Thrombosis Journal

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The risk factors of liver cirrhosis complicated with portal vein thrombosis and the efficacy and safety of anticoagulant therapy: a meta analysis

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Abstract

Objective To evaluate the risk factors of liver cirrhosis complicated with portal vein thrombosis and the efficacy and safety of anticoagulant therapy.

Methods Relevant literature was searched through PubMed, Cochrane library, Embase, Web of Science, Wanfang Medical Network and CNKI databases, and eligible literature was included. QUADS scale was used to evaluate the quality of the included literatures, and Stata15.1 software was used for meta-analysis and statistical processing.

Results For risk factors analysis for cirrhosis with Portal vein thrombosis, 19 literatures were included, including 1563 patients with cirrhosis with portal vein thrombosis and 2579 patients with cirrhosis without portal vein thrombosis, all of which were not treated with anticoagulation. The results of meta-analysis showed that compared with the PVT group, there was no significant difference in creatinine(Scr,MD = 0.09,95%CI: -0.03–0.22,P = 0.132)and total bilirubin(TBIL,MD = -0.00, 95%CI: -0.10 ~ 0.09,P = 0.948).There was significant difference in albumin(ALB,MD = -0.32, 95%CI:-0.43–0.21,P = 0.000)and PLT(PLT, MD = 0.15, 95%CI: 0.05–0.26, P = 0.004).And there was also no difference in hypertension history (OR = 0.78,95%CI:0.59 ~ 1.03,P = 0.079). In the study on the anticoagulant effect and safety of liver cirrhosis complicated with portal vein thrombosis, a total of 9 literatures were included. Among them,497 patients with liver cirrhosis complicated by portal vein thrombosis are treated with Anticoagulation treatment, and 633 patients with cirrhosis complicated by portal vein thrombosis without anticoagulation treatment. The analysis results showed that the thrombus recanalization situation of liver cirrhosis complicated with portal vein thrombosis after anticoagulation treatment was better than that of patients without anticoagulation (OR = 4.052,95%CI: 2.737–6.000,P = 0.000),and there was no significant difference in the occurrence of bleeding events between patients with anticoagulation and those without anticoagulation (OR = 1.017, 95%CI:0.735–1.407,P = 0.920). The Stata15.1Egger test showed no significant publication bias for all the results($P > 0.05$).

Conclusions Patients with liver cirrhosis complicated with low platelet and low albumin are more likely to develop PVT. Anticoagulation is helpful and safe for thrombolysis in patients with liver cirrhosis complicated with PVT.

Keywords Liver cirrhosis, Portal vein thrombosis, Risk factors, Anticoagulant therapy, Meta-analysis

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Introduction

Portal vein thrombosis (PVT) refers to the formation of thrombosis in the main portal vein and its branches,even the mesenteric vein or splenic vein. PVT can occur in a variety of clinical settings,including cirrhosis, malignancy,and inflammatory states.In patients with cirrhosis, the incidence of PVT is significantly increased,reaching 10%– 26%, due to portal hypertension,liver dysfunction and coagulation dysfunction [1].This complication may further aggravate portal hypertension,leading to gastroesophageal varices rupture bleeding,mesenteric ischemia and other serious consequences.Therefore, how to effectively prevent and treat PVT in patients with cirrhosis has become an important clinical topic.The pathogenesis is usually multifactorial,and it is believed that its occurrence is mainly determined by the interrelationship of the three physiological factors of the Virchow triad: the hypercoagulable state of blood, blood stasis, and intra vascular wall injury [2].However, the exact contribution of these factors to the development of PVT has not been fully elucidated.With the deepening of research,more and more evidence shows that thrombocytopenia,decreased albumin and coagulation dysfunction in patients with cirrhosis are high risk factors for PVT [3].Although the mechanism of PVT formation in patients with cirrhosis is well understood,there is no uniform risk factor prediction model.Therefore, it is of great clinical value to study the risk factors of liver cirrhosis complicated with PVT.

Although the diagnosis of PVT in cirrhosis has received more and more attention,many patients are only detected in routine imaging because of its hidden symptoms [3].Although this asymptomatic PVT does not cause immediate acute symptoms,prolonged thrombosis can aggravate portal hypertension,increase the risk of bleeding,and affect the patient's prognosis.In the treatment of PVT,anticoagulant therapy is a common clinical treatment [4].Its purpose is to promote the recanalization of thrombus and prevent the further expansion of thrombus or the formation of new thrombus.However,for patients with cirrhosis,anticoagulant therapy may carry a significant risk of bleeding,especially when there are existing complications such as portal hypertension and esophageal varicose veins.Some studies have shown that appropriate anticoagulant therapy can improve the recurrence rate of PVT in patients with cirrhosis without significantly increasing the risk of bleeding [4, 5].There is still some controversy about the anticoagulant treatment of cirrhosis combined with PVT.Therefore, this study focuses on the meta-analysis of the thrombotic recanalization and bleeding risk of patients with cirrhosis combined with PVT after anticoagulant treatment,and the risk factors of PVT in cirrhosis,hoping to provide certain clinical support.

Materials and methods

Retrieval method

The search was conducted independently by two researchers,liver cirrhosis (LC),portal vein thrombosis(PVT),risk factors,anticoagulation treatment was searched in Pubmed,Cochrane library, Embase,Web of Science,Wanfang Medical Network,CNKI and other databases with keywords. The literatures related to cirrhosis combined with PVT were selected.First, it is screened according to the title and abstract,and then carefully read the final selection of included literature. When there is a disagreement,the most important thing is to have an open and constructive discussion. Both parties should express their views based on the evidence and analysis results of the literature, and try to find common points of understanding or complementary explanations. If the parties cannot reach an agreement, consider bringing in a third-party expert to assess the point of dispute. Third-party experts can provide independent advice and advice to help resolve differences.

Inclusion and exclusion criteria

Inclusion criteria: ①**Study subjects:** patients with cirrhosis and PVT confirmed by imaging examination, clinical or histology were the experimental group, and patients with cirrhosis and no PVT were the control group; Liver cirrhosis with PVT treated with anticoagulation was the experimental group, and no anticoagulation was the control group. For patients treated with anticoagulation, screening ages ranged from 18 to 70 years,and all patients, regardless of PVT severity, were treated with prevention of bleeding events: endoscopic screening, interventional therapy (strip ligation) or/and pharmacological interventions depending on the presence and severity of esophageal varices. ②**Indicators**: hemoglobin (HB), platelet (PLT), serum creatinine (Scr), Albumin (ALB), and Total bilirubin(TBIL), Prothrombin(PT), Prothrombin activity(PTA), D-II polymers(D-II); Thrombus recanalization and bleeding after anticoagulant treatment; ③**Previous medical history**: history of hypertension, diabetes, splenectomy, smoking history, etc.④The language of publication is Chinese or English; Articles will be searched until October 2024.

Exclusion criteria:①The literature was in the form of review and repeated publication;②The literature data was not recorded completely.③The diagnosis of portal vein thrombosis was not confirmed by imaging. Acute PVT symptoms such as fever, abdominal pain, and intestinal obstruction were present.Contraindication of anticoagulation included allergy, history of cerebral

hemorrhage,uncontrolled bleeding, or sustained platelet count below 50 ×10^9/L.Liver malignancies and other malignancies, liver transplantation,Buga syndrome, PVT and Transjugular intrahepatic portal shunt (TIPS) caused by non-liver diseases.

Literature quality evaluation

Since this study was observational,QUADS (quality assessment of diagnostic accuracy studies) was used to evaluate the quality of the included documents.

Statistical methods

Stata15.1 software was used to conduct a meta-analysis of the literature data that met the criteria.Continuity variables were represented by mean difference (MD) and 95%CI.The odds ratio (OR) of bitaxonomic variables was used as the result evaluation method,and the effect size of each research index was represented by 95% confidence interval (CI). At the same time, the heterogeneity of the selected literatures was analyzed, and the I^2 statistic reflects the proportion of the heterogeneity in the total variation of the effect size.When $I^2 > 50\%$, we considered significant heterogeneity between studies.Subgroup analysis and meta-regression were used to explore the sources of heterogeneity, and sensitivity analysis was also available. Due to the large number of literatures required for subgroup analysis and regression analysis, and due to the limitation of the number of final literatures included in this study, we used STATA15.1 for sensitivity analysis of all literatures included. Sensitivity analysis can be based on the characteristics of the included studies, by eliminating some studies of low quality or using different efficacy evaluation criteria and exclusion criteria, and then conducting a combined analysis, comparing with the combined effect size before the exclusion, to explore the impact of the excluded studies on the combined effect size.Sensitivity analysis focuses on the comparison between the combined effect size and the original effect size obtained from repeated meta-analysis.The fixed-effect model was used for the studies with small heterogeneity ($P > 0.1$ and $I^2 < 50\%$).For all data results, $P < 0.05$ indicates statistical significance;meanwhile, Stata15.1 software is adopted to conduct Egger test on data results. If $P > 0.05$ indicates no significant publication bias.

Results

Features of the included literature

By searching the database,a total of 19 literatures were included in the analysis of the risk factors for PVT in cirrhosis,including 1563 patients with cirrhosis and 2579 patients without PVT.A total of 11 literatures were included in the analysis of the effect of anticoagulant therapy on cirrhosis combined with PVT, including 497 patients with cirrhosis combined with portal vein thrombosis and 633 patients with cirrhosis combined with portal vein thrombosis without anticoagulant therapy.The specific literature screening flow chart is shown in Fig. 1 below.

Specific features of the included literatures:

The basic information of anticoagulation therapy for liver cirrhosis complicated with portal vein thrombosis and the events of thrombosis recanalization and bleeding after anticoagulation in the included literatures are shown in Table 1:

Meta-analysis results of each observational index:

(1) Analysis of risk factors for liver cirrhosis complicated with portal vein thrombosis:

1 > Platelets (PLT)

A total of 12 papers [6–17] were included, including 675 patients with cirrhosis combined with PVT and 1159 patients with cirrhosis without PVT, with little heterogeneity (P =0.154,I2 =29.7%). After fixed-effect model analysis, the results showed that the platelet(PLT) of patients with cirrhosis combined with PVT was lower than that of patients with cirrhosis without PVT. There was statistical significance [MD =0.15,95%CI (0.05, 0.26), P= 0.004] (Fig. 2).

2 > Albumin (ALB), creatinine (Scr), total bilirubin (TBIL)

A total of 12 literatures included albumin(ALB)) [6, 8–12, 15, 17–21], including 638 cirrhosis patients with PVT and 915 patients without PVT, with little heterogeneity (P =0.029,I2 =48.8%).Fixed-effect model analysis was used.After analysis, the results showed that the albumin(ALB) of patients with PVT was lower than that of those without PVT, with statistical significance [MD =− 0.32,95%CI (− 0.43, − 0.21), P= 0.000] (Fig. 3A). A total of 14 literatures included total bilirubin(TBIL) [6–8, 10, 11, 13, 16–22], among which 676 patients with cirrhosis combined with PVT and 712 without, with little heterogeneity (*P* = 0.478,I2 =0.0%).Fixed-effect model analysis showed no difference between the two. There was no statistical significance [MD =− 0.00,95%CI (− 0.1, 0.09), P= 0.948](Fig. 3B). A total of 10 papers [6–8, 10, 13, 15, 16, 18, 20, 21] included serum creatinine(Scr), among which 536 patients with cirrhosis combined with PVT and 645 without, with little heterogeneity (P =0.632,I2 =0.0%). Fixed-effect model analysis showed no difference between the two. There was no statistical significance [MD =0.09,95%CI (− 0.03, 0.22), *P*= 0.132] (Fig. 3C). (Fig. 3A, B, C).

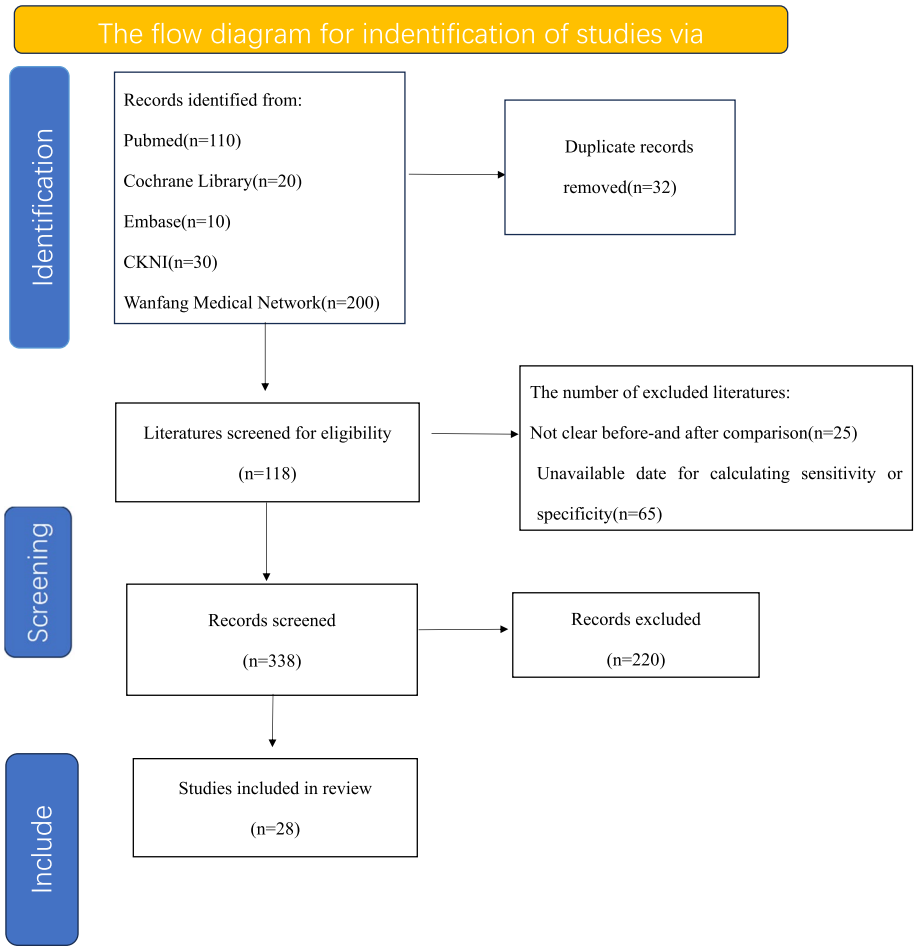

Fig. 1 Literature screening flow chart

3 > Hypertension history and PVT analysis results:

A total of 9 literatures included hypertension history, with little heterogeneity (P =0.415,I2 =2.3%), among which 545 patients with cirrhosis and 656 patients without PVT were analyzed by fixed-effect model, and the analysis results showed no significant difference between the two [OR =0.78,95%CI (0.59, 1.03). P= 0.079] (Fig. 4).

(2) Analysis of thrombosis recanalization and bleeding risk after liver cirrhosis combined with PVT anticoagulation:

1 > Results of thrombus recanalization after liver cirrhosis combined with PVT anticoagulation:

Thromboembolism after anticoagulation was included in a total of 9 literatures [23–31], among which 311 patients with cirrhosis combined with PVT undergoing anticoagulation and 411 patients without anticoagulation, with little heterogeneity (P =0.512,I2 =0.0%).The results of fixed-effect model analysis showed that thromboembolism after anticoagulation was better than that in patients without anticoagulation. There was statistical significance [OR =4.05,95%CI (2.74, 6.00), P= 0.000] (Fig. 5).

2 > Bleeding after liver cirrhosis combined with PVT anticoagulation results:

A total of 8 studies [23, 24, 27, 29–33] included bleeding after anticoagulation, including 87 patients with cirrhosis combined with PVT bleeding after anticoagulation and 116 patients without anticoagulation, showing little heterogeneity (P =0.521,I2 =0.0%). The results of fixed-effect model analysis showed no significant difference in bleeding after anticoagulation compared with non-anticoagulation patients [OR =1.02,95%CI (0.73, 1.41), P= 0.920] (Fig. 6).

Table 1 The basic information of included literature

Included literatures	Year	Anticoagulant Therapy	Thrombus Recanalization	Bleeding Events
Leonard Naymagon.et.al	2021	warfarin titrated to INR of 2–3 and enoxaparin-intervals 1 mg/kg twice daily rivaroxaban 20 mg daily (following a 21 day loading period of 15 mg twice daily) pixaban 5 mg twice daily (following a 7 day loading period of 10 mg twice daily) dabigatran 150 mg twice daily	complete resolution (41/86) PVT Extension (13/86)	Major Bleeding Events (17/86)
Jung Wha Chung.et.al	2014	Warfarin	Complete resolution/Partial Resolution (11/14)/(5/14) Non-response of thrombus (3/14)	-
Madalina Florescu.et.al	2021	200 U/kg enoxaparin was used firstly	Regression(30/54)	2 epistaxis,one oral bleeding and 7variceal bleeding
		Then oral anticoagulant with enoxaparin or Vitamin K antagonists was used	Progression(6/54) Stationary(18/54)	(10/54)
Ayako Sato.et.al	2023	(Rivaroxaban) direct oral anticoagulant followed by warfarin potassium and heparin	Complete resolution (5/21)2uppergastrointestinalbleeding	1 cerebral hemorrhage g(Endoscopic intervention)
			Extension (2/21)	1 with hemorrhoid (no one was bleeding fatal)
Zhiqi Zhang.et.al	2023	warfarin, rivaroxaban, dabigatran or low molecular weight heparin (LMWH) without limitations on dosing	Complete resolution(1/27) Partial Resolution(11/27) Progression(13/27)	Total Bleeding Events(4/27) Major Bleeding Events(cerebral hemorrhage)(1/27)
Bernhard Scheiner.et.al	2018	LMWH and followed by oral anticoagulation with phenprocoumon (target INR levels 1.5–2.0)	Resolution(7/16) Progression(2/16)	0/16
Hui Chen.et.al	2015	warfarin (target INR levels 1.5–2.0)	Resolution(15/22) Stationary(4/22) Progression(3/22)	No recording
Shenxin Lu.et.al	2024	warfarin(target INR levels 2–3) and nadroparin calcium 4100 IU/d for a period of 5 days If additional endoscopic therapy or other traumatic procedures were necessary	Complete recanalization(17/30) Partial recanalization(23/30) Exacerbation (extension/de novo) (0/30)	upper gastrointestinal contrast (2/30) Retroperitoneal(1/30)
Ming-hua Ai.et.al	2020	rivaroxaban 20 mg once daily Or dabigatran etexilate capsules 150 mg twice daily	Complete/partial recanalization(11/39) PVT progressive cases(3/39)	Hematuria(1/39) hemoptysis(1/39) Melena(1/39)

Publication bias detection results

In this study, the P values of all indicators were greater than 0.05, indicating that no significant publication bias existed (Table 2).

Discussion

As one of the complications of decompensation of cirrhosis, portal vein thrombosis is very important for early diagnosis and anticoagulation of acute portal vein thrombosis. Failure to detect and treat portal vein thrombosis can lead to mesenteric ischemia, which seriously threatens the life of patients. However, for patients with cirrhosis, the diagnosis of portal vein thrombosis is often found by chance. Therefore, how to identify the high risk factors of portal vein thrombosis at an early stage is crucial for the prevention of portal vein thrombosis [34]. Current studies have shown [35] that patients with cirrhosis have many risk factors that can easily lead to the formation of PVT, which are mainly divided into systemic and local factors. The portal vein system in cirrhosis is a local environmental factor, which is especially prone to thrombosis due to reduced blood flow in portal hypertension and inflammatory environment secondary to liver injury and intestinal translocation of bacteria

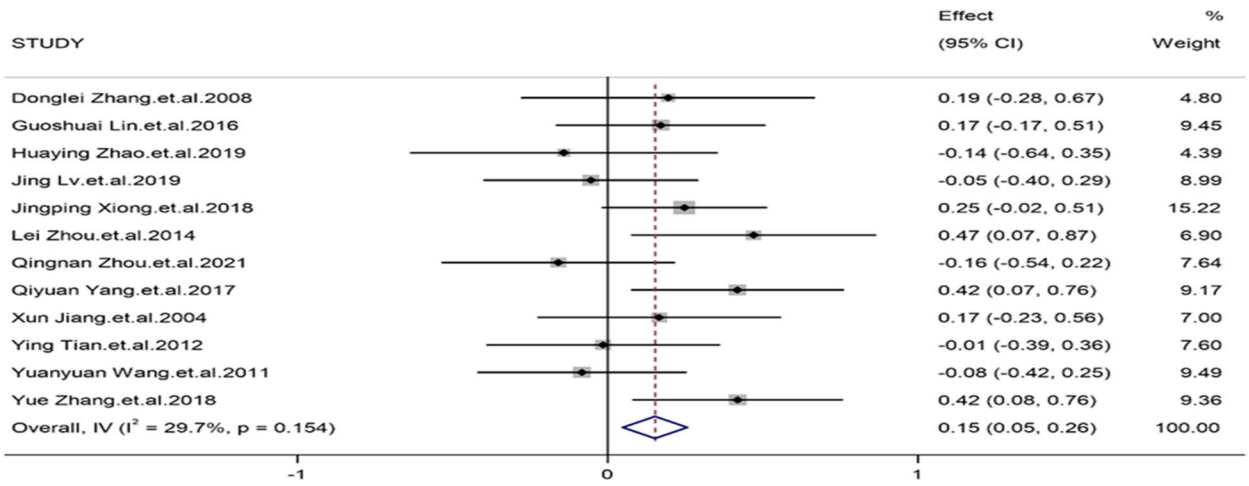

Fig. 2 Forest map of meta-analysis of PLT

or its by-products. Multiple systemic factors, including inherited and acquired embolism, extraperitoneal cancer, hormone therapy, and autoimmune diseases [36]. In our study, we found no difference in creatinine (P =0.132), total bilirubin (P =0.948) and hypertension (P =0.079) among patients with cirrhosis with portal vein thrombosis, while low albumin (P =0.000) and platelet decline (P =0.004) were risk factors for PVT in patients with cirrhosis.

The conclusion that platelet reduction is a risk factor for PVT in cirrhotic patients is also highlighted in the Baveno VII [37] consensus report that patients with low platelet counts are at higher risk for PVT, which seems paradoxical because logically, low platelet counts should be prone to bleeding. With the progression of cirrhosis and portal hypertension, the decrease of portal blood flow exceeds the protective effect of low platelet count on thrombosis. Therefore, the paradoxical finding that PVT increases while platelet count decreases may be related to the decrease of portal blood flow during the progression of portal hypertension [38]. Therefore, in the clinic, patients with cirrhosis complicated with thrombocytopenia, we need to be alert to the occurrence of PVT, and timely supplement platelet when necessary. Our study also found that cirrhosis patients with low albumin were more likely to form PVT, which may be related to albumin anti-oxidation and anti-platelet aggregation. This conclusion is consistent with the research conclusion of Stefania Basili [39] et al. Albumin can interfere with platelet activation by inhibiting Nox2-mediated oxidative stress. Albumin is known to exert its antioxidant effect by quenching active oxidant species (ROS) or by binding and inactivating free metals that would otherwise catalyze ROS formation. Nox2 is one of the most important cell producers of ROS, and inhibition of Nox2 activation is an important step in the platelet activation mechanism. Albumin can exert anti-platelet effects by inhibiting Nox2-derived ROS and ultimately inhibiting the formation of isoprostaglandins [40].Therefore, after the decrease of albumin, its anti-platelet aggregation effect is weakened, and it is easy to form thrombus.It can be seen that albumin is not only a nutritional indicator, but also a clotting indicator in patients with cirrhosis. Therefore, we need to pay attention to the albumin level of patients clinically and supplement it in time. When albumin is low, it can be supplemented intravenously to prevent portal vein thrombosis and hepatic encephalopathy. In addition, the results of this study also showed that creatinine, total bilirubin levels, and history of hypertension did not show a significant association in the development of PVT. These results suggest that although renal insufficiency and jaundice are common complications in the course of cirrhosis, they are not independent risk factors for PVT development. This finding provides a new way to further refine the risk assessment of PVT in clinic.

PVT can increase the risk of portal hypertension and related complications, as well as the complexity of liver transplantation and the risk of premature death after liver transplantation [41]. Anticoagulant therapy is a common treatment for patients with PVT, and non-cirrhotic patients with portal vein thrombosis often require anticoagulant therapy. At present, the clinically used anticoagulants are divided into heparin and oral anticoagulants. Low molecular weight heparin requires subcutaneous injection, so oral anticoagulants are suitable for long-term use. Warfarin is the most commonly used oral anticoagulant in clinical practice, but due to its narrow therapeutic window, large dose variation, and interaction

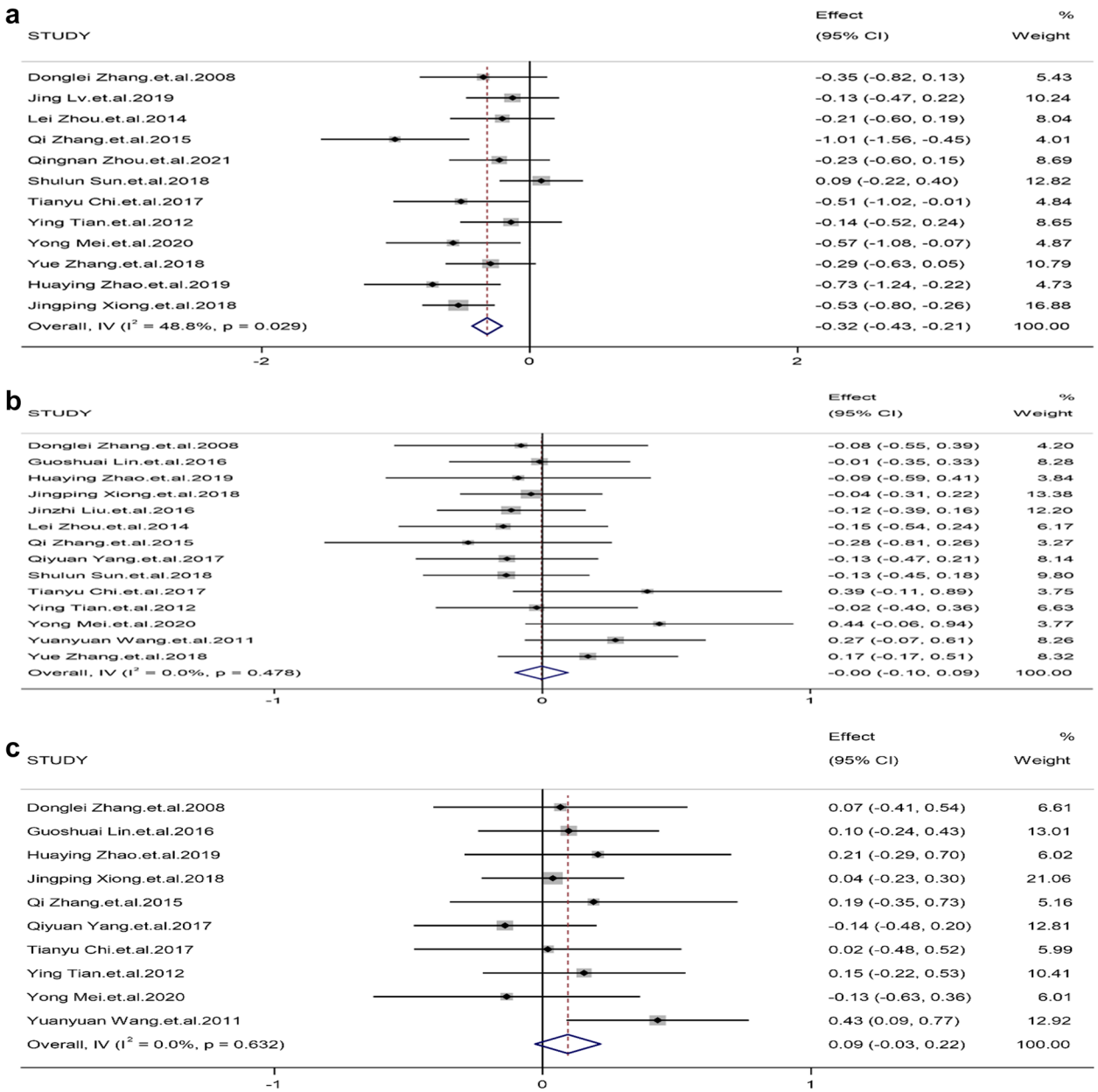

Fig. 3 Forest map of meta-analysis of albumin(ALB) (**A**). Forest map of meta-analysis of total bilirubin(TBIL) (**B**). Forest map of meta-analysis of serum creatinine (Scr) (**C**)

with a variety of foods, routine coagulation function testing is required, which is limited to some extent [42]. In DOACs, Dabigatran Etexilate Capsule is mainly metabolized by kidney, Apixaban and rivaroxaban are mainly metabolized by CYP3 A4 of liver cytochrome P450 [44], while Edoxaban is slightly metabolized by CYP3 A4, and apixaban is mainly eliminated by liver, followed by rivaroxaban and edoxaban. When the liver is not fully functional, on the one hand, it can lead to a decrease in the synthesis of clotting factors, and the decrease in plasma albumin level indirectly increases the anticoagulant effect of DOAC; on the other hand, the impaired liver function can affect its pharmacokinetic process in vivo, including first pass clearance after oral absorption, plasma protein binding, cytochrome P450 mediated metabolism, bile excretion and the influence on renal function. Current data on the safety and efficacy of oral anticoagulants in patients with liver disease are mainly derived from pharmacokinetic studies in subjects with mild to moderate liver injury (Child–pugh A or B) and small sample

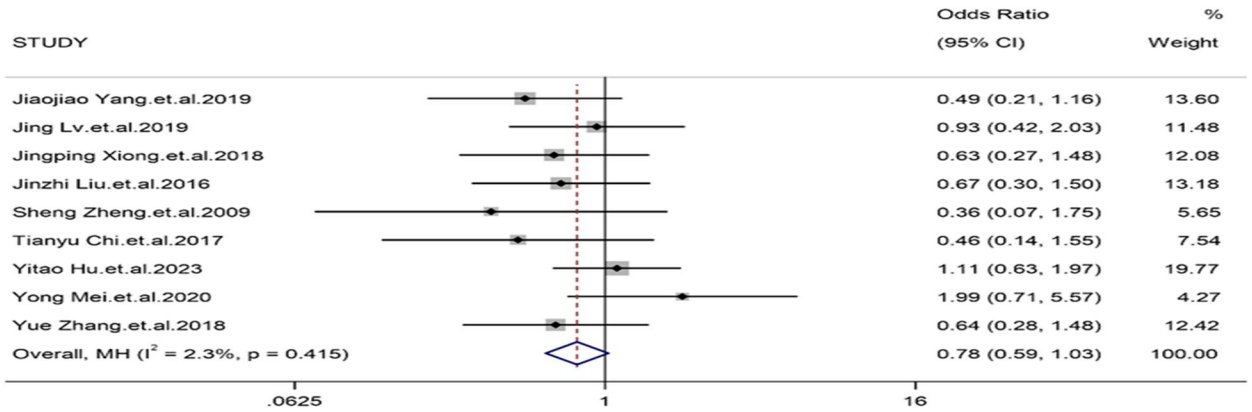

Fig. 4 Forest map of meta-analysis of Hypertension

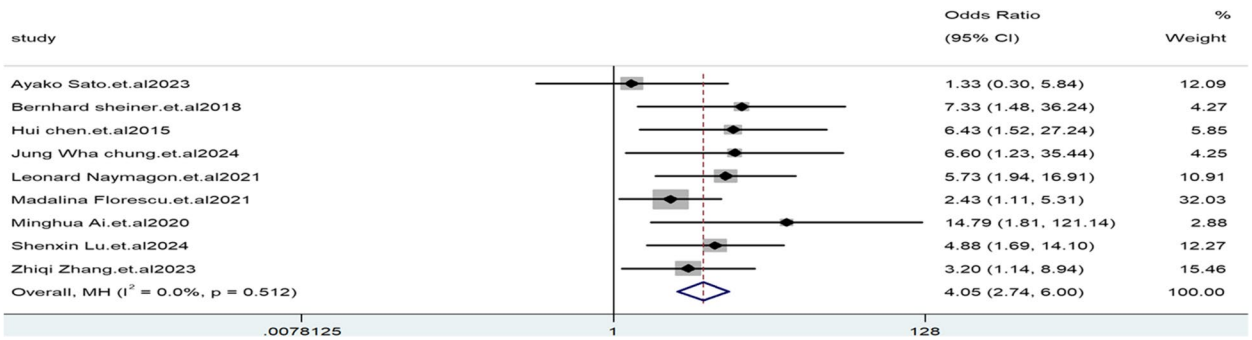

Fig. 5 Forest map of meta-analysis of Thrombus recanalization after anticoagulation

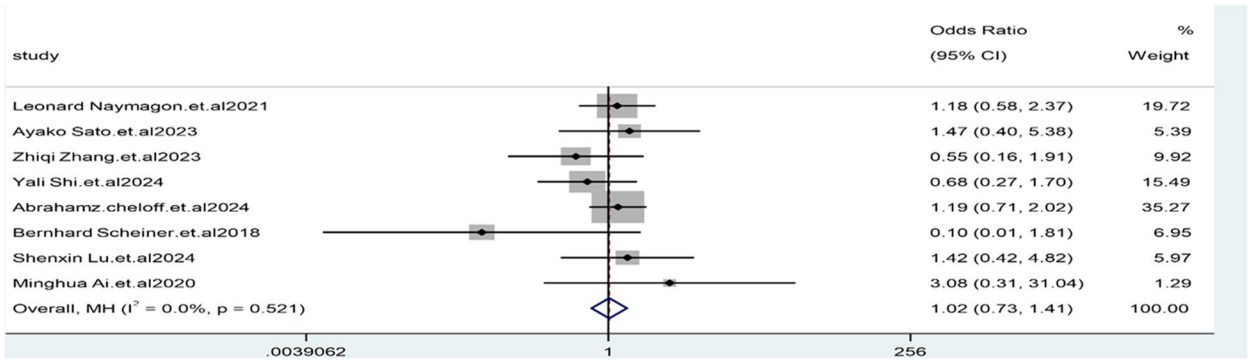

Fig. 6 Forest map of meta-analysis of Bleeding after anticoagulation

Table 2 Results of publication bias detection for each index

Indicator	PLT	ALB	TBIL	Scr	History of hypertension	Thrombus recanalization	Bleeding Events
P value	0.446	0.114	0.404	0.998	0.078	0.103	0.458

observational studies. Accidental overdose of DOACs and concurrent administration drugs that interact with DOACs or cause a relative excess of DOACs due to impaired kidney function, etc. If an overdose is suspected, whereas most DOACs have a half-life of about 12 h without bleeding. Before complications, only close

observation of the patient can be done, if necessary, in misuse activated charcoal can be taken orally within 2 to 4 h to reduce drug absorption. At present, there are some effective antagonists against DOACs-such as Andexanet alfa and idarucizumab are the currently approved specific reversal agents for oral factor (F)Xa inhibitors and dabigatran, respectively [45]. Moreover, more and more specific antagonists are gradually put into clinical trials. For patients with bleeding, corresponding hemostatic measures can be taken. For patients taking dabigatran, diuretics may be considered to promote their excretion [43]. Other treatment package include fluid therapy, infusion of red blood cells, platelets or fresh ice if necessary frozen plasma, etc., suitable patients can also consider the application of tranexamic acid and Vasopressin. If a patient has a fatal bleeding event, Prothrombin complex concentrate (PCC) is a concentrate of coagulation factors II, IX, and X or II, VII, IX, and X and the concentration of coagulation factors in PCC is approximately 25 times greater than in human plasma [46]. Our study found that anticoagulant therapy not only facilitates the recanalization of clots but also does not increase the incidence of bleeding. This suggests that anticoagulant therapy is safe for cirrhotic patients with portal vein thrombosis, which may be related to the recanalization of portal vein thrombosis after anticoagulant therapy, thereby reducing portal vein pressure, and the severity of esophageal and gastric varices, thereby reducing the incidence of gastrointestinal bleeding [42].

In conclusion, for patients with cirrhosis accompanied by albumin and platelet decline, timely supplementation is needed to prevent the occurrence of PVT. In addition, although the use of anticoagulant therapy does not significantly increase the risk of bleeding, it indicates that anticoagulant therapy has a good clinical application prospect in patients with cirrhosis. Although there are some differences in medical policies and anticoagulation programs in different countries, when starting an anticoagulation program, it should be carefully evaluated according to the specific clinical situation of patients and the risks and benefits of anticoagulation therapy to ensure effectiveness and safety. Future research should focus on how to optimize the individualized regimen of anticoagulation therapy and explore more new treatment options.

Limitations of this study: (1) Due to the short follow-up time of most of the included literatures in this study, the long-term efficacy and safety of anticoagulation therapy could not be fully evaluated; (2) Due to the limitation of literature search, it is impossible to explore and study the anticoagulant effect of different oral anticoagulants. (3) At the same time, meta-analysis studies on D-II polymer and PTA have not been conducted, and other indicators need to be further improved in the future to further improve the risk factors of cirrhosis complicated with portal vein thrombosis, so as to provide further support and basis for clinical treatment. (4) In addition, while DOACs is promising for use in patients with cirrhosis, its long-term safety needs more clinical evidence, especially in patients with severe liver insufficiency.

Acknowledgements
It is not suitable for our study.

Authors' contributions
Zhang Le and Ding Xiangchun were responsible for writing the content of the article and making pictures, Wang Xia and Ming Pu were responsible for organizing pictures and references, and Ma Lina and Ma Wanlong were responsible for revising the language of the article. All the authors contributed the same.

Funding
This study was supported by the Natural Science Foundation of Ningxia(2022 AAC02065)and the Key R&D Programs of Ningxia (2022 CMG02039) and the Fund for Less,Developed Regions of the Natural Science Foundation of China (81760363,81460301).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
An ethics statement is not applicable because this study is based on published literatures. Because our study is a meta-analysis,it is not necessary to get patient's consent.

Consent for publication
All authors agree to be published in the journal.

Competing interests
The authors declare no competing interests.

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Received: 4 November 2024 Accepted: 11 April 2025
Published online: 02 May 2025

References

1. Hepatobiliary Disease Study Group, Chinese Society of Gastroenterology, Chinese Medical Association. Consensus for management of portal vein thrombosis in liver cirrhosis (2020, Shanghai). J Dig Dis. 2021 Apr;22(4):176–186. https://doi.org/10.1111/1751-2980.12970. Epub 2021 Mar 7. Erratum in: J Dig Dis. 2021 May;22(5):295.
2. Ju C, Li X, Gadani S, Kapoor B, Partovi S. Portal Vein Thrombosis: Diagnosis and Endovascular Management. Rofo. 2022 Feb;194(2):169–180. English. https://doi.org/10.1055/a-1642-0990. Epub 2021 Oct 14.
3. Noronha Ferreira C, Marinho RT, Cortez-Pinto H, Ferreira P, Dias MS, Vasconcelos M, Alexandrino P, Serejo F, Pedro AJ, Gonçalves A, Palma S, Leite I, Reis D, Damião F, Valente A, Xavier Brito L, Baldaia C, Fatela N, Ramalho F, Velosa J. Incidence, predictive factors and clinical significance of development of portal vein thrombosis in cirrhosis: A prospective study. Liver Int. 2019Aug;39(8):1459–67. https://doi.org/10.1111/liv.14121. (Epub 2019 May 15).

4. Intagliata NM, Caldwell SH, Tripodi A. Diagnosis, Development, and Treatment of Portal Vein Thrombosis in Patients With and Without Cirrhosis. Gastroenterology. 2019May;156(6):1582-1599.e1. https://doi.org/10.1053/j.gastro.2019.01.265. (Epub 2019 Feb 13).
5. Senzolo M, M Sartori T, Rossetto V, Burra P, Cillo U, Boccagni P, Gasparini D, Miotto D, Simioni P, Tsochatzis E, A Burroughs K. Prospective evaluation of anticoagulation and transjugular intrahepatic portosystemic shunt for the management of portal vein thrombosis in cirrhosis. Liver Int. 2012 Jul;32(6):919–27. https://doi.org/10.1111/j.1478-3231.2012.02785.x. Epub 2012 Mar 21.
6. Zhang Donglei, Yang Ning. Risk factors related to portal vein thrombosis in cirrhotic patients. International Journal of Chinese Digestion,2008,16(27): 30106–3109. (in Chinese) https://doi.org/10.3969/j.issn.1009-3079.2008.27.018.
7. Lin Guoshuai, Xu Qin, Zhao Shuyi, et al. Analysis of clinical features and related risk factors of liver cirrhosis complicated with portal vein thrombosis. The Chinese journal of liver disease, 2016, 24 (7) : 513–517. The 10.3760 / cma. J.i SSN. 1007–3418.2016.07.006.
8. Zhao Huaying, Li Yunze, Wei Tianling, et al. Analysis of risk factors for liver cirrhosis complicated with portal vein thrombosis. Medical Information,2019,32(3):86–88,92. https://doi.org/10.3969/j.issn.1006-1959.2019.03.026.
9. Lv Jing, Dong Sisi, GU Hongtu, et al. Risk factors and TCM syndromic characteristics of portal vein thrombosis in cirrhosis. Journal of Clinical Hepatobiliary Diseases,2019,35(10):2210–2213.https://doi.org/10.3969/j.issn.1001-5256.2019.10.016.
10. Xiong Jingping, LIU Haiying, ZHANG Yuexin. Analysis of risk factors associated with portal vein thrombosis in cirrhosis. Liver,2018,23(3):206–209. https://doi.org/10.3969/j.issn.1008-1704.2018.03.007.
11. Zhou Lei, Kong derun. Risk factors of liver cirrhosis complicated with portal vein thrombosis. Journal of Anhui Medical University,2014(10):1505–1507.
12. Zhou Qingnan, Zhang Guo, Nongbing, et al. Analysis of risk factors for portal vein thrombosis in patients with liver cirrhosis. Chinese Journal of Clinical Oncology, 2019,14(4):360–363. (in Chinese) https://doi.org/10.3969/j.issn.1674-3806.2021.04.07.
13. Yang Qiyuan, Luo Duo, Shen Bo, et al. Analysis of risk factors for portal vein thrombosis in cirrhosis. Journal of Guangzhou Medical University,2017,45(5):18–21. (in Chinese) https://doi.org/10.3969/j.issn.2095-9664.2017.05.05.
14. Jiang Xuan, LIU Yulan, JIN Penghua, et al. Clinical analysis of portal vein thrombosis in liver cirrhosis. Chinese Journal of Digestion, 2004,24 (06):329–331.
15. Tian Ying, Chen Wenming, Zhang Donglei, et al. The multi-factor analysis of portal vein thrombosis in patients with cirrhosis. Chinese journal of refresher doctors, 2012, 35 (22) : 21–24. The 10.3760 / cma. J.i SSN. 1673–4904.2012.22.007.
16. Wang Yuanyuan, Wu Zigang, Du Yiping, et al. Clinical features of liver cirrhosis complicated with portal vein thrombosis. International Journal of Digestive Diseases,2011,31(4):239–242. (in Chinese) https://doi.org/10.3969/j.issn.1673-534X.2011.04.016.
17. Zhang Yue, Don Wenhua, Ma Zushuai. Analysis of risk factors and short-term prognosis of PVT in liver cirrhosis. Journal of Modern Integrated Chinese and Western Medicine,2018,27(6):612–614. (in Chinese) https://doi.org/10.3969/j.issn.1008-8849.2018.06.012.
18. Qi Z, Lianyi G. Analysis of risk factors for portal vein thrombosis in liver cirrhosis. Medicine and Philosophy. 2015;36(24):32–4 ((in Chinese)).
19. Sun Shulun, Wang Xiaoyan. Risk factors and prognostic methods of liver cirrhosis complicated with portal vein thrombosis. Journal of Clinical Medical Literature Electronic,2018,5(34):81,83. (in Chinese) https://doi.org/10.3877/j.issn.2095-8242.2018.34.041.
20. Chi Tian-Yu, Zhang Mei. Analysis of risk factors for venous thrombosis in cirrhosis. Journal of Gastroenterology and Hepatology,2017,26(1):17–19. (in Chinese) https://doi.org/10.3969/j.issn.1006-5709.2017.01.005.
21. Yong M, Zhilin Z, Xuhui Y, et al. Effect of P-selectin and D-dimer on early prediction of portal vein thrombosis in liver cirrhosis. Modern Digestion and Interventional Therapy. 2020;25(9):1231–4.
22. Liu Jinzhi Hu, Jianming NX. Risk factors and prognosis of liver cirrhosis complicated with portal vein thrombosis. Journal of Anhui Medical University. 2016;51(2):280–3 ((in Chinese)).
23. Sato A, Watanabe S, Iseki M, Yamada Y, Kobayashi R, Furuya M, Arai K, Ohshina E, Tashiro Y, Nozaka T, Matsuoka M, Yauchi M, Kobayashi K, Matsumoto T, Furumoto Y, Asano T, Azuma S. Anticoagulation against portal vein thrombosis reduces mortality and liver cirrhosis-related complications: A propensity score-matched study. Hepatol Res. 2023Nov;53(11):1096–104. https://doi.org/10.1111/hepr.13942. (Epub 2023 Jul 22).
24. Scheiner B, Stammet PR, Pokorny S, Bucsics T, Schwabl P, Brichta A, Thaler J, Lampichler K, Ba-Ssalamah A, Ay C, Ferlitsch A, Trauner M, Mandorfer M, Reiberger T. Anticoagulation in non-malignant portal vein thrombosis is safe and improves hepatic function. Wien Klin Wochenschr. 2018Jul;130(13–14):446–55. https://doi.org/10.1007/s00508-018-1351-y. (Epub 2018 Jun 18).
25. Chen H, Liu L, Qi X, He C, Wu F, Fan D, Han G. Efficacy and safety of anticoagulation in more advanced portal vein thrombosis in patients with liver cirrhosis. Eur J Gastroenterol Hepatol. 2016Jan;28(1):82–9. https://doi.org/10.1097/MEG.0000000000000482.
26. Chung JW, Kim GH, Lee JH, Ok KS, Jang ES, Jeong SH, Kim JW. Safety, efficacy, and response predictors of anticoagulation for the treatment of nonmalignant portal-vein thrombosis in patients with cirrhosis: a propensity score matching analysis. Clin Mol Hepatol. 2014Dec;20(4):384–91. https://doi.org/10.3350/cmh.2014.20.4.384. (Epub 2014 Dec 24).
27. Naymagon L, Tremblay D, Zubizarreta N, Moshier E, Mascarenhas J, Schiano T. Safety, Efficacy, and Long-Term Outcomes of Anticoagulation in Cirrhotic Portal Vein Thrombosis. Dig Dis Sci. 2021Oct;66(10):3619–29. https://doi.org/10.1007/s10620-020-06695-4. (Epub 2020 Nov 5).
28. Florescu MM, Costache A, Iacob SM, Pietrareanu C, Ester C, Cerban R, Dumitru R, Grasu M, Lupescu I, Gheorghe L. Anticoagulation Therapy for Portal Vein Thrombosis in Patients with Cirrhosis in a Tertiary Center Experience. J Gastrointestin Liver Dis. 2021Sep 21;30(3):374–9. https://doi.org/10.15403/jgld-3392.
29. Ai MH, Dong WG, Tan XP, Xu L, Xu C, Zhang Q, Zhang Y, Li J. Efficacy and safety study of direct-acting oral anticoagulants for the treatment of chronic portal vein thrombosis in patients with liver cirrhosis. Eur J Gastroenterol Hepatol. 2020Oct;32(10):1395–400. https://doi.org/10.1097/MEG.0000000000001846.
30. Lu S, Chen J, Zhang R, Luo T, Ma L, Xu P, Ding H, Zeng X, Wu B, Shi Y, Liu C, Mu Y, Chen S, Wang J. Comparative effectiveness of warfarin in cirrhotic patients with non-symptomatic portal vein thrombosis: a multicenter, randomized controlled trial. Expert Rev Gastroenterol Hepatol. 2024 Jan-Feb;18(1–3):5–12. https://doi.org/10.1080/17474124.2024.2307575. Epub 2024 Jan 29.
31. Zhang Z, Zhao Y, Li D, Guo M, Li H, Liu R, Cui X. Safety, efficacy and prognosis of anticoagulant therapy for portal vein thrombosis in cirrhosis: a retrospective cohort study. Thromb J. 2023Jan 30;21(1):13. https://doi.org/10.1186/s12959-023-00454-x.
32. Shi Y, Feng W, Cai J, Wang Z, Pu Y, Mao W, Zhan K, Chen D. Analysis of factors related to recanalization of portal vein thrombosis in liver cirrhosis: a retrospective cohort study. BMC Gastroenterol. 2024Jul 13;24(1):224. https://doi.org/10.1186/s12876-024-03322-8.
33. Cheloff AZ, Bonanni LJ, Kirschenbaum JD, Luke N, Engelman JL, Ross JL, Fuligni G, Northup PG. Treatment of portal vein thrombosis in cirrhosis is associated with no survival advantage: a retrospective controlled study. Hepatol Int. 2024 Oct 1. https://doi.org/10.1007/s12072-024-10734-x. Epub ahead of print.
34. Intagliata NM, Caldwell SH, Tripodi A. Diagnosis, Development, and Treatment of Portal Vein Thrombosis in Patients With andWithoutCirrhosis.Gastroenterology.2019May;156(6):1582–1599.e1.https://doi.org/10.1053/j.gastro.2019.01.265. Epub 2019 Feb 13.
35. Harding DJ, Perera MT, Chen F, Olliff S, Tripathi D. Portal vein thrombosis in cirrhosis: Controversies and latest developments. World J Gastroenterol. 2015Jun 14;21(22):6769–84. https://doi.org/10.3748/wjg.v21.i22.6769.
36. Ak C, Adali G, Sayar S, Agackiran A, Kulali F, Kahraman R, Ozturk O, Ozdil K. Portal vein thrombosis risk factors in liver transplant candidates. Hepatol Forum. 2022Sep 23;3(3):88–92. https://doi.org/10.14744/hf.2022.2022.0005.
37. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C; Baveno VII Faculty. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022 Apr;76(4):959–974. https://doi.org/10.1016/j.jhep.2021.12.022. Epub 2021 Dec 30. Erratum in: J Hepatol. 2022 Jul;77(1):271. https://doi.org/10.1016/j.jhep.2022.03.024.

38. Lisman T, Porte RJ. The role of platelets in liver inflammation and regeneration. Semin Thromb Hemost. 2010Mar;36(2):170–4. https://doi.org/10.1055/s-0030-1251501. (Epub 2010 Apr 22).
39. Basili S, Carnevale R, Nocella C, Bartimoccia S, Raparelli V, Talerico G, Stefanini L, Romiti GF, Perticone F, Corazza GR, Piscaglia F, Pietrangelo A, Violi F; PRO-LIVER Collaborators. Serum Albumin Is Inversely Associated With Portal Vein Thrombosis in Cirrhosis. Hepatol Commun. 2019 Mar 2;3(4):504–512. https://doi.org/10.1002/hep4.1317.
40. Davì G, Ferroni P. CD40-CD40L interactions in platelet activation. Thromb Haemost. 2005Jun;93(6):1011–2. https://doi.org/10.1160/TH05-04-0270.
41. Pignatelli P, Carnevale R, Di Santo S, Bartimoccia S, Sanguigni V, Lenti L, Finocchi A, Mendolicchio L, Soresina AR, Plebani A, Violi F. Inherited human gp91phox deficiency is associated with impaired isoprostane formation and platelet dysfunction. Arterioscler Thromb Vasc Biol. 2011Feb;31(2):423–34. https://doi.org/10.1161/ATVBAHA.110.217885. (Epub 2010 Nov 11).
42. Chen H, Turon F, Hernández-Gea V, Fuster J, Garcia-Criado A, Barrufet M, Darnell A, Fondevila C, Garcia-Valdecasas JC, Garcia-Pagán JC. Nontumoral portal vein thrombosis in patients awaiting liver transplantation. Liver Transpl. 2016Mar;22(3):352–65. https://doi.org/10.1002/lt.24387.
43. Simonetto DA, Singal AK, Garcia-Tsao G, Caldwell SH, Ahn J, Kamath PS. ACG Clinical Guideline: Disorders of the Hepatic and Mesenteric Circulation. Am J Gastroenterol. 2020Jan;115(1):18–40. https://doi.org/10.14309/ajg.0000000000000486.
44. Yao Hongyan.Pharmacokinetics and clinical application of novel oral anticoagulants. Intl Med Rev. 2022;28(19):2809–12. https://doi.org/10.3760/cma.j.issn.1007-1245.2022.19.032.
45. Levy JH, Shaw JR, Castellucci LA, Connors JM, Douketis J, Lindhoff-Last E, Rocca B, Samama CM, Siegal D, Weitz JI. Reversal of direct oral anticoagulants: guidance from the SSC of the ISTH. J Thromb Haemost. 2024Oct;22(10):2889–99. https://doi.org/10.1016/j.jtha.2024.07.009. (Epub 2024 Jul 17).
46. Franchini M, Lippi G. Prothrombin complex concentrates: an update. Blood Transfus. 2010;8(3):149–54. https://doi.org/10.2450/2010.0149-09.

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