

# Portal pressure decrease after esophagogastric devascularization and splenectomy in schistosomiasis: long-term varices behavior, rebleeding rate, and role of endoscopic treatment

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**ABSTRACT – Background** – Schistosomiasis is an endemic health problem affecting about four million people. The hepatosplenic form of the disease is characterized by periportal hepatic fibrosis, pre-sinusoidal portal hypertension and splenomegaly. Liver function is preserved, being varices bleeding the main complication of the disease. The surgical treatment used in the majority of centers for the prevention of rebleeding is esophagogastric devascularization and splenectomy. Most authors reported better results with the association of surgical and postoperative endoscopic treatment. **Objective** – The aim of this study was to compare the intra operative portal pressure decrease and esophageal varices behavior and rebleeding rates in patients submitted to surgical and postoperative endoscopic treatment after long-term follow-up. **Methods** – A retrospective study of 36 patients with schistosomiasis with, at least, one previous bleeding from esophageal varices rupture submitted to esophagogastric devascularization and splenectomy, added to endoscopic varices postoperative treatment was performed. Patients were stratified according to the intra operative portal pressure decrease in two groups: reduction below and above 30%. Long-term varices presence, size and bleeding recurrence were evaluated. **Results** – Regarding varices behavior, no significant influence was observed in both groups of portal pressure fall. Regarding bleeding recurrence, despite three times more frequent in the group with lower portal pressure fall, no significant difference was observed. All patients were submitted to postoperative endoscopic treatment. **Conclusion** – Esophageal varices banding, rather than portal pressure decrease, seems to be the main responsible factor for good results after combination of two therapies (surgery and endoscopy) for patients with portal hypertension due to schistosomiasis; further studies are necessary to confirm this hypothesis.

**HEADINGS** – Schistosomiasis mansoni. Portal hypertension, surgery. Endoscopy, rehabilitation. Esophageal and gastric varices. Ligation.

## INTRODUCTION

Schistosomiasis is an endemic health problem in Brazil affecting about four million people<sup>(1)</sup> and, two to ten percent of infected individuals will develop the hepatosplenic form of the disease, characterized by periportal hepatic fibrosis, pre-sinusoidal portal hypertension and splenomegaly<sup>(2)</sup>. In contrast to patients suffering from cirrhosis, the schistosomal population is represented by young, economically active individuals with preserved liver function<sup>(3,4)</sup>. However, as in cirrhotic individuals, when liver damage is installed, there is no option for medical treatment<sup>(2)</sup>. Liver function is preserved despite severe hepatic fibrosis, being digestive hemorrhage due to esophageal varices rupture the main and most fearsome complication of hepatosplenic schistosomiasis.

Studies have shown that one third of patients with hepatosplenic schistosomiasis may develop gastrointestinal bleeding due to esophageal varices rupture<sup>(5)</sup> with a mortality rate of up to 11.7% in the first bleeding episode<sup>(6)</sup>. The importance of this disease regarding public health was demonstrated by a survey from the

Brazilian Ministry of Health between 1998 and 2009 that showed an annual mortality rate estimated between 0.2 and 0.34 deaths per 100,000 inhabitants<sup>(1)</sup>.

With the ineffectiveness of drug and endoscopic therapy for esophageal varices bleeding control in these patients, surgical treatment has become since the late seventies a good therapeutic option<sup>(7)</sup>, especially for secondary prophylaxis. As the patient with schistosomiasis has preserved liver function, the surgical technique used in the majority of centers for the prevention of rebleeding is esophagogastric devascularization (EGDS) and splenectomy. This procedure, leads to acceptable results regarding bleeding control without the disadvantage of hepatic encephalopathy in the postoperative period. Although leading to good postoperative results<sup>(8)</sup>, the rebleeding rate after EGDS is considerable, ranging from 6 to 29%<sup>(9,10,11,12)</sup>. Meanwhile, Sakai et al. have shown a significant decrease in the postoperative bleeding rate when endoscopic therapy was associated in postoperative follow-up<sup>(12)</sup>, showing the need of a postoperative endoscopic program in patients submitted to EGDS<sup>(13,14)</sup>.

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Some studies have shown that EGDS decreases portal pressure<sup>(9,15)</sup>, leading to a consequent immediate decrease in varices size, increasing endoscopic treatment effectiveness after surgical treatment. Despite all this data, there is still a lack of information regarding late results and, it has already been shown that, the longer follow-up a higher incidence of rebleeding is observed<sup>(2,16)</sup>. Some authors brought into discussion if the strategy of EGDS associated to postoperative endoscopic treatment would really be the best therapeutic approach for these patients, despite the immediate significant decrease in portal pressure<sup>(10)</sup> and consequent varices size reduction. We have been using the association of both, surgical and postoperative endoscopic treatment, for rebleeding prophylaxis in schistosomotic patients as a routine since 1989<sup>(12)</sup>.

In the light of a huge endoscopic experience and better endoscopic equipment and, in a context where varices banding showed to be better than sclerosis, the place of surgical treatment for presinusoidal portal hypertension has to be reviewed.

The aim of this study was to compare the intraoperative portal pressure decrease with long-term esophageal varices behavior and rebleeding rates in patients submitted to EDGS and postoperative endoscopic treatment.

## METHODS

A retrospective study of 175 patients with presinusoidal portal hypertension (schistosomiasis) with previous bleeding from esophageal varices rupture submitted to EGDS at University of São Paulo Medical School and University of Goiás Medical School, between 1989 and 2005 was performed. From this cohort of patients, we selected a group of 40 patients that underwent EGDS within a protocol of intraoperative portal pressure measurements in order to a better understanding of portal hemodynamic and consequent surgical effects. All patients had schistosomiasis diagnosis based on epidemiological, clinical and laboratorial data, and confirmed by histopathology examination. The surgical procedure was performed electively in all patients with a minimum delay of 30 days from the last bleeding episode. Exclusion criteria were alcoholism, chronic hepatitis, portal vein thrombosis, clinical and laboratory evidence of hepatic failure, or histological evidence of another liver disease. All patients signed an informed consent and were aware of this study protocol. The both Institutions Ethics Committees approved this study.

Patients were submitted to preoperative upper digestive endoscopy, and postoperatively usually at the 30th postoperative day. Varices were assessed by number, location, and caliber and classified according to the adapted Paquet<sup>(11)</sup> and Palmer and Brick<sup>(5)</sup> endoscopic criteria (FIGURE 1).

Grade	Endoscopic findings
0	Absence of esophageal varices
I	Microvessels that sketch varicose strings located in the esophagogastric transition or in the distal esophagus
II	One or two fine-caliber varices (smaller than 3 mm diameter) located in the distal esophagus
III	Medium caliber varices (between 3 or 6 mm diameter) or more than varices up to 3 mm that may reach up to a third medium third of the esophagus.
IV	Thick caliber varices, larger than 6 mm diameter, in any part of the esophagus.

FIGURE 1. Endoscopic esophageal varices evaluation (adapted from Paquet and Palmer and Brick criteria).

EGDS was performed as previously reported<sup>(6)</sup>. A liver biopsy was performed in all cases to confirm diagnosis and exclude other causes of liver disease. During surgery, an 8 French catheter was introduced through a jejunal branch and settled inside the portal vein trunk. Portal pressure was measured twice. At the beginning and when the surgery was concluded. After the last measure the catheter was removed and the jejunal branch ligated. Patients were stratified according to the portal pressure decrease in two groups: reduction below 30% and above 30%.

In the postoperative period patients were submitted to routine endoscopic sclerosis and, in the last 10 years, to elastic band ligation of the remaining esophageal varices. Patients were submitted to endoscopic sessions every 2–4 weeks to obtain varices eradication. After the initial treatment stage, sessions were performed at 3, 6, and then every 12 months. Endoscopic treatment was repeated in cases of esophageal varices persistence or new vessels appearance, and if rebleeding occurred. All patients needed endoscopic treatment (sclerosis or banding) during follow-up due to recurrence or persistence of esophageal varices. All patients were kept on clinical and endoscopic surveillance and no medication as betablockers were used.

From this group of 40 patients, 4 lost follow-up being 36 patients eligible for this study; all patients were followed for at least five years.

Regarding the decrease in esophageal varices diameter, patients were divided into five groups:

Group A – when there was not any variation between the pre and postoperative evaluation; Group B - when the variation between the pre and postoperative period was 1 grade; Group C – variation of 2 grades;

Group D – variation of 3 grades; and

Group E – variation of 4 grades.

Regarding the occurrence of rebleeding, patients were classified if it was present (yes) or not (no).

The decrease in portal pressure was compared with the variation of varices diameter, during follow-up. If any increase in varices size during the postoperative endoscopic follow-up was observed, independently of the final result it was considered as a variation (Groups B to E). Likewise, the influence of intraoperative portal pressure fall was compared to the presence of bleeding recurrence.

The Kolmogorov Smirnov test was performed to analyze the evolution of varices size comparing the two periods (preoperative and postoperative). The Fisher exact test was used to compare de portal pressure reduction and bleeding relapse. The level of significance adopted was 5%.

## RESULTS

Thirty-six patients were included in the study, being 19 (52.7%) male and 17 (47.3%) female with a median age of 42 years (range: 20 to 56 years).

There was no operative mortality. All patients were followed for at least 5 years after surgery with a median follow-up of 10 years (ranging from 5 to 19 years).

Regarding portal pressure evaluation after EGDS, all presented a portal pressure decrease. Twenty-one (58.3%) patients presented a decrease below 30% and 15 patients (41.7%) a decrease above 30%.

The grade of varices caliber decrease at the last endoscopic evaluation had the following distribution: Grade A (no variation) = 4 patients; Grade B = 11 patients; Grade C = 2 patients; Grade D = 10

patients; Grade E = 9 patients. Thirty-two (88.9%) patients presented a varices size reduction compared with the preoperative evaluation.

When comparing the different grades of portal pressure reduction and its impact in postoperative varices behavior, a significant difference was observed showing that a higher portal pressure decrease was associated with a higher varices diameter reduction.

In the group with portal pressure decrease lower than 30%, we observed: three patients with grade A, three patients with grade B, two patients with grade C, seven patients with grade D and six patients with grade E variation. In the group with portal pressure fall higher than 30%, we observed: one patient with grade A, eight patients with grade C, three patients with grade D and three patients with grade E variation. (FIGURE 2).

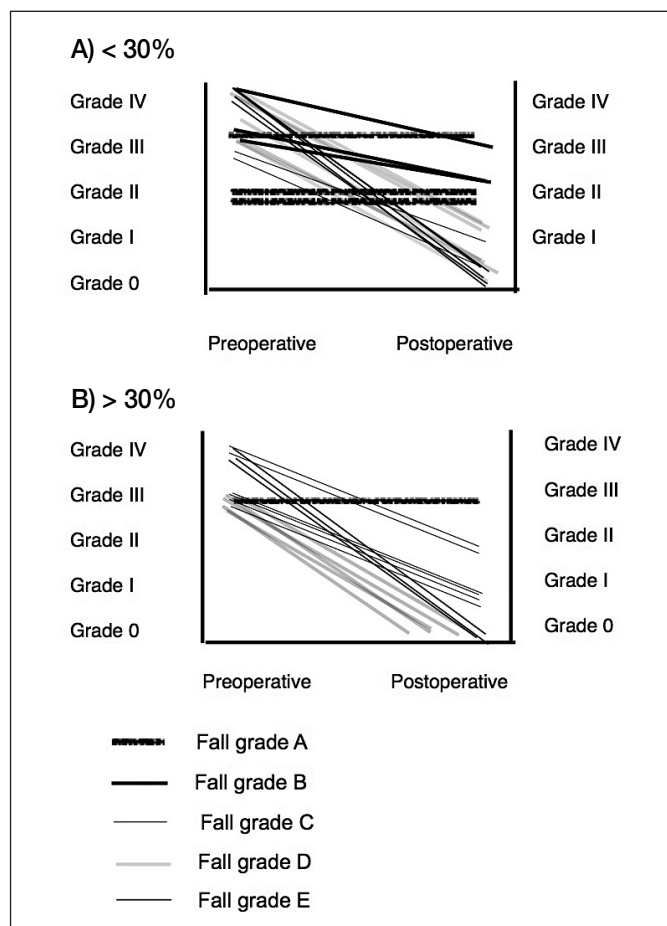


FIGURE 2 A/B. Varices evolution in patients with portal pressure decrease.

Despite a significant association between the portal pressure decrease and varices size reduction at the last endoscopic evaluation, during follow-up, most patients presented an increase in varices size that were endoscopically treated. In this way, regarding patients with portal pressure fall below 30%, 10 had varices size increase and 11 remained stable or presented size reduction, during long-term endoscopic follow-up; in the group with portal pressure fall higher than 30%, 10 had varices size increase and 5 remained stable or presented size reduction.

Four (11.1%) patients presented rebleeding due to esophageal varices rupture after EGDS. Three of these patients have had a

portal pressure decrease below 30% and only 1 above 30%. All bleeding episodes were controlled with endoscopic treatment and, no mortality was observed due to varices rebleeding. Despite two times more frequent in the group with lower portal pressure fall (6.3% vs 14.3%), no significant difference on the incidence of rebleeding was observed as shown on TABLE 1.

TABLE 1. Rebleeding rate according to intraoperative portal pressure decrease.

Pressure decrease (%)	Rebleeding				P
	No		Yes		
	n	%	n	%	
< 30	18	85.7	3	14.3	0.618
> 30	15	93.7	1	6.3	
Total	32	100.0	4	100.0	

Test: Fisher.

## DISCUSSION

The most threatening complication of schistosomiasis is esophageal or gastric variceal bleeding<sup>(2)</sup>. Although there are several studies showing options in the management of secondary bleeding prophylaxis in cirrhotic patients, results cannot be applied to patients with schistosomiasis because of the different pattern of portal hypertension (presinusoidal) and preserved liver function observed in these patients. Surgical treatment is adopted by specialized centers for rebleeding prophylaxis in schistosomal portal hypertension, nevertheless there is no consensus regarding the best technique to be employed<sup>(6)</sup>. Because of this, in both institutions (University of São Paulo Medical School and University of Goiás Medical School), medication as betablockers are preferably used in primary prophylaxis (if esophageal varices had not bleed yet). The ideal treatment goals are: avoidance of postoperative bleeding recurrence and portosystemic encephalopathy, maintenance of liver function, and the treatment of hypersplenism. Two major procedures have been widely applied, EGDS and distal splenorenal shunt. As the second option, a selective portal-systemic shunt, can lead to postoperative encephalopathy in up to 30% of patients, EGDS is the preferred technique performed in most groups for presinusoidal portal hypertension<sup>(6,8,12,17)</sup>. EGDS has the advantage of not triggering postoperative encephalopathy, but has the drawback of considerable rebleeding rates (up to 30%) from esophageal varices.

With the purpose of reducing bleeding recurrence rates, the routine association of postoperative endoscopic treatment with varices sclerotherapy, was introduced and reduced significantly the rebleeding rates comparing with EGDS alone<sup>(14,18)</sup>. In a study by Chaib et al.<sup>(19)</sup> evaluating early follow-up after EGDS, varices disappearance was observed in a smaller percentage compared with late follow-up, when endoscopic treatment was introduced, demonstrating an important role of this therapy in varices treatment<sup>(20)</sup>.

It is important to point out that many of these studies are from the nineties, when endoscopic resources were far inferior from nowadays. Currently, it is expected that with the endoscopic therapy evolution, better results can be achieved. These observations together with the data that endoscopic banding present better results than sclerotherapy for varices treatment<sup>(21)</sup> led us to question which treatment had more impact in varices behavior, surgery (EGDS) or endoscopic treatment. As all patients will

require endoscopic surveillance, the real role of EGDS in esophageal varices late behavior in patients submitted to the association of both therapeutic modalities need to be evaluated. Our study reemphasizes the need of revisiting the therapeutic approach of presinusoidal portal hypertension.

Recently, in a short follow-up study, Costa Lacet et al.<sup>(22)</sup> compared endoscopic sclerotherapy alone and associated to EGDS in treatment of esophageal varices in schistosomal portal hypertension, and showed that combined therapy was more effective for the prevention of recurrent esophageal variceal bleeding. Of course, it would have been better if this comparison were made with banding instead of sclerotherapy.

In order to understand the place of surgical treatment, we divided patients submitted to EGDS in two different categories based on the portal pressure fall immediately after operation as a beacon to determine if patients with greater fall evolved with a larger decrease in varices size during and after long-term follow-up (at least five years) and, if patients with lower portal pressure fall had a smaller decrease in varices size. Moreover, we tried to evaluate if a higher operative portal pressure fall have had any influence in bleeding recurrence.

Patients with a higher (>30%) portal pressure decrease, presented a significant reduction in esophageal varices size after long-term follow-up. This result suggested that the pressure fall caused by EGDS had influence in esophageal varices behavior at long-term follow-up. However, this data was related to the last endoscopic evaluation; when looking the varices size during follow-up, we found that a large number of patients independently from the portal pressure fall presented an increase of varices size needing endoscopic treatment. This behavior, leads us to question whether the most important role in the treatment is the endoscopy rather than surgery.

When the portal pressure fall levels were compared to bleeding recurrence, we did not observe any significant impact. Maybe, the small number of patients evaluated in this series should be the reason why a twofold difference however, not statistically significant.

Makdissi et al.<sup>(6)</sup> stated that, after EGDS, esophageal varices maintenance and recurrence are frequent, and long-term recurrence is the rule, but with significant decreases in both the caliber and number. Indeed, Ferraz et al.<sup>(8)</sup> obtained esophageal varices eradication in only 18.2% patients after EGDS alone, whereas eradication was possible in 52.7% when postoperative endoscopic treatment was associated. This data reemphasizes the need of lifelong endoscopic treatment for all patients.

In this series, we observed that a higher portal pressure decrease (>30%) after EGDS had no impact in bleeding recurrence however presented a significant impact in reducing esophageal varices size following endoscopic treatment. Although with no significance, a great number of patients, 20 (10 in >30% fall sample and 10 in <30% fall sample), had an increase in varices size during endoscopic follow up, showing the important role of endoscopic treatment in late results. The small number of patients evaluated, does not allow us to conclude which kind of treatment, surgery or endoscopic, or the association of both, is the key of good results.

This study emphasizes the need of long-term endoscopic treatment for patients submitted to surgical treatment of schistosomotic portal hypertension, independently of the effect of surgery on portal hemodynamics. Our results raised a discussion of which treatment is more important, surgery or endoscopic? Only a prospective, randomized study comparing the association of EGDS + endoscopic treatment versus band ligation alone, which is lacking in the literature, could answer this question.

In conclusion, it can be stated that endoscopic treatment after EGDS is essential for its long-term good results. The effective role of surgery could be questioned in further studies.

#### Authors' contribution

Tredicci TM: data collection. Silva Neto WDB: design, data analysis and paper writing. Herman P: design, data analysis and paper writing. Coelho FF: design and manuscript review. Makdissi FF: data collection.

Silva Neto WDB, Tredicci TM, Coelho FF, Makdissi FF, Herman P. Diminuição da pressão portal após desconexão ázigo-portal e esplenectomia na esquistossomose: comportamento a longo prazo das varizes, taxa de ressangramento e papel do tratamento endoscópico. *Arq Gastroenterol.* 2018;55(2):170-4.

**RESUMO – Contexto** – A esquistossomose é um problema de saúde pública endêmico, afetando cerca de quatro milhões de pessoas. A forma hepato-esplênica da doença é caracterizada por fibrose peri-portal, hipertensão pré-sinusoidal e esplenomegalia. A função hepática está preservada, sendo o sangramento por varizes a principal complicação da afecção. O tratamento cirúrgico usado pela maioria dos serviços para prevenção do ressangramento é a desconexão ázigo-portal e esplenectomia. Muitos autores reportaram melhores resultados com a associação do tratamento cirúrgico e o tratamento endoscópico pós-operatório. **Objetivo** – O objetivo deste estudo foi comparar a queda da pressão portal intraoperatória com o comportamento das varizes esofágicas e as taxas de ressangramento em pacientes submetidos a tratamento cirúrgico e endoscópico pós-operatório após seguimento de longo prazo. **Métodos** – Foi realizado um estudo retrospectivo de 36 pacientes esquistossomóticos com pelo menos um episódio de sangramento prévio por ruptura de varizes esofágicas, submetidos a desconexão ázigo-portal e esplenectomia, associada a tratamento endoscópico pós-operatório das varizes. Os pacientes foram divididos de acordo com a queda da pressão portal intraoperatória em dois grupos: redução menor e maior que 30%. Foram avaliadas a presença de tamanho das varizes a longo prazo e a recorrência do sangramento. **Resultados** – Levando-se em conta o comportamento das varizes, não foi observada influência significativa em ambos os grupos de queda de pressão portal. Com relação ao ressangramento das varizes, embora três vezes mais frequente no grupo com menor queda de pressão portal, não foi observada diferença estatística. Todos os pacientes foram submetidos a tratamento endoscópico pós-operatório. **Conclusão** – A ligadura elástica das varizes esofágicas, mais do que a queda da pressão portal, parece ser o principal fator responsável pelos bons resultados após a combinação das duas terapias (cirúrgica e endoscópica) para pacientes com hipertensão portal devido à esquistossomose. Estudos futuros serão necessário para confirmar esta hipótese.

**DESCRITORES** – Esquistossomose mansoni. Hipertensão portal, cirurgia. Endoscopia, reabilitação. Varizes esofágicas e gástricas. Ligadura.

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