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TITLE PAGE

Title:

Colonoscopy in patients with liver cirrhosis: success and safety issues.

Authors:

Elisabeth J Macken, MD[1]

Anton Steinhauser, MD[1]

Heiko U De Schepper, MD PhD[1]

Benedicte Y De Winter, MD PhD[2]

Tom G Moreels, MD PhD [1,2]

[1]Department of Gastroenterology and Hepatology, University Hospital Antwerp, Antwerp, Belgium

[2] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp

Corresponding author:

TG Moreels, MD, PhD

Department of Gastroenterology and Hepatology

University Hospital Antwerp

Wilrijkstraat 10

B-2650 Antwerp - BELGIUM

Tel: +3238213310

Fax: +3238214478

E-mail: tmoreels@gmail.com

List of abbreviations:

CIR: caecal intubation rate

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ABSTRACT

Background: Patients with liver cirrhosis undergo screening colonoscopy before liver transplantation. Screening colonoscopy is subject to specific quality criteria, among which caecal intubation rate. Several factors associated with failed caecal intubation have been identified.

Aims: We investigated whether liver cirrhosis influenced success and safety of screening colonoscopy.

Methods: Caecal intubation and complication rate of 93 candidates for liver transplantation due to liver cirrhosis were compared with the control rates of our endoscopy unit. Several patient and colonoscopy variables were taken into account.

Results: In patients with liver cirrhosis caecal intubation rate was only 83 %, whereas in the control group it was 94 % ($P<0.0001$). The presence of high volume ascites tends to compromise a successful colonoscopy. Serious complication rate was 0,4 % in controls without colonoscopy-related mortality. In the cirrhotic population two severe complications were encountered (2,2%, $P<0.05$) and one patient died due to colonic perforation and sepsis (mortality 1.1%).

Conclusions: Caecal intubation rate is significantly lower in patients with liver cirrhosis undergoing screening colonoscopy, possibly related to the presence of ascites. Complication and mortality rate of screening colonoscopy is significantly higher in patients being screened for liver transplantation.

Keywords: liver cirrhosis, colonoscopy, complication rate, caecal intubation rate

INTRODUCTION

Liver cirrhosis is a severe condition which often is characterized by jaundice, ascites, coagulation disorders, malnutrition and an immunosuppressive status. Besides treatment of the underlying disorder (e.g. abstinence of alcohol, treatment of hepatitis B or C), liver transplantation is the only structural treatment that can be offered (1). Contra-indications for transplantation include severe cardiopulmonary disease, active alcohol or substance abuse, active infection or uncontrolled sepsis, inability to comply with medical treatment and extrahepatic malignancy (2). To evaluate the latter, extensive screening is performed to exclude a malignancy before accepting the patient on a liver transplantation list. In general, computed tomography scan of the lungs and abdomen are performed, as well as ultrasound and mammography of the female breasts, gynaecological investigation, blood test including prostate specific antigen and upper and lower gastrointestinal endoscopy (3). Moreover, patients with liver cirrhosis may have a higher risk of developing colorectal cancer (4).

In order to detect polyps and colorectal cancer, as well as other mucosal pathology, conventional colonoscopy is considered the gold standard (5). However, complete colonoscopy is not always feasible. Possible reasons for failure of caecal intubation are sigmoid loop formation, long and tortuous redundant colon, postoperative fixation of colonic segments, and patient discomfort (6). Other factors that may compromise caecal intubation are older patient's age, female gender, low body mass index, diverticular disease, previous abdominal or pelvic surgery, and colonoscopy carried out in private office practice (7,8).

Little is known regarding the effect of liver cirrhosis on the success and complication rate of colonoscopy. Several studies report on the endoscopic results of colonoscopy in cirrhotic patients, but caecal intubation rate (CIR) in liver cirrhosis patients remains unknown (3,4,9-13). Moreover, data on safety of colonoscopy in cirrhotic patients are little. Patients

with decompensated liver cirrhosis tend to have further water retention due to bowel preparation (13). And the risk of postpolypectomy bleeding appears to be dependent on the Child-Pugh score (14,15).

In the present study we retrospectively analysed CIR and complication rate of screening colonoscopy in patients with liver cirrhosis who were candidate for liver transplantation in our hospital. Results were compared with the overall colonoscopy quality outcomes of our endoscopy unit as measured in 2009 (16).

MATERIALS AND METHODS

The Antwerp University Hospital database of all patients listed for liver transplantation was used, starting from 2003. Furthermore, all patients screened for liver transplantation, but who failed to be listed due to contra-indications or progressive disease and death were also included. All colonoscopy reports were retrospectively reviewed. Patients without liver cirrhosis, but who were transplanted because of e.g. polycystic liver disease, acute hepatic failure, Caroli syndrome, amyloidosis, neuro-endocrine liver tumour, etc. were excluded from analysis. Furthermore, a history of colonic surgery or inadequate bowel cleansing were also considered exclusion criteria (5). Finally, procedures performed with endoscopes other than the conventional 133 cm long Olympus (CFQ-160I) or Fujinon (EC-450WM) were also excluded. Data on patient's age, sex, Child-Pugh score and presence of ascites were retrospectively collected as well as depth of endoscope insertion, endoscopist (trainee or supervisor), bowel preparation, type of sedation, endoscopic findings, type of endoscope and year of examination. Reason for failed caecal intubation and subsequent examinations were also registered. Since our unit is a training unit, colonoscopy is performed both by trainees and supervisors.

As controls, we used the 2009 quality control data on colonoscopy of our unit (16). In this study all colonoscopies performed at the Antwerp University Hospital performed in 2009 were analyzed. Procedures with no or insufficient bowel cleansing were excluded, as were colonoscopies performed in colons with partial surgical resections or with other endoscopes than conventional 133 cm long colonoscopies, resulting in 1269 eligible colonoscopies. Patients with liver cirrhosis who underwent screening colonoscopy in 2009 were eliminated from the overall 2009 control group. Endoscopic findings were divided into two groups. The first group encompassed normal findings or small insignificant findings such as diminutive polyps. The second group encompasses significant findings such as large polyps, visible vessels or angiodysplastic lesions at risk for future bleeding, or carcinoma.

Age categories were divided into decades. Results are expressed as mean with standard error of the mean (SEM) or in percentage where applicable. Statistical analysis based on Chi-square cross tables were used to analyze the relationships between caecal intubation and the other variables. To exclude intervariable interference binary logistic regression was used. SPSS program 19.0 was used and a P value less than 0.05 was considered statistically significant.

RESULTS

In total, 133 patients were screened for liver transplantation due to chronic liver disease. Of 24 patients no endoscopic report could be retrieved (14 patients did not undergo colonoscopy, 10 patients had their colonoscopy in another referring hospital). 11 patients were transplanted for another medical condition than liver cirrhosis and were excluded, as well as 4 patients in whom colonoscopy was performed using a longer (160 cm) colonoscope.

One patient with incomplete colonoscopy due to insufficient bowel cleansing was equally excluded, leaving 93 patients for study analysis.

The male-female ratio was 58:35 (62% male, 38% female) with a mean age of 55±1 years (range 23 – 73 years). In the 2009 control group male-female ratio was 1:1 with patients' mean age of 58±1 years. The majority of patients with liver cirrhosis had Child-Pugh score B (41 of 93 cases). The caecum was reached in 77 patients representing a CIR of 83%, whereas in the 2009 control group CIR was 94 % (Chi square test, $P<0.0001$). Possible reasons for this lower CIR were further analysed. There was no difference in CIR related to the patients' sex and age groups (Chi square test, $P>0.05$) (Figure 1). Comparing the three classes of the Child-Pugh score, there appeared to be a higher success rate in Child-Pugh A (CIR of 92%). However, no statistically significant correlation was noted between CIR and Child-Pugh classification (Chi square test, $P>0.05$) (Figure 2). The presence of ascites tended to influence CIR: 91% in patients without ascites vs. 75% and 77% in patients with moderate and severe ascites respectively (Chi square test, $P>0.05$) (Figure 3). There were no significant differences in CIR when taking into account bowel preparation. Most procedures were performed under conscious sedation using midazolam with or without fentanyl. Only 3 procedures were performed under general anesthesia, whilst 3 procedures have been carried out without any sedation. All 6 procedures were successful. Using both Chi-square and binary logistic regression none of these variables appeared to be significant to explain the lower CIR in patients with liver cirrhosis.

Incomplete colonoscopy was due to a redundant colon, pain or loop formation. Failure occurred mostly in the ascending or transverse colon, though 3 procedures were stopped at the level of the sigmoid colon. After failed colonoscopy, computed tomography (CT) colonography was performed, or colonoscopy was repeated using a single-or double-balloon

enteroscope, or in one case by merely repeating the colonoscopy a week later. In 37% no further action was undertaken to investigate the rest of the colon (Table 1).

In 18 colonoscopies (19%) significant endoscopic findings were encountered, such as large polyps, angiodysplastic lesions or visible vessels at risk for bleeding and one caecal tumour. Serious complication rate was 0,4 % (5/1269 patients) in the 2009 control group: 2 perforations, 2 episodes of severe bradycardia and 1 rebleeding was seen during or shortly after the procedure. There was no colonoscopy-related mortality. In the cirrhotic population 2 severe complications were encountered (2,2%, $P<0.05$). One patient died the day after procedure due to sepsis (mortality 1.1%). Postmortem examination revealed a small post-polypectomy colonic perforation. The second patient developed an umbilical herniation 6 days after the procedure, probably related to the air insufflation during colonoscopy. One case of spontaneous bacterial peritonitis was seen 3 weeks after the colonoscopy, but this was considered too long to be possibly related. No post-polypectomy bleeding was encountered.

DISCUSSION

Routine endoscopy of liver transplant candidates has been debated (17). However, current standard clinical practice includes both upper and lower gastrointestinal screening endoscopy. Moreover, recent data suggests an increased risk of colorectal cancer in patients with liver cirrhosis (4). Therefore, screening colonoscopy seems warranted in the routine work-up of all patients with liver cirrhosis who are candidate for liver transplantation. Several colonoscopy quality indicators have been defined, of whom caecal intubation rate and complication rate are very important (5). Several patient-related factors implicating both CIR and complication rate have previously defined (6-8). Also the presence of liver cirrhosis has been identified as a possible factor jeopardizing the success and safety of colonoscopy. There

appears to be an increased risk of water retention and electrolyte disturbances due to the bowel preparation, and the risk of post-polypectomy bleeding increases with the Child-Pugh score (13-15).

The present study further elaborated on the potential risks of performing colonoscopy in patients with liver cirrhosis screened for liver transplantation. Retrospective colonoscopy quality control in our endoscopy unit in 2009 revealed an overall acceptable CIR (94%) and complication (0.4%) and mortality (0%) rate (16). However, in the present study, CIR (83%) was significantly lower in patients with liver cirrhosis screened for transplantation. Moreover, complication (2.2%) and mortality (1.1%) rate was significantly higher in cirrhotic patients. In contrast to previous reports, no post-polypectomy bleeding was encountered (15). Further analysis suggested that the presence of ascites may lead to lower CIR. External abdominal compression may help to guide the endoscope and to avoid loop formation (18,19). This may not be feasible in the presence of high volume or tense ascites, explaining the lower success rate of colonoscopy. Moreover, with the colon surrounded by liquid, there is less internal compression from the abdominal wall, increasing the risk of bowel distension, loop formation and stretching of the mesentery. Therefore, paracentesis to reduce intra-abdominal ascites volume prior to colonoscopy may be warranted. Although this has never been investigated in patients with ascites due to liver cirrhosis, international guidelines advice that the abdomen be emptied of fluid before colonoscopy in patients with peritoneal dialysis in order to prevent post-colonoscopy peritonitis (20). In these patients, the risk of colonoscopy-induced peritonitis (within 24 hours after the procedure) is 6-8%, and can be prevented by the combination of emptying the abdomen and prophylactic administration of antibiotics before colonoscopy (20,21). However, in contrast to patients with peritoneal dialysis, the risk of developing post-colonoscopy peritonitis in patients with ascites due to liver cirrhosis is probably lower, since no specific data are exist on this topic (22). In the present study, 1

episode of bacterial peritonitis was encountered 3 weeks after colonoscopy, but this was considered too long to be related.

Other factors, like age and sex did not influence CIR in patients with liver cirrhosis. The role of anesthesia was also studied. In total 3 cirrhotic patients underwent colonoscopy under general anesthesia, and 3 without any sedation, all of whom were successful. Most procedures were performed under conscious sedation using midazolam with or without fentanyl. One could argue that the higher failure rate in cirrhotic patients was due to less general anesthesia than in the control group. Moreover, because of hepatic metabolisation of midazolam, less sedation is warranted in cirrothic patients. When we exclude procedures under general anesthesia from the cirrhotic population and from the control group a failure rate to reach the caecum of 17,8% and 6,5% respectively is obtained, still leaving a significant difference between the two groups. Despite the higher complication rate in the cirrhotic population, screening colonoscopy remains important in candidates for liver transplantation, since significant endoscopic findings, like polyps or even colorectal carcinoma were seen in 19% of the patients.

In conclusion, complication rate and mortality of screening colonoscopy were significantly higher in cirrhotic patients being screened for liver transplantation. Moreover, caecal intubation rate was significantly lower in cirrhotic patients, possibly related to the volume of ascites. A prospective study will be undertaken to address this topic.

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FIGURE LEGENDS

Figure 1: Age and caecal intubation rate. No statistically significant correlation was found between age category and caecal intubation rate in patients with liver cirrhosis (Chi square test).

Figure 2: Child-Pugh classification and caecal intubation rate. Although no statistically significant correlation was found between Child-Pugh classification and caecal intubation

rate, Child-Pugh classification B and C resulted in lower caecal intubation rate (Chi square test).

Figure 3: Volume of ascites and caecal intubation rate. Although no statistical significant correlation was found between volume of ascites and caecal intubation rate, higher ascites volumes resulted in lower caecal intubation rate (Chi square test).