Digestive and Liver Disease 46 (2014) 152–156

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Liver, Pancreas and Biliary Tract

Impact of portal vein thrombosis on the efficacy of endoscopic variceal band ligation

Alessandra Dell'Era[a,b,*], Francesca Iannuzzi[a,b], Federica M. Fabris[b], Paola Fontana[a,b], Raffaella Reati[a,b], Paolo Grillo[d], Alessio Aghemo[c], Roberto de Franchis[a,b], Massimo Primignani[b]

[a] Department of Medical Sciences, Università degli Studi di Milano – IRCCS Fondazione Cà Granda Ospedale Policlinico di Milano, Milan, Italy
[b] Gastroenterology 3 Unit – IRCCS Fondazione Cà Granda Ospedale Policlinico di Milano, Milan, Italy
[c] Gastroenterology 1 Unit – IRCCS Fondazione Cà Granda Ospedale Policlinico di Milano, Milan, Italy
[d] Epidemiology Unit – IRCCS Fondazione Cà Granda Ospedale Policlinico di Milano, Milan, Italy

ARTICLE INFO

Article history:
Received 6 February 2013
Accepted 20 August 2013
Available online 29 September 2013

Keywords:
Esophageal varices
Endoscopic band ligation
Portal vein thrombosis

ABSTRACT

Background: Influence of portal vein thrombosis on efficacy of endoscopic variceal banding in patients with cirrhosis or extrahepatic portal vein obstruction has never been evaluated. Aim of the study was to assess influence of thrombosis on rate and time to eradication in cirrhosis and extrahepatic portal vein obstruction undergoing banding, compared to cirrhotic patients without thrombosis.
Methods: Retrospective analysis of 235 consecutive patients (192 with cirrhosis without thrombosis, 22 cirrhosis and thrombosis and 21 extrahepatic portal vein obstruction) who underwent banding. Banding was performed every 2–3 weeks until eradication; endoscopic follow-up was performed at 1, 3, 6 months, then annually.
Results: Eradication was achieved in 233 patients. Median time to eradication in cirrhotic patients with portal vein thrombosis vs. cirrhotic patients without thrombosis was 50.9 days (12–440) vs. 43.4 days (13–489.4); log-rank: 0.04; patients with extrahepatic portal vein obstruction vs. cirrhotic patients without thrombosis 63.9 days (31–321.6) vs. 43.4 days (13.0–489.4); log-rank: 0.008. Thrombosis was shown to be the only risk factor for longer time to eradication.
Conclusions: Portal vein thrombosis per se appears to be the cause of a longer time to achieve eradication of varices but, once eradication is achieved, it does not influence their recurrence.

1. Introduction

Thrombosis of the portal vein may occur in the setting of an established cirrhosis [1] or as extrahepatic portal vein obstruction (EHPVO) in patients without a pre-existing liver disease, mostly with malignancy, abdominal infection or inflammation, myeloproliferative disorders or hereditary/acquired prothrombotic conditions [2,3]. Acute EHPVO, if not promptly relieved, leads to the formation of the portal vein cavernoma, a network of hepatopetal vessels which partly restores the portal flow to the liver, but does not prevent the development of portal hypertension. Bleeding from esophageal varices is one of the most dreaded complications of portal hypertension since, in spite of all the achievements of the last decades, it still is associated with high mortality rates [4]. Therefore, it is mandatory to start a prophylaxis of variceal bleeding, either to prevent first bleeding in patients with high risk varices [5,6] or to prevent rebleeding once varices have bled [5,6]. Endoscopic band ligation of esophageal varices (EVL) is a therapeutic option to prevent bleeding from high risk esophageal varices (EV) [5–23] or rebleeding in patients with liver cirrhosis or EHPVO [5,6,24–28].

Many patients with liver cirrhosis who need to undergo EVL for primary or secondary prophylaxis of variceal bleeding have an associated, usually non-occlusive portal vein thrombosis (PVT). As of today, the influence of portal vein thrombosis, either EHPVO or complicating liver cirrhosis, on the efficacy of EVL has never been assessed.

Aims of this study were to assess the influence of PVT on the eradication rate and time to eradication of EV in patients undergoing EVL. Secondary end-points were the recurrence rate of EV and time to recurrence, bleeding from EV and bleeding-related mortality.

* Corresponding author at: Gastroenterology Unit – Ospedale L. Sacco, Via GB Grassi 74, 20157 Milan, Italy. Tel.: +39 02 3904 2207/2925; fax: +39 02 3904 2337.
E-mail address: alessandra.dellera@unimi.it (A. Dell'Era).

1590-8658/$36.00
http://dx.doi.org/10.1016/j.dld.2013.08.138

2. Patients and methods

2.1. Study cohort

This is a retrospective analysis of consecutive patients referred to the Gastroenterology 3 Unit of the IRCCS Fondazione Ca' Granda Ospedale Policlinico of Milan for EVL between February1995 and February 2009. In the setting of primary prophylaxis for cirrhotic patients without PVT, EVL was performed for contraindication, intolerance or failure of haemodynamic response to beta-blockers; for cirrhotic patients with PVT, EVL was performed in order to minimize the risk of bleeding before starting oral anticoagulation. Inclusion criteria were: (a) cirrhosis diagnosed by histology or unequivocal clinical, laboratory and ultrasound findings or portal vein thrombosis in the absence of parenchymal liver disease, (b) for patients in primary prophylaxis: presence of high risk varices [2] and for patients in secondary prophylaxis: varices of any grade, (c) at least 6 months of follow-up, and (d) written informed consent to the procedures. Exclusion criteria were the presence of advanced-stage hepatocellular carcinoma and portal vein thrombosis due to neoplastic vascular invasion. Forty-nine patients were excluded from the analysis because of a follow-up less than 6 months. Two hundred and thirty-five patients entered the study: 192 patients with cirrhosis without PVT, 22 with cirrhosis with PVT and 21 with EHPVO. EVL was indicated for primary prophylaxis of esophageal variceal bleeding in 123 patients with cirrhosis and in 7 with EHPVO, to prevent rebleeding in 91 patients with cirrhosis and 14 with EHPVO.

2.2. Endoscopic band ligation

Endoscopic band ligation was performed in all patients within one month from the indication and then every 2–3-weeks until eradication was achieved. Band ligation was initially performed with the single-band device; then with multiband ligation devices (SpeedBand, Boston Scientific Medi-Tech, Natick, MA, or Six Shooter Saeed Multi-Band ligator, Wilson Cook Medical Inc., Winston-Salem, NC) when they became commercially available, under light e.v. sedation with midazolam, by placing up to 7 bands per session.

Anticoagulation was discontinued 5 days before and 14 days after the banding session to allow the procedure; during this period patients were given LMWH at prophylactic dose.

2.3. Diagnosis of portal vein thrombosis

In all cases portal vein thrombosis was diagnosed at abdominal ultrasonography, showing solid echoes within the portal vein, and confirmed in many cases by computed tomography scanning or magnetic resonance angiography.

2.4. Definitions of end-points

Eradication of esophageal varices: varices were considered eradicated when they had disappeared or were too small for further ligation because it was not possible to aspirate them into the ligation device.

Time to eradication of esophageal varices was defined as the time from the date of the first EVL to 30 days after the date of the follow up upper gastrointestinal endoscopy showing eradication of EV.

Recurrence of esophageal varices was defined as the reappearance of esophageal varices which could be ligated.

Time to recurrence of esophageal varices was defined as the time from the date of eradication to the date of the endoscopy showing recurrence of esophageal varices.

Bleeding-related mortality was defined as any death within 6 weeks of the date of bleeding, according to international consensus guidelines [29].

2.5. Follow-up

After eradication, patients underwent repeat endoscopy at 1, 3, 6 months and then yearly to monitor variceal recurrence. Variceal recurrences were treated with repeat band ligation. All patients underwent clinical reassessment every 6 months or more often if needed.

Median follow-up was 31 months (range 6–149) with no difference between the three groups.

2.6. Statistical analysis

The statistical analysis was performed by SPSS statistical package (SPSS Inc., Chicago, IL, USA). Data are reported as frequencies, medians with range or mean ± s.d., ANOVA test, Kruskal–Wallis H test and χ^2 test were used as appropriate. Actuarial probability of eradication and recurrence of EV was evaluated by the Kaplan–Meier method. Comparison between different groups was made by the Log Rank test. Identification of factors influencing time to eradication of EV was performed by logistic regression analysis. Statistical significance was established at a p value of less than 0.05.

3. Results

Two-hundred and 35 patients were enrolled in the study, 72% men, mean age 59.2 ± 12.2 years. The characteristics of the study population are shown in Table 1: cirrhotic patients with or without PVT were prevalently males and did not differ for any of the clinical or biochemical parameters evaluated. On the other hand, patients with EHPVO had no male predominance, were significantly younger and had a higher platelet count (reflecting the existence of a chronic myeloproliferative neoplasm as the underlying cause of EHPVO in many of them). Moreover, in patients with cirrhosis and PVT, the latter was mostly partial, whereas it was complete (i.e. portal vein cavernoma) in those with EHPVO. Further characteristics of PVT in patients with cirrhosis and EHPVO are shown in Table 2.

Clinical presentation of EHPVO was acute in 43% of patients (presentation being abdominal pain, intestinal infarction) and chronic in 57%. As for aetiology of PVT, it was due to myeloproliferative disease in 77% of patients (5% PV, 24% ET, 24% MF, 10% PV and then MF; 14% unclassifiable myeloproliferative neoplasia); in 5% of patients MPD was associated to eterozygous prothrombin mutation and in 5% of patients the thrombophylic risk factor was factor V Leiden mutation. In 15% of patients the cause of thrombosis was perinatal pylephlebitis. No risk factor for EHPVO could be found in 3% of patients. Anticoagulant therapy was performed in 62% of patients. Complete recanalization was not achieved in any patient. When clinically indicated patients were treated for underlying myeloproliferative disease with oncocarbide (38%) or anti-JAK2-targeted therapy (5%). 24% of patients received no therapy. Sixty-two percent of patients were on non selective beta-blockers therapy.

3.1. Primary end-points

3.1.1. Eradication rate

All patients included in the study achieved eradication except two patients, one with cirrhosis without PVT and one with cirrhosis and PVT.