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ORIGINAL ARTICLE

Association between portal vein thrombosis and risk of bleeding in liver cirrhosis: A systematic review of the literature

Xingshun Qi[a,b,*], Chunping Su[c], Weirong Ren[b,d], Man Yang[b,e], Jia Jia[b,f], Junna Dai[a], Wenda Xu[a], Xiaozhong Guo[a,*]

[a] *Department of Gastroenterology, General Hospital of Shenyang Military Area, Shenyang 110840, China*
[b] *Xijing Hospital of Digestive Diseases, Fourth Military Medical University, Xi'an 710032, China*
[c] *Library of Fourth Military Medical University, Xi'an 710032, China*
[d] *Department of Digestive Diseases, Sanmenxia Central Hospital, Henan University of Science and Technology, Xiaoshan Road, Sanmenxia 472000, China*
[e] *Department of Gastroenterology, Songgang People's Hospital, Shenzhen 518105, China*
[f] *Department of Digestive Diseases, Shaanxi Provincial People's Hospital, Xi'an 710068, China*

Summary
Aims: A systematic review of the literature was conducted to explore the association of portal vein thrombosis (PVT) with the risk of bleeding in liver cirrhosis.
Methods: PubMed, EMBASE, and Cochrane library databases were searched for all relevant papers, which compared the prevalence of bleeding at baseline and/or incidence of bleeding during follow-up between cirrhotic patients with and without PVT.
Results: Eighteen papers were eligible for this systematic review. The heterogeneity among studies was marked with regards to the treatment modalities, sources of bleeding, lengths of follow-up, and ways of data expression. But most of their findings were homozygous and suggested that the cirrhotic patients with PVT were more likely to have previous histories of bleeding at their admission and to develop de novo bleeding and/or rebleeding during the short- and long-term follow-up. The association of PVT with the risk of bleeding might be weakened in the multivariate analyses. Additionally, as for the cirrhotic patients with gastric variceal bleeding treated with medical/endoscopic therapy, the association of PVT with the risk of rebleeding remained controversial in 2 studies; as for the cirrhotic patients undergoing transjugular intrahepatic portosystemic shunts for the management of variceal bleeding, a pre-existing PVT was not associated with the risk of rebleeding.

* Corresponding authors. Department of Gastroenterology, General Hospital of Shenyang Military Area, No. 83 Wenhua Road, Shenyang 110840 China. Tel.: +86 24 288 976 03; fax: +86 24 288 511 13.
E-mail addresses: xingshunqi@126.com (X. Qi), guo_xiao_zhong@126.com (X. Guo).

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Conclusions: Based on a systematic review of the literature, there was a positive association between the presence of PVT and risk of bleeding in liver cirrhosis in most of clinical conditions. However, whether PVT aggravated the development of bleeding during follow-up needed to be further explored.

Introduction

Gastroesophageal varices can be found in approximately 50% of cirrhotic patients at the time of diagnosis [1,2]. The development of varices is primarily attributed to an increased portal pressure caused by fibrosis and regenerative nodules (as the hepatic venous pressure gradient is more than 10 mmHg, varcies will develop [3]). Once the varices are ruptured, the mortality is up to 15—20% within 6 weeks and as high as 40% within 1 year [4,5]. The most common predictors for the first occurrence or recurrence of variceal bleeding include the diameter of varices, red signs on endoscopy, and Child-Pugh score [6]. Recently, the researchers also have cast more attention to the effect of portal vein thrombosis (PVT) on the development of variceal bleeding in liver cirrhosis [7,8], because it can further elevate the resistance to portal inflow. The important topic may influence the risk stratification of variceal bleeding, thereby improving the algorithm for the management of variceal bleeding in liver cirrhosis. Herein, we systematically review the relevant literature to clarify the association between PVT and risk of bleeding in liver cirrhosis.

Methods

Search strategy and study selection

As previously described, we retrieved all papers regarding PVT via the PubMed, EMBASE, and Cochrane library databases [9,10]. After this systematic search, more recently published publications were also hand-searched. Among the clinical studies with more than 10 patients, we further identified the studies that evaluated the association between PVT and risk of bleeding in liver cirrhosis. Exclusion criteria were as follows:

- only malignancy was enrolled;
- PVT developed after surgery, therapeutic endoscopy, or interventional treatments;
- PVT developed in non-cirrhotic patients;
- the control group (i.e., patients without PVT) was missing;
- the association between PVT and risk of bleeding was not evaluated.

Data extraction

We extracted the following characteristics of the included studies: first author, publication year, study design, enrolment period, target population, treatment modalities, total number of observed patients, and number of patients with PVT. Additionally, we collected the data regarding the proportion of bleeding in cirrhotic patients with and without PVT. If the original data were not reported, we collected the odds or hazard ratios to express the difference in the proportion of bleeding between the two groups. Data were not synthesized, because they were expressed in different ways.

Grade of evidence

The evidence was classified into high- and low-grade. The evidence was of high-grade, if any one of the 2 following points was met:

- a multivariate analysis was performed to explore the statistically significant difference;
- if only a univariate analysis was performed, the baseline Child-Pugh class or MELD score should be matched between patients with and without PVT.

Otherwise, the evidence was of low-grade.

Results

Characteristics of studies

Initially, 10,936 papers regarding PVT were identified. Among them, 14 papers were eligible for this systematic review [11—24] (Fig. 1). Another 4 eligible papers, which were published after the systematic search, were also identified by hand searching [25—28]. Thus, 18 studies were finally included. The characteristics of included studies were summarized in Table 1. According to the regions, 5 studies were performed in China Taiwan, 5 studies in Italy, 3 studies in USA, 2 studies in France, 1 study in Canada, 1 study in Switzerland, and 1 study in France and Belgium. According to the enrolment periods, 3 studies were launched before 1990, 5 studies between 1990 and 2000, and 10 studies after 2000. According to the publication forms, 2 studies were published in abstracts, and 16 studies in full-texts. Hepatocellular carcinoma was excluded in 7 studies, but not in 9 studies. The information regarding the exclusion of hepatocellular carcinoma was not reported in 2 other studies. The prevalence of PVT in liver cirrhosis was 7—25%.

Multivariate analyses were performed in 8 studies [11,13,14,17,18,23,24,28], and only univariate analyses were performed in 10 others. Of these studies without multivariate analyses, 5 had similar proportions of

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