

**Case Report**
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## A Combined Treatment of Life-threatening and Difficult to Treat Bleeding Gastro-oesophageal Varices in a Patient with Cirrhosis and Portal Cavernomatosis

Simone Di Cola<sup>1\*</sup>, Adriano De Santis<sup>1</sup>, Emanuela De Santis<sup>1</sup>, Piergiorgio Nardis<sup>2</sup>, Stefano Pontone<sup>3</sup>, Mario Corona<sup>2</sup> and Pierleone Lucatelli<sup>2</sup>

<sup>1</sup>Department of Translational and Precision Medicine, Sapienza University, Viale Dell'Università 37, 00185, Rome, Italy

<sup>2</sup>Department of Radiological Oncological and Anatomic-Pathological Sciences, Sapienza University, Viale Regina Elena 324, 00161, Rome, Italy

<sup>3</sup>Department of Surgical Sciences, Sapienza University, Viale Regina Elena 324, 00161, Rome, Italy

### ABSTRACT

Balloon-occluded retrograde transvenous obliteration (BRTO) is an endovascular secondary prophylactic approach to gastroesophageal variceal (GOV) bleeding. However, standard primary prophylaxis is often ineffective and GOV bleeding is more severe than esophageal variceal (EV) bleeding. Portal vein thrombosis and its evolution to cavernomatosis are common complications of cirrhosis. There are no data in the literature on the safety of BRTO in patients with portal cavernomatosis and on the risk of excessively increasing portal hypertension in patients with esophageal varices at risk of bleeding. Portal cavernomatosis is a relative contraindication to TIPS placement. Furthermore, in our knowledge there are no great experiences on the combined use of BRTO and TIPS and no information in patients with portal cavernomatosis.

We report the case of a 66-year-old woman with hepatitis C virus-related liver cirrhosis. The patient had re-current EV bleeding, the new onset of a large GOV2, and portal cavernomatosis. We performed EV band ligation (EVBL) followed by BRTO to treat the GOV2, which had not bled previously. No complications occurred and an improvement in liver tests was observed after treatment. Following a further episode of bleeding from esophageal varices we decided to perform TIPS placement.

The combination of EVBL and BRTO as primary prophylaxis of GOV2 bleeding is safe and effective also in patient with portal cavernomatosis. An improvement in liver tests was also observed, likely due to increased portal flow through the cavernoma. The combined use of BRTO and TIPS is safe and effective to control esophageal and gastroesophageal varices.

### \*Corresponding author

Simone Di Cola, Department of Translational and Precision Medicine, Sapienza University, Viale Dell'Università 37, 00185, Rome, Italy.  
 Tel: +39 3348331802; E-mail: simone.dicola@uniroma1.it

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### Introduction

Gastroesophageal varices (GOV) are a complication of portal hypertension. According to Sarin's classification, GOV2s are defined as the extension of esophageal varices along the greater curve. Most GOVs are fed by afferents supplied by the left gastric vein, posterior gastric vein, short gastric or gastroepiploic vein, and especially the gastrosplenic shunt [1]. However, it is increasingly evident that GOVs are different entities than esophageal varices (EV). GOV bleeding is more severe, with higher morbidity and mortality rates and greater therapeutic difficulties [2]. In fact, variceal ligation is often impossible, while sclerotherapy is inadequate for the high flow within the varicose vein. Although transjugular intrahepatic portosystemic shunt (TIPS) placement

is the reference standard procedure for secondary prophylaxis, recent evidence shows that it is not as effective for GOVs as it is for EVs due to physiopathologic differences. More recently, embolization of the shunt has been proposed as an alternative therapeutic option that seems to achieve better results as secondary prophylaxis in the management of GOVs when directly drained by the shunt. Shunt embolization has recently been included in the American and European guidelines for secondary prophylaxis of GOV bleeding [3,4].

We successfully treated a patient with hepatitis C virus (HCV)-related liver cirrhosis and portal cavernomatosis, a history of EV bleeding that was refractory to endoscopic and pharmacological therapy, and the new onset of a large GOV2 (3cm). Primary prophylaxis of GOV2 bleeding consisted of the combination of EV ligation followed by balloon-occluded retrograde transvenous obliteration (BRTO), which was performed without complications. Only several months later the patient presented a new episode

of bleeding from esophageal varices; we therefore decided to evaluate the feasibility of TIPS despite the presence of the por-tal cavernoma. The procedure was considered feasible and performed without periprocedural problems. The combined use of TIPS and BRTO in patient with portal cavernomatosis has been shown to be safe and effective.

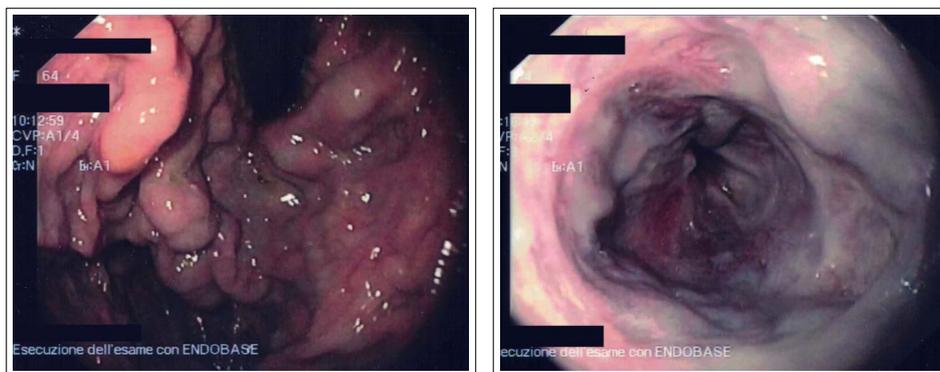
**Case Presentation**

**Chief Complaint**

A 66-year-old woman was admitted to our department due to the detection of a very large (F3) EV with red wale marks and a voluminous (3 cm) GOV2 at routine gastroscopy (Figure 1).

**History of Past and Present Illness**

The patient had HCV-related liver cirrhosis that was treated in 2003 with pegylated interferon and ribavirin, with achievement of a sustained virological response. The only dis-ease complication, otherwise compensated, was a long history of EVs with two bleeding episodes (most recently in 2011). For this reason, the patient was under treatment with beta blockers and underwent sev-eral EVBL sessions, which did not result in EV eradication. Endoscopy depicted a new onset GOV2 (Figure 1).



**A**

**B**

**Figure 1:** Presence of large gastroesophageal varices in the fundus of the stomach (A); Esophageal vari-ces with signs of previous ligatures (B)

**Family History:** No Family History of Gastrointestinal Disease

**Physical Examinadon Upon Admission**

On admission the patient was in good clinical condition.

**Laboratory Examinadon**

The patient was hemodynamically stable and had mostly normal blood tests with the exception of mild anemia (Hb 10.8 gr/dL) and thrombocytopenia (PLT 52.000/mm3). The Child-Pugh score was A5 and the Model for End-Stage Liver Disease (MELD) value was 11 (Table 1).

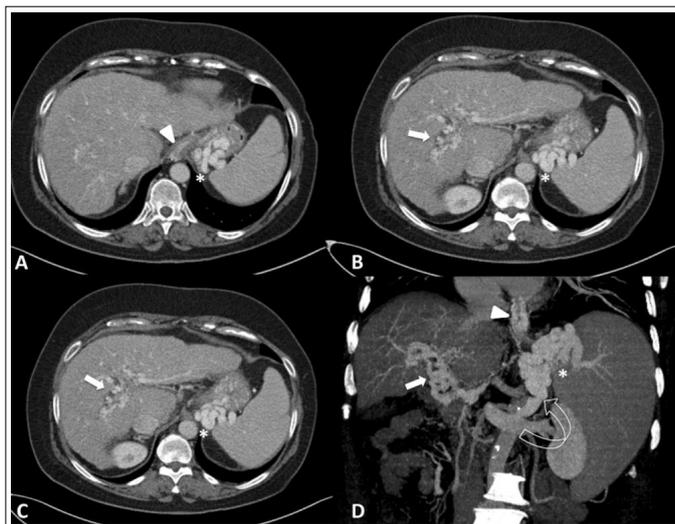
**Table 1: Laboratory Findings Pre and Post Brto**

PARAMETER	UoM	Pre-BRTO	Post-BRTO	1-Month Follow-Up
Hemoglobin	g/dL	10.8	11.7	11.4
White Blood Cells (Neu %)	x10 <sup>6</sup> /L	1940 (58%)	3720 (70%)	2170 (59%)
Platelets	x10 <sup>9</sup> /L	52000	49000	41000
GOT	U/L	26	28	36
GPT	U/L	17	17	34
γ-glutamyltransferase	U/L	20	19	36
Alkaline Phosphatase	U/L	44	62	74
Total/direct Bilirubin	mg/dL	1.18/0.55	0.91/0.41	1.03/0.46
Total Proteins	gr/dL	6.3	8	7.8
Albumin	gr/dL	3.7	4.5	4.2
INR	ratio	1.37	1.13	1.15
Creatinine	mg/dL	0.79	0.70	0.89
MELD		11	8	8

**GOT:** Glutamic Oxaloacetic Transaminase; **GPT:** Glutamic-Pyruvic Transaminase; **Meld:** Model of End-Stage Liver Disease

### Imaging Examination

Abdominal CT scan demonstrated the presence of a hypertrophied left splenorenal shunt draining a 3-cm GOV. Moreover, the presence of a portal cavernomatosis was identified (Figure 2).



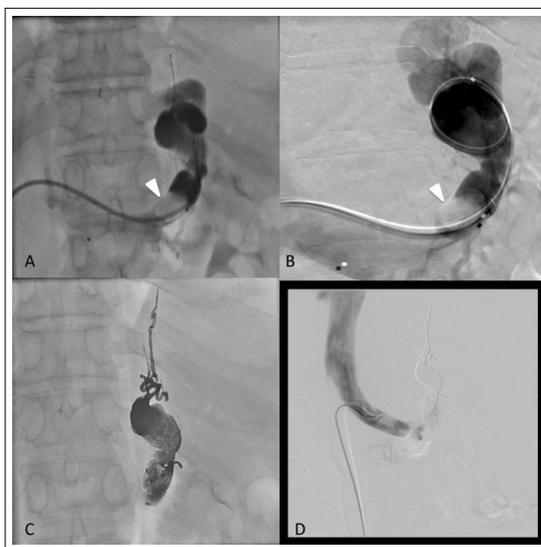
**Figure 2:** Preprocedural enhanced CT venous phase. A-C: axial images; D: coronal oblique multiplanar reconstruction depicting the cavernous transformation of the portal vein (white arrow) and presence of gastroesophageal varices (white arrowhead) associated with a large (3 cm) GOV2 drained by a hypertrophied left splenorenal shunt (curved white arrow)

### Treatment

Considering the high risk of bleeding and patient history of varix worsening despite pharmacological prophylaxis and previous bleeding, the patient was referred for TIPS placement. However, the pre-procedural review of radiological images highlighted the technical impossibility of performing an intrahepatic shunt due to the presence of portal cavernomatosis. We therefore decided to perform EVBL, followed within one week by BRTO. Performing EVBL earlier reduced the risk of variceal bleeding after BRTO, which can increase portal pressure. However, we considered the placement of TIPS difficult due to the presence of portal cavernomatosis and not effective in treating voluminous GOV2.

### BRTO Procedure

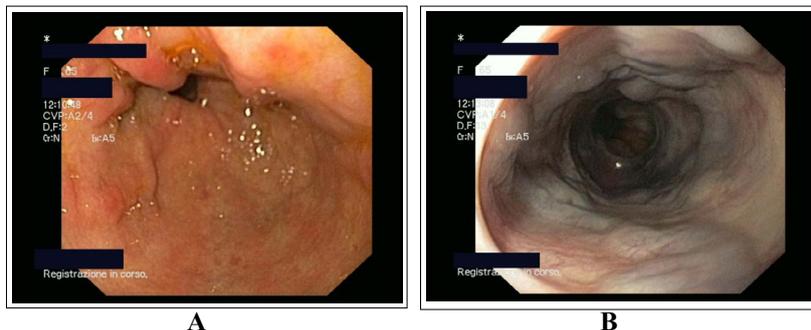
BRTO was performed via the right common femoral vein access. Once superselective catheterization of the hypertrophied left splenorenal shunt with a 7 Fr balloon guiding catheter (FlowGate, Stryker Neurovascular) was achieved, balloon inflation was performed in order to achieve contrast media stasis. This permitted flow reversal within the shunt and the visualization of a large GOV2. Embolization was then performed coaxially using a 2.7 Fr microcatheter (Progreat, Terumo Tokyo Japan) with the injection of liquid embolic agent Onyx 34 (ev3 Neurovascular, Irvine, CA) under continuous fluoroscopic guidance. Angiography performed at the end of the procedure confirmed the complete occlusion of the shunt, and no complications occurred (Figure 3).



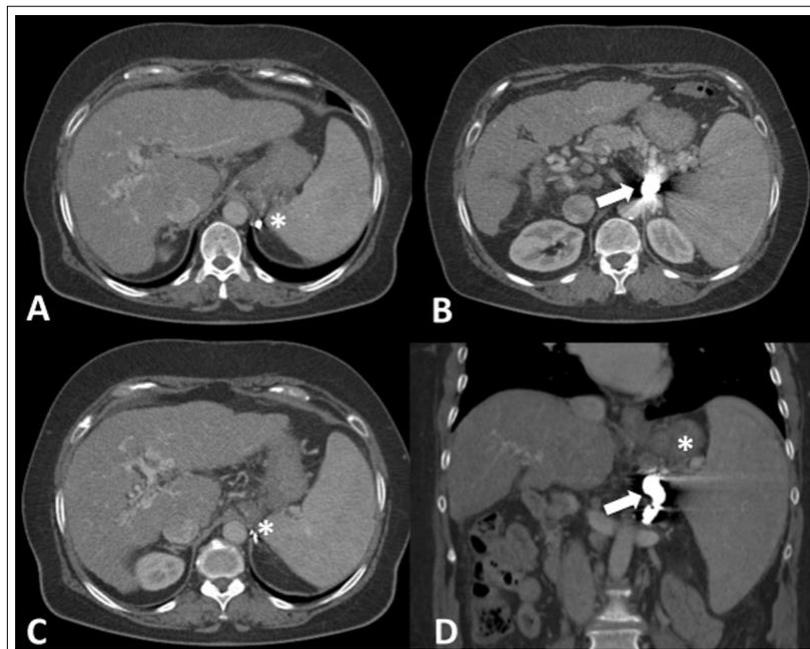
**Figure 3:** Intraprocedural X-rays. Superselective catheterization of the hypertrophied left splenorenal shunt with a 7 Fr balloon guiding catheter (FlowGate, Stryker Neurovascular). After balloon inflation, contrast media stasis is appreciable (A). Subsequent angiography with the inflated balloon confirmed flow reversal within the shunt and the visualization of a large GOV2 (B). Onyx cast used to embolize the splenorenal shunt is shown (C). Angiography confirmed the complete occlusion of the shunt (D)

### Outcome and Follow-Up

Biochemical controls were performed two weeks after the procedure. An improvement in the MELD value was observed (Table 1). In particular, a marked improvement in liver prothrombin synthesis (international normalized ratio (INR), total protein, and albumin) and bilirubin was noted. A gastroscopy one month later showed F2 varices without red wale marks and the absence of the GOV2. EVs were again ligated (Figure 4). An abdominal CT scan one month after the procedure confirmed the complete obliteration of the splenorenal shunt (Figure 5). During this period, the patient did not suffer gastrointestinal bleeding. At the one-month follow-up, biochemical controls confirmed sustained improvement in MELD and hemoglobin values (Table 1).



**Figure 4:** Absence of large gastroesophageal varices in the fundus of the stomach (A); F2 esophageal varices without red mark signs before ligation with 4 bands (B)



**Figure 5:** Postprocedural enhanced CT venous phase. Axial images (A-C). Coronal multiplanar reconstruction depicting complete exclusion of both the GOV2 (asterisk) and left splenorenal shunt (white arrow) (D)

### TIPS Placement

After another episode of melena and two endoscopic variceal ligations of esophageal varices we decide to propose TIPS placement. The patient performed another abdominal CT-scan that showed an improvement of the diameter of the vessels into the cavernoma (probably due to the increase in portal vein flow after the obliteration of the voluminous gastro-renal shunt). This change made TIPS placements feasible. After this procedure the value of HVPg was reduced from 25 mmHg to 11 mmHg. As expected MELD value is increased after the procedure ( as you can see in Table 2).

**Table 2: Laboratory Findings Pre and Post Tips**

PARAMETER	UoM	Post-TIPS	1-Month Follow-Up
Hemoglobin	g/dL	12.3	12.7
White Blood Cells (Neu %)	x10 <sup>6</sup> /L	5570 (88%)	6900 (68%)
Platelets	x10 <sup>9</sup> /L	49000	53000
GOT	U/L	40	53
GPT	U/L	32	48
γ-glutamyltransferase	U/L	32	32
Alkaline Phosphatase	U/L	46	163
Total/direct Bilirubin	mg/dL	1.17/0.5	2.93/0.68
Total Proteins	gr/dL	7.8	7.8
Albumin	gr/dL	3.8	4.4
INR	ratio	1.39	1.2
Creatinine	mg/dL	1,07	1.11
MELD		11	13

### Discussion

GOVs are complications of portal hypertension and are present in 20% of patients with EVs [5]. However, GOVs have a worse prognosis due to more severe bleeding and higher mortality rates [1]. An endoscopic approach is very difficult due to the position of GOVs (particularly GOV2s) and sclerotherapy is often ineffective due to the high flows. Although GOV progression correlates with worsening portal hypertension, GOVs are present at lower portal pressures as compared to EVs (11-18 mmHg vs. 16-24 mmHg) [5,-7]. In a cohort study, 6% of patients with GOV bleeding had baseline HVPG levels <12 mmHg [8]. Furthermore, it has been found that most GOVs are fed by gastrosplenic shunts. While EVs show an “uphill” venous outflow (77-100%) through the azygos/hemiazygos venous system, the GOV system is more complex and shows downward or mixed drainage [9]. This demonstrates physiopathologic differences between GOVs and EVs, which could explain why TIPS placement has shown different results in GOV as compared to EV management [10,11]. It was observed that 50% of patients with TIPS had persistent GOVs, and a rebleeding rate of 27% was reported [12].

Our patient had a history of EVs refractory to endoscopic and drug therapy. At the gastroscopy a massive GOV2 was detected. Although the patient had experienced two bleeding episodes, GOVs had never been documented in previous gastroscopies. The patient was a candidate for a more aggressive secondary prophylactic approach to GOV bleeding. TIPS is appropriate for F3 EVs, but the discovery of a portal cavernomatosis made its placement difficult. Cavernomatosis is not an absolute contraindication to TIPS placement and in selected units with extensive experience TIPS can often be performed even in the presence of cavernomatosis and is recommended for patients at high risk of bleeding [13]. However, in this setting the TIPS procedure has a lower rate of technical success, around 70% vs. 100% in patients with no cavernomatosis or partial portal vein thrombosis [14]. Secondly, radiological images demonstrated that the portal cavernoma was not in direct communication with the splenorenal shunt. Therefore, due to the increased procedural risk of performing TIPS on a portal vein cavernomatosis and the reduced effectiveness of TIPS on GOVs, we opted to proceed with BRTO.

BRTO was first performed in 1994, though it has only recently received increased attention for GOV management, with excellent results in terms of efficacy and safety [15]. It is performed by

inserting a balloon catheter into an outflow shunt (gastric-renal or gastric-inferior vena cava) through the femoral or internal jugular vein and subsequently blocking blood flow with the balloon, followed by the injection of a sclerosing agent directly into the EVs. Like TIPS, it has recently been included in American and European guidelines as secondary prophylaxis of GOV bleeding [3,4]. The main concern related to BRTO is the increase in portal hypertension due to the closure of a vent valve in the splanchnic circle [16]. However, BRTO appears to enhance liver performance by improving liver flow, as opposed to TIPS [17]. Indeed, liver function was improved after obliteration, with a reduction in the MELD value from 11 to 8 (Table 1) despite the presence of portal cavernomatosis. In particular, we noted an improvement in hepatic protein synthesis (INR from 1.37 to 1.13; total proteins from 6.3 gr/dL to 8 gr/dL, and albumin from 3.7 gr/dL to 4.5 gr/dL).

In order to avoid worsening portal hypertension and EV bleeding risk with BRTO, we first performed EVBL followed by BRTO after a 1-week clinical and laboratory follow-up. The innovation of this clinical case was that BRTO was used as primary prophylaxis due to the high risk of EV bleeding and since the presence of cavernomatosis. However, some experienced centers have used BRTO as primary prophylaxis. We therefore preferred to perform BRTO directly without attempting an endoscopic approach given the patient’s clinical context. Endoscopic follow-up showed the absence of GOVs and the presence of ligated F2 EVs without red wale marks. An abdominal CT scan confirmed the complete obliteration of the shunt (Figure 4).

However about 5 months later she presented a new hospitalization for melena and the emergency gastroscopy showed F2 varices with red marks, subjected to ligation. The patient was then subsequently admitted to our varicose vein control department. Gastroscopy revealed the presence of F2 varices again without red marks. In consideration of the numerous episodes of bleeding and the persistence of esophageal varices, the possibility of placing the TIPS was re-evaluated. The radiologists considered the procedure feasible thanks to the increase in portal vein diameter after shunt obliteration. The ultrasound and endoscopic control at 1 month showed good functioning of the shunt. There is little experience on the combined use of TIPS and BRTO in patient with esophageal and gastroesophageal varices and to our knowledge there are no studies on the combined use in patients with portal cavernomatosis.

## Conclusions

The presence of portal cavernomatosis rendered TIPS placement unfeasible, so we decided to perform a two-step procedure: EVs were treated with ligation while GOVs were treated with BRTO. EVBL was performed earlier since obliteration of the shunt can cause increased portal pressure and consequent EV bleeding. The use of BRTO as primary prophylaxis has been shown to be effective and safe in the treatment of GOV2s. EV ligation was effective in preventing bleeding due to the increase in portal hypertension after shunt obliteration. Liver function was improved after obliteration, most likely due to increased liver flow.

Bleeding from esophageal varices did not occur immediately after the shunt obliteration but after 5 months. It is therefore likely that the bleeding is independent of the increased portal flow following the obliteration but that it reflects the pre-existing important portal hypertension that had already caused several bleedings from esophageal varices in the past. It is also possible that the improvement in portal flow could increase the diameter of the venous vessels of the cavernoma and therefore render TIPS placement feasible. In fact, by re-evaluating the case following the further persistence of esophageal varices and their bleeding, the placement of TIPS was performed. The combined use of TIPS and BRTO is therefore safe and feasible even in patients with portal cavernomatosis.

**Author Contributions:** Di cola S was a major contributor in writing the manuscript. Di cola S, De Santis A, De Santis E, Lucatelli P, Corona M, Pontone S and Nardis P contributed substantially to the acquisition, analysis and interpretation of data. Lucatelli P and Corona M performed the balloon-occluded retrograde transvenous obliteration and Transjugular PortoSystemic Shunt, Pontone S performed the esophageal variceal ligation. De santis A and Di cola S provided critical revision of the article and final approval of the version to be published.

All authors read and approved the final version of the manuscript

**Supported by Informed Consent:** patient has granted us informed consent to publish this case report.

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**Care Checklist (2016) Statement:** the authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Core Tip:** This Case highlights the efficacy and safety of BRTO in the management of gastric varices for the prevention of their bleeding in presence of portal cavernomatosis. It also confirms the data from the literature on improving liver function. There is little experience on the combined use of TIPS and BRTO and to our knowledge there are no studies on the combined use in patients with portal cavernomatosis.

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