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SHORT COMMUNICATION VENOUS INTERVENTIONS

# Liver Growth and Portal Hypertension Improvement After Percutaneous Recanalization of Chronic Portal Vein Thrombosis in Non-Cirrhotic Participants

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**Abstract**

*Purpose* To evaluate liver function improvement and volume gain after percutaneous recanalization of chronic portal vein thrombosis (PVT) in non-cirrhotic patients.

*Materials and Methods* In this retrospective study, five non-cirrhotic participants between 21 and 67 years old with secondary chronic PVT (4–21 years from diagnose) were submitted to percutaneous portal vein recanalization, followed by varices and shunts embolization.

*Results* After a mean of 12.6 months, all portal veins remained patent and there was complete resolution of portal hypertension (PH) symptoms in all participants. There was a significant increase in liver volume of 39.8 ± 19.0% ($p = 0.042$), platelets count of 53120 ± 20188/µl ($p = 0.042$), and a significant decrease in total bilirubin levels from 1.04 ± 0.23 mg/dL to 0.51 ± 0.09 mg/dL ($p = 0.043$). We also found a non-significant increase in albumin levels from 3.88 ± 0.39 g/dL to 4.38 ± 0.27 g/dL ($p = 0.078$) and decrease in spleen diameter from 16.88 ± 4.03 cm to 14.15 ± 2.72 cm ($p = 0.068$).

*Discussion* In this retrospective study, even with a small number of participants, we were capable of showing a median of 39.8% increase in liver volume, laboratorial liver function improvement, platelets count and resolution of PH symptoms, including gastroesophageal varices disappearance after portal vein recanalization followed by shunt embolization.

*Conclusion* In this small series of cases, recanalization of chronic PVT in non-cirrhotic participants was feasible, successful and safe despite the prolonged time of occlusion. This is a new and promising approaching to an old and still challenging disease.

**Keywords** Chronic portal vein thrombosis · Portal vein recanalization · Portal hypertension · Portosystemic shunt

**Abbreviations**

| | |
|---|---|
| CT | Computed tomography |
| GI | Gastrointestinal |
| HE | Hepatic encephalopathy |
| INR | International normalized ratio |
| MELD | Model for end-stage liver disease |
| PVT | Portal vein thrombosis |
| PH | Portal hypertension |
| TIPS | Transjugular intrahepatic portosystemic shunt |

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## Introduction

Complete or partial portal vein thrombosis (PVT) is considered the major cause of extrahepatic portal hypertension (PH) in non-cirrhotic participants. It is a life-threating disease and has many causes, such as cancer, thrombophilia, inflammatory diseases, Budd Chiari syndrome and after major abdominal surgeries, however, one third of the cases remains as idiopathic [1–3]. In acute phase, anticoagulation with lower molecular heparin or vitamin K antagonists reaches 53–71% complete or partial recanalization [4]. When flow patency is not achieved, symptoms of PH like ascites, upper and lower digestive bleeding, splenomegaly and hepatic encephalopathy (HE) [5, 6] can develop. With disease progression, there is a decrease of liver volume and function can decrease as well [7]. In general, these patients are treated with beta-blockers, diuretics and sometimes, maintained with oral anticoagulants for the rest of their lives when prothrombotic disorders are found or in order to prevent thrombus extension into mesenteric and splenic territories. Frequent paracentesis and upper gastrointestinal (GI) endoscopy with varices ligation are usually performed but as years goes by, major bleeding episodes or refractory HE can become fatal. For these life threatening episodes, transjugular intrahepatic portosystemic shunt (TIPS) or shunt occlusion are the treatments of choice [8].

Unfortunately, TIPS can progress into HE [6, 9] and shunt occlusion can increase other PH manifestations.

Liver transplantation is often not considered a treatment option due to anatomic incompatibility, low MELD scores, greater operative time, frequent rethrombosis and is only considered when severe hepatic insufficiency develop [6].

## Materials and Methods

In this retrospective case series, five consecutive non-cirrhotic participants (4 males and 1 female) between 21 and 67 years old with secondary chronic PVT (4–21 years) were treated with percutaneous portal vein recanalization and varices / portal-systemic shunts embolization. The baseline etiologies of PVT were: post splenectomy due to lymphoma, inflammatory disease, post bariatric surgery (2 cases) and umbilical vein access. All of them had recurrent manifestations of PH such as upper GI bleeding, refractory encephalopathy and portal biliopathy. None of the participants had thrombophilic conditions.

Preprocedural contrast enhanced multiphasic abdominal computed tomography (CT) was accessed in all patients. Complete PVT extending through secondary intrahepatic portal vein branches or distally into splenic or superior mesenteric vein was considered an exclusion criteria and was not found in this case series.

Procedures were performed under general anesthesia, a transhepatic approach with a NPAS access set (Cook, USA) and ultrasound guidance was used to access a pervious intrahepatic portal branch. A Brite Tip 7 French (F) sheath (Cordis, USA) was placed in portal vein next to its occlusion site. Once the percutaneous access was secured, anticoagulation with non-fractioned heparin was initiated. The occluded vessel was recanalized with a 5F KMP catheter (Cook, USA) and a hydrophilic 0,035 inch Glidewire (Terumo, Japan). Angioplasty of the occluded portal vein was performed progressively up to 10 mm with Advance balloon catheters (Cook, USA), inflated to its nominal pressure. A 12 mm Zilver stent (Cook, USA) was placed if there was residual stenosis greater than 50% or any vascular dissection. Portosystemic shunts and major gastroesophageal varices were embolized with Amplatzer II (Abbott, USA), Microplex Coils (Microvention, Japan) and a 1:2 mixture of cyanoacrylate glue (Glubran 2, GEM, Italy) and Lipiodol (Guerbet, France). The hepatic tracts were embolized with 0,035 inch Nester coils (Cook, USA) and the same solution of glue and lipiodol described before (Figs. 1, 2, 3 and 4).

All participants were discharged up to five days after the intervention with Rivaroxaban (Xa factor inhibitor) prescription for at least one year.

Abdominal multiphasic CT scan and GI endoscopy was performed 1, 12 and 24 months after the intervention.

Hepatic volumetry and spleen diameter were calculated using Horus 4.0.0 software before, 1 month and up to 2 years after angioplasty, as well as blood samples analysis to check for any improvement in hepatic function.

Continuous variables were reported as mean ± standard deviation, Wilcoxon test was used to compare results. Statistical tests were based on a 2-sided significance level of 0.05. SPSS software, version 21.0 (IBM, New York, USA), was used for statistical analyses.

## Results

Baseline characteristics of participants, blood tests results, liver volume and spleen diameter are described in Table 1.

Technical success was achieved in 100%. After a median time of 12.6 ± 7.5 months, all portal veins remained patent. There was an increase in liver volume (39.8 ± 19.0%; $p = 0.042$), platelets count (53,120 ± 20,188/µl; $p = 0.042$), International Normalized Ratio (INR) from 1.14 ± 0.15 to 1.29 ± 0.16 ($p = 0.043$), albumin levels (3.88 ± 0.39 g/dL

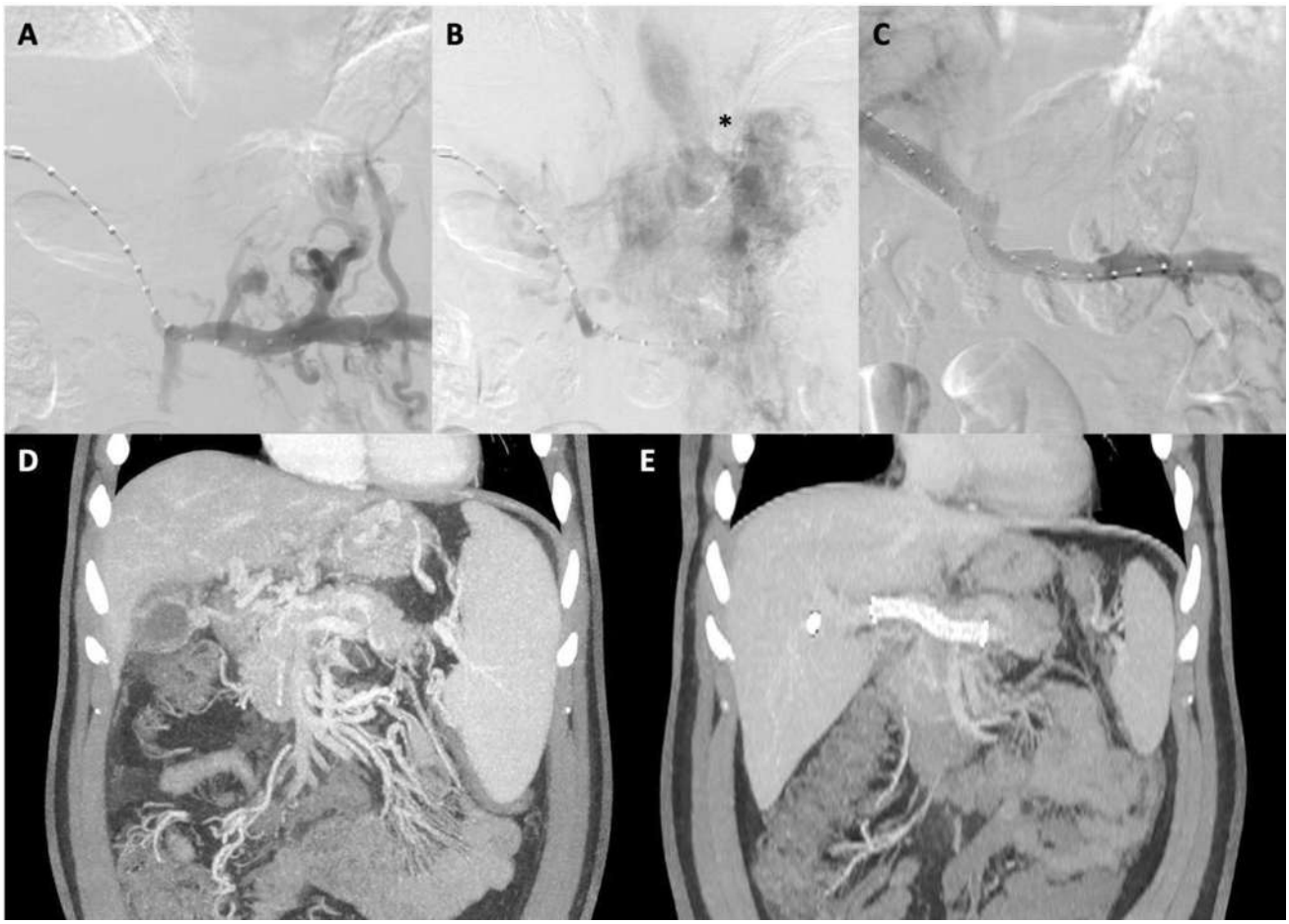


**Fig. 1** Portal vein recanalization in a 48 years old male participant with 5 years portal vein occlusion due to intestinal inflammatory disease. **A** Early digital subtraction splenoportography after portal recanalization though transhepatic access showing huge fugal collaterals, and major gastric and esophagus varices (*) better depicted on the late phase (**B**). **C** Digital subtraction splenoportography after portal vein recanalization with a 12 × 80 mm Zilver self-expanding nitinol stent (Cook, USA) showing complete resolution of portal vein occlusion and disappearance of all collateral flow. **D** Computed tomography (CT) scan, coronal view with intravenous contrast in portal phase, before recanalization showing portal vein chronic occlusion, a small, ischemic liver, splenomegaly and an important collateral venous network including gastric varices and cavernous transformation of the portal vein. **E** CT scan one year after portal vein recanalization, coronal view in portal phase showing patent stent in portal vein, with important liver growth, spleen volume reduction and disappearance of all venous collateral network

to 4.38 ± 0.27 g/dL; $p = 0.078$) and white blood cells count 5038 ± 2733/μL to 6844/μL ± 2846/μL; $p = 0.35$) and a decrease in total bilirubin levels (1.04 ± 0.23 mg/dL to 0.51 ± 0.09 mg/dL; $p = 0.043$) and spleen diameter (16.88 ± 4.03 cm to 14.15 ± 2.72 cm; $p = 0.068$).

There were complete disappearance of gastroesophageal varices on upper GI endoscopy and resolution of all other PH related symptoms such as ascites, portal biliopathy and encephalopathy in all patients.

There was a single episode of peri-hepatic bleeding requiring blood transfusion and arterial embolization one day after portal vein recanalization.

In one participant, we did not use a primary stent because of the excellent result after balloon angioplasty. After six months he developed an important restenosis with the presence of a portal pseudoaneurysm. Another intervention was needed, where we placed two 11 mm Viabahn covered stents (Gore, USA) restoring portal vein flow and integrity (Fig. 3).

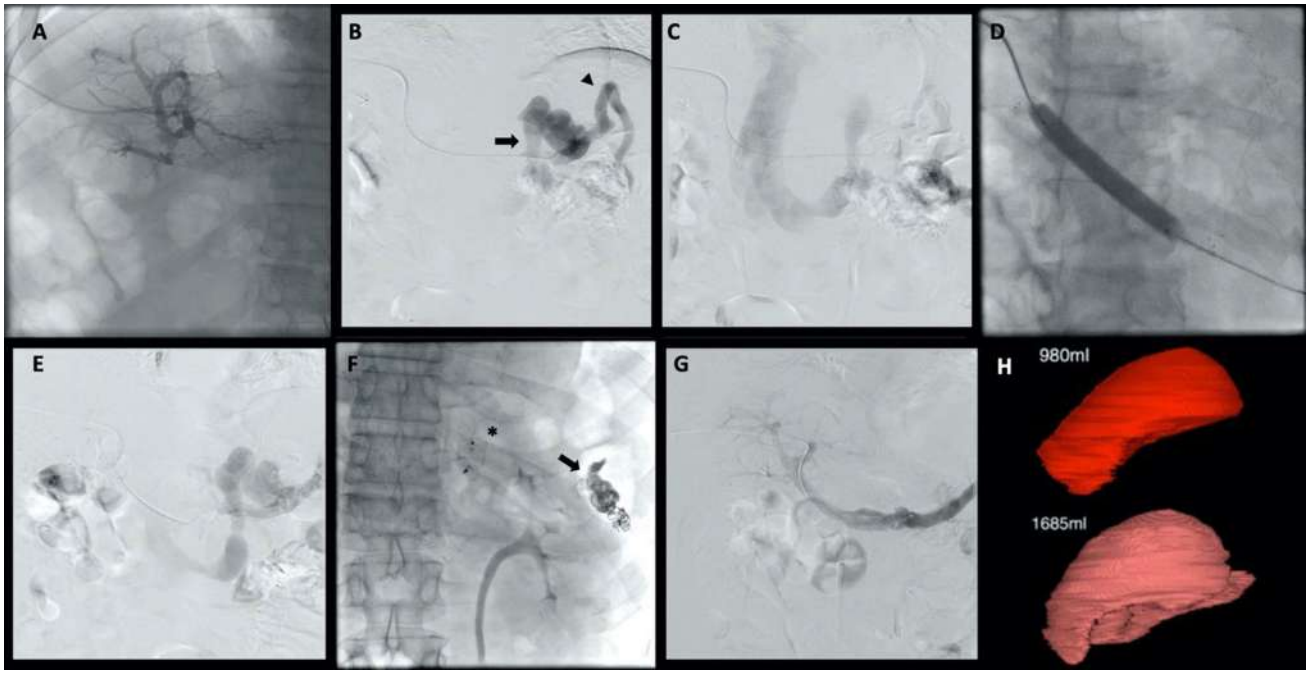


**Fig. 2** 54 years old male with an 8 years portal vein occlusion after sleeve gastrectomy, with portal hypertension and overt hepatic encephalopathy. **A** Transhepatic portography showing a complete occlusion at the main trunk. **B** Early digital subtraction splenoportography after portal vein recanalization showing fugal flow through splenorenal (arrow) and splenoretroperitoneal (arrow head) shunts, better depicted in the late phase (**C**). **D** Balloon angioplasty after deployment of a 12 × 80 mm Zilver self-expandable nitinol stent (Cook, USA) covering the occlusion zone. **E** Digital subtraction splenoportography showing absence of flow into the portal vein immediately after its recanalization due to shunt "steal". **F** Splenorenal shunt occlusion (*) with a 22 mm Amplatzer plug II (Abbott, USA) by femoral vein access and splenoretroperitoneal occlusion (arrow) with coils and an 1:2 emulsion of cyanoacrylate and lipiodol (Guerbet, France) solution. **G** Digital subtraction splenoportography immediately after shunts occlusion showing restoration of hepatic flow through the recanalized portal vein. **H** Hepatic volumetry before and 2 years after portal vein recanalization showing a 72% volume increase

## Discussion

There is no specific guideline recommending intervention in chronic non-cirrhotic PVT patients. They are usually treated with the same protocol as cirrhotic ones, which includes anticoagulation and variceal endoscopic ligation. In cases of refractory GI bleeding and in the absence of contraindications, TIPS is usually considered the treatment of choice [7].

Nevertheless, the physiopathology of chronic PVT in a non-cirrhotic patient (pre-sinusoidal PH) is completely different from a cirrhotic one (sinusoidal PH), and placing a TIPS may worse liver ischemia and add the risk of developing hepatic encephalopathy and hepatic disfunction in the future.

In fact, during these procedures we were able to see some interesting hepato-petal shunts, feeding those ischemic livers. One participant had as unique, petal recanalization of the umbilical vein that have completely disappeared after portal vein recanalization (Fig. 5).

In this retrospective study, even with a small number of participants, we were capable of showing for the first time a median of 39,8% increase of liver volume, platelets count, laboratorial liver function improvement and resolution of PH symptoms after portal vein recanalization in non-cirrhotic patients.

The oldness of thrombosis (4–21 years) was not an impediment to revascularization. We believe that the most important predictor of success is the presence of patent intrahepatic main portal branches and a splenic-mesenteric junction, so it gives you a good in and outflow after treatment. It is fundamental to occlude any important portal-systemic shunt if it is still present after angioplasty, to ensure portal vein patency, otherwise, the blood will still flow to the less resistance territory and may lead to rethrombosis. Chronic thrombosis extending through

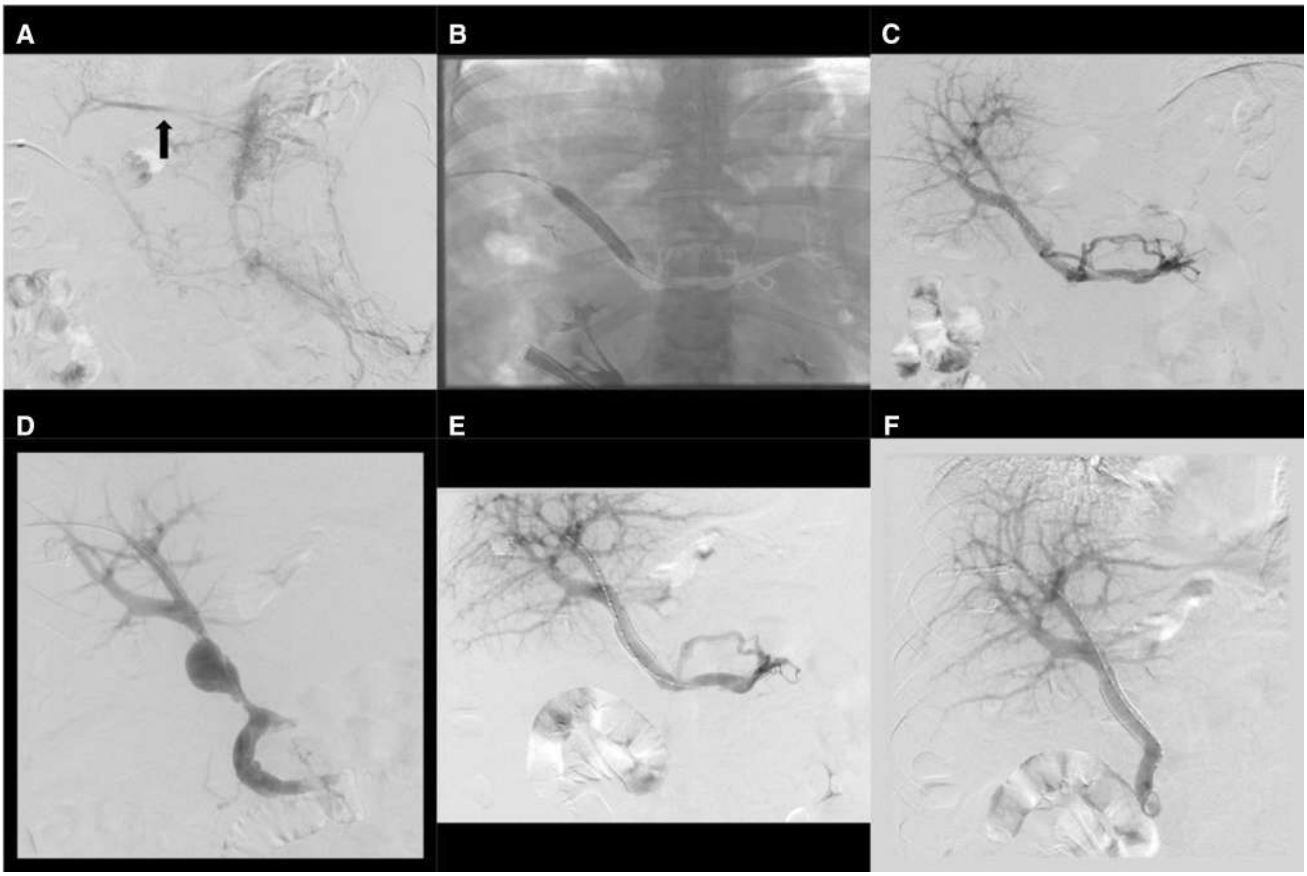


**Fig. 3** 39 years old male with a 6 years chronic portal vein occlusion after sleeve gastrectomy. **A** Digital subtraction splenoportography after portal vein recanalization showing important collateral flow though splenoretroperitoneal shunts, gastric varices and a direct gastric-portal shunt to the left portal vein (arrow). **B** Portal vein angioplasty with a 10 × 60 mm balloon catheter. **C** Digital subtraction splenoportography after balloon catheter angioplasty showing restoration of portal vein flow and complete resolution of all the collateral vein network. Due to this excellent result, we decided not to stent the portal vein. **D** Digital subtraction portography six months after portal vein recanalization showing proximal and distal restenosis with a large portal pseudoaneurysm. Digital subtraction splenoportography (**E**) and mesenteric phlebography (**F**) after two overlapped 11 × 50 mm Viabahn covered stent (Gore, USA) placement showing complete resolution of the restenosis and pseudoaneurysm with a patent portal vein

secondary portal branches will not give a good outflow after recanalization and distal thrombosis into the superior mesenteric or splenic veins will probably not give a good inflow after recanalization, mainly because of the development of multiple shunts and collaterals pathways that should be hard to manage in order to ensure redirection of flow into the reopened portal vein. These scenarios mentioned above are considered predictors of poor response to treatment and should not be treated with this technique in our opinion.

Another important aspect to discuss is the need to place a stent after balloon catheter angioplasty of the portal vein. As it is very common to find residual portal vein dissection or stenosis after angioplasty and by the fact that the only patient primarily treated without a stent developed later on a portal restenosis and pseudoaneurysm, we decided to always place a nitinol self-expandable stent to ensure good long-term patency and a vascular matrix to guide endothelization.

The indication of the use of anticoagulants and for how long it should be used is still an unanswered question. Although the use of direct-acting oral anticoagulants to treat PVT is still an off-label indication, several studies

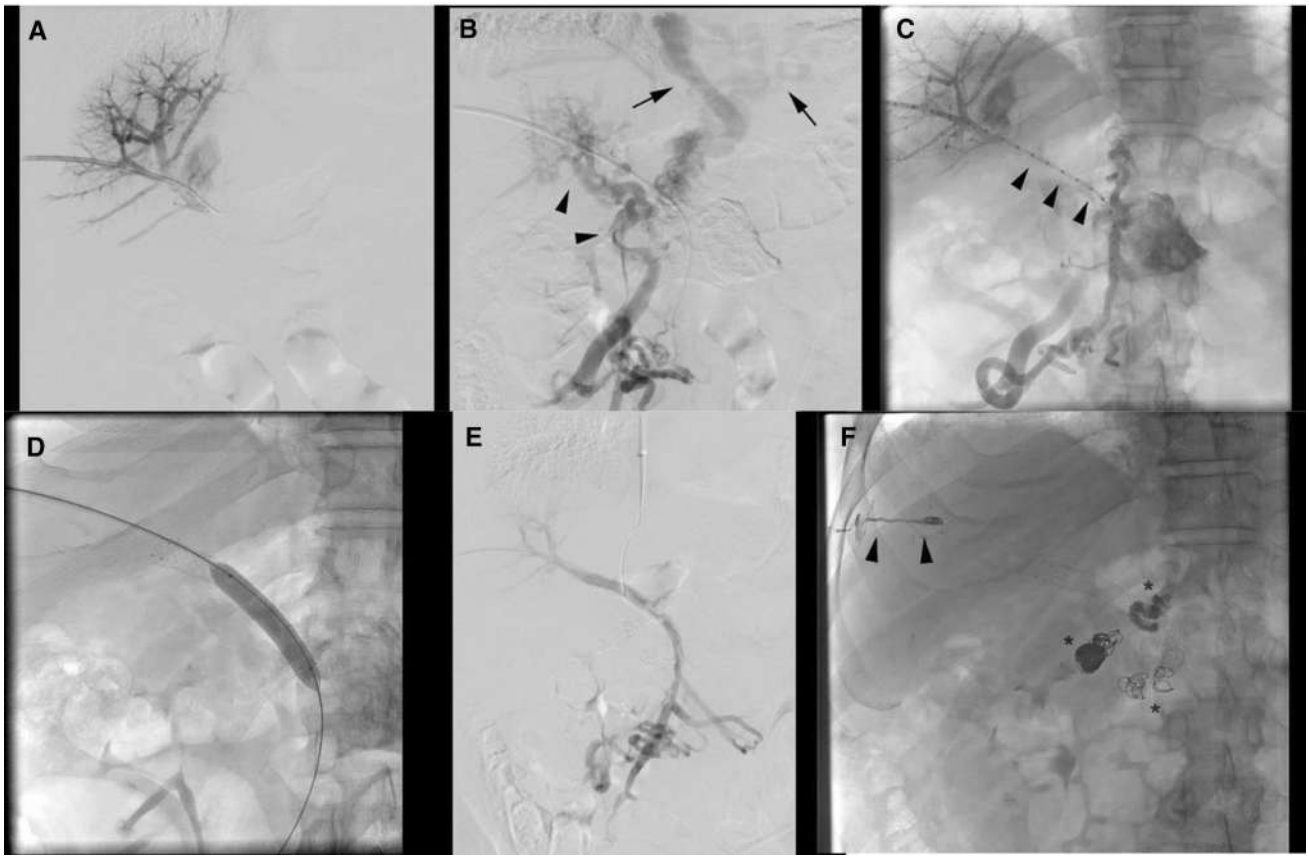


**Fig. 4** 67 years old male with a 4-year-old portal vein thrombosis after splenectomy due to Lymphoma. **A** Transhepatic, digital subtraction portography showing portal vein occlusion at the junction of the right and left portal veins. **B** Superior mesenteric digital subtraction phlebography after portal vein recanalization showing cavernous transformation of the portal vein, fed by mesenteric collaterals (arrow heads) and huge gastroesophageal varices (arrows). **C** Simultaneous contrast injection in the portal vein and in the superior mesenteric vein showing a 9 cm chronic occlusion of the portal vein (arrow heads). **D** Portal vein angioplasty with a 10 × 80 mm balloon catheter after the deployment of a 12 × 100 mm Zilver self-expanding nitinol stent (Cook, USA) in the occlusion zone. **E** Superior mesenteric digital subtraction angiography after portal vein angioplasty and collateral network occlusion showing hepato-petal flow through the recanalized portal vein. **F** Final radiography showing collateral veins occlusion, including gastroesophageal varices (*) with Coils and a 1:2 emulsion of cyanoacrylate with lipiodol (Guerbet, France) and percutaneous track embolization (arrow heads) with coils and the same solution of glue and lipiodol previously described

describe the safety and efficacy of this group of drugs for treating thrombosis in unusual sites [10].

Hepatic transplant is rarely indicated to this group of participants, mostly because they usually have low Model for End-Stage Liver Disease (MELD) scores or because of the absence of a vascular anatomy suitable to it. Additionally, stenting beyond the splenic-mesenteric junction may impair a future possibility of liver transplantation.

The retrospective analysis, the small number of participants were the most important limitations of our study. To confirm our findings larger and prospective studies are necessary.

## Conclusion

In this small series of cases, recanalization of chronic PVT in non-cirrhotic patients was feasible, successful and safe despite the prolonged time of occlusion. Additional benefits of percutaneous revascularization were an important volumetric enlargement of the liver, resolution of PH

**Table 1** Blood analysis results, liver volume and spleen diameter evaluation during follow-up period

| TABLE 1 | Time (months) | White Blood Cels (/μL) | Platelets (/μL) | INR | Total Bilirrubin (mg/dL) | Albumin (g/dL) | Hepatic Volume (ml) | Volume Increase | Spleen Diameter (cm) |
|---|---|---|---|---|---|---|---|---|---|
| Participant 1: 48Y; Male, 5y—inflammatory PVT | T0 | 2700 | 51.000 | 1.14 | 0.8 | 3.9 | 1487 | * | 19.4 |
| | T1 | 5410 | 88.000 | 1.37 | 1.0 | 4.5 | 1852 | 25% | 16.0 |
| | T24 | 5670 | 140.000 | 1.25 | 0.5 | 4.5 | 2061 | 39% | 14.6 |
| Participant 2: 54y; Male, 8y—Bariatric Surgery | T0 | 8500 | 141.000 | 1.25 | 1.3 | 3.4 | 980 | * | 10.9 |
| | T1 | 4000 | 164.000 | 1.15 | 0.5 | 3.4 | 1196 | 22% | 11.1 |
| | T12 | 5100 | 183.000 | 1.34 | 0.4 | 4.2 | 1685 | 72% | 10.2 |
| Participant 3: 39y; Male, 6y—Bariatric Surgery | T0 | 4230 | 110.000 | 1.15 | 1.3 | 4.1 | 1418 | * | 18.0 |
| | T1 | 4570 | 98.000 | 1.00 | 0.7 | 4.2 | 1880 | 32% | 17.0 |
| | T12 | 7090 | 153.000 | 1.30 | 0.5 | 4.8 | 1890 | 33% | 15.5 |
| Participant 4: 67y, Male, 6y - Splenectomy | T0 | 7300 | 375.000 | 0.90 | 1.0 | 3.6 | 1476 | * | * |
| | T1 | 9160 | 352.000 | 1.04 | 0.4 | 4.0 | 1702 | 15% | * |
| | T12 | 11,670 | 423.000 | 1.05 | 0.5 | 4.2 | 1960 | 33% | * |
| Participant 5: 21y, Female, 21y, Umbilical Vein Access | T0 | 2460 | 51.000 | 1.27 | 0.8 | 4.4 | 921 | * | 19.2 |
| | T1 | 6900 | 75.900 | * | 1.0 | 4.6 | 1137 | 23% | 16.4 |
| | T3 | 4690 | 94.600 | 1.49 | 0.6 | 4.2 | 1124 | 22% | 16.3 |

*PVT* Portal Vein Thrombosis, *INR* International normalized ratio, *Hb* Hemoglobin

*Missing or inexistent data

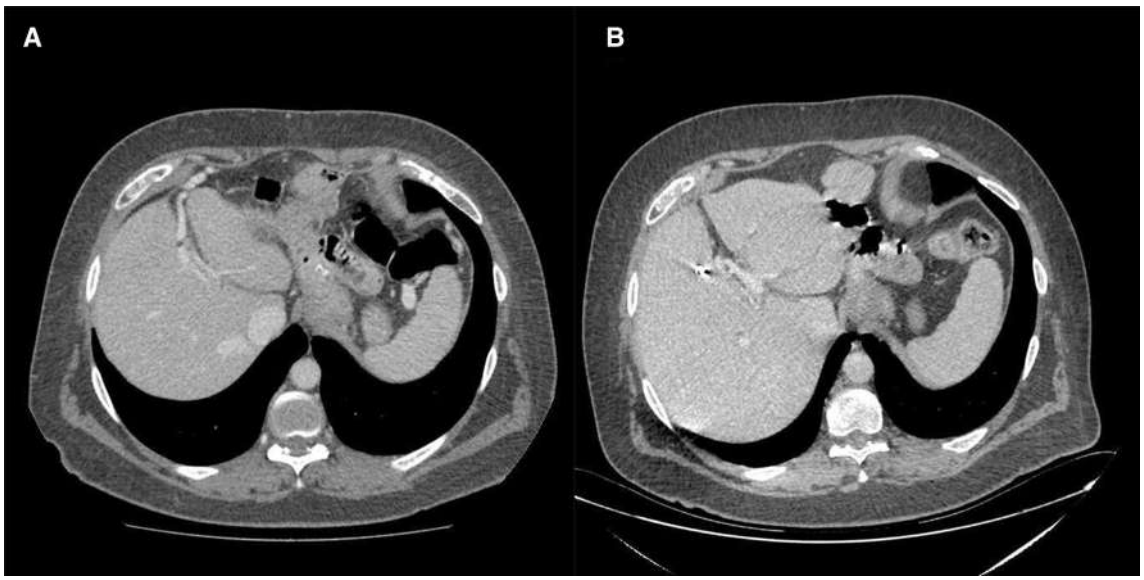


**Fig. 5** **a** Computed tomography (CT) scan with intravenous contrast (portal phase) before recanalization in participant #2 demonstrates a small volume, ischemic liver with para-umbilical vein recanalization with hepato-petal flow; **b** CT scan in the same participant, one year after portal recanalization, showing a significant increase in the liver volume with complete disappearance of the para-umbilical vein

symptoms, laboratorial liver function improvement and elevation in platelets count. This is a new and promising approaching to an old and still challenging disease.

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**Declarations**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Human and Animal Rights** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and

with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

**Consent for Publication** For this type of study consent for publication is not required.

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