxis
Postoperative days 1–3 Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Antithrombotic prophylaxis
Daily review of discharge criteria Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Antibiotic prophylaxis
Ileus prevention (MgO/Macrogol/Lactulose) Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Postoperative days 1-3
Free fluids/normal diet POD 1 Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Daily review of discharge criteria
Intravenous fluids discontinued POD 1 Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Ileus prevention (MgO/Macrogol/Lactulose)
Oral analgesia POD 1 Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Free fluids/normal diet POD 1
Normal diet POD 2 Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Intravenous fluids discontinued POD 1
Removal of urinary catheter POD 2 Stop epidural/intravenous analgesia POD 3	Oral analgesia POD 1
Stop epidural/intravenous analgesia POD 3	Normal diet POD 2
	Removal of urinary catheter POD 2
Full mobilization POD 3	Stop epidural/intravenous analgesia POD 3
	Full mobilization POD 3

#### Table 2 Functional recovery criteria

1. Pain control with oral analgesia only

2. No intra-venous fluid support

3. Full mobilization to preoperative level

4. Eating of solid food

5. Normal serum bilirubin or returning toward normal ranges

resection in an ERAS setting [20] were invited by email to participate in this retrospective study. A total of 11 European high-volume centers (>25 cases/year) [21] participated (see list below). The last 15 consecutive patients who underwent liver surgery in each hospital were selected and reviewed (open–close procedures and biliodigestive/vascular anastomoses were excluded). Included patients were all admitted and operated on between 2010 and 2012. All patients received perioperative care according to local protocols.

### ERAS experience

Three of the 11 centers indicated that they had formally implemented ERAS protocol for liver surgery. The implementation of ERAS principles in these three centers was achieved by multidisciplinary involvement, including a liver surgeon, an anesthetist, recovery ward nursing staff, and a researcher. In addition, all Dutch centers in this study had already gained experience with the ERAS program for colonic surgery as most of them participated in a nationwide structured implementation plan [22, 23]. The other hospitals were aware of the ERAS programs for liver and colonic surgery, but a structured implementation and evaluation had not yet been performed. Centers that had implemented the ERAS liver surgery program used the FR criteria (Table 2) to assess readiness for discharge. In the other centers the operating surgeon or physician on call was responsible for discharge and no strict criteria were applied.

### Data and statistics

Data were anonymously collected in an Oracle 10 database (Oracle Corp., Redwood Shores, CA, USA) with OpenClinica<sup>®</sup> trial software for online data capture and management (Ikaza Research, Cambridge, MA, USA) and analyzed using SPSS ver. 19 (SPSS Inc., Chicago, IL, USA). Basic analyses were performed using descriptive statistics. To describe the compliance in the complete cohort based on results of individual centers, a randomeffect logistic regression analysis was used. This adjusts for the heterogeneity of compliance among centers. The constant in the logistic regression model was transformed to an overall cohort compliance, except for three items that did not fit into the model (weighted median was used in these cases). Comparison between groups was performed using the Mann–Whitney U and Wilcoxon signed-ranks tests as appropriate. All statistical tests were two-sided, and P < 0.05 was considered statistically significant.

### Results

Patient and surgical characteristics

A total of 165 patients were included in this study. Baseline patient characteristics are given in Table 3. Surgical details with regard to type of incision and resection are given in Table 4. Overall morbidity and the distribution of postoperative surgical complications according to the Clavien–Dindo grading system can be found in Table 5.

## Primary end points

Overall compliance with the ERAS core elements varied among the assessed centers (Fig. 1). None of the participating hospitals were shown to be "fully" compliant with

**Table 3** Baseline characteristics of patients (N = 165)

Median age (range) (years)	62 (19-89)
Male gender	83 (50)
ASA grade	
Ι	21 (13)
П	111 (67)
III	32 (19)
Missing	1 (1)
Malignancy	150 (91)

Values in parentheses are percentages, unless indicated otherwise ASA American Society of Anesthesiologists

**Table 4** Surgical characteristics of patients (N = 165)

Incision	
Laparoscopic	22 (13)
Kocher's/J-shaped	81 (49)
Bilateral subcostal	19 (12)
Mercedes	12 (7)
Median	13 (8)
Other <sup>a</sup>	11 (7)
NA	7 (4)
Liver resection	
Minor (<3 segments or non-anatomical)	93 (56)
Major (≥3 segments)	45 (27)
Simultaneous non-hepatic	27 (16)
Туре	
Wedge resection/segmentectomy	46 (28)
Bisegmentectomy	23 (14)
Right hepatectomy	24 (15)
Left hepatectomy	2 (1)
Deroofing/enucleation	1 (1)
Extended right hepatectomy	4 (2)
Extended left hepatectomy	2 (1)
Multiple wedge resections/segmentectomies	35 (21)
Major ( $\geq$ 3 segments)	10 (6)
Other <sup>b</sup>	28 (17)
Major ( $\geq$ 3 segments)	3 (2)

Values in parentheses are percentages

NA not available

<sup>a</sup> Thoracoabdominal and xiphopubic incisions

<sup>b</sup> Hepatic resections combined with RFA or nonhepatic procedures

the complete set of core ERAS elements. Centers provided a median number of 9 (range = 7–12) of pre-, peri-, and postoperative care items according to the ERAS protocol. Five hospitals were partially compliant (11 or more items) and the remaining six hospitals were poorly compliant to the core elements. A summary of the overall compliance per ERAS element across all units (N = 165 patients) is given in Tables 6 and 7.

Table 5Morbidity $(N = 165)$	
Overall morbidity	47 (28)
Clavien–Dindo	
Grade I	8 (5)
Grade II	26 (16)
Grade IIIa	6 (4)
Grade IIIb	2 (1)
Grade IVa	5 (3)
Grade IVb	-
Grade V (death)	-
Readmissions	3 (2)

Values in parentheses are percentages

## Preoperative

Median compliance of the centers with preoperative core items was partial (66 %, 2 of 3 elements, range = 1–3). All centers provided preoperative counselling, predominantly on procedural issues and complications. Three centers provided extensive counselling, with attention to postoperative elements such as early oral feeding and mobilization, FR, and discharge criteria. No record of preoperative counselling could be found for 2 % of the patients. For 94 % (60–100) of the patients, preoperative fasting was reduced to a minimum. Anxiolytic premedication was not given to 43 % (13–100) of the patients.

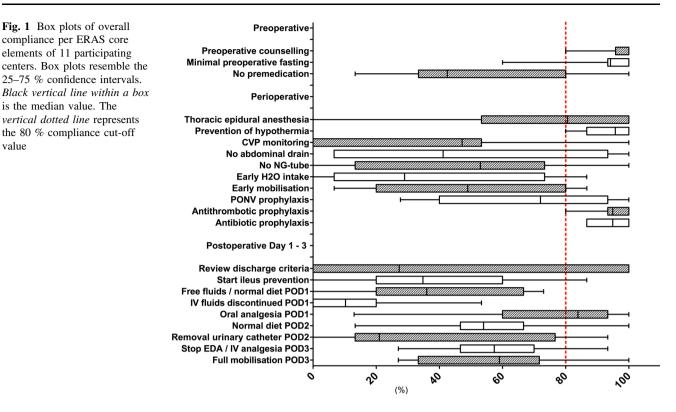
### Perioperative

Median compliance with perioperative core items was partial (50 %, 5 of 10 elements, range = 4-7). Ninety-six percent (87-100) of the patients received active prevention of hypothermia and 81 % (0-100) received thoracic epidural anesthesia. In 13 % (0-13), the procedure was laparoscopically performed, and in 49 % (26-100), a right subcostal incision was used. In 47 % (0-100) of the patients, the central venous pressure (CVP) was closely monitored and kept below 5 mmHg during parenchymal transection. In 53 % (0-100) of the patients, nasogastric tubes (NGT) were removed immediately after the operation, and in 41 % (7–100), abdominal drains were not used. In contrast to antithrombotic and antibiotic prophylaxes, prophylaxis for postoperative nausea and vomiting (PONV) was frequently provided, but not as per routine in all patients.

#### Postoperative

Median compliance of the centers with postoperative core items was poor (22 %, 2 of 9 elements, range = 0-6).

value



Early oral fluid intake, directly after surgery, was commenced in only 42 % (7-87) of the patients on POD 0, and only 36 % (0-73) tolerated free fluids or a normal diet on POD 1 (independent of the extent of liver surgery). After surgery patient-controlled intravenous (PCIA) or epidural analgesia (PCEA) was started in 83 % (0-93) of the patients as the standard of care. Oral analgesia was provided to 90 % (13-93) of patients, but in 14 % oral pain medication was not started until POD 2. Mobilization was achieved in only 50 % (13-93) of the patients on POD 1. In 56 % (0-73) of the patients, IV support was discontinued on POD 3. Urinary catheters were removed on POD 3 in 52 % (0–93), and they were usually not removed until the day of or the day after thoracic epidural anesthesia was discontinued. Signs of return of bowel function (flatulence and/or stool) were seen in 71 % (13-93) of patients on POD 3.

## Secondary end points

Data on the day of discharge and the time to FR are depicted in Fig. 2. The median length of stay (LOS) after surgery was 7 (range = 1–27) days and 31, 49, and 64 % of all patients were discharged on POD 5, 6, and 7, respectively. Using the FR criteria, a majority of the patients could be considered functionally recovered on median POD 5 (1-24). This difference between discharge and time to FR was statistically significant (P < 0.001).

Eighty-one percent (N = 133) of the patients were not discharged on the day that FR criteria were fulfilled. In 29 % of patients, complications were responsible for prolonged hospitalization (Table 5). Although time to FR and LOS were in favor of the centers that were partially compliant with the ERAS program, differences did not reach statistical significance (Figs. 3, 4).

## Discussion

This study evaluated the current perioperative care in 11 high-volume European liver surgery centers by assessing compliance with an ERAS program. Perioperative care varied considerably among the centers. All of the participating institutions had already adopted a median of 9 (range = 7-12) elements of the ERAS care program as part of modern surgical practice. None of the centers had implemented the complete set of core elements. Interestingly, pre- and perioperative elements had the best implementation, but the centers were especially poor at complying with ERAS elements in the postoperative phase. In addition, a significant discrepancy between the patient's recovery and actual discharge was observed.

Every center consistently provided preoperative counseling, limited the fasting period, actively prevented hypothermia during surgery, and systematically administered antithrombotic and antibiotic prophylaxes. Also,

### Table 6 Compliance with ERAS elements

	N/total N (%)	Overall median compliance (range)
Preoperative		
Preoperative counselling	162/165 (98)	96 (80-100)
Assessment of discharge arrangements	120/165 (73)	73 (0–100) <sup>a</sup>
Assessment of mobility	122/164 (74)	74 (0-100) <sup>a</sup>
Daily review of discharge criteria	45/165 (27)	27 (0-100) <sup>a</sup>
Normal oral diet up to 6 h + clear fluid intake up to 2 h	155/165 (94)	94 (60–100)
No anxiolytic premedication	91/162 (56)	43 (13-100)
Perioperative		
Thoracic epidural anesthesia (EDA)	119/165 (72)	81 (0-100)
Prevention of hypothermia	157/160 (98)	96 (87-100)
Laparoscopy/right subcostal incision	102/159 (64)	65 (13-87)
CVP monitoring (CVP < 5 mmHg)	47/102 (46)	47 (0–100)
No postoperative nasogastric tube	72/161 (45)	53 (0-100)
No routine use of abdominal drain	76/165 (46)	41 (7-100)
Postoperative day (POD) 0		
PONV prophylaxis	110/164 (67)	72 (27–100)
Antithrombotic prophylaxis	157/164 (96)	95 (80-100)
Antibiotic prophylaxis	155/162 (96)	95 (87-100)
Oral fluid intake	100/162 (62)	42 (7-87)
Mobilization at all	13/150 (9)	6 (7–87)
Start oral analgesia	86/163 (51)	51 (7-100)
Use of patient-controlled analgesia (EDA or IV)	132/165 (80)	83 (0–93)
POD 1		
Nasogastric tube removed	107/160 (67)	66 (0-100)
Tolerance of free fluids/normal diet	63/165 (38)	36 (0-73)
Mobilization at all/out of bed	82/160 (51)	50 (7-87)
No intravenous fluids	17/165 (10)	10 (0-53)
Oral analgesia	129/165 (78)	84 (13-100)
Use of patient-controlled analgesia (EDA or IV)	114/165 (69)	75 (0–93)
CAD removal	14/161 (9)	5 (0-60)
Flatulence and/or stool	15/148 (10)	10 (0-20)
POD 2		
Normal diet	101/165 (61)	54 (13-100)
Mobilization out of bed	118/159 (74)	76 (13–93)
No intravenous fluids	34/165 (21)	19 (0-67)
Oral analgesia	135/165 (82)	86 (13–93)
Use of patient-controlled analgesia (EDA or IV)	91/165 (55)	54 (0-87)
CAD removal	41/159 (26)	21 (0-93)
Flatulence and/or stool POD 3	59/145 (41)	41 (0-67)
Normal diet	120/165 (73)	73 (13–93)

Table 6	continued
---------	-----------

	N/total N (%)	Overall median compliance (range)
Full mobilization	81/151 (57)	59 (27–100)
No intravenous fluids	76/165 (46)	56 (0-73)
Oral analgesia	139/165 (84)	90 (13-93)
Use of patient-controlled analgesia (EDA or IV)	46/165 (28)	25 (0-87)
CAD removal	85/157 (54)	52 (0-93)
Flatulence and/or stool	108/154 (70)	71 (13–93)
Use of cathartics and/or laxatives	61/165 (37)	35 (0-87)

Overall median compliance represents all assessed centers (N = 11) CVP central venous pressure, PONV postoperative nausea and vomiting, IV intravenous, CAD catheter à démeure

<sup>a</sup> Weighted median

PONV prophylaxis, the use of epidural anesthesia, and patient-controlled analgesia already had a prominent place. In contrast to the aforementioned care elements, other ERAS components were absent or suboptimally implemented. The partial or poor compliance and wide variation among the centers mirror this.

During the preoperative phase, anxiolytic medication was commonly used. Two striking perioperative observations were the widespread use of abdominal drains and NGT. In addition, the CVP during parenchymal transection was poorly documented. In the postoperative phase, the resumption of oral intake, removal of the urinary catheter, use of laxatives, and mobilization were only poorly implemented.

Based upon previous studies, it is known that preoperative counseling on the role and expectations of the patient in the recovery period could further optimize postoperative recovery and satisfaction [24, 25]. Also, the use of anxiolytic premedication could negatively influence gastrointestinal motility and, although it is safe to use short-acting benzodiazepines in day surgery [26], their efficacy for major surgery remains unclear.

Important accumulated evidence for the perioperative phase has shown that the necessity of abdominal drains can be questioned after uncomplicated liver resection [27]. Equally, it is well known that it is safe to remove NGTs directly after abdominal surgery [28]. The use of an NGT is even associated with an increased risk of developing postoperative pulmonary complications [28, 29].

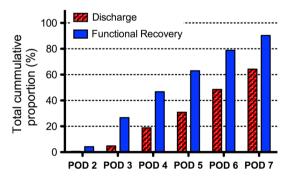
There is an ongoing discussion concerning central venous pressure monitoring (CVP <5–10 mmHg). Low CVP can be utilized to minimize back bleeding during parenchymal transection and to avoid excessive administration of IV fluids [30–32]. However, it could be argued

Table 7 Compliance with ERAS core elements per center

	Cente	rs									
	A	В	С	D	Е	F	G	Н	Ι	J	K
Preoperative											
Preoperative counselling (%)	100	100	100	100	100	100	100	80	93	100	100
Minimal preoperative fasting (%)	60	100	100	100	100	100	100	80	93	100	100
No anxiolytic premedication (%)	13	67	80	40	40	27	80	100	87	20	53
Perioperative											
Thoracic epidural analgesia (%)	100	93	100	80	87	93	100	53	7	0	80
Prevention of hypothermia (%)	87	93	93	100	80	100	100	100	87	100	100
CVP monitoring (%)	13	33	13	53	7	0	0	100	20	73	0
No routine drainage of the peritoneal cavity (%)	67	53	100	93	100	27	53	7	7	7	87
No standard nasogastric drainage (%)	27	40	13	67	73	7	53	0	13	87	100
Start intake of water/free fluids (%)	7	40	80	0	47	13	67	0	0	80	87
Early mobilization (%)	7	47	33	53	20	13	80	87	40	87	73
PONV prophylaxis (%)	80	27	93	73	93	47	100	40	93	33	60
Antithrombotic prophylaxis (%)	93	80	93	93	100	100	100	100	100	93	100
Antibiotic prophylaxis (%)	100	100	87	93	100	87	93	100	93	100	87
Postoperative days 1-3											
Daily review of discharge criteria (%)	0	0	0	100	0	0	100	0	0	0	100
Ileus prevention (%)	27	13	40	87	27	60	20	27	0	80	27
Free fluids/normal diet POD 1 (%)	20	33	20	73	47	33	67	0	7	53	67
Intravenous fluids discontinued POD 1 (%)	0	0	0	0	0	0	53	0	33	20	7
Oral analgesia POD 1 (%)	100	87	93	100	60	93	93	13	73	53	93
Normal diet POD 2 (%)	40	67	47	100	53	67	40	13	73	100	73
Removal of urinary catheter POD 2 (%)	0	47	7	13	13	7	0	27	40	93	33
Stop epidural/intravenous analgesia POD 3 (%)	27	80	53	73	53	33	60	60	93	60	40
Full mobilization POD 3 (%)	27	73	60	80	40	27	33	67	100	33	33

Total N = 165, with 15 patients per center

CVP central venous pressure, PONV postoperative nausea and vomiting, POD postoperative day



**Fig. 2** Discharge versus functional recovery, P < 0.001. Cumulative proportion of all patients (N = 165) who were discharged on POD 2–7 and who were functionally recovered (FR). *POD* postoperative day

that CVP monitoring is not strictly necessary in minor hepatectomies, which represent a majority in the present study.

Lastly, patient-controlled analgesia may help to reduce opioid use and its associated side effects [33]. However,

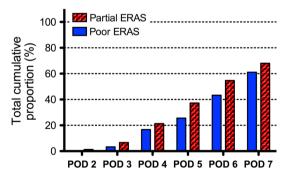
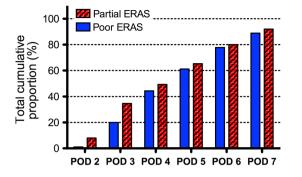


Fig. 3 Discharge in partial ERAS centers (N = 5) versus poor ERAS centers (N = 6), P = 0.166. Cumulative proportion of patients who were discharged on POD 2–7

there is debate concerning the role of epidural catheters (EDA). Although frequently used in the participating centers, they are no longer used in an increasing number of other hospitals that perform liver surgery. Not only can the technique be contraindicated, e.g., because of the presence



**Fig. 4** Functional recovery in partial ERAS centers (N = 5) versus poor ERAS centers (N = 6), P = 0.149. Cumulative proportion of patients who were functionally recovered on POD 2–7

of coagulopathy, it can also cause potentially serious complications such as epidural hematoma, abscess, or paralysis [34]. The epidural catheterization is more time-consuming than intravenous analgesia and fails to provide adequate analgesia in >20 % of the patients [35].

It may be felt that ERAS principles are not uniformly applicable to all patients and other factors (e.g., age, comorbidity, indication for surgery, and extent of liver resection) could play a role. There are good alternatives to core elements that would not deter from the ERAS principles. Postoperative pain has traditionally been managed by intravenous or epidural analgesia. It can be argued whether the inclusion of thoracic epidural analgesia as a core element reflects current clinical practice. The use of wound catheters with a local anesthetic [36–38] or the use of intrathecal morphine [39] has been shown to be safe and effective also in an ERAS setting for liver surgery [40, 41]. Furthermore, alternatives to reduce CVP or monitor it could serve as a substitute and may be sufficient [42, 43].

In the postoperative phase, the still abundant use of NGTs could explain why early intake of water on POD 0 was achieved in only less than one third of the patients and why only half of the patients tolerated a normal diet on POD 2. A quick return to a normal diet has been shown to be safe for both major upper abdominal and colorectal surgeries [44, 45]. In addition, to promote the return of normal bowel function or prevent a postoperative ileus, standard use of laxatives has been shown to be effective [4, 5]. Lastly, few patients mobilized out of bed before POD 2. The use of drains, lack of daily mobilization goals, and relatively late removal of catheters can explain this observation.

A secondary outcome was the length of hospital stay versus the time to FR. It is generally agreed that it is medically justified to discharge patients when criteria for full FR are met [4, 5, 20]. In keeping with literature data [4, 19], a discrepancy was found between discharge and time to FR. A majority of patients (63 %) principally were functionally recovered on median POD 5 (range = 1-24),

while only 31 % were discharged at that time. Factors influencing this delay could have been poor organization of discharge logistics, cultural differences, and deviant patient expectations. Unfortunately, it was not possible to assess all five FR criteria because serum bilirubin values were inconsistently available. Bilirubin values were therefore assumed normal since the majority of the liver resections in this study were minor procedures.

The retrospective assessment of the data, the selection of participating centers, and their varying experience with ERAS principles may have biased our results. However, this design was deliberately chosen so as to not influence the behavior of medical and nursing staff in perioperative care during a full prospective assessment. Both large and small hepatic centers were allowed to participate and this could also have influenced our results. However, the large number of minor resections in this study and the participation of several high-volume European centers with varying experience with ERAS protocols do provide a reflection of daily practice in liver surgery and therefore increase external validity.

Based on this study several recommendations can be made that could eventually lead to further optimization of care and potentially improve postoperative outcomes. Change of current practice and implementation of an enhanced-recovery care pathway are desirable but will require multidisciplinary efforts [19, 46]. Although counseling is already part of preoperative care in that information on the procedure and possible complications is provided, there should be more emphasis on the recovery period with respect to pain control, early mobilization, resumption of intake, and time of discharge. Furthermore, administration of preoperative anxiolytic medication should not be the standard. Recommendations for the perioperative phase include the selective monitoring of the CVP and abandoning the standard use of abdominal drains and the dogmatic use of NGT. For patients undergoing liver surgery, the use of NGTs is not needed at all and seems very conservative. In combination with adequate PONV prophylaxis, a safe and quick return to a normal diet may be facilitated. In addition, laxatives can be provided in a standard manner, urinary catheters should be removed earlier, and daily mobilization goals should be determined. Lastly, predefined discharge criteria should be checked daily to minimize a delay in discharge after FR.

The findings of this study are clinically relevant to liver surgeons as they aim for a universally accepted and standardized perioperative care program. The findings may help to provide the standardization needed for comparability in clinical audits and trials. Future research should clarify the role of the individual components in ERAS programs and investigate to what extent an element contributes to the improvement of outcomes. Several recent studies [8–10] have already demonstrated the additional value of ERAS programs with predefined discharge criteria. In addition, safe and effective alternatives or new elements should be embraced.

# Conclusion

Perioperative care among centers that perform liver resections varied substantially and elements of enhancedrecovery programs had already been implemented as part of daily surgical practice. Other elements can be further optimized based on ERAS principles. This may standardize care and improve recovery after liver surgery. Acknowledgments The authors thank all participating centers for their support and contribution to this study: in the Netherlands: Maastricht University Medical Center, Maastricht; Academic Medical Center, Amsterdam; Erasmus Medical Center, Rotterdam; University Medical Center Utrecht, Utrecht; Maxima Medical Center, Veldhoven; Medical Spectrum Twente, Enschede; Jeroen Bosch Hospital, Den Bosch; Radboud University Nijmegen Medical Center, Nijmegen; in Belgium: University Hospital Leuven, Leuven; in Germany: University Hospital Aachen, Aachen; and in Italy: San Raffaele Hospital, Milan.

Conflict of interest The authors declare no conflicts of interest.

Appendix

Hosp Com	oital: plicati	Ptn.nr: ons:	Date of birth:	ASA
		on (<30 days): yes /no		
	perati			Comments:
Date				
Yes	No			
		Preoperative counselling (if y	es, specify)	
		Assessment of discharge arra		
		Assessment of discharge and	angements	
		Preoperative mobility assess		
		Preoperative mobility assess		Commonte:
	of adn			Comments:
Date	of adn	Preoperative mobility assess		Comments:
Date Yes	of adm : No	Preoperative mobility assess	ment	Comments:
Day Date Yes	of adn	Preoperative mobility assess	ment	Comments:
Date Yes	of adm : No	Preoperative mobility assess	ment	Comments:
Date Yes	of adm : No	Preoperative mobility assess	ment	Comments:
Date Yes	of adm : No	Preoperative mobility assess nission: Pre-anaesthetic medication (	ment f yes, specify)	Comments:
Date Yes	of adm : No	Preoperative mobility assess	ment f yes, specify)	Comments:
Date Yes	of adm : No	Preoperative mobility assess nission: Pre-anaesthetic medication (	ment f yes, specify)	Comments:

Day	of sur	gery (peroperative):	Comments:
Date			
Yes	No		
		Preoperative fasting (if yes, specify regime and hours before surgery)	
Surg			
Yes	No		Comments:
		Minimal invasive incisions / laparoscopy (specify type of surgery)	Type of incision: Type of surgery:
		CAD	
		Use of abdominal drains	
	esthes	iology	
Yes	No	Antibiotic prophylaxis (before incision)	Comments:
		Arterial line	
		Intravenous infusion	
		CVP catheter	
		Hemodynamic monitoring	
		Anaesthesia (specify type)	
		Epidural (if yes, location)	
		Upper and lower body air-warming device > 36 °C	
		Nasogastric decompression tube	
		CVP <5 mmHg perioperative	
		PONV prophylaxis (specify)	
		Antithrombotic prophylaxis (LMWH)	

Arterial line removed         CVP catheter removed         Nasogastric decompression tube removed (if used)	Yes	No		Comments:
			Arterial line removed	
Nasogastric decompression tube removed (if used)			CVP catheter removed	
			Nasogastric decompression tube removed (if used)	

Reco	overy /	Ward (POD 0):	Comments:
Date	:		
Yes	No		
		Use of analgesia (PCA / Epidural / PCEA)	
		Daily pain assessment	
		CAD	
		Patient journal	
		Oral analgesics (if yes, specify)	
		IV fluids	
		Oral intake of water / carbohydrate drinks	
		Mobilisation (if yes, specify)	
		(Semi-) solid food intake in the evening	
		Laxatives (if yes, specify type, dosage and duration)	
		Stools/flatulence	

DOD 4 (ward):					
	POD 1 (ward): Comments: Date:				
Yes	No				
		Use of analgesia (PCA / Epidural / PCEA)			
		Daily pain assessment			
		CAD			
		Oral analgesics			
		IV fluids			
		Normal diet / patient drinks 1.5 L + solid food intake			
		Mobilisation (if yes, specify)			
		Laxatives			
		Stools/flatulence			
		Standard postoperative laboratory tests (specify)			
		Ready for discharge (if yes, specify criteria)			
	_		-		
POD Date			Comments:		
		1			
Yes	No				
Ш		Use of analgesia (PCA / Epidural / PCEA)			
		Daily pain assessment			
		CAD			
		Oral analgesics			
		IV fluids			
		Normal diet			
		Mobilisation (if yes, specify)			
		Laxatives			
		Stools/flatulence			
		Ready for discharge (if yes, specify criteria)			

POD 3: Comments: Date:			Comments:
			Yes
		Use of analgesia (PCA / Epidural / PCEA)	
		Daily pain assessment	
		CAD	
		Oral analgesics	
		IV fluids	
		Normal diet	
		Mobilisation (if yes, specify)	
		Laxatives	
		Stools/flatulence	
		Standard postoperative laboratory tests (specify)	
		Ready for discharge (if yes, specify criteria)	
		Discharge arrangements made	

POD 4:			Comments:	
Date	Date:			
Yes	No		-	
		Discharged		
		If not discharged: care continued as on POD3?		

POD 5:			Comments:
Date:			
Yes	No		
		Discharged	
		If not discharged: care continued as on POD4?	

POD 6:			Comments
Date:			
Yes	No		
		Discharged	
		If not discharged: care continued as on POD5?	

#### References

- Kehlet H, Wilmore DW (2002) Multimodal strategies to improve surgical outcome. Am J Surg 183(6):630–641
- Spanjersberg WR, Reurings J, Keus F, van Laarhoven CJ (2011) Fast track surgery versus conventional recovery strategies for colorectal surgery. Cochrane Database Syst Rev 2:CD007635
- MacKay G, O'Dwyer PJ (2008) Early discharge following liver resection for colorectal metastases. Scott Med J 53(2):22–24
- van Dam RM, Hendry PO, Coolsen MM, Bemelmans MH, Lassen K, Revhaug A et al (2008) Initial experience with a multimodal enhanced recovery programme in patients undergoing liver resection. Br J Surg 95(8):969–975
- Hendry PO, van Dam RM, Bukkems SF, McKeown DW, Parks RW, Preston T et al (2010) Randomized clinical trial of laxatives and oral nutritional supplements within an enhanced recovery after surgery protocol following liver resection. Br J Surg 97(8):1198–1206
- Lin DX, Li X, Ye QW, Lin F, Li LL, Zhang QY (2011) Implementation of a fast-track clinical pathway decreases postoperative length of stay and hospital charges for liver resection. Cell Biochem Biophys 61(2):413–419
- Coolsen MM, Wong-Lun-Hing EM, van Dam RM, van der Wilt AA, Slim K, Lassen K et al (2013) A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. HPB (Oxford) 15(4):245–251
- Sanchez-Perez B, Aranda-Narvaez JM, Suarez-Munoz MA, Eladel-Delfresno M, Fernandez-Aguilar JL, Perez-Daga JA et al (2012) Fast-track program in laparoscopic liver surgery: theory or fact? World J Gastrointest Surg 4(11):246–250
- Ni CY, Yang Y, Chang YQ, Cai H, Xu B, Yang F et al (2013) Fast-track surgery improves postoperative recovery in patients undergoing partial hepatectomy for primary liver cancer: a prospective randomized controlled trial. Eur J Surg Oncol 39(6):542–547
- Schultz NA, Larsen PN, Klarskov B, Plum LM, Frederiksen HJ, Christensen BM et al (2013) Evaluation of a fast-track programme for patients undergoing liver resection. Br J Surg 100(1):138–143
- Wong-Lun-Hing EM, Lodewick TM, Stoot JH, Bemelmans MH, Olde Damink SH, Dejong CH et al (2012) A survey in the hepatopancreatobiliary community on ways to enhance patient recovery. HPB (Oxford) 14(12):818–827
- Brustia P, Renghi A, Gramaglia L, Porta C, Cassatella R, De Angelis R et al (2003) Mininvasive abdominal aortic surgery. Early recovery and reduced hospitalization after multidisciplinary approach. J Cardiovasc Surg (Torino) 44(5):629–635
- Barbieri A, Vanhaecht K, Van Herck P, Sermeus W, Faggiano F, Marchisio S et al (2009) Effects of clinical pathways in the joint replacement: a meta-analysis. BMC Med 7:32
- Arsalani-Zadeh R, ElFadl D, Yassin N, MacFie J (2011) Evidence-based review of enhancing postoperative recovery after breast surgery. Br J Surg 98(2):181–196
- Rawlinson A, Kang P, Evans J, Khanna A (2011) A systematic review of enhanced recovery protocols in colorectal surgery. Ann R Coll Surg Engl 93(8):583–588
- Spelt L, Ansari D, Sturesson C, Tingstedt B, Andersson R (2011) Fast-track programmes for hepatopancreatic resections: where do we stand? HPB (Oxford) 13(12):833–838
- Lassen K, Coolsen MM, Slim K, Carli F, de Aguilar-Nascimento JE, Schafer M et al (2012) Guidelines for perioperative care for pancreaticoduodenectomy: enhanced recovery after surgery (ERAS<sup>®</sup>) society recommendations. Clin Nutr 31(6):817–830
- Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF et al (2011) Laparoscopy in combination with fast track

multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). Ann Surg 254(6):868–875

- Maessen J, Dejong CH, Hausel J, Nygren J, Lassen K, Andersen J et al (2007) A protocol is not enough to implement an enhanced recovery programme for colorectal resection. Br J Surg 94(2):224–231
- 20. van Dam RM, Wong-Lun-Hing EM, van Breukelen GJ, Stoot JH, van der Vorst JR, Bemelmans MH et al (2012) Open versus laparoscopic left lateral hepatic sectionectomy within an enhanced recovery ERAS<sup>®</sup> programme (ORANGE II-Trial): study protocol for a randomized controlled trial. Trials 13(1):54
- Fong Y, Gonen M, Rubin D, Radzyner M, Brennan MF (2005) Long-term survival is superior after resection for cancer in highvolume centers. Ann Surg 242(4):540–544 discussion 544–547
- 22. Maessen JM, Hoff C, Jottard K, Kessels AG, Bremers AJ, Havenga K et al (2009) To eat or not to eat: facilitating early oral intake after elective colonic surgery in the Netherlands. Clin Nutr 28(1):29–33
- 23. Gillissen F, Hoff C, Maessen JM, Winkens B, Teeuwen JH, von Meyenfeldt MF et al (2013) Structured synchronous implementation of an enhanced recovery program in elective colonic surgery in 33 hospitals in The Netherlands. World J Surg 37(5):1082–1093. doi:10.1007/s00268-013-1938-4
- Disbrow EA, Bennett HL, Owings JT (1993) Effect of preoperative suggestion on postoperative gastrointestinal motility. West J Med 158(5):488–492
- Kiecolt-Glaser JK, Page GG, Marucha PT, MacCallum RC, Glaser R (1998) Psychological influences on surgical recovery. Perspectives from psychoneuroimmunology. Am Psychol 53(11):1209–1218
- Walker KJ, Smith AF (2009) Premedication for anxiety in adult day surgery. Cochrane Database Syst Rev 4:CD002192
- Gurusamy KS, Samraj K, Davidson BR (2007) Routine abdominal drainage for uncomplicated liver resection. Cochrane Database Syst Rev 3:CD006232
- Nelson R, Tse B, Edwards S (2005) Systematic review of prophylactic nasogastric decompression after abdominal operations. Br J Surg 92(6):673–680
- Pessaux P, Regimbeau JM, Dondero F, Plasse M, Mantz J, Belghiti J (2007) Randomized clinical trial evaluating the need for routine nasogastric decompression after elective hepatic resection. Br J Surg 94(3):297–303
- 30. Lesurtel M, Selzner M, Petrowsky H, McCormack L, Clavien PA (2005) How should transection of the liver be performed? A prospective randomized study in 100 consecutive patients: comparing four different transection strategies. Ann Surg 242(6): 814–822 discussion 822–823
- Wang WD, Liang LJ, Huang XQ, Yin XY (2006) Low central venous pressure reduces blood loss in hepatectomy. World J Gastroenterol 12(6):935–939
- McNally SJ, Revie EJ, Massie LJ, McKeown DW, Parks RW, Garden OJ et al (2012) Factors in perioperative care that determine blood loss in liver surgery. HPB (Oxford) 14(4):236–241
- 33. Ong CK, Seymour RA, Lirk P, Merry AF (2010) Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: a qualitative systematic review of analgesic efficacy for acute postoperative pain. Anesth Analg 110(4):1170–1179
- Cook TM, Counsell D, Wildsmith JA (2009) Major complications of central neuraxial block: report on the third national audit project of the Royal College of Anaesthetists. Br J Anaesth 102(2):179–190
- 35. McLeod G, Davies H, Munnoch N, Bannister J, MacRae W (2001) Postoperative pain relief using thoracic epidural analgesia: outstanding success and disappointing failures. Anaesthesia 56(1):75–81

- Basu S, Tamijmarane A, Bulters D, Wells JK, John TG, Rees M (2004) An alternative method of wound pain control following hepatic resection: a preliminary study. HPB (Oxford) 6(3):186–189
- Liu SS, Richman JM, Thirlby RC, Wu CL (2006) Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: a quantitative and qualitative systematic review of randomized controlled trials. J Am Coll Surg 203(6):914–932
- Forastiere E, Sofra M, Giannarelli D, Fabrizi L, Simone G (2008) Effectiveness of continuous wound infusion of 0.5 % ropivacaine by on-Q pain relief system for postoperative pain management after open nephrectomy. Br J Anaesth 101(6):841–847
- 39. De Pietri L, Siniscalchi A, Reggiani A, Masetti M, Begliomini B, Gazzi M et al (2006) The use of intrathecal morphine for postoperative pain relief after liver resection: a comparison with epidural analgesia. Anesth Analg 102(4):1157–1163
- 40. Koea JB, Young Y, Gunn K (2009) Fast track liver resection: the effect of a comprehensive care package and analgesia with single dose intrathecal morphine with gabapentin or continuous epidural analgesia. HPB Surg 2009:271986
- 41. Revie EJ, McKeown DW, Wilson JA, Garden OJ, Wigmore SJ (2012) Randomized clinical trial of local infiltration plus patient-

controlled opiate analgesia versus epidural analgesia following liver resection surgery. HPB (Oxford) 14(9):611-618

- Lentschener C, Ozier Y (2002) Anaesthesia for elective liver resection: some points should be revisited. Eur J Anaesthesiol 19(11):780–788
- 43. Zhu P, Lau WY, Chen YF, Zhang BX, Huang ZY, Zhang ZW et al (2012) Randomized clinical trial comparing infrahepatic inferior vena cava clamping with low central venous pressure in complex liver resections involving the Pringle manoeuvre. Br J Surg 99(6):781–788
- 44. Andersen HK, Lewis SJ, Thomas S (2006) Early enteral nutrition within 24 h of colorectal surgery versus later commencement of feeding for postoperative complications. Cochrane Database Syst Rev 4:CD004080
- 45. Lassen K, Kjaeve J, Fetveit T, Trano G, Sigurdsson HK, Horn A et al (2008) Allowing normal food at will after major upper gastrointestinal surgery does not increase morbidity: a randomized multicenter trial. Ann Surg 247(5):721–729
- Ahmed J, Khan S, Gatt M, Kallam R, MacFie J (2010) Compliance with enhanced recovery programmes in elective colorectal surgery. Br J Surg 97(5):754–758