TRASHEPATIC LEFT GASTRIC VEIN EMBOLIZATION IN THE TREATMENT OF RECURRENT HEMORRHAGING IN PATIENTS WITH SCHISTOSOMIASIS PREVIOUSLY SUBMITTED TO NON-DERIVATIVE SURGERY

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ABSTRACT – Context - Non-derivative surgical techniques are the treatment of choice for the control of upper digestive tract hemorrhages after schistosomotic portal hypertension. However, recurrent hemorrhaging due to gastroesophagic varices is frequent. Objective - To evaluate the outcome of treatment based on embolization of the left gastric vein to control the reoccurrence of hemorrhages caused by gastroesophagic varices in patients with schistosomiasis previously submitted to non-derivative surgery. Methods - Rates of reoccurrence of hemorrhages and the qualitative and quantitative reduction of gastroesophagic varices in patients undergoing transhepatic embolization of the left gastric vein between December 1999 and January 2009 were studied based on medical charts and follow-up reports. Results - Seven patients with a mean age of 39.3 years underwent percutaneous transhepatic embolization of the left gastric vein. The mean time between azigoportal disconnections employed in combination with splenectomy and the percutaneous approach was 8.4 ± 7.3 years, and the number of episodes of digestive hemorrhaging ranged from 1 to 7 years. No episodes of reoccurrence of hemorrhaging were found during a follow-up period which ranged from 6 months to 7 years. Endoscopic postembolization studies revealed reductions in gastroesophagic varices in all patients compared to preembolization endoscopy. Conclusions - Percutaneous transhepatic embolization of the left gastric vein in patients with schistosomiasis previously submitted to surgery resulted in a decrease in gastroesophagic varices and was shown to be effective in controlling hemorrhage reoccurrence.

HEADINGS - Schistosomiasis. Portal hypertension. Esophageal and gastric varices. Embolization, therapeutic.

INTRODUCTION

Mansonic schistosomiasis is the second most prevalent parasitosis globally after malaria. There are an estimated 250 million individuals infected with schistosomiasis in over 70 countries, 20 million of whom carry the severe form of the disease. Schistosomiasis is associated with 200,000 deaths per year, mainly due to upper digestive tract hemorrhaging secondary to schistosomotic portal hypertension^(10, 11, 32).

Surgical management is the treatment of choice in schistosomotic patients who present with digestive hemorrhaging due to gastroesophagic varices. The most commonly used is the non-derivative methods with include a range of different azigoportal disconnections employed in combination with splenectomy (APDS) or otherwise⁽¹⁾.

Besides yielding good clinical outcomes in the treatment of digestive hemorrhaging due to gastro-

esophageal varices, these approaches are advantageous over venous derivations in schistosomotic patients due to their treatment of hypersplenism, lesser technical difficulty, lower morbidity, and chiefly because they do not lead to hepatic encephalopathy postoperatively. However, non-derivative techniques are associated with a higher incidence of recurrent hemorrhaging and portal vein thrombosis^(1, 2, 13, 14, 15, 16, 17, 20, 24, 33, 35).

The rate of recurrence of bleeding after treatment using non-derivative techniques varies. Splenectomy plus gastroesophagic devascularization for example, presents a recurrence rate of between 6% and $29\%^{(6, 16, 28)}$.

Recurrent bleeding after non-derivative surgery has been ascribed to several factors: partial gastroesophagic devascularization, isolated splenectomy, portal vein thrombosis, rechanneling of the gastroesophagic system and other causes of upper digestive tract hemorrhaging unrelated to the surgical procedure⁽¹⁾.

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Against this background, schistosomotic patients submitted to non-derivative surgery for the treatment of high digestive tract hemorrhaging caused by gastroesophagic varices require constant outpatient follow-up. During follow-up sessions, digestive endoscopies are performed to assess gastroesophagic varices which tend to diminish in size rather than disappear. Depending on the service, the endoscopic program for eradicating gastroesophagic varices may be compulsory or selective, the aim of which is to prevent recurrent bleeding⁽¹⁶⁾.

Despite surgical and complementary endoscopic treatment, some patients present bleeding episodes. In 1999, our service recorded a hemorrhagic recurrence rate of 23.1% (6 out of 26 patients) in schistosomotic patients who were previously submitted to APDS in combination with endoscopic eradication of gastroesophagic varices. In two of these patients (33.3%), bleeding was not controllable using endoscopic or occlusion with a Sengstaken-Blakemore balloon. These cases underwent emergency mesenteric-caval derivation surgery but died due to subsequent complications.

Our group proposed an alternative to surgical treatment of recurrent hemorrhage due to gastroesophagic varices in schistosomotic patients previously undergoing non-derivative surgery, who continued to bleed despite complementary endoscopic treatment. The transhepatic left gastric vein embolization is a minimally invasive option which is more conducive to the survival of this patient group. This procedure, initially proposed by Lunderquist et al.⁽²¹⁾ was only elected exceptionally in our service to control digestive hemorrhaging in this specific patient group.

Given the peculiarities of this patient group, particularly previous surgery for venous disconnection, coupled with the lack of data on use of transhepatic percutaneous embolization of the left gastric vein in schistosomotic patients, the aim of this study was analyze the benefits that this technique effectively provides these patients in the medium to long term.

METHODS

This study had its project approved by the Ethics Committee on Human Research, Protocol no. 313/2008 on 18/12/2008.

Data was collected retrospectively from charts of schistosomotic patients who manifested recurrent hemorrhage due to gastroesophagic varices after non-derivative surgery and that were refractory to endoscopic treatment. The patients were referred by the Liver Surgery and Portal Hypertension Team of the Surgery Department of our service for angiographic study of the portal system, performed by the team from the Discipline of Vascular Surgery of the same department. Patients submitted to transhepatic percutaneous embolization of the left gastric vein between December 1999 and January 2009 were included.

All patients presented the same diagnosis of schistosomiasis, based on the preoperative investigation protocol (Kato Katz or rectal biopsy) and/or results of intra-operative hepatic biopsy. In addition, these patients had undergone previous non-derivative surgery for the treatment of digestive hemorrhage secondary to schistosomotic portal hypertension. All patients presented at least one episode of recurrence of digestive hemorrhaging postoperatively due to gastroesophagic varices, despite undergoing an endoscopic sclerotherapy program.

During the study period spanning from December 1999 to January 2009, a total of 10 previously operated schistossomotic patients were referred for treatment of rebleeding due to gastroesophagic varices by transhepatic percutaneous embolization of the left gastric vein.

One patient refused the treatment and was excluded from the study. A further two patients were submitted to transhepatic percutaneous portography without embolization. In addition to age and gender, the following variable were gathered from medical records and outpatient reports^(16, 24).

Data on previous surgical procedure: date, locale and surgical technique employed.

Post-operative events: occurrence of cavernomatous transformation of the portal vein, digestive hemorrhaging secondary to gastroesophagic varices, digestive endoscopy, endoscopic sclerotherapy treatment.

Transhepatic percutaneous embolization procedure: date of procedure, type of anesthesia, ultra-sound guided punction, material used for embolization, and early complications (within 30 days of procedure).

Post-embolization follow-up: late complications (30 days or more after the procedure), outpatient follow-up period, recurrent hemorrhaging and post-embolization endoscopic study.

Table 1 shows the characteristics of recurrent hemorrhaging due to gastroesophagic varices in the population studied, plus time to manifestation of rebleeding after non-derivative surgery and number of rebleeding episodes. All study subjects presented normal liver function throughout the outpatient follow-up period.

The endoscopic assessment criteria adopted was based on the comparison of endoscopy findings pre and post embolization, according to the simplified classification of Beppu et

TABLE 1. Time from surgical treatment non-derivative and the manifestation of rebleeding and the number of episodes of rebleeding of seven patients

| No. | Time (y) between surgery non derivative and the rebleeding | Number of gastrointestinal bleeding |
|--------|--|---|
| 1 | 0,5 | 7 |
| 2 | 19 | 4 |
| 3 | 11 | 2 |
| 4 | 4 | 2 |
| 5 | 5 | 1 |
| 6 | 5 | 2 |
| 7 | 3 | 4 |
| Median | 5 | 2 |

(y): yea

al. (4) which considers the number and size of gastroesophagic varices, and appearance of signs of eminent or active bleeding on endoscopy study.

A descriptive statistical analysis of the data (post-operative events, type of anesthesia, ultra-sound guided punction, material used for embolization, early complications, late complications, recurrent hemorrhaging and post-embolization endoscopic study) obtained in this study was carried out.

RESULTS

All patients undergoing surgery had a detailed surgical report describing the gastroesophagic devascularization and splenectomy technique employed to treat portal hypertension, standardized by De Capua Jr.⁽¹³⁾, together with data pertaining to the diagnostic investigation for schistosomiasis and rationale behind indication for surgery.

All procedures for transhepatic percutaneous embolization of the left gastric vein were performed within our service. The decision to perform general endovenous anesthesia was taken on a case-by-case basis according to the following criteria: hemodynamic stability, technical difficulties and patient cooperation. The other patients were submitted to the procedure under local anesthesia. Guided ultrasound for punction of the intra-hepatic portal vein was used whenever possible. Of the seven patients, three (42.8%) were operated under general anesthesia and two (26.8%) had ultrasound guided puncture during embolization of the left gastric vein.

Systematic review of medical charts and archived images of the procedures performed allowed confirmation of the surgical technique adopted for left gastric vein embolization. The choice of materials employed to obliterate the left gastric vein was found to follow no standard. This was likely due to the urgent nature of the intervention and/or lack of availability within the service. The products used for definitive troncular embolization of the vein were as follows: Gelfoam® associated with N-butyl 2-cyanoacrylate cement (Histoacryl®) in 57% of the procedures (four patients), absolute alcohol associated with cement in 14% of the procedures (one patient) and Gianturco coils associated with absolute alcohol in 29% (two patients).

Figure 1A-F depicts the main steps involved in the procedure for transhepatic percutaneous embolization of the left gastric vein.

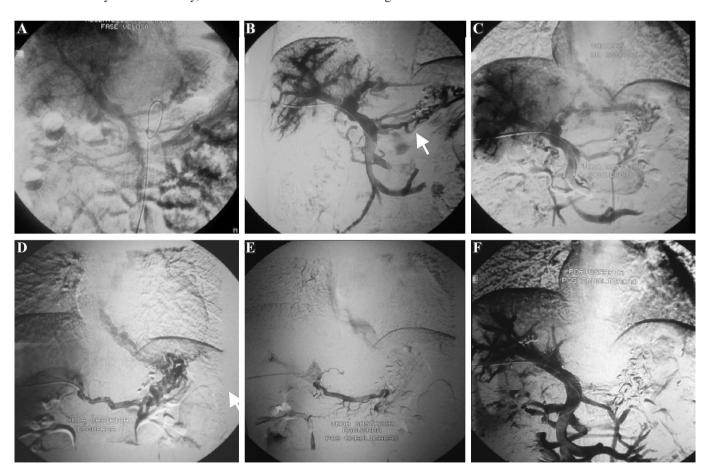


FIGURE 1. Transhepatic percutaneous embolization of the left gastric vein of patient no.5, performed on 15th February 2000. (A) Arterial portography. (B) Transhepatic portography. (C) Late transhepatic portography. (D) Selective catheterization of the left gastric vein. Gastroesophagic varices (arrow). (E) Selective angiography of the left gastric vein after embolization revealing occlusion of the gastroesophagic varices. (F) Control transhepatic portography after embolization showing absence of collateral circulation

With regard to the occurrence of cavernomatous transformation of the portal vein after APDS in the study population, only two patients (29%) presented this characteristic.

No short or long-term complications were noted in the group of seven patients submitted to embolization.

The results obtained demonstrate that clinically that no rebleeding occurred during the post-embolization outpatient follow-up period (median = 1,25 years with min = 0,5 and max =7,25). In addition, during the outpatient follow-up period, a significant reduction in the number and/or size of the gastroesophagic varices was evident in all patients who underwent embolization.

Table 2 shows the endoscopic findings for the study population at 3 time points: pre-embolization, post-embolization (medium term) and post-embolization (long term) among patients followed for at least 5 years.

responsible for venous congestion goes unidentified, particularly in patients previously undergoing APDS.

In our institution, the guidelines on treatment of recurrent hemorrhaging due to gastroesophagic varices in schistosomotic patients previously submitted to non derivative surgery have been standardized. Pursuant to these standards, the treatment of choice for recurrent hemorrhaging due to gastroesophagic varices is the endoscopic treatment, while transhepatic percutaneous embolization of the left gastric vein is indicated only under exceptional circumstances.

Only two studies^(26, 27) are available in the literature describing treatment of schistosomotic patients with digestive hemorrhaging due to gastroesophagic varices by embolization of the hepatofugal collateral circulation. Both studies are by the same author, although the first study is only a preliminary report. The second study describes the long-

TABLE 2. Endoscopic findings pre-, post-embolization and 5 years after embolization

| No. | EDA preembolization | EDA postembolization | EDA after 5 years |
|-----|-------------------------|----------------------|-------------------|
| 1 | 4L + bleeding | 3T + 1L | - |
| 2 | 2L + 1T | 2T | 1T |
| 3 | Varices free | Varices | - |
| 4 | 1L + 2M | 3T | - |
| 5 | 1L + 1M + 1T + bleeding | 3T | 3T + 1M |
| 6 | 2L + 1M + 1T + bleeding | 3 M | - |
| 7 | 2L + bleeding | 3T | - |

EDA: endoscopic assessment; L: large varices; M: medium varices; T: thin varices

DISCUSSION

In a 1980 study, Haddad⁽¹⁸⁾ detected esophageal varices in all patients after APDS. These findings corroborate the results reported by other authors in the literature, describing persistence of varices after non-derivative surgical management, although both size and number were substantially reduced post operatively^(7, 29, 30, 35, 38).

Given that rebleeding rates reported in the literature of between 6% and 29% rise with longer outpatient follow-up time^(6, 7, 12, 28, 33, 34, 35), coupled with the fact that surgical treatment is clearly unable to eliminate the factors triggering portal hypertension in the liver, we can conclude that no methodology is sufficiently reliable to be able to guarantee successful outcomes for this type of therapeutic procedure. Moreover, we found few reports on treatment of schistossomotic patients with recurrent hemorrhaging after non-derivative surgery.

Regarding the factors described in the literature to explain rebleeding secondary to gastroesophagic varices, 86.7% of rebleeding episodes were associated with portal vein thrombosis, partial gastroesophagic devascularization or rechanneling of the gastroesophagic venous system, or all these factors concomitantly⁽¹⁾. However, whereas treatment of recurrent bleeding entails endoscopic programs for the eradication of varices, often scant emphasis is placed on accurate diagnosis of the cause of bleeding, i.e. the collateral circulation route

term results of embolization, through direct access to the left gastric vein by laparotomy, as the primary treatment during the acute bleeding phase in 100 patients with portal hypertension. This approach was associated with a 5-year rate of bleeding recurrence of 12%. However, the study casuistic comprised schistosomotic and cirrhotic patients and contained no details regarding patient profile and presented other inconsistencies which prevented further conclusions from being drawn concerning treatment options for schistosomotic patients.

The remaining studies in the literature highlight percutaneous embolization as a treatment alternative to venous derivation surgery in cirrhotic patients with acute bleeding that offers lower morbidity and mortality and less impact on hepatic encephalopathy but high rates of recurrent hemorrhaging ranging from 36% to 81% (3, 5, 21, 22, 23, 36, 40, 41, 42, 43, 44).

It is noteworthy that between 1985 and 2009, the Surgery Department carried out around 440 APDS operations for the treatment of digestive hemorrhaging in schistosomotic patients. However, after the 7th post-operative month, a large proportion of patients had discontinued outpatient follow-up sessions⁽¹⁶⁾.

Despite the large number of operations performed by this service and the rate of around 15% (16,35) of hemorrhagic recurrence due to gastroesophagic varices in previously operated patients, only 10 patients who had unsuccessful outcomes after endoscopic treatment of recurrent hemorrhaging were

referred for possible percutaneous treatment. However, out of the 10 patients referred, only 7 were submitted to embolization and consequently included in this study.

Nevertheless, in order to ascertain the technical success rate, it is necessary to explore the reasons behind the failed attempts at left gastric vein embolization seen in the two patients who agreed to undergo transhepatic percutaneous portography and who were not embolized. The technical failure was due to two specific situations: cavernomatous transformation of the portal vein, and failure to identify the left gastric vein.

In the first case involving a failed attempt at embolization of the left gastric vein, the patient presented a clinical picture of portal vein thrombosis on the 13th post-operative day after APDS. Four years later the subject presented rebleeding as a result of gastroesophagic varices and was referred to an endoscopic program for eradicating varices. In view of the poor outcomes of endoscopic treatment, the patient was submitted to angiography study to investigate the cause of bleeding. The exam revealed the presence of a permeable left gastric vein, and percutaneous embolization was therefore indicated. However, technical difficulties involved in the cavernomatous transformation of the portal vein rendered selective catheterization of the left gastric vein impossible. The patient was later successfully reoperated to perform ligature of the left gastric vein.

However, two other patients who presented cavernomatous transformation of the portal vein were also submitted to successful percutaneous embolization, in spite of the difficulties presented by this anatomic alteration.

In the second case involving failed embolization of the left gastric vein, the patient was referred for emergency embolization after the first bleeding episode as a result of failed endoscopic treatment. Despite the previous angiography by arterial portography during the percutaneous transhepatic embolization procedure, no venous branch was found to be significantly contributing to the formation of gastroesophagic varices. Accordingly, no embolization procedure was carried out. We considered this particular case a technical failure which stemmed from indication of the procedure or the inability to identify the collateral circulation during the percutaneous approach. In spite of these mitigating factors the patient did not manifest any further bleeding episodes during outpatient follow-up.

Based on the two cases outlined above, a technical success rate of 77.8% was calculated, since these cases were deemed technical failures and were thus included in the population of this study (seven patients).

However, taking into account only the seven patients who were effectively embolized in this study, the results found based on the review of the patients' medical records showed that no bleeding episodes occurred during the post-embolization outpatient follow-up period.

Moreover, a significant reduction in gastroesophagic varices in number and/or size of varices was found on endoscopic pre and post embolization studies in patients submitted to embolization. In addition, in the sample studied

two patients were followed up for longer than 5 years and revealed no relevant changes on late endoscopy compared to the first endoscopic assessment post-embolization. Both of these patients presented several episodes of rebleeding during post-operative and pre-embolization periods despite endoscopic treatment.

Notwithstanding the small sample size, these results suggest long-term benefits of embolization in this specific patient group. These findings corroborate the hypothesis of this study which predicted clinically better outcomes after embolization in this specific group of schistossomotic patients previously submitted to non-derivative surgical treatment, compared to the results found in the literature for the same treatment in cirrhotics under different circumstances.

Our patients differed from the other cases reported in the literature in four main aspects: firstly, schistosomotic patients are generally afflicted by portal hypertension and have preserved hepatic function. Second, such patients no longer manifest changes consistent with hypersplenism after splenectomy, contributing to improved coagulation⁽²⁵⁾. The third aspect concerns the anatomic changes brought about by APDS. It is known that, anatomically, the main blood supply route to the cardiotuberosity venous plexus is the left gastric vein. Another study⁽³⁹⁾ demonstrated that 25% of patients with portal hypertension can present multiple left gastric veins. Previously operated patients manifest a lesser number of routes available to recruit for collateral circulation, as a result of the venous ligatures performed during surgery, involving not only the left gastric vein but also the other plexus veins. The fourth and final aspect concerns the contribution of the splenectomy in reducing the flow in the portal vein^(6, 16, 38).

Based on these findings, we believe that this specific patient profile represents the most suited group for indication of the procedure of transhepatic percutaneous embolization of the left gastric vein. We also hold the view that in previously operated patients with persistent and/or rechanneled left gastric vein, the chances of success following endoscopic treatment in the medium to long term are slim, mirroring results obtained after splenectomy alone, a technique known to be relatively ineffective and associated with hemorrhage recurrence rates of up to 54%^(6, 31). Perhaps in a different scenario, armed with the appropriate knowledge of hepatofugal circulation of each case of hemorrhagic recurrence due to gastroesophagic varices, the transhepatic percutaneous procedure for embolization of the left gastric vein may have played a greater role in the management of these patients. This is unlikely to have eliminated the need for the endoscopic eradication program but would certainly have led to improved portal hypertension control and consequently fewer endoscopic interventions^(4, 8, 9, 18). Akin to Bengmark et al.⁽³⁾, we consider the choice of material a pivotal factor in the success of the procedure. However, despite the lack of standardization of embolizing agents owing to the limits inherent to a philanthropic service, all patients were submitted to embolization of the left gastric vein using at least one definitive embolizer, coil or cement based, as per recommendations by several authors(3, 5, 21, 22, 23, 36, 37, 40, 41, 42, 43, 44).

Despite the absence of standard embolizing agents, the small sample size and the satisfactory results achieved using embolization of the left gastric vein proved insufficient to allow us to reach any conclusions on the best option available.

Although no complications ensued, short or long term, in the population of seven patients submitted to embolization of the left gastric vein, it is important to note the occurrence of a case of pneumothorax during transhepatic percutaneous punction of the portal vein in a patient excluded from the study due to technical failure of transhepatic percutaneous embolization of the left gastric vein. This incident occurred when the procedure was being performed under general anesthetic and ultrasound guided punction. In this specific case, owing to the anthropometric characteristics of the patient and an expected difficulty in performing transhepatic punction, a surgical planned was devised to render this procedure feasible using anesthetic support in conjunction with a radiologist to aid the punction activity.

Nevertheless, these additional safeguards were unable to prevent the occurrence of the complication. In the literature, the occurrence of complications stemming from transhepatic percutaneous punction have been described in up to 12% of cases, with a hemorrhage rate of 6% and plural complications incidence of $3.2\%^{(19)}$.

The small sample size precluded the drawing of more in-depth conclusions regarding the use of general anesthetic or the merit of ultrasound-guided punction. However, the sole complication described would not have been prevented by the use of either of these approaches.

Despite the small number of patients evaluated, the results of this study showed that the endoscopic treatment of gastroesophageal varices that developed after APDS in schistosomotic patients was not effective to prevent bleeding in long term, but the transhepatic percutaneous embolization of the left gastric vein procedure shows better results. Further studies should be conducted to establish treatment protocols for schistosomotic patients that have rebleeding after APDS. It should establish whether the indication of the transhepatic percutaneous embolization of the left gastric vein procedure may, in some cases, replace the endoscopic sclerotherapy.

CONCLUSION

The results presented in this study allow us to conclude that indication of transhepatic percutaneous embolization of the left gastric vein in only exceptional circumstances should be reviewed in the guidelines for treatment of schistosomotic patients with recurrent hemorrhaging due to gastroesophagic varices previously submitted to non-derivative surgical treatment. We believe this therapeutic option to be a good therapeutic alternative for treatment in this patient group, particularly after determining hepatofugal circulation, an investigation which should be included in the treatment flow diagram for these patients.

Saad PF, Razuk A, Telles GJP, Park JH, Esteves FP, Caffaro RA. Embolização transhepática da veia gástrica esquerda no tratamento da recidiva hemorrágica em esquistossomóticos submetidos previamente a cirurgia não derivativa. Arq Gastroenterol. 2012;49(4):238-44.

RESUMO - Introdução - A cirurgia por técnicas não derivativas é o tratamento de escolha para o controle da hemorragia digestiva alta secundária à hipertensão portal esquistossomótica. Contudo, a recidiva hemorrágica em decorrência das varizes gastroesofágicas é um evento frequente. O programa de erradicação endoscópica das varizes gastroesofágicas tem o objetivo de prevenir e/ou tratar a recidiva hemorrágica, porém nem todos os doentes respondem ao tratamento. Objetivo - Avaliar o sucesso do tratamento de embolização da veia gástrica esquerda no controle da recidiva hemorrágica por varizes gastroesofágicas nos doentes esquistossomóticos submetidos previamente a cirurgia não derivativa. Métodos - Foram estudadas, por meio de dados colhidos nos prontuários médicos e dos protocolos de seguimento ambulatorial, a incidência da recidiva hemorrágica e a diminuição quantitativa e qualitativa das varizes gastroesofágicas em detrimento das varizes gastroesofágicas dos doentes encaminhados para embolização transhepática da veia gástrica esquerda no período de dezembro de 1999 até janeiro de 2009. Resultados - Sete doentes com média etária de 39,3 anos foram encaminhados para embolização percutânea transhepática da veia gástrica esquerda. O tempo médio decorrido entre a DAPE e a abordagem percutânea foi de 8,4 ± 7,3 anos e o número de episódios de hemorragia digestiva variou de um a sete neste período. Nenhum episódio de ressangramento foi verificado na população do estudo durante o período de acompanhamento, que variou de 6 meses a 7 anos. Após estudo endoscópico pós-embolização, todos os doentes apresentaram diminuição das varizes gastroesofágicas em comparação à endoscopia pré-embolização. Conclusão - A embolização percutânea transepática da veia gástrica esquerda nos doentes esquistossomóticos, previamente operados, determinou a redução das varizes gastroesofágicas e foi eficiente no controle do ressangramento para a população estudada.

DESCRITORES – Esquistossomose. Hipertensão portal. Varizes esofágicas e gástricas. Embolização terapêutica.

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