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Management of colorectal cancer in patients with cirrhosis: A retrospective, case-matched study of short- and long-term outcomes

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ABSTRACT

Background: Few studies have assessed access to postoperative chemotherapy and survival in cirrhotic patients with colorectal cancer. Aim of this study was to analyse short and long-term outcomes in these patients compared to non-cirrhotics.
Methods: A retrospective, single-centre, comparative, case-matched study comparing 40 cirrhotic patients who had undergone colorectal resection between January 2006 and January 2014, and a matched cohort of 80 non-cirrhotic patients. Data collection included rate of postoperative outcomes, chemotherapy regimen, overall and disease-free 3-year survival.
Results: Cirrhotics had more major postoperative complications than non-cirrhotics (57.5% vs. 26.5%, respectively; $p = 0.002$) but no difference in anastomotic leakage ($p = 0.1$); a higher mortality rate ($p = 0.0006$) was observed in Child–Pugh class B patients. Cirrhotics had no difference in adjuvant chemotherapy rate compared to non-cirrhotics (55% vs. 65%, respectively $p = 0.8$); 3-year overall survival was 71% in the Child A group vs. 92% in non-cirrhotics ($p = 0.03$).
Conclusion: Despite a higher postoperative complication rate and a lower overall survival of cirrhotic patients compared to non-cirrhotics, cirrhosis had no impact on oncological outcomes and access/tolerance to postoperative chemotherapy. Thus cirrhosis should not be considered as a contraindication to curative treatment of colon cancer.

1. Introduction

The incidence of cirrhosis is increasing in parallel with that of hepatitis and non-alcoholic steatohepatitis, and is associated with an increased risk of developing colorectal cancer.

The indications for surgery in cirrhotic patients have recently been broadened, mostly due to better understanding and management of cirrhosis, the perioperative period and postoperative complications. Nevertheless, cirrhosis is still associated with an increased risk of postoperative morbidity (up to 3.7-fold for cirrhosis alone and up to 14.3-fold for cirrhosis and portal hypertension) [1].

It is well established that the prognosis of cirrhotic patients is correlated with the Child–Pugh score; the spontaneous 5-year survival rate ranges from 70% for Child–Pugh A patients to 20% for Child–Pugh C patients [2].

Given the high postoperative morbidity and the low spontaneous survival of cirrhotic patients, it is essential to investigate the therapeutic management of colorectal cancer in this population. However, few studies have assessed long-term survival and access to postoperative chemotherapy in cirrhotic patients with colorectal cancer. Hence, the objective of the present study was to collect and analyse data on short- and long-term outcomes in these cirrhotic patients.

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2. Patients and methods

2.1. Population

From January 2006 to January 2014, 40 cirrhotic patients underwent a colorectal resection for colorectal cancer (2.1% of the 1866 patients operated for colorectal cancer during this period) at Amiens University Hospital (Amiens, France). These cirrhotic patients were compared with a cohort of 80 non-cirrhotic controls.

2.2. Study design

This was a retrospective, single-centre, comparative, case-matched study. Preoperative, operative and postoperative data were retrieved from our institution's database. The cirrhotic patients were compared with a cohort of 80 non-cirrhotic controls matched 1:2 for age, gender, tumour site and TNM stage ($n = 50$ matched with Child A patients and $n = 30$ matched with Child B patients). All patients were considered for perioperative morbidity.

2.3. Data collection

The following data were collected: demographic and clinical data (gender, BMI, age, Child Pugh stage, portal hypertension and the aetiology of cirrhosis), tumour-related data (site and stage), surgical data (surgical approach, operating time, the type of anastomosis, and the rate of conversion from laparoscopy to laparotomy), postoperative outcomes (complications of surgery, according to the Clavien-Dindo classification [3]), oncological data (initiation of chemotherapy, the chemotherapy regimen and the completion of chemotherapy), and survival data (overall, disease-free and cancer-specific survival, and cause of death).

2.4. Endpoints

The study endpoints were peri-operative and early postoperative outcomes (laparoscopy and conversion rates, and overall and cirrhosis-related postoperative complications), oncological outcomes (the proportion of patients starting chemotherapy and completing chemotherapy) and survival (overall and disease-free survival, and causes of death) in the Child A, Child B and matched non-cirrhotic groups. The reasons for death in the Child A group were also analysed.

2.5. Definitions

2.5.1. Cirrhosis

Patients were only included if they had pathologically confirmed cirrhosis. This encompassed cirrhosis (i) confirmed preoperatively or (ii) suspected preoperatively and then confirmed per-operatively with a liver biopsy during the colectomy. Patients with F4 fibrosis (defined as the most advanced stage of fibrosis in the Metavir classification) were considered to be cirrhotic [4]. Patients were classified according to the Child–Pugh classification as Child A (5 to 6 points), Child B (7 to 9 points) and Child C (10 to 15 points) [5].

2.5.2. Surgical technique and postoperative care

The surgical approach was chosen as a function of the patient's general conditions and surgical history, and was validated in a surgical team meeting. For right hemicolectomy, a laterolateral hand-sewn anastomosis was created. For left colectomy and proctectomy, a lateroterminal stapled anastomosis was created. Drainage was not applied systematically during colon surgery and was only considered in patients with preoperative ascites. For proctectomy, a pelvic drain was always left in place. A running skin suture was used for cirrhotic patients. Gastric tubes were removed before the patient left the operating theatre and refeeding was initiated on postoperative day (POD) 1. Bladder tubes were removed on POD1 after colectomy or POD 5 after proctectomy.

2.5.3. Postoperative complications

Clavien I and II complications were considered to be minor, Clavien III and IV complications were considered as major and Clavien V were postoperative mortality. Postoperative complications were defined up to the 30 postoperative days. Anastomotic fistula was screened for (on a CT scan or during reoperation) and defined as any leak of the anastomosis or bowel cul-de-sac.

2.5.4. Adjuvant chemotherapy

As recommended by the American Society of Colon and Rectal surgeons, adjuvant chemotherapy (Folfox IV for 12 cycles) was suggested for all patients with stage III and IV colon and rectal cancers [6–8].

2.5.5. Survival

Overall survival was defined as the time between tumour resection and death or the date of last follow-up. Disease-free survival was defined as the time between tumour resection and any recurrence.

2.6. Statistical analysis

Continuous variables are reported as the median (range) and categorical variables are reported as percentages. A χ^2 test or Fisher's exact test were used for comparisons of categorical data, and a t test or a Mann–Whitney test were used for comparisons of continuous variables, as appropriate. Survival was analysed according to the Kaplan–Meier method in all the population and in Child A patients [2], given the known, strong correlation between the Child–Pugh score and survival and the small number of patients in the Child B group.

All statistical analyses were performed using SPSS for Windows® software (version 15.0, SPSS Inc., Chicago, IL, USA). A p value below 0.05 was considered to be statistically significant.

3. Results

Forty cirrhotic patients were matched with 80 non-cirrhotic patients. Twenty-five cirrhotic patients (62.5%) were Child–Pugh class A and were matched with 50 non-cirrhotic patients. The remaining 15 cirrhotic patients (37.5%) were Child–Pugh class B and were matched with 30 non-cirrhotic patients. The proportion of males was 72.5% ($n = 29$) in the cirrhotic group also 72.5% in the control group ($n = 58$). The mean age was 63.2 in the cirrhotic group and 64.3 in the control group. The characteristics of the study population (the Child A group, the Child B group and the matched non-cirrhotic groups) are shown in Table 1. The groups did not differ significantly in terms of age, gender, tumour site or TNM stage (Table 1).

In the Child A group, the aetiology for cirrhosis was alcohol abuse in 48%, non-alcoholic steatohepatitis (NASH) in 20%, hemochromatosis in 4%, viral hepatitis in 4% and an unknown aetiology in 24%. Three patients had portal hypertension. None of the Child A patients had preoperative ascites.

In the Child B group, the aetiology for cirrhosis was alcohol in 40%, NASH syndrome in 20%, viral hepatitis in 13% and an unknown aetiology in 27%. None of the Child B patients had portal hypertension; 2 Child B patients had preoperative ascites and were treated preoperatively with a transjugular intrahepatic portosystemic shunt (TIPS).