Evaluation of a fast-track programme for patients undergoing liver resection

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Background: Recent developments in perioperative pathophysiology and care have documented evidence-based, multimodal rehabilitation (fast-track) to hasten recovery and to decrease morbidity and hospital stay for several major surgical procedures. The aim of this study was to investigate the effect of introducing fast-track principles for perioperative care in unselected patients undergoing open or laparoscopic liver resection.

Methods: This was a prospective study involving the first 100 consecutive patients who followed fast-track principles for liver resection. Catheters and drains were systematically removed early, and patients were mobilized and started eating and drinking from the day of surgery. An opioid-sparing multimodal pain treatment was given for the first week. Discharge criteria were: pain sufficiently controlled by oral analgesics alone, patient comfortable with discharge and no untreated complications.

Results: Median length of stay (LOS) for all patients was 5 days, with 2 days after laparoscopic versus 5 days following open resection \((P < 0.001)\). Median LOS after minor open resections (fewer than 3 segments) was 5 days versus 6 days for major resections (3 or more segments) \((P < 0.001)\). Simple right or left hemihepatectomies had a median LOS of 5 days. The readmission rate was 6.0 per cent and 30-day mortality was zero.

Conclusion: Fast-track principles for perioperative care were introduced successfully and are safe after liver resection. Routine discharge 2 days after laparoscopic resection and 4–5 days after open liver resection may be feasible.

Introduction

Recent developments in perioperative pathophysiology and care indicate that multimodal rehabilitation (fast-track surgery or enhanced recovery programmes) hasten recovery and decrease morbidity and hospital stay following several major surgical procedures⁴–⁸. Key elements involve preoperative patient information, short-acting general anaesthetic agents, limited use of catheters, drains and tubes, opioid-sparing analgesia, and enforced early mobilization and oral nutrition.

Liver surgery has traditionally been regarded as major surgery, and liver resections accepted as high-risk procedures undertaken in specialist centres. There are few published data for intended enhanced recovery after liver resection⁹,¹⁰. In a Danish national study (2002–2007) the median length of stay (LOS) after liver resection was 9 days and that after right hemihepatectomy 15 days¹¹.

Shorter LOS has been reported after laparoscopic liver resection, but it is unclear whether this is due to the minimally invasive technique or whether a similar decrease in LOS can be reached following open surgery with an optimized fast-track programme¹²,¹³. These fast-track principles are also needed to achieve the full potential for fast recovery in laparoscopic operations for gastrointestinal cancers¹⁴.

The aim of this study was, in a prospective setting, to investigate the effect of multimodal rehabilitation in unselected patients having a liver resection of any type,
Fast-track programme after liver resection

The primary endpoints were patient safety and LOS.

Methods

From January 2011, fast-track principles for liver resections were introduced and a prospective study involving the first 100 consecutive patients was performed. All patients had surgery in a high-volume hepatobiliary unit, Rigshospitalet, University of Copenhagen, acting as a tertiary referral centre for the eastern part of Denmark (2·3 million people). The centre has an annual volume of more than 200 resections, mostly for colorectal cancer liver metastases (CRLM).

All patients who had been informed of the protocol by a clinical project nurse before admission were included. The only exclusion criteria were limitations in project nurse capacity or hilar cholangiocarcinoma, because of the necessity of hepaticojejunostomy for biliary reconstruction. Included patients who were not resected, because their disease was more widespread than expected, were excluded and replaced by the next consecutive patient who had a resection undertaken. If a laparoscopic operation was converted to open surgery, the patient changed category to open resection.

Liver resections were categorized as laparoscopic (non-anatomical wedge resections, or resection of 1 or 2 segments), minor open resection (fewer than 3 segments including multiple non-anatomical resections) or major open resections (3 or more segments). New standard operation procedures were introduced for each category (Table 1). A transverse incision in the right upper quadrant extended upwards in the midline was used for open resections. If possible, an upper midline incision was used for resections within or confined to the left lateral segment.

All patients were informed about the planned operation by a liver surgeon in the outpatient clinic. Clinical project nurses then systematically informed patients about the optimized perioperative care; patients were seen at least once by a project nurse after surgery and again in the outpatient clinic as close as possible to postoperative day (POD) 10, and were then followed up twice by telephone calls before receiving any chemotherapy.

Patients received a well defined multimodal pain treatment for 1 week, including 1 g paracetamol every 6 h (individual prescription in the major open resection group), 200 mg celecoxib every 12 h, and 300 mg gabapentin in the morning and 600 mg in the evening. All patients, except those in the laparoscopic group, had epidural analgesia (Th8–Th9, bupivacaine and morphine) for 0–48 h after surgery (from POD 0 to the morning of POD 3).

The focus of the anaesthetic procedure was to secure sufficient perfusion of vital organs while minimizing blood loss. Central venous pressure below 6 mmHg was achieved by 10° reverse Trendelenburg, pharmacological intervention with glyceryl trinitrate, and fluid restriction. Monitoring of vital signs included cardiac output, central venous saturation, central venous pressure, urine output and invasive arterial blood pressure recording15–17.

Patients were discharged to the ward and mobilized from POD 0, except for those having the most advanced open resections and patients with an American Society of Table 1 Standard perioperative care principles for the three categories of liver resection

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic resection</th>
<th>Minor open resection</th>
<th>Major open resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidural analgesia</td>
<td>No</td>
<td>POD 0–3 morning</td>
<td>POD 0–3 morning</td>
</tr>
<tr>
<td>Analgesics: gabapentin + celecoxib + paracetamol</td>
<td>Yes (local analgesia in incisions)</td>
<td>Yes</td>
<td>Yes (paracetamol: individual assessment)</td>
</tr>
<tr>
<td>Nasogastric tube removed</td>
<td>Yes</td>
<td>Optional</td>
<td>Mandatory (out POD 1)</td>
</tr>
<tr>
<td>immediately after surgery</td>
<td></td>
<td>POD 0</td>
<td>Optional stay in perioperative department POD 0</td>
</tr>
<tr>
<td>Abdominal drain</td>
<td>No</td>
<td>POD 0</td>
<td>POD 0</td>
</tr>
<tr>
<td>Sent to ward</td>
<td></td>
<td>Optional POD 0</td>
<td>Mandatory (out POD 1)</td>
</tr>
<tr>
<td>Removal of urinary catheter</td>
<td>POD 0</td>
<td>POD 1 (morning)</td>
<td>POD 0</td>
</tr>
<tr>
<td>Peripheral intravenous catheter</td>
<td>Closed POD 0</td>
<td>Closed POD 0</td>
<td>POD 1</td>
</tr>
<tr>
<td>Routine blood tests</td>
<td>Removed POD 1</td>
<td>Removed POD 1</td>
<td>Removed POD 1</td>
</tr>
<tr>
<td>Laxatives: chewing gum (1/2 h t.i.d.) + magnesia 1 g</td>
<td>POD 1</td>
<td>POD 1</td>
<td>POD 1–3</td>
</tr>
<tr>
<td>Mobilization</td>
<td>POD 0: out of bed &gt; 2 h</td>
<td>POD 0: out of bed 2 h</td>
<td>POD 0: out of bed 2 h</td>
</tr>
<tr>
<td>Discharge</td>
<td>POD ≤ 1: out of bed &gt; 8 h + walking exercise t.i.d.</td>
<td>POD ≤ 1: out of bed &gt; 8 h + walking exercise t.i.d.</td>
<td>POD ≤ 1: out of bed &gt; 8 h + walking exercise t.i.d.</td>
</tr>
<tr>
<td></td>
<td>Aim at discharge POD 2–3</td>
<td>Aim at discharge POD 5</td>
<td>Aim at discharge POD 5</td>
</tr>
</tbody>
</table>

POD, postoperative day; t.i.d., three times daily.
Anesthesiologists physical status of 3, who were managed in a high-dependency unit on the first postoperative night. All patients were encouraged to drink and eat from POD 0. The aim was to achieve discharge at POD 3 (approximately 72 h) following laparoscopic resection and POD 5 after open resection, although earlier discharge was an option in all groups. Criteria for discharge were: pain sufficiently controlled by oral analgesics, patient comfortable with discharge and no untreated surgical complications. Assessment of pain was done at rest and activity at POD 1 and POD 3, using a 100-mm visual analogue scale (VAS)\(^{18}\).

Complications were graded I – V according to the Dindo – Clavien classification\(^{19}\).

### Statistical analysis

Continuous data are expressed as median (range). The Mann–Whitney U test was used to compare groups. Data were analysed using SPSS\(^{®}\) version 19-0 for Windows\(^{®}\) (IBM, Armonk, New York, USA) and SigmaStat\(^{®}\) version 3-1 (Systat Software, Chicago, Illinois, USA). \(P < 0.050\) was considered statistically significant.

### Results

The first 100 consecutive included patients underwent surgery and were discharged between the beginning of January and the end of August 2011. Patient demographics and the types of resection performed are shown in Tables 2 and 3. Six intended laparoscopic resections were converted to open resections and were included in the minor open resection group.

Median postoperative LOS after laparoscopic resection was 2 days, compared with a median of 5 days for open resection \((P < 0.001)\). Median LOS after minor open and major open resections was 5 and 6 days respectively \((P < 0.001)\). Some 67.0 per cent of all patients were discharged on POD 5 or earlier.

When extensive procedures were excluded (central resections, extended right and left hepatectomies, hepatectomy in combination with other resections or radiofrequency ablation (RFA) of the other hemiliver), patients having classical right and left hemihepatectomies had a median LOS of 5 days, similar to the minor open resection group \((P = 0.236)\). Patients having a more extensive resection, central resection, right or left hepatectomy in combination with other resections or RFA, had a median LOS of 7 days, and only one patient was discharged at POD 5 (extended right hepatectomy). There was no significant difference in LOS between patients having a liver resection for hepatocellular carcinoma (HCC) and those having resection for CRLM or other reasons.

Complications graded according to the Dindo–Clavien classification are shown in Table 4. There was no difference in complications between the groups, but a tendency towards more severe complications in the major resection group compared with laparoscopic and minor open resection groups, primarily because of relative hepatic insufficiency. The grade IIIb complications were wound infection (1 patient) and wound dehiscence (3). When patients with grade III–IV complications were excluded, median LOS following major resections was 5 days.

There was one readmission in the laparoscopic group (asthma not related to surgery), one in the minor open resection group (wound dehiscence), two in the major open resection group (both wound dehiscence) and two at local hospitals (1 for suspected pulmonary embolism and one for pain). Thirty-day mortality was zero. One patient with HCC, hepatitis C virus infection and cirrhosis died...
on day 50. The death was caused by recurrence of HCC and liver insufficiency.

Median pain scores (VAS) in the laparoscopic group on POD 1 and 3 were 2 and 0 respectively. Pain scores in the minor and major open resection groups were both 1 on POD 1, and 1 and 0 respectively on POD 3.

**Discussion**

Introduction of the systematic use of evidence-based principles for perioperative care in liver resection accelerated postoperative recovery, achieving a LOS of 2–6 days. The readmission rate was 6–0 per cent, with no deaths within 30 days. Minor and major open resections were done with the same incision. There were no differences in pain score or time to bowel function among the groups. These results demonstrate a significant decrease in LOS after liver resection compared with the results of the national Danish study (2002–2007), which included the authors’ unit.

In a similar population managed within an enhanced recovery after surgery (ERAS) programme, Van Dam and colleagues reported a median LOS of 6 days after open liver resection, significantly lower than the LOS in their control group. MacKay and O’Dwyer reported a median LOS of 4 days in a small series of 12 resections for CRLM following fast-track principles, although only three of these resections were major. Capussotti and co-workers achieved a mean LOS of 8–8 days in a population of 126 patients, comparable to the present population. By comparison, a large population operated on over a decade at Memorial Sloan-Kettering Cancer Center without the use of predefined fast-track principles had a mean LOS of 7–7 and 9–1 days respectively for simple and complex resections of fewer than three segments, and 11–1 and 12–6 days for simple and complex resections of three or more segments.

The present study implied a tendency towards a higher frequency of complications in the major resection group, especially hepatic insufficiency. It is not clear whether this rate of complications following major resection reflects the size and function of the liver remnant as a limiting factor in relation to fast recovery and discharge, although it is well known that the extent and complexity of liver resection is related to the risk and severity of complications, including hepatic insufficiency.

Not surprisingly, patients in the laparoscopic resection group had a significantly shorter LOS than those in the open resection groups (2 versus 5 days), although they followed the same principles for perioperative and postoperative care. This might be due to a combination of the minimally invasive technique and the selection of relatively simple procedures in patients without previous liver resections. A median LOS of 2 days after laparoscopic...
liver resection has not been achieved before, although it is accepted that the laparoscopic group consisted of selected patients with no previous liver resections. Selection of less challenging patients needing small non-anatomical resections, resection of the left lateral segment and first-time resections are characteristic of many, although not all, series 12, 13, 24–26.

A limitation in this comparison of LOS between the open and laparoscopic resection groups was that patients in the open resection group received epidural analgesia until POD 3 per protocol, making discharge before POD 4 difficult. Interestingly, there was no significant difference in pain score at POD 1 and POD 3 between the groups.

Drains were rarely used for minor open resections, but placed routinely following major open resections. Only one patient was suspected of having a minor bile leak, but this stopped spontaneously. There is no evidence that abdominal drainage after liver resection reduces the rate of re-intervention for postoperative haemorrhage or bile leakage, and, because drains represent a significant impediment to achieving early mobilization, they are not used routinely at the authors’ centre 27–29.

The introduction of fast-track principles with early discharge might have led to an increased rate of readmission. A readmission discharge might have led to an increased rate of readmission impediment to achieving early mobilization, they are not bile leakage, and, because drains represent a significant rate of reintervention for postoperative haemorrhage or


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