What are the Particularities of Colorectal Surgery in Cirrhotic Patients

Gilles Manceau¹, Clarisse Eveno², Charles Sabbagh³

¹Digestive Surgery Department, Hôpital de la Pitié Salpêtrière, APHP Paris, France

²Digestive Surgery Department, CHU Lille, France

³Digestive Surgery Department, CHU Amiens-Picardie, France

Corresponding author:
Professor Charles Sabbagh
Digestive Surgery Department
CHU Amiens-Picardie, France
E-mail: sabbagh.charles@chu-amiens.fr

Rezumat

Care sunt particularitățile chirurgiei colorectale la bolnavii cirofici

Obiectivul acestei lucrări a fost de a trece în revistă întreaga literatură despre chirurgia colorectală, cu scopul de a defini în mod cât mai adecvat indicațiile chirurgicale și specificul tratamentului acestuia. Analiza publicațiilor a fost efectuată conform metodologiei Autorității Naționale pentru Sănătate (Haute Autorité de Santé - HAS), prin consultarea bazei de date PubMed (Medline), de la începutul lunii ianuarie 1995 până la sfârșitul lunii iunie 2015.

Cuvinte cheie: colorectal, intervenție chirurgicală, ciroză

Abstract

This work's objective was to review the entire literature on colorectal surgery in order to best define the surgical indications and their management specificities. The literature analysis was carried out according to High Authority for Health (HAS) methodology, by consulting the PubMed database (Medline), from the beginning of January 1995 until the end of June 2015.

Key words: colorectal, surgery, cirrhosis

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Introduction

The cirrhotic patient colonic surgery rules are based on little data, of heterogeneous quality, originating mainly from general surgery data, and colorectal surgeons and oncologists are unfamiliar with this situation. In the report of the French association of surgery on cirrhotic patient surgery, only 84 cases of colon cancer were reported over a period of 7 years (1985-1992) (1). Data from the Oxford Record Linkage Study database suggested that, compared to the general population, the risk of developing colon cancer was 2.04 times higher in cirrhotic patients². This recommendation's purpose was to clarify the cirrhotic patient colonic surgery characteristics.

Documented Research

The literature analysis was carried out according to the High Authority for Health (HAS) methodology, by consulting the PubMed database (Medline), from the beginning of January 1995 until the end of June 2015, with the starting equation: [cirrhosis (Title/Abstract) or liver disease (Title/Abstract)] and [colorectal (Title/Abstract) or colon (Title/Abstract) or rectal (Title/Abstract)] and surgery (Title/Abstract). The search was limited to articles published in either English or French.

A works of interest manual selection by titles reading was then achieved, from the obtained references. Editorials, clinical cases and literature reviews were excluded. This research was completed by analysing the references of the selected articles and by using the PubMed "Similar articles" link (*Table 1*).

Surgical Indications

The main indication analysed is that of colorectal cancer. Two cohort studies and a retrospective case-control study assessed the risk of colon cancer in patients with cirrhosis (2,3,4). In 1999, Sorensen et al. reported the results of a Danish national cohort study of 11,605 patients (3). In this study, compared to

the general population, patients with cirrhosis were 1.5 times more likely to develop colon cancer. This risk was different depending on the aetiology. The alcoholic origin risk was higher (standardized incidence ratio (SIR): 1.5, 95% confidence interval (CI): 1.1-2.1), but not for primary biliary cirrhosis (SIR: 2.7, 95% CI: 1.0 to 5.8) or viral origin (SIR: 1.5, 95% CI: 0.9 to 2.5). In 2008, Goldacre et al. confirmed these results in a cohort study of 599,308 patients in the United Kingdom (2). The authors found that compared to the general population, patients with cirrhosis were 2.04 times more likely to develop colon cancer. They also confirmed that the risk was higher for patients with alcoholic cirrhosis (relative risk: 2.81, 95% CI: 1.40 to 5.04), but not for other aetiologies (risk relative: 1.84, 95% CI: 0.95 to 3.23) (2).

Furthermore, in cases of primary biliary cirrhosis, the use of ursodesoxycolic acid (UDCA) does not reduce the risk of colorectal adenoma (13% vs 24%, $p = 0.16$) after an average interval of 45.6 ± 27.6 months but the risk of recurrence in the form of adenoma was significantly lower with the use of UDCA ($p = 0.001$)(4).

Alcoholic cirrhosis patients have an increased risk of developing colon cancer compared to a non-cirrhotic population.

Table 1. Final analysis of the documentary research

Level of scientific evidence provided by the literature	Articles
<i>Level 1</i>	
High-power randomized controlled trials	
Méta-analyse d'essais comparatifs randomisés	
Decision analysis based on well-conducted data	
<i>Level 2</i>	
Low-power randomized controlled trials	
Well-conducted non-randomized comparative studies	
Cohort studies	
<i>Level 3</i>	
Case-control study	
<i>Level 4</i>	
Comparative studies with significant biases	
Retrospective studies	
Case series	

Technical Specificities

In pre-operatively

Place of TIPS preoperatively

In order to reduce the post-operative complications risk, particularly higher in portal hypertension cases, we could propose to set up a TIPS, which will make possible the decrease of the ascites rate and deviation veins, and therefore the reduce of postoperative complications rate (5). Two retrospective monocentric series evaluated TIPS before surgery (including colorectal surgery) (6,7).

Azoulay et al. (6) were the first to study the use of TIPS in the preoperative management of seven patients with cirrhosis and portal hypertension (including two colon cancers). This study's authors found a significant decrease in the Child-Pugh score with this treatment (6 vs 5, $p = 0.03$). In a case-control study, Vinet et al. (7) compared the results of 18 patients with TIPS and 17 without TIPS. Most of the procedures performed were colectomies (74%, $n = 26/35$). There were no significant differences between the TIPS and non-TIPS groups in terms of intraoperative blood loss, postoperative complications rate, length of stay (17.4 days versus 22.6 days), overall survival rate at one month (83% vs. 88%) and overall survival rate at one year (54% vs. 63%) TIPS was not an independent predictor of survival (HR: 1.39, 95% CI: from 0.42 to 4.61, $p = 0.58$).

The installation of a TIPS before colorectal surgery cannot be recommended systematically in patients with portal hypertension. It is nevertheless a therapeutic defence to be considered in the case of portal hypertension.

Intraoperative

Surgical Approach

Two monocentric retrospective series and two cohort studies evaluated the surgical approach in cirrhotic patients (7,15-17). In 2004, Martinez et al. (8) reported a series of 17 cirrhotic patients laparoscopy operated for colon surgery (12 Child A and 5 Child B). The

conversion rate was 29% ($n = 5/17$), the post-operative morbidity rate was 29% ($n = 5/17$) but there were no anastomotic fistulas or post-operative deaths. Postoperative complications were hematoma on a trocar scar, anastomotic haemorrhage, and superficial wall infection (8). In 2005, Cobb et al. (9) reported the results of 50 cirrhotic patients laparoscopy operated. Only four of these patients (8%) had had a colectomy. The authors reported a post-operative morbidity rate of 16% ($n = 8/50$), the absence of postoperative mortality and a 3 days average length of stay (range: 1-9 days). The authors concluded that cirrhosis was not a contraindication to laparoscopy. These data are difficult to analyse due to surgical procedures heterogeneity and the lack of morbidity clear definition. In addition, cirrhotic patients were not compared to non-cirrhotic patients. In their cohort study, Montomoli et al (10) studied the mortality risk factors at 30 days after surgery for colorectal cancer in cirrhotic patients. The mortality excess risk, compared to non-cirrhotic patients, was greater for laparoscopy operated patients compared to laparotomy operated patients, but without any direct comparison being carried out. Under laparoscopy, the mortality risk in cirrhotic patients was increased by 6.82 times compared to liver disease-free patients, operated on the same approach. The laparotomy mortality risk was 3-times higher.

In a cohort study of 145,600 patients, Kang et al (11) studied the high surgical risk patients laparoscopy feasibility (patients over 70 years old or obese or smoking, or with organ failure, including 4% of cirrhotic patients). The authors found a decrease in postoperative mortality (OR = 0.6), a shorter length of stay, a decrease in postoperative complications (OR = 0.53), a decrease in the urinary tract infections rate (OR = 0.64), a decrease in the anastomotic fistulas rate (OR = 0.69) and a decrease in the parietal complications rate (OR = 0.46) under laparoscopy, as compared to laparotomy.

In conclusion, little data is available on the surgical approach. A single study SUGGESTS an increased risk of postoperative mortality in

laparoscopy colorectal surgery.

Laparoscopy is not contraindicated in cirrhotic patients.

Protective anastomosis-stoma

A cohort study evaluated colon surgery anastomotic fistula risk factors. In this study by Leichtel et al. (12) involving 4340 patients, cirrhosis was not one of the criteria studied as such, but the presence of ascites ($p = 0.67$) and a consumption of more than 2 glasses of alcohol per day ($p = 0.22$) were not anastomotic fistula risk factors. However, in the meta-analysis by Mc Dermott et al. (13) including 451 studies, excessive alcohol consumption was an anastomotic fistula independent risk factor. The authors determined that consuming more than 21 drinks per week increased the risk of anastomotic fistula by 7. (RR: 7.18, 95% CI: 1.2 - 43).

In conclusion, no literature data makes it possible to establish a direct link between cirrhosis and anastomotic fistula.

A practices modification based solely on the presence of cirrhosis is not recommended.

Drain

No specific data is available in the literature.

No recommendation can be made as to the interest of abdominal drainage in colorectal surgery in cirrhotic patients.

In post-operative

Adjuvant chemotherapy in colorectal cancer

Six retrospective studies have evaluated colon cancer adjuvant chemotherapy value (14-19). There are few data available on cirrhotic patients chemotherapy specific characteristics; this is partly due to the fact that cirrhotic patients are excluded from randomized controlled trials which assess the post-operative chemotherapy impact on colon cancer survival (20).

Hepatotoxicity of chemotherapy

The potential hepatotoxicity of oxaliplatin has been reported. Oxaliplatin can induce sinusoidal obstruction syndrome which, in

turn, can lead to portal hypertension, haemorrhagic varices, ascites and thrombocytopenia (14). Nguyen-Khac et al. studied the hepatotoxicity of chemotherapy in a monocentric retrospective series of 50 non-cirrhotic patients with colorectal hepatic metastases. There were 18 cases (36%) of severe sinus dilation, 13 cases (26%) of portal fibrosis, 7 cases (14%) of perisinusoidal fibrosis, 6 cases (12%) of regenerative nodular hyperplasia, and 2 cases (4%) of fatty liver. Perisinusoidal fibrosis was more common after chemotherapy in general (21% versus 0%, $p = 0.04$) and LV5FU2 (50% vs 0%, $p = 0.02$). Sinus dilation was more frequent with oxaliplatin treatment (54.5% versus 23.5%, $p = 0.05$) and a low body mass index ($25.6 \pm 4.7 \text{ kg/m}^2$ versus $29 \pm 3.7 \text{ kg/m}^2$, $p = 0.003$) (15).

Chemotherapy in the cirrhotic patient

In a prospective, recent observational study, Madbouly et al. analysed the adjuvant chemotherapy results in portal hypertension patients. The 5-fluorouracil (5-FU) / folinic acid group received a bolus of 5-FU (450 mg/m^2) and folinic acid (20 mg/m^2) per day for 5 days every 28 days for 6 cycles. The Folfox 4 group received oxaliplatin (85 mg/m^2) for 2 hours on the first day, folinic acid (200 mg/m^2) on the first and second day, a loading dose of 5-FU (400 mg/m^2) as a bolus of 5-FU (600 mg/m^2) for 22 hours on D1 and D2 for 6 cycles. There were more new oesophageal varices at 3 years (8% vs. 40%, $p = 0.003$), more bleeding from the upper digestive tract at 3 years (8% vs. 35%, $p = 0.01$) and more ascites at 3 years in the Folfox group (5% vs. 25%, $p = 0.03$).

Results of surgery for cancer

Short-term results: morbidity and mortality

Three cohort studies, a prospective study and two retrospective series, a review of the literature evaluated the postoperative morbidity and mortality in cirrhotic patients (5,10,21-25).

Mortality

In a cohort of 2.8 million people, Csikesz et al. (5) found that cirrhosis (18,355) patients,

and portal hypertension cirrhosis (4,214) patients presented mortality risk factors (relative risk [95% CI] of 3.7 [2.6 to 5.2] and 14.3 [97-21], respectively). In this study, no details were given on these patients cause of death.

In a more recent cohort study, Lin et al. (21) also found cirrhosis as a risk factor for mortality after non-hepatic surgery, but with a mortality rate increased by 1.88 times compared to the general population. An analysis based on the type of surgery showed that, after a digestive procedure, the risk was higher than in the general population (RR: 2.58, 95% CI: 1.98 to 3.35). In 2009, Nguyen et al. (24) reported in a cohort study, the results of patients having had a colectomy (aetiology not known). The mortality rate was 5% in the general population, 14% for cirrhosis patients and 29% for portal hypertension cirrhosis patients ($p < 0.0001$). When only elective procedures were considered, the mortality rate was also higher in cirrhotic patients (hazard ratio: 3.91; 95% CI: 03.12 to 04.09) and in cirrhotic patients with portal hypertension (hazard ratio: 11, 3; 95% CI: 8.46 to 15.1). Similarly, in emergency, the mortality rate was higher in cirrhotic patients (hazard ratio: 2.4; 95% CI: 2.07 to 2.79) and cirrhotic patients with portal hypertension (hazard ratio: 5.8; 95% CI: 4.9 to 7.6). In multivariate analysis, the independent risk factors for mortality were cirrhosis, portal hypertension, old age, colectomy and co-morbidities (cardio-vascular history, congestive heart failure, chronic renal failure, paraplegia, and malnutrition). In a retrospective study of 41 patients, Meunier et al. (22) found that preoperative peritonitis ($p < 0.05$), postoperative complications ($p < 0.04$), postoperative infections ($p < 0.01$) and total colectomy ($p < 0.02$) were risk factors for mortality in univariate analysis in cirrhotic patients. Patients who underwent a total colectomy had a 100% mortality rate (3 patients in this series). Deaths were linked to ascites fluid infection, anastomotic fistulas, hepatocellular insufficiency, gastrointestinal bleeding and respiratory failure (22). In a retrospective comparative study of 30,927 patients, conducted based on the ground data of American College

of Surgeons National Surgical Quality Improvement Program between 2005 and 2007, Ghaferi et al. (23) highlighted an over-risk of mortality in cirrhotic patients (3.4% vs 13.3%, $p < 0.001$). The authors also studied the risk of death according to the MELD score. The risk of death was multiplied by 9 when the MELD was > 15 and the risk of death was 2.6 times higher when the MELD was < 15 .

In a Danish cohort study, Montomoli et al. (10) studied the risk factors for 30-day mortality. After surgery for colon cancer, the authors found that cirrhotic patients had 2.5 times the risk of death at 30 days compared to patients without liver disease.

Cirrhosis and portal hypertension increase the risk of death with colorectal surgery.

General Complications

Nguyen et al. (24) found an increase in overall morbidity in cirrhotic patients (OR: 1.35; 95% CI: 1.2-1.52) and in portal hypertension cirrhotic patients (OR: 1.82; IC 95 %: 1.55 to 2.15) (5% versus 14% and 29%, respectively, $p = 0.0001$), but no details on the type of postoperative complications were given. Meunier et al. (22) identified ascites as the only predictor of overall morbidity. In their cohort study, Ghaferi et al. Found an increased risk of major complications in cirrhotic patients compared to non-cirrhotic patients (15.8% vs 26.4, $p < 0.001$) (23).

Postoperative morbidity after colon surgery is increased in cases of portal hypertension cirrhosis.

Long-term result

A retrospective studies meta-analysis assessed furthermore the risk of developing liver metastases in patients with cirrhosis and colon cancer (26). Sixteen studies were included in this meta-analysis. During oncological follow-up (from the diagnosis of colon cancer to the death of the patient), the proportion of patients with metastases was 22% in the group of cirrhotic patients (378/1738 patients) and 50% in the group of non-cirrhotic patients (14 068/37 306 patients). This meta-analysis suggested that

the risk of liver metastases was lower in cirrhotic patients (RR = 0.53, 95% CI = 0.42 to 0.66, $I^2 = 71\%$). The major bias of this meta-analysis was the inclusion of autopsy series ($n = 14$) and surgical series ($n = 2$). Furthermore, no interval between the diagnosis of cancer and the evaluation of the hepatic parenchyma was available (27,28). Among the studies included in the meta-analysis, the surgical series by Lascone et al. (28) reported a liver metastasis rate in cirrhotic patients ($n = 171$) of 4.7% (8/171) and a rate in non-cirrhotic patients ($n = 543$) of 32% (174/543) ($p < 0.001$).

In a monocentric series involving 40 cirrhotic patients and matched by age, gender, tumour site and TNM stage, Sabbagh et al. did not demonstrate a significant difference for recurrence-free survival and specific cancer-related survival. Overall survival was significantly worse in cirrhotic patients suggesting a prognosis mainly related to cirrhosis (29).

In conclusion, cirrhotic patients may have a lower risk (-86% in the surgical series and -41% in the autopsy series) of developing liver metastases.

Rectal Surgery Specificities

Analysis of the literature shows that there is currently no study specifically carried out on cirrhotic patients undergoing rectal surgery. Likewise, no data could be found concerning the morbidity of radiotherapy / radio-chemotherapy-adjuvant therapy in this type of patient. The results reported below come from subgroup analyses from series comprising colorectal surgery operated patients.

Two studies (a cohort study and a retrospective study) evaluated postoperative outcomes after rectal excision for cancer in the cirrhotic patient (10,22). Postoperative mortality increased significantly in rectal cancer operated cirrhotic patients (LE2) (10). The Danish population study by Montomoli et al. (10) included 13,498 patients with rectal cancer operated between 1996 and 2009, including 104 patients (0.8%) with non-cirrhotic liver disease and 58 (0.4%) hepatic cirrhosis. 10 30-

day mortality rates were 6.4% in patients without liver disease, 10.6% in those with non-cirrhotic liver disease and 19% in those with cirrhosis. Cirrhosis was an independent factor in postoperative mortality in multivariate analysis (RR = 2.84; 95% CI: 1.52-5.30).

Regarding the surgical approach, the study by Kang et al. (11), which evaluated laparoscopy feasibility and advantages, as compared to laparotomy in 9547 patients considered to be at high surgical risk and electively undergoing colorectal surgery, included 1257 anterior resections (13%) and 388 abdominoperineal amputations (4%). In multivariate analysis, after adjustment according to the type of surgery performed (colic vs. rectal), laparoscopy was significantly associated with a decrease in the postoperative mortality rate, anastomotic fistula, parietal complications, ileus, urinary tract infections, respiratory failure, length of hospital stay and hospital costs (LE2).

In the randomized trial of Merad et al. (30) that evaluated the pelvis prophylactic drainage value in the prevention of surgical complications after subperitoneal colorectal anastomosis or coloanal anastomosis, the cirrhosis history and the intraoperative ascites presence were considered as anastomosis integrity possible risk factors, and were used to check the good comparability of the two groups after randomization. However, no study has shown that these two criteria increase the rate of anastomotic fistula after rectal surgery. Thus, cirrhosis should not by itself justify the achievement of a systematic bypass stoma, especially since the presence of an ostomy in a cirrhotic patient can lead to complications (ascites infection, ascites leakage peristomal, peristomal varicose veins with bleeding, stoma disinsertion and peristomal disruption).

Cirrhosis increases the risk of death after rectal surgery. Laparoscopy seems to be a valid approach in rectal surgery in cirrhotic patients. No modification of practices can be recommended concerning the making of a protective ostomy and the setting up of a prophylactic drainage of the pelvis after rectal surgery in the cirrhotic patient.

Non-surgical Alternatives Place

There is no data in the literature on the place of non-surgical treatments.

Conflict of Interest

The authors declare no conflict of interests.

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