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

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ABSTRACT

*Background and aim:* Aim of the study was to assess the impact of ERAS approach ("fluid restrictive and drainless") on open liver resections for HCC comparing their outcome with open resections in pre-ERAS period and with laparoscopic surgery.
*Study design:* 207 patients undergoing minor liver resection for HCC were divided into three groups: Group A, open minor resections in pre-ERAS period (95 patients); Group B, laparoscopic ERAS resections (55 patients); Group C, open ERAS resections (57 patients).
*Results:* Blood loss was lower in group C and B compared with group A. Postoperative morbidity was 26.5% in group A, 16.3% in group B and 12.1% in group C ($p < 0.05$). Ascites was less frequent in group B (7.5%) and C (6.2%) compared with group A (12%). Median time for functional recovery in group B (3 days) and C (3 days) was shorter compared with group A (5 days).
*Conclusions:* Laparoscopic approach confirms to be associated with reduced blood loss and postoperative morbidity. In patients who cannot be candidates to minimally-invasive approach, ERAS management seems to allow blood loss and postoperative morbidity reduction: indeed, results achieved in this group of patients are more similar to those of laparoscopy than to pre-ERAS open surgery.


## 1. Introduction

Over the last two decades laparoscopic surgery has evolved to became the approach of choice for many abdominal procedures, including liver resections (LR) [1–3]. Patients with hepatocellular carcinoma (HCC) have the most outstanding benefits from laparoscopic liver resection (LLR) in terms of intraoperative blood loss and postoperative morbidity reduction and postoperative length of stay shortening, mainly as a result of a decreased impact of surgery on wall portosystemic shunts [4–6]. Nevertheless, the type of surgery/procedure itself is not the only variable that influences recovery and hospital length of stay. Indeed, the widespread of minimally-invasive liver surgery has not only contributed to the evolution of the surgical technique but also innovation of patients management. The application of multimodal perioperative care protocols initially adopted in minimally-invasive surgery and commonly referred as fast track or enhanced recovery programmes (Enhanced Recovery After Surgery, ERAS) has achieved significant improvements in the outcome of variety of surgical procedures [7]. Targeting factors that delay postoperative recovery (pain, gut dysfunction and immobility) and combining a series of interventions to reduce peri-operative stress and organ dysfunction, such programmes have shown to accelerate postoperative recovery and reduce length of stay, without affecting rate of postoperative complications [8]. Thanks to encouraging results, together with recent development in surgical field, many elements of ERAS programme have been more widely introduced into many tertiary centres performing hepatobiliary surgery worldwide and applied even to conventional open surgery [9,10]. Patients affected by HCC, requiring liver resection but unsuitable for laparoscopy, might benefit from fast-track management since they have a baseline higher risk of postoperative complications due to peri-operative stress, but no specific report exists. Primary endpoint of the study was to assess the impact of ERAS approach ("fluid restrictive and drainless") in

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patients undergoing open LR for HCC comparing their short term outcome with patients undergoing open resection in pre-ERAS period and with patients undergoing laparoscopic surgery. Secondary endpoint was to assess overall impact of ERAS management (both in open and laparoscopic surgery) on perioperative outcome of patients with HCC.

## 2. Materials and methods

### 2.1. Study population

From January 2004 to May 2014, 1583 hepatic resections were performed at the Hepatobiliary Surgery Division of San Raffaele Hospital in Milano, with a programme of laparoscopic liver resection starting in 2005 (ERAS management on principle) and introduction of fast-track management protocols for all resections in 2011. 364 (23%) resections were performed in patients affected by HCC and, among these, 249 were minor resections. Re-resections were excluded from analysis as well as hepatic resections combined to other major abdominal procedures (e.g. biliary-enteric anastomosis), so that study population consisted of 207 patients undergoing as many procedures.

Patients were divided in three groups according to perioperative management protocol and to surgical approach. In particular Group A consisted of 95 patients undergoing open LR in pre-ERAS period, Group B consisted of 55 patients undergoing minor LLR and Group C was composed of 57 patients undergoing open LR in ERAS period. Breakdown of patients inclusion within years is shown in Fig. 1.

### 2.2. Preoperative workup

Preoperative assessment included standard liver function tests (to assess Child Pugh classification) and serum tumour markers, abdominal ultrasonography, thoracoabdominal imaging. Patients who were potential candidates for LR were systematically evaluated at weekly multidisciplinary meetings, including liver surgeons, radiologists and medical oncologist to define the final indication for the surgical procedure and both the type and the resection technique.

### 2.3. Surgical technique

Laparotomy was performed through a right subcostal extended to midline incision. For laparoscopic resections the patient was placed in the "French" position, with the first surgeon standing between the patient's legs, with one assistant on each side. Usually a 4-trocar configuration was used with a 15-mm port for 30° laparoscope. Hepatic transection was performed using the Sono-Surg system (Olympus, Tokyo, Japan) that integrates both the ultrasonic coagulating cutter and the conventional ultrasonic dissector [11]. Pringle's manoeuvre was used on demand to control intraoperative bleeding.

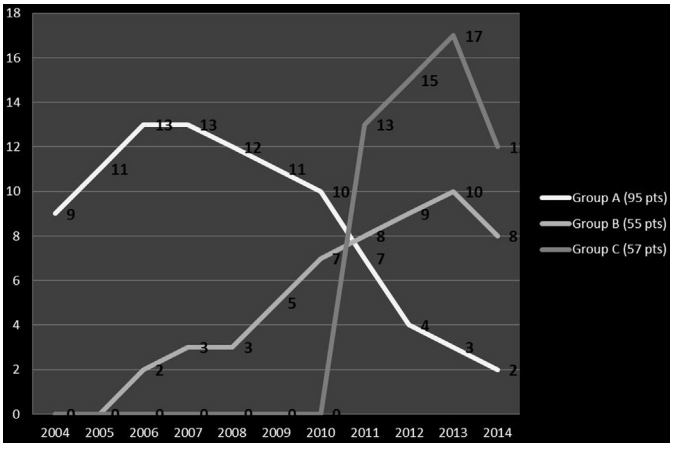


**Fig. 1.** Breakdown of patients inclusion according to year, stratified per Group.

### 2.4. Perioperative management

The ERAS multimodal evidence-based recovery protocol was adapted from the initial model to elective liver surgery [9], with the main goal to enhance functional recovery. Definition of functional recovery was based on the following criteria (when all are met, the patient is considered functional recovered):

- Adequate pain control with oral analgesics.
- Independently mobile (mobile at preoperative level).
- Tolerance of solid food: fluid and solid food intake is monitored and must be returned to normal tolerance level. Tolerance is considered to be normal when oral intake of water or normal food is resumed and continued for at least 24 h. Furthermore prophylaxis of postoperative nausea and vomiting (PONV), which obviously influences the intake, is always performed.
- Normal or decreasing serum bilirubin.
- No intravenous fluids.

### 2.5. Outcome evaluation

Data regarding general characteristics of patients and disease were recorded. Intraoperative and postoperative outcome were evaluated, including morbidity and mortality. Postoperative complications were reviewed for 90 days following liver resection and were graded retrospectively according to Dindo-Clavien classification of surgical complications [12]. Postoperative mortality was defined as any death during postoperative hospitalization or within 90 days after resection. PLF was defined according to ISGLS definition [13].

Specific issue regarding ERAS management (nasogastric tube and drainage placement, oral feeding, mobilization, bowel canalization, adequate pain control with oral analgesics, time for functional recovery, agreement for discharge, rate of readmission, length of stay) were also collected and analyzed.

### 2.6. Statistical analysis

Demographic, pathologic, operative details, and surgical outcomes between groups were compared using the $\chi^2$ test or Fisher's exact test for categorical data and the Mann–Whitney $U$ test for ordinal data. All data were expressed as mean plus the standard deviation or median and range. Significance was defined as $p < 0.05$. All analyses were performed using the statistical package SPSS 18.0 (SPSS, Chicago, IL, USA).

## 3. Results

### 3.1. Patients and disease characteristics

Patients and disease characteristics are summarized in Table 1. All the patients in Group A had Child A liver function, while a minority was Child B in Groups B and C (respectively 7.3% and 3.5%). A different distribution of lesions within liver segments was recorded comparing the three groups: in particular lesions in laparoscopic segments (II-III-IVb-V-VI) were 44.2% in Group A, 94.5% in Group B and 3.5% in Group C ($p = 0.043$).