European Journal of Surgical Oncology 45 (2019) 1439–1445

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Defining enhanced recovery after resection of peri-hilar cholangiocarcinoma

L.M. Quinn [a, *], K. Mann [b], R.P. Jones [a], S. Bathla [b], S. Stremitzer [b], D.F. Dunne [c], C. Lacasia [b], S.W. Fenwick [b], H.Z. Malik [b]

[a] Institute of Translational Medicine, University of Liverpool, Liverpool, UK
[b] Northwest Hepatobiliary Centre, University Hospital Aintree, Liverpool, UK
[c] Department of Hepatopancreatobiliary Surgery, Royal Liverpool University Hospital, Liverpool, UK

ARTICLE INFO

Article history:
Received 13 December 2018
Received in revised form
18 March 2019
Accepted 25 March 2019
Available online 28 March 2019

ABSTRACT

Introduction: Enhanced recovery after surgery (ERAS) for peri-hilar cholangiocarcinoma (pCCA) has not been described in the literature. This study examined patients undergoing pCCA resection within a standard post hepatectomy ERAS pathway to define achievable targets suitable for these patients.
Methods: Patients undergoing pCCA resection at University Hospital Aintree (January 2009–October 2017) were identified. Achievement of key ERAS outcomes was assessed. Patients were stratified on incidence of major complications and pre-operative cardiopulmonary exercise testing. Chi Square and Mann Whitney analyses were undertaken as appropriate. Achievable ERAS targets were derived from patients who did not develop a major complication.
Results: 46 patients underwent resection with enhanced recovery. Median age 65 (24 male: 22 female). Key ERAS outcomes in patients who did not experience major complications are described as medians (interquartile range): length of stay 8 days (6–13), duration critical care 2 days (2–4), inotropes 6 h (0–24), epidural 3 days (3–4), early mobilization day 1 (1–2), full mobilization day 3 (3–4), urinary catheter removal day 4 (3–5), NGT removal day 1 (1–2) and restoration oral nutrition day 2 (2–4). Patients deemed high risk pre-operatively or those who developed major complications post-operatively required significantly longer critical care ($p = 0.008$ and $p = 0.002$ respectively). Other ERAS targets remained achievable in similar timeframes.
Conclusions: ERAS for pCCA is achievable. Applicable ERAS standards are defined which take into account minor complications. High risk patients and those with major complications can be appropriately managed in an ERAS pathway, though there is increased need for critical care support.

Introduction

Enhanced recovery after surgery (ERAS) for patients undergoing resection of peri-hilar cholangiocarcinoma (pCCA) has not been adequately described, and an appropriate ERAS target based pathway has not been defined. Significant variation exists in the care of patients with pCCA [1]. ERAS employs a fast track multimodal strategy to minimize variation in post-operative care and accelerate recovery [2]. Principles are derived from colorectal surgery but distinct differences exist which may impede implementation in HPB surgery [3].

ERAS has been shown to be effective in patients undergoing hepatectomy, but the addition of a biliary-enteric reconstruction means current targets for standard hepatectomy may not be appropriate. In colorectal liver metastasis (CRLM) resections, ERAS shortens hospital inpatient stay and critical care admissions without increases in morbidity or mortality [4]. Randomised clinical trials of ERAS versus standard care in open hepatectomy reaffirmed this and with improved quality of life [5]. Similar results are demonstrated following primary liver cancer resection [6]. Systematic reviews on ERAS in CRLM surgery conclude ERAS is safe and effective [7]. These studies had limited patient numbers, [8] and peri-hilar CCA resection is poorly represented and sometimes intentionally excluded from these studies. The ERAS society

* Corresponding author. Hepatobiliary Research Fellow, Institute of Translational Medicine, University of Liverpool, Sherrington Building, Ashton Street, Liverpool, L69 3GE, UK.
E-mail address: L.M.Quinn@liverpool.ac.uk (L.M. Quinn).

https://doi.org/10.1016/j.ejso.2019.03.033
0748-7983/

guidelines for liver surgery were published in 2016 [9] Significant components of this guideline, such as omission of abdominal drainage and nasogastric drainage may not be applicable to pCCA resection.

The feasibility of applying ERAS in patients undergoing peri-hilar cholangiocarcinoma resection was demonstrated by Yip et al., where a small number of the overall series were included in a standard ERAS hepatectomy model [10]. Studies describing specific and achievable ERAS components in patients undergoing pCCA resection are absent. This study sought to examine patients undergoing peri-hilar CCA resection within a standard post hepatectomy ERAS pathway to define a pathway with achievable targets suitable for these patients.

Methods

Study population

All patients undergoing resection for peri-hilar cholangiocarcinoma at University Hospital Aintree (Liverpool, UK) between January 2009 and October 2017 were identified from a prospectively maintained database. Patients with tumours considered as peri-hilar disease and included in the study were those considered type 2–4 using the modified Bismuth-Corlette system [11]. Intra-hepatic cholangiocarcinoma, Bismuth-Corlette Type 1 and distal common bile duct disease were excluded. Peri-hilar cholangiocarcinoma was histologically confirmed on the resected specimen in all patients.

Study centre

The study centre was designated a UK test site for ERAS in liver surgery supported by the UK Department of Health.

ERAS design

The ERAS pathway applied to those patients undergoing peri-hilar CCA resection required modification on an individual patient basis from the standard hepatectomy pathway applied in non-CCA resection. The standard ERAS pathway has been previously described in the literature (Fig. 1).

Pre-operative assessment and risk stratification

The integrated ERAS liver pathway commences at the supraregional hepatobiliary specialist multi-disciplinary team (MDT) meeting where those patients with potentially resectable peri-hilar CCA are identified.

Preoperative assessment included a clinical review by a single lead anaesthetist, and a preoperative cardio-pulmonary exercise test (CPET). Patients were classified as low, intermediate or high risk by a dedicated hepatobiliary consultant anaesthetist in conjunction with CPET outcome. All patients with a relative oxygen uptake <11 ml/kg/min on CPET were classified as high risk [12].

Patients with obstructive jaundice underwent pre-operative biliary drainage with either endoscopic retrograde cholangiopancreatography and metallic stenting or a percutaneous transhepatic approach. Where indicated, biliary drainage was undertaken prior to CPET assessment. Adequate drainage of the future liver remnant was undertaken to reduce the risk of postoperative hepatic failure (PHF) [13].

Staging laparoscopy was undertaken in all patients to exclude the presence of radiologically occult metastases [14]. All resected patients were admitted electively to level 2 or 3 care on completion of resectional surgery.

Anaesthetic management

Patients could eat and drink until 6 h pre-operatively, with clear fluids up until 2 h before surgery. All patients underwent a thoracic epidural (unless contraindicated). Two large bore cannula, internal jugular central venous lines and urinary catheter were used prior to incision.

An arterial line with cardiac output monitoring was used to guide fluid management and perfusion optimization. The pulse contour continuous cardiac output (PiCCO) was employed for all resections.

Low central venous pressures were achieved with a combination of thoracic epidural, fluid restriction, and nitrate infusion as required. All patients received prophylactic intravenous antibiotics. Hypothermia was prevented using routine intra-operative monitoring and air warming systems. Calf compression stockings and devices were used throughout for venous thrombotic prophylaxis. Optimal glycaemic control was ensured throughout.

Surgical procedure

A reverse L-shaped incision was used in all cases. Frozen sections of proximal and distal bile duct resection margins were sent for histopathological analysis prior to completion of resection. Liver parenchyma was transected with Cavitron Ultrasonic Surgical Aspirator, with or without intermittent inflow occlusion. Biliary reconstruction encompassed retrocolic hepatico-jejunosotomy formation and a jejuno-jejunostomy. Blakes drains were routinely used in all patients. Where portal venous or arterial resection was indicated, IV unfractionated heparin was administered for 48 h or until conversion to low molecular weight heparin on the critical care unit.

Post-operative analgesia

Epidural analgesia was delivered using Levobupivacaine 0.1% and Fentanyl 2mcg via thoracic epidural. Ideally this was discontinued by the 3rd post-operative day with application of a single Fentanyl patch to facilitate transition to oral analgesia. The dedicated pain management team supported all pain management.

Peri-operative care plan

Patients were admitted on the morning of surgery unless this was precluded by clinical or social circumstances. Patients were considered eligible for discharge when tolerating full oral dietary intake, pain control was adequate, passing flatus and urine satisfactorily, and demonstrating normal clinical and acceptable biochemical indices (daily routine blood tests were tailored according to patient progress). Patients had to be deemed independently mobile and safe for discharge by both the ward nursing staff and physiotherapist ensuring all discharge criteria were met. Adherence to all ERAS components were documented in the case notes. All patients were followed up in the hepatobiliary outpatient clinic within 1 week of discharge. All patients received specialist nurse telephone clinic appointment follow-up after discharge.

Data collection and statistical analysis

Standard demographic and clinico-pathological data were retrieved from paper and electronic case notes on each patient.

Data collected included preoperative assessment (including cardiopulmonary exercise testing), operative factors, duration of critical care, duration of inotropes/vasopressors, duration of epidural analgesia, post-operative mobilization (sat out of bed at

Time Point	Goals
Referral	Discussion of referral and review of imaging in MDT
First clinic appointment	Patient education, discussion of full care pathway Discussion of operative intervention and associated risks/complications
Pre-operative assessment	Cardiopulmonary exercise testing Assessment in pre-operative assessment clinic Review by dedicated liver anaesthetist
Day of admission	Review of operative intervention Review of expectations of enhanced recovery
Surgery	Minimize use of drains No use of nasogastric drainage Selective critical care admission
Post-operative Day 1	Sat out of bed at least 8 hours 4 walks of 30m or more Respiratory physiotherapy review Review by acute pain team Commence full diet as tolerated Discharge planning meeting
Post-operative Day 2	Maintain oral intake If epidural in use place Fentanyl patch (25 mcg/hr) at 22:00 If PCA aim to convert to oral analgesia Sat out of bed at least 8 hours 4 walks of 40m or more
Post-operative Day 3	Removal of epidural analgesia Discontinue supplemental oxygen if saturations within normal range Maintain oral intake Sat out of bed at least 8 hours 4 walks of 60m or more Plan discharge
Post-operative Day 4-6	Maintain oral intake Sat out of bed at least 8 hours 4 walks of 60m or more Discharge if: Tolerating full oral intake Pain adequately controlled Passing flatus and urine normally Normal routine observations Independently mobile and deemed safe for discharge Patient and family happy to proceed to discharge
Day 1 post-discharge	Phone review with cancer specialist nurse

Fig. 1. Standard hepatectomy ERAS pathway.

least 8 h, 4 walks of 30 m or more), duration of urinary catheterization, duration of nasogastric drainage and restoration and maintenance of enteral nutrition as tolerated, use of surgical and radiological drains, complications, discharges and 30 day re-admissions.

Complications were stratified using the Dindo-Clavien system [15]. Major complication was defined as having complication Grade IIIa or above.

To identify achievable ERAS targets, statistical analyses compared outcomes in those who experienced major complications with those who experienced minor or no complications at all. An achievable ERAS target was considered as the median achieved in those patients without a major postoperative complication.

To determine the applicability of ERAS to higher risk patients a separate analysis examined their achievement of these ERAS targets. All statistical analyses were undertaken using IBM SPSS Statistics (version 25) software. Continuous variables were analysed with Mann Whitney *U* test and categorical data with Chi-Square test. Continuous data is presented as medians with range and interquartile range (IQR).

Results

Study cohort

60 patients underwent resection of peri-hilar cholangiocarcinoma. Patients had a median age of 65 years (range 54–76 years) and were evenly distributed between gender (32 male and 28 female). Disease demographics and operative approaches are described in Table 1.

Preoperative biliary drainage of the future remnant liver was undertaken in the majority of patients (54 of 60).

Resection of the portal vein was undertaken in 20 of 60 patients. R0 resection margin was achieved in 45 of 60 of cases (75%).

There were ten inpatient deaths, eight of these occurring in patients who underwent extended parenchymal resection with portal vein resection.

Complications are outlined in Table 2.

Four further patients were excluded from ERAS analysis due to incomplete datasets.

46 patients completed the ERAS pathway with full datasets and

Table 1
pCCA patient and disease demographics.

Characteristic	Value (n = 60)
Sex, no (%)	
-Female	28 (47%)
-Male	32 (53%)
Age (median)	65
ASA	
1–2	48 (80%)
3–4	12 (20%)
Preop drainage, no (%)	54 (90%)
Anaerobic Threhold, median (range) mls/kg/min	11.7 (7.6–25.1)
Operation type, no (%)	
-Radical bile duct resection	11 (18%)
-Left hemihepatectomy, seg 1 + Extra-hepatic Bile Duct (EHBD) Resection	13 (22%)
-Right hemihepatectomy, seg 1 + EHBD	6 (10%)
-Left trisectionectomy, seg 1 + EHBD	15 (25%)
-Right trisectionectomy, seg 1 + EHBD	15 (25%)
Portal vein resection, no (%)	20 (33%)
T stage, no (%)	
-T1	9 (15%)
-T2	42 (70%)
-T3	7 (12%)
-T4	2 (3%)
N stage, no (%)	
-N0	38 (63%)
-N1	22 (37%)
R0 margin, no (%)	45 (75%)
Grade, no (%)	
-Poor	14 (23%)
-Moderate	31 (52%)
-Well	16 (27%)
Lymphovascular invasion, no (%)	29 (48%)
Perineural invasion, no (%)	51 (85%)

underwent further analysis. 20 (44%) were classified as high risk on pre-operative CPET.

Morbidity

Major complications (Clavien-Dindo $\geq$ IIIa) occurred in 18 patients (39%). 22 patients experienced minor complications (Clavien-Dindo $\leq$ IIa). 6 patients had a complication free index admission.

ERAS parameters

Achievements of key ERAS parameters are demonstrated in Table 3. An achievable ERAS pathway in pCCA resection based on those patients who developed minor complications or had a complication free admission is summarised in Fig. 2.

Table 2
Complications.

Grade	Complications before 90 days
Grade 2	
Sepsis requiring IV antibiotics	38
Bile leak without IR drainage	12
Ascites (medically managed)	7
Acute coronary syndrome	3
Thromboembolic event	3
Grade 3	
Abdominal abscess with IR drainage	7
Bile leak with IR drainage	6
Repeat laparotomy	4
Grade 4	
Multi-organ dysfunction syndrome	10

Critical care admission

Median duration of admission to high dependency/intensive care unit was 3 days (range 1–21 days, IQR 2–5 days). Examining those patients without major complications, the median critical care duration reduced significantly to 2 days (range 1–7 days, IQR 2–4 days, p = 0.002).

Inotropic support

Median duration of inotropic/vasopressor support was 12 h (range 6–60 h, IQR 6–36 h). In those without major complications, duration of inotropic support was significantly less (median 6 h, range 0–48 h, IQR 0–24 h, p = 0.003).

Epidural analgesia

Median duration of epidural analgesia was 72 h (range 24–120 h, IQR 72–96 h) with no significant difference observed in those without major complications (median 72 h, range 48–96 h, IQR 72–96 h, p = 0.294).

Mobilization

Median time to sitting out of bed >8 h was 2 days (range 1–4 days, IQR 1–2 days). In patients who did not experience major complications this reduced to post-operative day 1 (range 1–4 days, IQR 1–2 days) but did not achieve statistical significance (p = 0.156).

The median time to patients achieving 4 walks of 30 m was 4 days (range 2–11, IQR 3–4 days). In the subgroup without major complications this improved significantly to 3 days (range 1–6 days, IQR 3–4 days, p = 0.042).

Table 3
Achievement of key ERAS targets.

ERAS Parameter (Median time to achievement/IQR)	Full cohort	Major complication subgroup	Minor/no complication subgroup	Significance (Mann-Whitney *U* test)	High risk cohort	Low risk cohort	Significance (Mann-Whitney *U* test)
Critical care admission	3 days [2–5]	5 days [3–7]	2 days [2–4]	P = 0.002	4 days [3–7]	2 days [1–3]	p = 0.008
Inotropic/vasopressor support	12 h (0–24)	24 h (24–48)	6 h (0–24)	P = 0.003	24 h (0–48)	12 h (0–24)	p = 0.258
Epidural duration	72 h (72–96)	96 h (72–96)	72 h (72–96)	P = 0.294	3 days [3,4]	3 days [3,4]	p = 0.197
Urinary catheterization duration	4 days [3–6]	6 days [4–10]	4 days [3–5]	P = 0.001	2 days [1,2]	2 days [1,2]	p = 0.656
Time to sitting out of bed >8 h	2 days [1,2]	2 days [1–3]	1 day [1,2]	P = 0.156	4 days [3–5]	3 days [3,4]	p = 0.177
Time to full mobilization	4 days [3,4]	4 days [3–6]	3 days [3,4]	P = 0.042	5 days [3–8]	4 days [3–5]	p = 0.407
Duration of nasogastric drainage	1 day [1–3]	1 day [1–6]	1 day [1,2]	P = 0.422	1 day [1–5]	1 day [1,2]	p = 0.139
Time to restoration of enteral nutrition	2 days [2–4]	2 days [2,3]	2 days [2–4]	P = 0.881	2 days [2–4]	2 days [1–3]	p = 0.197
Length of stay	13.5 days (8–21)	23 days (18–46)	8 days [6–13]	P = 0.00001	14 days (8–27)	8 days [7–16]	p = 0.095

Urinary catheterization

Median duration of urinary catheterization was 4 days (range 3–30 days, IQR 3–6 days), which in those without major complications was largely unchanged (median 4 days, range 3–6 days, IQR 3–5 days, p = 0.001) despite achieving statistical significance.

Restoration of enteral nutrition

Median duration of nasogastric drainage was 1 day (range 1–30, IQR 1–3 days) and unchanged in those without major complications (median 1 day, range 1–10 days, IQR 1–2 days day, p = 0.422).

Median time to enteral feeding (full diet as tolerated) was post-operative day 2 (range 1–11, IQR 2–4 days). In those without major complications, this remained 2 days (range 1–7 days, IQR 2–4 days, p = 0.881).

11 patients had temporary ileus requiring further nasogastric drainage.

Surgical drainage

Drains were inserted in all patients at surgery and cannot represent an enhanced recovery target. 23 of the 46 patients (50%) were discharged with surgical drains in situ, with subsequent removal at the outpatient clinic.

Length of stay

Median length of stay for the entire cohort was 13.5 days (range 5–76 days, IQR 8–21 days). In those without major complications this reduced significantly to 8 days (range 5–17 days, IQR 6–13 days, p = 0.001).

30-day readmission

The 30-day readmission rate was 9/46 (20%). Indications for readmission included sepsis in 4 patients (1 collection required radiological drainage) and hepatic artery pseudo-aneurysm formation in 2 patients (stented successfully). 3 additional patients were readmitted for liver insufficiency, poor oral intake and anaemia respectively.

High risk patients

Comparative analysis of ERAS achievement in the pre-operative CPET determined high and low risk cohort, demonstrated no significant difference in the majority of key ERAS targets (Table 3).

However, patients considered high risk on pre-operative CPET required significantly longer critical care admission (median 4 days, range 2–21 days, IQR 3–7 days) than those deemed low risk (median 2 days, range 1–7 days, IQR 1–3 days) (p = 0.008).

High risk patients required longer duration of inotropic/vasopressor support (median 24 h, range 12–60 h, IQR 12–48 h) compared to low risk patients (median 12 h, range 0–48 h, IQR 0–24 h), however this did not achieve statistical significance (p = 0.258).

High risk patients had a trend towards longer duration of inpatient length of stay (median 14 days, IQR 8–27 days, compared to 8 days in low risk patients, IQR 7–16 days) but this was not statistically significant (0.095).

Discussion

Enhanced recovery after resection for peri-hilar cholangiocarcinoma is achievable, and targets have been defined (Table 3). ERAS principles can be applied to both high and low risk anaesthetic groups and those who develop major and minor complications. Morbidity following pCCA resection is high and adjustments for this must be incorporated into ERAS care.

pCCA patients require significant pre-operative work-up. The ERAS pathway begins at the time of decision to operate. We utilized CPET outcome to stratify patients as high or low risk and successfully identified those patients requiring increased critical care admission.

Patients who develop major complications and those at higher pre-operative risk as defined by CPET, [16] require a tailored approach and expectations of ERAS target achievement should be lower. These patients required longer inotropic support and prolonged critical care admission with increased length of inpatient stay. Crucially, ERAS remains achievable across the remaining core components and being deemed high risk pre-operatively or the development of a complication should not preclude engagement with ERAS pathways.

Effective pain management is fundamental to successful enhanced recovery. Epidural usage reduces the need for systemic opioids and reduced impairment of gut motility [17]. Our findings are in keeping with this. The incidence of ileus was low. Early commencement of oral clear fluid and diet in a stepwise fashion is feasible.

Adherence to early mobilization is key to successful enhanced recovery following standard liver resection.[10] Early mobilization is achievable by sitting patients out of bed at day 2 and mobilizing at day 3–4 (when appropriate). Early removal of urinary catheters may help facilitate this.

Biliary anastomoses above the confluence are high risk for anastomotic leak [18]. Surgical drains were used in all patients and

Time Point	Goals
Referral	Discussion of referral and review of imaging in MDT Referral for biliary drainage if required
First clinic appointment	Patient education, discussion of full care pathway Discussion of operative intervention and associated risks/complications
Pre-operative assessment	Cardiopulmonary exercise testing Assessment in pre-operative assessment clinic Review by dedicated liver anaesthetist
Day of admission	Review of operative intervention Review of expectations of enhanced recovery
Surgery	Thoracic epidural (unless contraindicated) Routine nasogastric drainage and surgical drains for all patients Routine PiCCO intra-operative monitoring Critical care admission for all patients (Level II/III as required +/- inotropic support)
Post-operative Day 1	Review of inotropic support (if indicated) Review +/- removal of nasogastric tube Sat out of bed at least 8 hours where feasible Respiratory physiotherapy review Review by acute pain team Commence oral fluids as tolerated Daily review of drain output
Post-operative Day 2	Commence full oral intake as tolerated Place Fentanyl patch (25 mcg/hr) at 22:00 Critical care discharge planning review Continue respiratory physiotherapy and pain team review Sat out of bed at least 8 hours
Post-operative Day 3	Removal of epidural analgesia Discontinue supplemental oxygen if saturations within normal range Maintain oral intake as tolerated Sat out of bed at least 8 hours 4 walks of 30m or more Plan to remove urinary catheter if adequately mobile Arrange discharge to elective hepatobiliary ward where appropriate
Post-operative Day 4-8	Maintain oral intake Remove surgical drains when output satisfactory 4 walks of 40m or more Increase mobilization to 4 walks of 60m or more

Fig. 2. ERAS pathway for peri-hilar cholangiocarcinoma resection.

therefore cannot be considered an ERAS target. Minor bile leak was prevalent with the surgically placed drain providing adequate control. Patients were safely discharged home when medically fit with surgical drains in situ reducing length of stay without impact on 30-day readmission.

Length of stay is an objective component for measuring the success of an ERAS program [19]. We have demonstrated a safe and achievable discharge at 8 post-operative days in patients with minor or no complications, without impact on readmission rate.

This is the first study to examine ERAS in peri-hilar CCA resection and defines achievable enhanced recovery pathway parameters. This retrospective study was undertaken in an established ERAS centre. We did not seek to demonstrate superiority of ERAS to standard post-operative care in minimizing complications. Prospective randomised studies with increased patient numbers would further elucidate the potential benefits of ERAS in this complex cohort.

Enhanced recovery should be considered for all peri-hilar cholangiocarcinoma patients undergoing resection. Patients deemed high risk on pre-operative assessment or those who develop major complications may require increased critical care admission, cardiovascular support and overall length of stay, but should not be precluded from ERAS enrolment. ERAS standards have been defined which take into account development of minor complications. These standards are safe, achievable and should be applied.

Conflicts of interest statement

The authors declare no conflict of interest for the submitted paper.

Funding

No sources of funding.

References

[1] Coelen RJ, Huiskens J, Olthof PB, Roos E, Wiggers JK, et al. Compliance with evidence-based multidisciplinary guidelines on perihilar cholangiocarcinoma. United European Gastroenterol J 2017 Jun;5(4):519–26.

[2] Spanjersberg WR, Reurings J, Keus F, van Laarhoven CJ. Fast track surgery versus conventional recovery strategies for colorectal surgery. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007635.
[3] Hall TC, Dennison AR, Bilku DK, Metcalfe MS, Garcea G. Enhanced recovery programmes in hepatobiliary and pancreatic surgery: a systematic review. Ann R Coll Surg Engl 2012 Jul;94(5):318–26.
[4] Dunne DF, Yip VS, Jones RP, McChesney EA, Lythgoe DT, et al. Enhanced recovery in the resection of colorectal liver metastases. J Surg Oncol 2014 Aug;110(2):197–202.
[5] Jones C, Kelliher L, Dickinson M, Riga A, Worthington T, et al. Randomised clinical trial on enhanced recovery versus standard care following open liver resection. Br J Surg 2013;100(8):1015–24.
[6] Ni CY, Yang Y, Chang YQ, Cai H, Xu B, et al. Fast-track surgery improves postoperative recovery in patients undergoing partial hepatectomy for primary liver cancer: a prospective randomized controlled trial. Eur J Surg Oncol 2013 Jun;39(6):542–7.
[7] Ahmed EA, Montalti R, Niccolini D, Vincenzi P, Coletta M, et al. Fast track program in liver resection: a PRISMA compliant systematic review and meta-analysis. Medicine (Baltim) 2016;95(28):e4154.
[8] Coolsen MM, Wong-Lun-Hing EM, van Dam RM, van der Wilt AA, Slim K, et al. A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. HPB 2013 Apr;15(4):245–51.
[9] Melloul E, Hübner M, Scott M, Snowden C, Prentis J, et al. Guidelines for perioperative care for liver surgery: enhanced recovery after surgery (ERAS) society recommendations. World J Surg 2016 Oct;40(10):2425–40.
[10] Yip VS, Dunne DF, Samuels S, Tan CY, Lacasia C, et al. Adherence to early mobilisation: key for successful enhanced recovery after liver resection. Eur J Surg Oncol 2016 Oct;42(10):1561–7.
[11] Bismuth H, Nakache R, Diamond T. Management strategies in resection for hilar cholangiocarcinoma. Ann Surg 1992 Jan;215(1):31–8.
[12] Older P, Hall A. Clinical review: how to identify high-risk surgical patients. Crit Care 2004 Oct;8(5):369–72.
[13] Kennedy TJ, Yopp A, Qin Y, Zhao B, Guo P, et al. Role of preoperative biliary drainage of liver remnant prior to extended liver resection for hilar cholangiocarcinoma. HPB 2009 August;11(5):445–51.
[14] Bird N, Elmasry M, Jones R, Elniel M, Kelly M, et al. Role of staging laparoscopy in stratification of patients with perihilar cholangiocarcinoma. Br J Surg 2017;104(4):418–25.
[15] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
[16] Dunne DF, Jones RP, Lythgoe DT, Pilkington FJ, Palmer DH, et al. Cardiopulmonary exercise testing before liver surgery. J Surg Oncol 2014 Sep;110(4):439–44.
[17] Nimmo SM, Foo ITH, Paterson HM. Enhanced recovery after surgery: pain management. J Surg Oncol 2017 Oct;116(5):583–91.
[18] Kadaba RS, Bowers KA, Khorsandi S, Hutchins RR, Abraham AT, et al. Complications of biliary-enteric anastomoses. Ann R Coll Surg Engl 2017 Mar;99(3):210–5.
[19] Neville A, Lee L, Antonescu I, Mayo NE, Vassiliou MC, et al. Systematic review of outcomes used to evaluate enhanced recovery after surgery. Br J Surg 2014 Feb;101(3):159–70.