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**Cost-benefit analysis of the implementation of an enhanced recovery
program in liver surgery**

Gaëtan-Romain Joliat¹, Ismaïl Labgaa¹, Martin Hübner¹, Catherine Blanc², Anne-Claude Griesser³, Markus Schäfer¹, Nicolas Demartines¹

Departments of Visceral Surgery¹ and Anesthesiology², and Medical Directorate³, University Hospital of Lausanne (CHUV), Lausanne, Switzerland

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Correspondence to:

Nicolas Demartines, MD, FACS, FRCS

Professor and Chairman

Department of Visceral Surgery

University Hospital CHUV

Rue du Bugnon 46

1011 Lausanne, Switzerland

Phone: +41 21 314 24 00

Fax: +41 21 314 24 11

E-mail: demartines@chuv.ch

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Abstract (word count: 250)*Background*

Enhanced recovery after surgery (ERAS) programs have been shown to ease the postoperative recovery and improve clinical outcomes for various surgery types. ERAS cost-effectiveness was demonstrated for colorectal surgery but not for liver surgery. The present study aim was to analyze the implementation costs and benefits of a specific ERAS program in liver surgery.

Methods

A dedicated ERAS protocol for liver surgery was implemented in our department in July 2013. The subsequent year all consecutive patients undergoing liver surgery were treated according to this protocol (ERAS group). They were compared in terms of real in-hospital costs with a patient series before ERAS implementation (pre-ERAS group). Mean costs per patient were compared with a bootstrap T-test. A cost-minimization analysis was performed.

Results

Seventy-four ERAS patients were compared with 100 pre-ERAS patients. There were no significant pre- and intraoperative differences between the two groups, except for the laparoscopy number (n=18 ERAS, n=9 pre-ERAS, p=0.010). Overall postoperative complications were observed in 36 (49%) and 64 patients (64%) in the ERAS and pre-ERAS groups, respectively (p=0.046). The median length of stay was significantly shorter for the ERAS group (8 vs. 10 days, p=0.006).

The total mean costs per patient were €38'726 and €42'356 for ERAS and pre-ERAS (p=0.467). The cost-minimization analysis showed a total mean cost reduction of €3'080 per patient after ERAS implementation.

Conclusions

ERAS implementation for liver surgery induced a non-significant decrease in cost compared to standard care. Significant decreased complication rate and hospital stay were observed in the ERAS group.

Introduction

Enhanced recovery after surgery (ERAS) programs are standardized multimodal perioperative care aiming to reduce the patient's response to surgical stress and to decrease the postoperative complication risk [1]. Fewer postoperative complications and improved recovery lead to a shorter length of hospital stay (LoS). ERAS has been shown to be beneficial on a clinical and economic level in colorectal surgery [2–4]. Therefore, ERAS programs have been extended to other types of surgery, including liver surgery [5–10], but few studies compared an ERAS pathway for liver surgery to a conventional perioperative management [11–14]. The preliminary results have shown that ERAS for liver surgery appears to be safe and feasible [12–17]. Moreover, some studies showed a diminution of postoperative complications or LoS [18–20].

Formal guidelines for ERAS in liver surgery have not been published yet. However, general recommendations for ERAS in liver surgery based on ERAS protocol in pancreas surgery [21] encompass the use of preoperative counseling, carbohydrate beverages, reduced preoperative fasting, optimized fluid balance, avoidance of premedication, standardized postoperative analgesia, early postoperative nutrition, and early postoperative mobilization.

While implementing a new clinical perioperative pathway should first and foremost result in clinical benefits for the patients, it should also be preferentially cost-beneficial in order to convince the financial hospital authorities to invest in such a project and to contribute to reduce the health care costs.

The study aim was to compare the complete real in-hospital costs for liver resections before and after systematic implementation of an ERAS pathway for liver surgery in an ERAS-dedicated tertiary center.

Material and Methods

ERAS protocol and patient groups

ERAS was first implemented for colorectal surgery in our department in May 2011. The members of the multidisciplinary team had received beforehand a formal training provided by the ERAS[®] Society. ERAS protocol for liver surgery was implemented in the department of Visceral Surgery at the University Hospital of Lausanne (CHUV, Switzerland) in July 2013. This protocol was developed by the local ERAS team based on previous ERAS protocols for pancreas [21] and colorectal [22] surgery. This liver protocol encompasses a list of diverse pre-, intra-, and postoperative items that are summarized in detail in *Table 1*.

From July 2013 to July 2014 all consecutive liver resections were included into ERAS. Major hepatectomy was defined as resection of ≥ 3 Couinaud segments, and minor hepatectomy as resection of one to two liver segments. Wedge resections were defined as non-anatomical partial resections of liver segments.

The ERAS group (from July 2013 to July 2014) was compared to a pre-ERAS group that included a cohort of 100 consecutive patients who underwent liver surgery before the implementation of ERAS for liver surgery. No power analysis was performed because it was estimated a priori that selecting a cohort of 70 to 80 consecutive ERAS patients would permit to draw a firm statistically-based conclusion.

The study was retrospective. However, all data were prospectively recorded in our liver database for both periods, prior and after ERAS implementation. Data collection was performed by a dedicated and fully trained ERAS nurse. The study was approved by the local ethics committee (protocol number 362/14) and was registered online on Research Registry (UIN: researchregistry443).

Perioperative parameters

Operating time was calculated from incision to skin closure, whereas anesthesia time was calculated from the patient entry in the operating room (OR) until the patient was awake. Postoperative complications were graded according to the validated Clavien classification [23] and the comprehensive complication index (CCI) [24]. Grade I-II were defined as minor complications and grade III-IV as major complications [23]. Postoperative death during the hospital stay or during the 30 postoperative days was defined as grade V [23]. Formal ERAS validated discharge criteria were: control of pain with oral analgesia only, no intravenous fluids, independent mobilization, and sufficient oral intake (at least 2/3 of a normal meal). LoS was defined from operation day until day of discharge. Data about readiness for discharge were not collected. Even though readiness for discharge is more realistic than LoS, this concept may be more subjective (based on doctors' appreciations) than the actual hospital LoS. That is why LoS was calculated based on objective figures. Readmission rate was defined as the number of patients needing a rehospitalization within 60 days of surgery. Overall compliance was calculated as the number of fulfilled pre-, intra-, and postoperative items divided by the total number of predefined enhanced recovery measures (expressed in %). For the pre-ERAS group, it was assessed if some ERAS items were already applied, and overall compliance was then calculated.

Analysis of the costs

A comprehensive analysis of all real costs was performed for every patient according to a method previously used by our group [3]. Briefly, all pertinent intraoperative costs and pre-/postoperative costs were considered. The intraoperative costs included the disposable material used during the operation and the anesthesia as well as OR costs. The anesthesia costs integrated the anesthesiologist and anesthesia nurse costs (based on the duration of the anesthesia in minutes) as well as the materials and medications used for the anesthesia. The

OR costs were based on the OR occupation in minutes. The pre- and postoperative costs included the following items: intensive care unit (ICU)/intermediate care (IC), medical care, nursing care, physiotherapy, medication, blood test, laboratory, radiology, pathology, housing, administration, and other costs. The medical care costs included all costs related to the doctors' clinical activities, except for the anesthesiologist costs accounted in the anesthesia and OR costs. The costs of nursing care represented the costs of the ward and did not include the ICU and IC costs. They were based on the Project of Research in Nursing (PRN), which determines the prospective nursing time needed per patient based on a validated 249-item list [25]. The housing costs were calculated per day of hospitalization. The administrative costs were counted per admission. Finally, the other costs covered the social work division, the priest, and the occupational therapy. Detailed data were furnished by the account department of our hospital and represented the real costs of each patient case.

All costs were primarily in Swiss Francs (CHF). The used exchange rate to euros (€) was the one current on March 8, 2015: CHF1=€0.94. No correction for general price difference between the two periods (ERAS and pre-ERAS) was made.

Cost-minimization analysis and sensitivity analysis

A cost-minimization analysis was performed, i.e., hospital savings per patient were calculated. This present analysis was made by the subtraction of the standard care costs per patient to the ERAS-specific costs per patient and the ERAS costs per patient. The ERAS-specific costs included the salary of the ERAS-dedicated nurse (fixed costs), the costs of the quarterly ERAS liver meetings (fixed costs), the ERAS database (variable costs, depending on the patient number), the patient carbohydrates drinks (variable costs, depending on the patient number), and the patient logbook costs (variable costs, depending on the patient number).

A sensitivity analysis was undertaken as well. As fixed costs are independent from the patient number and are allocated on an individual basis, large variations due to the number of patients can appear. We therefore calculated the cost-minimization by varying the patient number by $\pm 50\%$ (i.e., calculating the ERAS-specific costs for 37 and 111 patients).

Subgroup analysis

A subgroup analysis was performed for all hepatic resections that were performed by laparotomy. Mean total costs were calculated and compared using a bootstrap T-test.

Statistical analysis

A Mann-Whitney U test or a T-test was used to compare continuous variables depending on the distribution type and the homogeneity of the variances. Categorical (discrete) variables were compared using a Fisher's exact test or a Chi-square test. The arithmetic means were used because they represent informative and explicit figures from a pharmaco-economic standpoint. Moreover, a resampling was performed for the cost analysis by using the bootstrap method because of its simplicity, its property to derive confidence intervals from a complex sample distribution, and its robustness of estimation. A bootstrap T-test was used to compare the different costs. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS®19 (IBM, Armonk, New York, USA) and GraphPad Prism®5.

Results

Patient characteristics and surgical details

A total of 174 patients were enrolled for further analysis: 74 in the ERAS group and 100 in the pre-ERAS group. Demographic, preoperative, and surgical data were comparable in the ERAS and pre-ERAS groups, except for laparoscopy that was more frequently performed in the ERAS group (n=18 vs. n=9, p=0.010). *Table 2* resumes the patient characteristics and the surgery type performed.

Compliance and perioperative outcomes

In terms of compliance to the ERAS protocol, the overall rate including all pre-, intra-, and postoperative ERAS items was 73.8% in the ERAS group compared to 48.7% in the pre-ERAS group (p<0.001). The readmission rate 60 days after the operation was not significantly different between the two groups (6/74=8% and 7/100=7%, p=0.780).

The perioperative data are summarized in *Table 3*. There was no difference in the operating time and the anesthesia time between the ERAS and pre-ERAS groups. The overall complication rate was significantly lower in the ERAS group compared to the pre-ERAS group (36/74=49% vs. 64/100=64%, p=0.046). If one subdivides the complications into minor (I-II) and major (III-IV) there were no differences between the ERAS and pre-ERAS groups. Median CCI was lower for the ERAS group (8.7 vs. 20.9, p=0.044). The median LoS was significantly shorter for the ERAS group (8 vs. 10 days, p=0.006). The median ICU stays were 0 and 1 day for the ERAS and pre-ERAS groups (p<0.001), while the median IC stays were 2 and 3 days (p=0.002), respectively.

Analysis of the costs

The mean (SD) total costs/patient were €38'726 (31'608) for the ERAS group and €42'356 (26'898) for the pre-ERAS group (p=0.467). The mean intraoperative costs/patient

for the ERAS and pre-ERAS groups were €10'793 (6'228) and €9'981 (4'440) respectively ($p=0.236$). The mean pre-/postoperative costs/patient were €27'933 (27'635) for the ERAS group and €32'375 (25'224) for the pre-ERAS group ($p=0.271$). The pre-, intra- and postoperative costs are summarized in detail in *Table 4* and *Figure 1*. All mean costs/patient were lower for the ERAS group except for the anesthesia and OR, the nursing care, the housing, the administration, and the social service, occupational therapy and priest costs.

Cost-minimization analysis and sensitivity analysis

The difference of mean total costs/patient between the pre-ERAS and ERAS groups was €'630 (-9%), meaning that the total mean costs of ERAS/patient were €'630 less expensive than the ones of the pre-ERAS group.

In the ERAS-specific costs, fixed ERAS costs included the crude salary of the ERAS-dedicated nurse (€31'845 per year) and the costs of the ERAS liver meetings (€50/meeting for the used material and the preparation time, at least 4 meetings/year). As the ERAS-dedicated nurse was also responsible for ERAS colorectal and ERAS pancreas during the same period of time, we divided her salary by three. Fixed ERAS costs/patient were therefore: $27'282/74+200/74=€371$. The variable ERAS costs were the ERAS database (€100/patient), the patient carbohydrate drinks (€75/patient), and the patient logbooks (€4/patient). ERAS-specific costs were thus calculated to be €50/patient.

The final total gain/patient for the ERAS group was €'080 (-7%).

If we vary the number of patients by $\pm 50\%$, the ERAS-specific costs/patient would be €22 for 37 patients and €427 for 111 patients, leading to a final total gain for ERAS/patient of €'708 (-6%) and €'203 (-8%), respectively.

Subgroup analysis

Regarding the operations performed by laparotomy, there were 55 patients in the ERAS group and 92 patients in the pre-ERAS group. Both groups showed similar demographics and surgical details. The total mean costs/patient was €42'234 (39'526) for the ERAS group and €45'584 (35'985) for the pre-ERAS group (difference: €3'350, $p=0.657$).

Discussion

The present study assessing the real costs of implementation of an ERAS protocol for liver surgery demonstrated in our cohort a non-significant decrease in costs compared to standard management but a significant decrease in complications and LoS.

The main savings engendered by the implementation of ERAS for liver surgery were found in the ICU/IC costs (€'578/patient), but were not statistically significant ($p=0.174$). The majority of patients included in the ERAS protocol did not need to stay in the ICU, while the median length of ICU stay was one day for the pre-ERAS group ($p<0.001$). Moreover, the reduction of ICU stay for the ERAS group was also coupled to a shorter IC stay compared to the pre-ERAS group (2 *vs.* 3 days, $p=0.002$). This cannot be explained by a difference of operation complexity (major *vs.* minor hepatectomy) as the ERAS and pre-ERAS groups were similar in this regard ($p=0.643$) and the operation durations were comparable ($p=0.188$). With ERAS liver implementation, patients were routinely scheduled for IC unit if needed, or for the standard ward. Only in rare case of extended major hepatectomy, patients were postoperatively transferred to the ICU. The fact that IC unit stay was also shorter for the ERAS group suggests an enhanced recovery in the early postoperative days and a lower rate of patients necessitating continuous monitoring. This could be related to the standardized anesthesia protocol that emphasized the postoperative analgesia, the postoperative nausea and vomiting prophylaxis, the fluid intake, and the early diet, and/or to the standardized care maps guiding the postoperative phase [26,27].

The second main absolute gain in the ERAS group but not statistically significant was related to the medical care costs (€'052/patient). This can be linked, if there is a gain as it was not significant, to the reduced overall complication rate and LoS observed in the ERAS group. A postoperative complication results in increased medical resources (consultation,

non-surgical procedures, etc), therefore increasing the medical care costs [28,29]. ERAS also had a significant cost-benefit effect on the radiology and a non statistically significant cost-benefit effect on the medication. The radiology costs represented the main statistically significant savings of the ERAS group with a gain of €58/patient ($p=0.021$). In the ERAS group, fewer medications were used and fewer radiological exams were performed postoperatively. These can be an effect of the implementation of ERAS, can be due to the diminution of postoperative complications, or can just be due to the standardization of the postoperative management with the clinical care maps [27], or a mix of the three previous explanations. Costs are frequently linked to LoS, and LoS differ widely from country to country. The most important factor for one country is the difference between the LoS before and after ERAS implementation rather than the absolute LoS. The same is true for ICU and IC stays that depend on local habits and infrastructures; the important point being the difference in ICU and IC needs before and after ERAS implementation more than the absolute numbers.

Conversely, the ERAS group had significantly higher anesthesia/OR costs and not significantly higher nursing care costs. As the anesthesia and OR times were not different between the two groups, the difference of costs mainly lies in the material and drugs used during anesthesia. The standardized anesthesia protocol and the routine prophylactic use of postoperative nausea and vomiting prevention by droperidol, ondansetron, and bethamethasone only explain a small part of this difference, as the prophylaxis costs are low. The higher number of laparoscopies in the ERAS group had no impact on the material and drugs used during anesthesia. Of note, the number of thoracic epidurals was similar in both groups (54/74 ERAS group vs. 79/100 pre-ERAS group, $p=1$). No clear explanation was therefore found for this increase in anesthesia and OR costs. Regarding the nursing care costs, as the ICU and IC median stays were shorter, the patients with higher PRN number (i.e.,

representing the case complexity in terms of nursing actions) [25] were transferred earlier to the ward, therefore increasing this part of the costs at the beginning of their hospital stay.

LoS was found to be shorter for the ERAS group. There was nevertheless no repercussion on the mean housing costs/patient. No difference of mean housing costs was indeed found between the ERAS and pre-ERAS groups ($p=0.058$). This is explained by the constant annual increase (inflation) of the basal rate of hospital housing costs throughout the years. It is not clear why a diminution of complications and a shorter LoS did not translate into significant overall cost difference. One explanation could be related to the large found confidence intervals inherent to the bootstrap method and related to the p -value. It is nevertheless interesting to notice that implementation of ERAS had positive outcomes for the patients without increasing the costs, meaning that ERAS was cost-effective. This also justifies the investment costs necessary to implement ERAS.

ERAS for liver surgery was previously shown to be feasible and safe [12–15]. Two systematic reviews showed a decrease in complications and/or a reduction of LoS without an increase of the readmission rate, corroborating the results of this present study [18,19]. A study by Dunne *et al.* including hepatectomies for colorectal metastasis found that as ERAS experience increases with time, a progressive diminution of hospitalization time and critical care admission was noticed [30]. However, reduced LoS may be associated with higher rate of readmissions as reported by Connor *et al.* [11]. It has to be emphasized that the present study showed a significant shorter LoS after ERAS implementation, but the readmission rate did not increase and remained low. Hospital discharge was based on formal discharge criteria.

As shown by previous studies, implementation of ERAS protocols in gastrointestinal surgery needs initial investments, but is then associated with an important gain per patient for both financial and clinical aspects (significant diminution of complications, reduction of LoS, quicker recovery) [2,3,31–33]. Once the implementation phase is done, financial gains appear

and continue over time, giving considerable savings proportionally to the increasing number of patients included in the protocol. Regarding the real costs of the implementation of an ERAS pathway for liver surgery, data are for the moment non-existent. A simulation study from Faujour *et al.* was recently published and estimated that after ERAS implementation in different specialties, an overall gain of €180/hospital day for all the surgical units could be obtained [34]. In this study ERAS was implemented in five French units of digestive (including liver surgery), orthopedic, and urology surgeries. Their outcomes were based on estimations and not on real costs as in the present study. In our department, ERAS was already implemented in colorectal surgery since 2011, so costs of education and training of the team were not included in this analysis.

Comparing the overall cost data of this study to the results published for colorectal surgery [3], the absolute cost difference between ERAS and pre-ERAS is more important in liver surgery (€3'080 vs. €1'651). This is partly explained by the fact that the overall costs for liver surgery are higher than for colorectal surgery. The observed not significant overall cost difference between ERAS and pre-ERAS in the present study can be explained by the fact that even though there is an important absolute difference (i.e., €3'080) between the two groups, the relative difference is rather small (-7%). Nevertheless, the present study suggests benefits of ERAS implementation in liver surgery.

The present study has several limitations that must be addressed. First, the higher number of laparoscopies in the ERAS group may in part explain the results. Laparoscopy as single measure has been shown to improve and fasten recovery [35,36]. Therefore the higher percentage of laparoscopic cases in the ERAS group entails a bias, as we do not know exactly to which extent the benefits are due to ERAS, laparoscopy, standardization, or all together. To minimize this bias, a subgroup analysis was performed with the patients operated by laparotomy. The difference of total mean costs/patient between pre-ERAS and ERAS

(€'350) was not different from the total mean costs calculated in the entire cohort (€'620, laparotomy and laparoscopy patients). These findings support the fact that laparoscopy did not play a major role in the cost benefits observed in the ERAS group. Second, the ERAS and pre-ERAS groups were retrospectively analyzed inducing all possible limitations of a retrospective study (e.g., underreporting of complications, missing data). However, the data have been prospectively recorded in our liver database for several years, and the same database was used for both periods. Moreover, the validated Clavien classification of complications and the CCI were systematically used and provided a recognized objective evaluation of complications for both periods. Finally, only costs linked to the primary hospitalization were calculated (in-hospital costs), the costs for postoperative rehabilitation and recovery time before returning to work were not taken into account in the current analysis. However, despite the lack of actual data on rehabilitation after ERAS, it can be assumed that outpatient recovery may also become easier and faster in ERAS patients [37]. To support this statement discharge was based on formal pre-established criteria, and readmission rates were similar.

ERAS-skeptics may argue that it is difficult to differentiate between the positive benefits of the ERAS program itself and the systematization of care induced by the ERAS care maps. They are right, there is nothing magical in ERAS. However, care maps belong to ERAS programs with systematization of care, and the final goal achieved is of importance: a significant decrease in complication rate. Whether it comes from the pathophysiology of ERAS, from the systematization, or from both matters little but this deserves further investigation beyond the present study aim. Of note, the ERAS-specific costs of this present analysis were half of the ones that were published for implementation of ERAS in colorectal surgery [3] because the costs of the courses to educate the team to the ERAS concept were not necessary and therefore not included. Finally, one can challenge if Swiss results may be

extrapolated to other countries. In fact, the importance of the present results lies in the cost, complication rate, and LoS differences between pre- and after ERAS implementation more than in the absolute numbers. For this reason, it can be suggested that the present outcomes may also be observed in other countries.

In conclusion, implementation of ERAS for liver surgery showed a non-significant decrease in costs in our institution. It also led to a significant reduction of the overall complication rate and LoS.

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Disclosures

Gaëtan-Romain Joliat, Ismaïl Labgaa, Martin Hübner, Catherine Blanc, Anne-Claude Griesser, Markus Schäfer, and Nicolas Demartines have no conflicts of interest or financial ties to disclose.

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Table 1. ERAS protocol for liver surgery used in our department compared to the pre-ERAS period.

ERAS single item	ERAS protocol	Pre-ERAS period
<i>Preoperative</i>		
Counseling and education	Preadmission counseling and written information at the outpatient clinic*	None
Fasting	Clear fluids until 2h before surgery, solids 6h before surgery	Clear fluids and solids 6h before surgery
Carbohydrate drinks	800 ml the evening before surgery and 400 ml 2h before surgery	None
Premedication	No premedication	Anesthesiologist-dependant
Thromboprophylaxis	LMW heparin 12h before surgery and during hospitalization, and IPC	LMW heparin 12h before surgery and during hospitalization
Oral bowel preparation	No routine use	No routine use
<i>Intraoperative</i>		
PONV prophylaxis	Droperidol + ondansetron +/- bethamethasone if no contraindication	No routine use
Hypothermia prevention	Active warming with air blanket	Active warming with air blanket.
Antibiotic prophylaxis	Cefuroxime 1.5 g at induction	Cefuroxime 1.5 g at induction
Balanced IV fluids	Intraoperative crystalloids quantity depending on the operation avoiding salt and water overload. Postoperative crystalloids 1000 ml for the first 24h then 500 ml/24h for the first postoperative days	No policy
<i>Postoperative</i>		
Nasogastric tube	No routine use	No routine use
Postoperative analgesia	Epidural or systemic morphine and paracetamol (if no hepatic failure) and metamizole. Oral oxycodone-naloxone (when epidural is removed, usually on POD 3). NSAIDs from POD 5 instead of metamizole	No routine use of epidural
Abdominal drains	No routine abdominal drainage	Surgeon-dependant
Urinary catheter	Removal on POD 3	Removal depending on the surgeon
Nutrition	Free fluids 4h after surgery. Normal diet from POD 1. Two nutritional supplements per day	Free fluids on day 1, then depending on the patient's evolution
Laxatives	Oral magnesium hydroxide twice a day until day of hospital discharge	No routine use
Mobilization	Out of bed at least 2h on the day of surgery. From POD 1 at least 8h out of bed	No protocol
Systematic audit	Systematic audit, meeting every 3 months	None

* Preadmission counseling is performed by the ERAS-dedicated nurse and consists mainly of information on the ERAS protocol and the patient logbook. PONV: postoperative nausea and vomiting. IV: intravenous. LMW: low molecular weight. IPC: intermittent pneumatic compression. POD: postoperative day. NSAIDs: nonsteroidal anti-inflammatory drugs.

Table 2. Patient demographics and surgical details.

	ERAS group (n=74)	Pre-ERAS group (n=100)	P-value
Age (years)*	60.5 (50-68.25)	64 (57.25-69.75)	0.061
Gender (W/M)	31 (42%)/43 (58%)	40/60	0.876
Body mass index (kg/m ²)	25.3 (21.6-29)	24.8 (22.3-27.8)	0.812
ASA score I-II/III†	56 (76%)/18 (24%)	72/28	0.607
Active smokers	19 (26%)	26	1.000
No alcohol consumption	36 (49%)	59	0.218
Cirrhosis	4 (5%)	12	0.186
Diabetes	14 (19%)	19	1.000
Immunosuppression	4 (5%)	1	0.165
Preoperative chemotherapy	29 (39%)	54	0.066
Preoperative PV embolization‡	11 (15%)	26	0.092
Preoperative bile duct stenting	4 (5%)	3	0.460
Open/laparoscopy	56 (76%)/18 (24%)	91/9	0.010
Hepatectomy**			
Major	30 (41%)	45	0.643
Minor	36 (49%)	44	0.643
Wedge resection	8 (10%)	11	1.000
WHO performance§			
0/1/2/3/4	31 (42%)/40 (54%)/2 (3%)/1 (1%)	56/42/1/1	0.288
Diagnoses			
HCC¶	10 (14%)	16	0.675
Colorectal metastasis	31 (42%)	46	0.645
Cholangiocarcinomas	9 (11%)	9	0.616
Other cancers	4 (5%)	13	0.123
Benign lesions#	20 (28%)	16	0.090

* Medians are expressed with interquartile range. † American Society of Anesthesiologists score. ‡ PV: portal vein. ** Major hepatectomy was defined as resection of 3 or more Couinaud segments. § World Health Organization performance index: 0=asymptomatic, 1=symptomatic, ambulant, 2=symptomatic, <50% in bed, 3=symptomatic, >50% in bed, 4=bedbound. ¶ Hepatocellular carcinomas. # Benign lesions included adenomas, cystadenomas, echinococcosis, biliary cysts, and polycystic liver diseases.

Table 3. Perioperative outcomes.

	ERAS group (n=74)	Pre-ERAS group (n=100)	P-value
Operating time, min*	254.5 (188.3-351)	279 (208-359)	0.188
Anesthesia time, min	354 (273.3-436.8)	375 (300-454.5)	0.115
Pedicular clamping	45 (61%)	53	0.355
Complications	36 (49%)	64	0.046
Minor (I-II)	25 (34%)	42	0.345
Major (III-IV)	10 (14%)	20	0.313
Deaths (V)	1 (1%)	2	1.000
CCI†	8.7 (0-21.3)	20.9 (0-29.6)	0.044
Length of stay, days	8 (6-11)	10 (7-15.5)	0.006
ICU stay, days‡	0 (0-0)	1 (0-2)	<0.001
IC stay, days**	2 (1-3.25)	3 (2-4)	0.002
Overall compliance (%)§	73.8 (52.4-89.1)	48.7 (37.4-59.3)	<0.001
Readmission at 60 days	6 (8%)	7	0.780

*Medians are expressed with interquartile range. †Comprehensive complication index. ‡Intensive care unit.

**Intermediate care. §Overall compliance represents the number of fulfilled items divided by the total number of enhanced recovery measures (%).

Table 4. Detailed costs for the ERAS and pre-ERAS groups in euros.

	ERAS			Pre-ERAS			Mean difference	Inferior CI	Superior CI	P-value
	Mean (SD)	Inferior CI	Superior CI	Mean (SD)	Inferior CI	Superior CI				
Total intraoperative	10 793 (6 228)	9 399	12 668	9 981 (4 440)	8 797	11 332	812	-1 322	3 190	0.236
Disposable materials	1 923 (1 468)	1 595	2 304	2 675 (3 510)	2 058	3 418	-752	-1 545	-44	0.079
Anesthesia and operating room	8 870 (5 208)	7 804	10 364	7 306 (3 235)	6 740	7 914	1 564	223	3 234	0.039
Total pre- and postoperative	27 933 (27 635)	18 722	40 146	32 375 (25 224)	24 840	41 456	-4 442	-17 980	9 958	0.271
ICU/IC	5 754 (12 365)	3 509	8 960	8 332 (12 704)	6 190	10 970	-2 578	-6 092	1 296	0.174
Medical care	9 015 (18 459)	5 397	13 748	10 067 (15 072)	7 338	13 361	-1 052	-6 283	4 252	0.709
Nursing care	4 986 (5 289)	3 913	6 308	4 185 (3 251)	3 547	4 898	801	-437	2 343	0.242
Physiotherapy	500 (710)	304	787	607 (699)	471	769	-106	-364	201	0.452
Medication	1 232 (3 142)	675	2 039	2 008 (3 013)	1 515	2 688	-776	-1 641	198	0.091
Blood	538 (1 281)	308	857	827 (1 847)	523	1 235	-290	-743	194	0.252
Laboratory	1 430 (1 862)	1 060	1 898	1 861 (1 987)	1 480	2 269	-431	-990	172	0.158
Radiology	701 (1 322)	422	1 025	1 259 (1 857)	912	1 630	-558	-1 018	-81	0.021
Pathology	1 293 (997)	1 085	1 540	1 312 (757)	1 177	1 475	-19	-299	271	0.882
Housing	1 964 (1 818)	1 586	2 385	1 480 (1 004)	1 281	1 689	484	30	939	0.058
Administration	415 (0)	415	415	347 (46)	338	357	67	58	77	0.001
Others*	105 (289)	50	184	89 (125)	68	116	16	-47	95	0.659
Total	38 726 (31 608)	28 121	52 814	42 356 (26 898)	33 638	52 788	-3 630	-19 302	13 148	0.467

ICU: intensive care unit, IC: intermediate care, SD: standard deviation, CI: 95% confidence interval.

* Others included the social work, the chaplain/priest, and the occupational therapy costs.

Figure 1. Box-Whisker plots of intraoperative, pre-/postoperative, and total mean cost differences between the two groups (ERAS minus pre-ERAS) in euros.

