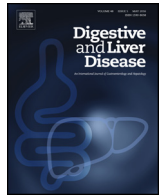




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Liver, Pancreas and Biliary Tract

Elective endoscopic variceal ligation is not a risk factor for bacterial infection in patients with liver cirrhosis

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ABSTRACT

Background: Patients with cirrhosis are at high risk of bacterial infections. Invasive procedures are generally believed to increase this susceptibility.

Aims: We investigated the incidence of bacterial infections in cirrhotic patients undergoing elective endoscopic variceal ligation (EVL).

Methods: We enrolled 60 consecutive cirrhotic patients who underwent a total number of 112 elective EVL procedures. One to seven bands were applied at each session until variceal eradication. Markers of inflammation/infection and blood cultures were obtained before and 24 h after EVL.

Results: Aetiology of liver disease was metabolic in 27 (45%), viral in 21 (35%), alcoholic in 12 (20%) patients. Child–Pugh class A/B/C distribution was 29/26/5, respectively, 23 (38%) patients had ascites and 15 (25%) had hepatocellular carcinoma. Blood cultures were negative in all samples before EVL, whereas 3/112 (2.7%) cultures tested positive after endoscopy. *Streptococcus mitis* and *Staphylococcus epidermidis* were isolated in 1 and 2 cases, respectively. None of these three patients developed any features of clinically relevant infection, suggesting that the positive cultures were an expression of a transient bacteraemia with no clinical sequelae.

Conclusions: Bacterial infection is an uncommon occurrence after elective EVL in cirrhotic patients, and antibiotic prophylaxis is not necessary in this clinical setting.

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1. Introduction

Bacterial infections are a frequent event in liver cirrhosis [1] and there is evidence that invasive procedures (i.e. surgical, endovascular or endoscopic interventions) increase the risk of septic complications, particularly in patients with more advanced disease [2]. Transient episodes of bacteraemia may occur during routine endoscopic examinations because of mucosal trauma and the consequent translocation of the endogenous microbial flora into the bloodstream [3]. In patients with advanced liver disease, this mech-

anism is favoured by the portal hypertension, which along with the acquired immunodeficiency characterising liver cirrhosis might increase the chances of bacterial infection [4,5]. Endoscopic variceal ligation (EVL) is nowadays the most frequently applied invasive procedure in cirrhotic patients, and the treatment of choice not only for acute episodes of variceal haemorrhage, but also for primary and secondary prophylaxis of the bleeding itself [6]. Up to now, the incidence of post-procedure bacteraemia in cirrhotic patients undergoing elective EVL has been investigated in a limited number of studies, all evaluating the presence of bacteria in blood cultures collected within the first two hours from the end of the procedure, with extremely heterogeneous results [7–13]. Additionally, data with regards to the occurrence of bacterial infections after or throughout serial sessions of prophylactically performed elective EVL to eradicate oesophageal varices are scarce [9,12], whereas there are clear indications for antibiotic prophylaxis for patients

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with acute portal-hypertensive gastrointestinal bleeding undergoing EVL [3,6]. The aim of this prospective study was to assess the incidence of bacteraemia and of clinically relevant infections in patients with liver cirrhosis undergoing elective EVL.

2. Methods

2.1. Subjects

This prospective study enrolled 60 cirrhotic patients [51 males (85%), mean age 66.2 ± 11.1 years] with severe portal hypertension and high risk of oesophageal variceal bleeding, consecutively hospitalized at the Liver Unit of the Messina University Hospital from March 2015 to October 2016, who underwent one or multiple elective sessions of EVL for primary or secondary prophylaxis until complete eradication (no further ligation possible [14]). Exclusion criteria were active variceal bleeding, clinical/biochemical evidence of sepsis or recent (within 4 weeks) or ongoing antimicrobial therapy at the time of the EVL procedure. Clinical and demographic characteristics were prospectively recorded. Child–Pugh and Model of End-stage Liver Disease (MELD) scores were calculated for each patient before EVL.

2.2. Blood tests and blood cultures

Biochemistry and clotting were obtained on admission. Full blood count, inflammatory indexes such as C-reactive protein (C-RP) and procalcitonin (PCT), as well as blood cultures from a peripheral venepuncture (a total amount of 20 ml of whole blood was inoculated – 10 ml each time – into a set of aerobic and anaerobic mediums) were performed before and 24 h after EVL. Blood samples were collected after skin antisepsis with 70° GL ethanol, using throwaway gloves, and blood was immediately transferred to the culture bottles, after replacing the original needle with a new one and disinfecting the flask top.

Full blood count and biochemistry were also performed at 48 and 72 h post-procedure.

2.3. Endoscopy

Elective EVL was performed by two expert endoscopists (SP and PC) with an autoclave-sterilized multiple-band ligator (Speedband Superview Super 7TM, Boston Scientific, USA). Disposable banders were used. One to seven rubber bands were applied at each session. Patients underwent the procedure under deep sedation and were kept on nil by mouth for the following 24 h. None of the patients received antibiotic prophylaxis before or after the intervention. An upper gastrointestinal endoscopy with possible further ligation was repeated every 4–8 weeks until complete eradication of the varices was achieved. The endoscopic sessions in which banding was planned but not performed because complete variceal eradication was documented were excluded from the study. A control oesophagogastroduodenoscopy was performed at 3–6 months post-eradication, followed by a routine endoscopic follow-up every 6–12 months [14,15].

2.4. Ethics

The study has been performed in accordance with the ethical standards of the Declaration of Helsinki and its later amendments. All patients gave their informed consent to participate in the study and the protocol was approved by the ethics Committee of the University Hospital of Messina.

2.5. Statistics

Continuous variables were tested for normal distribution by Kolmogorov–Smirnov test and are presented as mean \pm standard deviation (SD) or median and range, as appropriate. Categorical variables were compared with the χ^2 test or the Fisher's exact test.

Normally distributed continuous variables were compared with the Student *t*-test or, if they were not normally distributed, by the Mann–Whitney test. The linear relationship between continuous variables was assessed by Pearson's correlation coefficient or Spearman's rank correlation, according to distribution. Significance testing was two-sided and set to less than 0.05. The statistical package SPSS version 20.0, January 2004 was used for the analysis.

3. Results

Demographic, clinical and biochemical characteristics of the 60 patients included in the study are reported in Table 1. The aetiology of cirrhosis was metabolic (non-alcoholic fatty liver disease/steatohepatitis) in 27 (45%), viral in 21 (35%) and alcoholic in 12 (20%) cases. The distribution of patients within Child–Pugh classes was as follows: 29 (48.3%) class A, 26 (43.3%) class B and 5 (8.4%) class C. Mean Child–Pugh score was 6.8 ± 1.65 and 23 (38%) patients had clinically or radiologically detectable ascites. Mean MELD score was 10.65 ± 3 . Nine (15%) patients had medium size varices with red marks and 51 (85%) large varices, respectively, according to the currently accepted classification [6]. Fifteen (25%) patients had a diagnosis of hepatocellular carcinoma and did not receive any loco-regional or systemic treatment over the observational period until oesophageal varices eradication. Thirty-two (52%) patients were on treatment with proton pump inhibitors (median dose 20 [range 20–40] mg/day). Forty-seven (78%) patients were receiving non-selective beta-blockers – 40 of them (87%) were

Table 1
Demographic, clinical and biochemical characteristics of 60 cirrhotic patients undergoing elective endoscopic variceal ligation.

Age years, mean \pm SD	66 \pm 11
Male sex, n (%)	51 (85)
Aetiology, n (%)	
Viral	21 (35)
Alcoholic	12 (20)
Metabolic	27 (45)
Child–Pugh class, n (%)	
A	29 (48.3)
B	26 (43.3)
C	5 (8.4)
Child–Pugh score, mean \pm SD	6.8 \pm 1.65
MELD, mean \pm SD	10.65 \pm 3
Ascites, n (%)	23 (38)
Varices size (medium + RWM/large), n (%)	9/51 (15/85)
Number of procedures per patient median (range)	2 (1–4)
Portal vein thrombosis, n (%)	16 (27)
Primary/secondary prophylaxis, n (%)	47(78)/13(22)
Bands per procedure, median (range)	5 (1–7)
Hepatocellular carcinoma, n (%)	15 (25)
Diabetes, n (%)	28 (46.6)
Arterial hypertension, n (%)	30 (50)
Haemoglobin g/dl, median (range)	11.23 (7.1–15.8)
White blood cells/mm ³ , median (range)	3,900 (1,700–14,500)
Platelets/mm ³ , median (range)	83,500 (31,000–592,000)
c-RP mg/dl, median (range)	0.5 (0.1–6.6)
PCT ng/ml, median (range)	0.1 (0.03–2.09)
Therapy with NSBBs n (%)	46 (76.6)
Therapy with PPIs, n (%)	32 (53)

Abbreviations: SD, standard deviation; MELD, Model of End-stage Liver Disease; RWM, red wall marks; c-RP, C-reactive protein; PCT, procalcitonin; NSBBs, non-selective beta-blockers; PPIs, proton pump inhibitors.

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