

## EVOLUTIONAL PROFILE OF THE ESOPHAGEAL VARICES AFTER SPLENECTOMY ASSOCIATED WITH LIGATION OF THE LEFT GASTRIC VEIN AND SCLEROTHERAPY IN SCHISTOSOMAL PORTAL HYPERTENSION

*Perfil evolutivo das varizes esofágicas pós esplenectomia associada à ligadura da veia gástrica esquerda e escleroterapia na hipertensão portal esquistossomótica*

João **BATISTA-NETO**, Luciano Becker **TOGNETTI**, Laércio Tenório **RIBEIRO**,  
Maria do Carmo **BALWANI**, Tadeu **MURITIBA**, Elton Elton Correa **ALVES**

From the Group of Liver, Bile Ducts, Pancreas and Portal Hypertension Surgery, General Surgery and Specialties Service, University Hospital Prof. Alberto Antunes, Faculty of Medicine, Federal University of Alagoas, Maceio, Brazil.

**ABSTRACT - Background** – The schistosomiasis affects 200 million people in 70 countries worldwide. It is estimated that 10% of those infected will develop hepatosplenic status and of these, 30% will progress to portal hypertension and esophagogastric varices, whose expression is through gastrointestinal bleeding with significant mortality in the first bleeding episode. Multiple surgical techniques have been developed to prevent re-bleeding. **Aim** - To evaluate the evolutionary profile of esophageal varices after splenectomy + ligation of the left gastric vein associated with endoscopic sclerotherapy in schistosomal portal hypertension. **Methods** - Prospective and observational study including schistosomiasis patients with previous history of upper digestive hemorrhage and underwent to splenectomy + ligation of the left gastric vein and sclerotherapy. The variables were: evolutionary profile of esophageal varices before and after surgery and re-bleeding rate. **Results** - The sample included 30 patients, 15 patients for each gender. The age ranged from 19 to 74 years (median = 43 years). There was a reduction in the degree, caliber and red spots in all patients ( $p < 0.05$ ). The eradication of varices with sclerotherapy was achieved in 86.7% and with surgery alone in 15.4%. The mean follow-up was 28 months, ranging from two to 76 months. Were carried from one to seven sessions of sclerotherapy and the average was three per patient to eradicate varices. Four (13.3%) did not complete the follow-up. The re-bleeding rate was 16.7%. **Conclusion** - There was a reduction of the degree, caliber and red spots of esophageal varices in all patients.

**HEADINGS** - Hypertension, portal. Esophageal and gastric varices. Splenectomy. Schistosomiasis.

### Correspondence:

João Batista Neto,  
e-mail: jbatista19@uol.com.br

Financial source: none

Conflicts of interest: none

Received for publication: 04/10/2012

Accepted for publication: 06/12/2012

**DESCRIPTORES** - Hipertensão portal. Varizes esofágicas e gástricas. Esplenectomia. Esquistossomose.

**RESUMO – Racional** - A esquistossomose mansônica afeta 200 milhões de pessoas em 70 países do mundo. Estima-se que 10% dos infectados evoluirão para a forma hepatoesplênica e, destes, 30% progredirão para hipertensão portal e varizes esofagogástricas, cuja expressão será através de hemorragia digestiva com mortalidade relevante no primeiro episódio hemorrágico. Múltiplas técnicas cirúrgicas foram desenvolvidas para prevenir o ressangramento. **Objetivo** - Avaliar o perfil evolutivo das varizes esofágicas após esplenectomia + ligadura da veia gástrica esquerda associada à escleroterapia endoscópica na hipertensão portal esquistossomótica. **Método** - Estudo prospectivo, observacional, de pacientes esquistossomóticos com antecedentes de hemorragia digestiva alta, submetidos à esplenectomia + ligadura da veia gástrica esquerda e escleroterapia. As variáveis estudadas foram perfil evolutivo das varizes esofágicas antes e após a operação e índice de recidiva hemorrágica. **Resultados** - Amostra foi constituída por 30 pacientes distribuídos, quanto ao gênero, em 15 doentes para cada sexo. A idade variou de 19 a 74 anos (mediana=43 anos). Houve redução do grau, calibre e red spots em todos os pacientes ( $p < 0,05$ ). A erradicação das varizes com escleroterapia foi alcançada em 86,7% e exclusivamente com a operação em 15,4% dos pacientes. O tempo de seguimento médio foi de 28 meses, variando de dois a 76 meses. Foram realizadas de uma a sete sessões de escleroterapia e média de três por paciente para erradicar as varizes. Quatro pacientes (13,3%) não completaram o seguimento. A recidiva hemorrágica foi de 16,7%. **Conclusão** - Houve redução do grau, calibre e dos red spots das varizes esofágicas em todos os pacientes.

## INTRODUCTION

The schistosomiasis affects 200 million people in 70 countries worldwide, and another 600 million are at risk of being infected. It's estimated that 10% of those infected will develop the hepatosplenic form and of these, 30% will progress to portal hypertension and esophagogastric varices, whose expression is through gastrointestinal bleeding in up to 40% of their patients with significant mortality in the first hemorrhagic episode<sup>15,32</sup>.

Multiple surgical techniques have been developed to prevent (secondary prophylaxis) rebleeding, which may occur in the following year by up to 70% of those who had their first hemorrhagic episode, if untreated<sup>16</sup>.

Splenectomy associated with ligation of the left gastric vein (SLLGV) is used in hepatosplenic schistosomiasis since the 60s, in our region and service<sup>15,28</sup>. The importance of the left gastric vein to maintain the gastroesophageal varices plexus have been demonstrated. The ligation remains being indicated in cases of rebleeding of splenectomized when it has not been ligated<sup>3,25</sup>.

With the domain of the technique of sclerotherapy of esophageal varices, through flexible endoscopes in the 80s, our service<sup>23</sup> began the sclerotherapeutic treatment of residual varices after SLLGV, following the intention to eradicate them with lower morbidity and mortality than surgical ligation of varices<sup>10,15,28</sup> or azygoportal disconnection<sup>22,25</sup>, and obtain similar rates of rebleeding.

The eradication of esophageal varices after SLLGV without sclerotherapy reaches rates of 18.2%<sup>12</sup>. In a prospective study<sup>24</sup> of 20 cases with assessment at 30, 60 and 90 days after SLLGV, observed partial reduction in all degrees and calibers of varices without statistical significance. Underwent sclerotherapy, these varices are controlled up to 80-90% of cases<sup>12,20,29,31</sup>. The combination of sclerotherapy after surgical treatment without shunt is a controversial procedure, adopted by authors with vast experience<sup>12,20,29,31</sup> and considered dispensable by others<sup>6,17,24</sup>, who use it only in rebleeding.

The aim of this prospective study is to analyze the endoscopic evolutionary profile of the esophageal varices after SLLGV associated with sclerotherapy, motivated by the paucity of published literature.

## METHOD

Patients were studied in a prospective, observational and consecutive surgical protocol in the General Surgery and Specialties Service of the University Hospital Prof. Alberto Antunes at Federal University of Alagoas, Maceio, Brazil. The study was approved by the Ethics Committee at the same hospital and all participants authorized their inclusion in the project and signed an informed consent.

The inclusion criteria were: 1) to have a clinical diagnosis, epidemiological, sonographic and histological diagnosis of schistosomiasis with recent history of upper gastrointestinal bleeding exclusively by esophageal varices; 2) classified as Child A or B (MELD <10); 3) had viral markers for hepatitis B and C negative.

Exclusion criteria were patients with: 1) chronic alcoholism; 2) chronic hepatitis; 3) mixed hepatopathy; 4) portal system thrombosis at Doppler; 5) clinical and laboratory data of uncontrollable hepatic, renal or cardiac insufficiency or ultrasound evidence/histopathological of another hepatopathy.

All patients received preoperative treatment for schistosomiasis with praziquantel. Prophylaxis for sepsis after splenectomy was performed with vaccination for pneumococcus, meningococcus and Haemophilus influenza.

### Surgical procedure

Abdominal access was performed by subcostal incision of Kocher at left. The main surgical steps were: 1) access to the omental bursa; 2) prior ligation of the splenic artery in the upper border of the pancreas; 3) splenectomy by a standardized technique<sup>28</sup>; 4) complete devascularization of the greater gastric curvature; 5) ligation of the left gastric vein by accessing on its origin<sup>15</sup>; 6) wedge liver biopsy. Antibiotic prophylaxis with cefazolin was made during anesthetic induction. There wasn't platelets infusion in thrombocytopenia until 30.000/cm<sup>3</sup>. There was reserving of platelets for lower rates, but there was no need to use. Hemoglobin less than 7 g was corrected to achieve it in the pre or intraoperative with packed red blood cells.

### Endoscopic procedure

Endoscopy was performed in the pre and postoperative and varices were classified according to Paquet<sup>26</sup> to the degree and caliber. The presence of red spots or congestive gastropathy was noted and just as any other mucosal changes. The sclerotherapy sessions were held at least 45 days after the operation to complete or electively treat residual varices. Sclerotherapy was performed with injection solution of ethanolamine diluted to 3%, into the varices, in sessions spaced every 15 days or monthly until full eradication of varices. Follow-up was set at 6, 12, 24 months, according to each case and consecutively.

The variables studied (end point) were: 1) evolutionary profile of endoscopic varices pre and postoperative (minimum of 45 days after SLLGV) according to the degree, caliber and presence or absence of red spots<sup>26</sup>; 2) the post-sclerotherapy evolution; 3) index of rebleeding.

### Clinical outcome / complications

Surgical complications were divided into related to the surgical procedure or secondary to portal

hypertension. Regarding rebleeding established itself as relapse patients who presented hematemesis, melena or blood taste sensation in the mouth, at any stage of the disease considered controlled. Endoscopy was performed to determine the cause.

### Statistical Analysis

Statistical analysis was performed by paired Student t test with 95% CI for the degree and caliber of esophageal varices, the results were considered significant with  $p < 0,05$ , using the computer program SPSS<sup>13</sup>. The presence or absence of red spots was analyzed by Fisher's exact test by Epidat 3.1, the results were considered significant with  $p < 0,05$ .

## RESULTS

The sample consisted of 30 patients, 15 males and 15 females, median age was 43 years (19-74 years). The mean hospital stay was six days (four to 25 days). The mean follow-up was 28 months (two to 76 months) and performed in 86.7% (26/30) of patients. Two patients had endoscopic report of preoperative misplaced and four did not complete the sessions of sclerotherapy.

There was a reduction in the degree and caliber of the varices in all patients, with statistical significance ( $p < 0.05$  and Tables 1 and 2).

**TABLE 1** – Evolutional profile of endoscopic esophageal varices pre and postoperative as the degree presented, according to Paquet<sup>26</sup> (N = 30)

Classification of esophageal varices according to the degree							
PERIOD	Incipient	1	2	3	4	Incomplete assessment	Total
Preoperative	1(3,3%)	1(3,3)	8(26,6)	9(30)	9(30)	2(6,6)	30 (100%)
Postoperative	4(13,3%)	6(20)	4(13,3)	10(33,3)	2(6,6)	4(13,3)	30 (100%)

Paired Student t test with CI = 95%:  $p < 0,05$ .

The increased number of patients with esophageal varices degrees 1 and 3 postoperatively was due to the degree reduction in patients with higher degree of them.

There was total eradication of varices in 15.4% (4/26) of patients in the first endoscopy (minimum 45 days) after SLLGV without sclerotherapy.

Sclerotherapy of esophageal varices after SLLGV was completed in all patients whose varices persisted after the operation (84.6% - 22/26) and its control was performed with one to seven sclerotherapy sessions, an average of three sessions per patient.

Complications related to surgery were: pancreatic fistula, incisional hernia and insufficient ligation of the hilum - one for each patient. Seven patients (23,3%) had complications related to portal hypertension: ascites (6); melena (2); liver failure (1) who died at 68 months of follow up; gynecomastia (1) that ceded to the suppression of the diuretic. There was no hospital mortality.

**TABLE 2** – Evolutional profile of endoscopic esophageal varices pre and postoperative in the caliber presented, according to Paquet<sup>26</sup> (N = 30).

Classification of esophageal varices according the caliber						
PERIOD	PERIOD	Thin	Medium	Thick	Incomplete assessment	Total
Preoperative	0 (0%)	1 (3,3)	15 (50)	12 (40)	2 (6,6)	30 (100%)
Postoperative	4 (13,3%)	8 (26,6)	8 (26,6)	8 (26,6)	2 (6,6)	30 (100%)

Paired Student t test with CI = 95%:  $p < 0,05$ .

Regarding the presence of red spots, was obtained a reduction of 61,5% (n = 16) to 15,4% (n = 3), respectively in the pre and postoperative of SLLGV. This variation was statistically significant using the Fisher exact test ( $p = 0.0018$  with 95% CI), ie,  $p < 0,05$ . The overall rebleeding occurred in 16,7% (5/30), manifested by mild symptoms that did not require transfusion.

## DISCUSSION

The progress of endoscopic therapy in the last 20 years of the last century for esophageal varices provided to schools that adopt methods without surgical shunts in schistosomal be able to approach them without surgically exposing the morbidity of surgical ligation of varices intraesophageal, though low<sup>1,2,6,7,10,11,15,21,23,25,27,30</sup>. Kelner<sup>15,16</sup> has always considered that the surgical treatment of schistosomal portal hypertension did not need very large disconnection, like azygoportal disconnection + splenectomy, establishing itself in the pathophysiology of the disease. He proposed that splenectomy associated with sclerotherapy or band ligation, would be sufficient procedures to obtain satisfactory results, may be added the ligation of the left gastric vein, because no technique cure the patient, and all options are palliative. There is no consensus on the best technique to be used in schistosomal portal hypertension<sup>14,16,21,27</sup> although the Brazilian Society of Hepatology in a recent consensus<sup>5</sup> has indicated azygoportal disconnection + splenectomy as ideal method for secondary prophylaxis for variceal bleeding in schistosomal. There are no reliable studies scientifically sufficient to eradicate the controversy<sup>19</sup>.

Ferraz et al.<sup>12</sup> reported varices eradication in 52.7% when associated sclerotherapy with SLLGV, a lower rate than this study, 84.6%. They pointed out, however, the difficulty of patients returning to the complementary endoscopic treatment sessions. This fact was also identified in this study, although fewer (15.4%), perhaps because it was prospective and consequently generate higher compliance in doctor / patient relationship. The eradication of varices without sclerotherapy in the aforementioned study<sup>12</sup> was 18.2% of esophageal varices, similar to this (15.4%). The red spots were reduced significantly from 61.5% to 15.4% in this series, consistent with a recent study<sup>9</sup>.

The rebleeding rate of 16.7% in this study was consistent with other séries<sup>12,21,29,31</sup> and appears to be related to the degree of fibrosis<sup>4</sup>, more intensely marked

by thrombocytopenia<sup>33</sup>. This claim is disputed by other authors<sup>2</sup>, which relate the severity of hepatosplenic schistosomiasis to intrahepatic sinusoidal obstruction and not to fibrosis.

Sakai<sup>29</sup>, said to be easier to control endoscopic esophageal varices in schistosomiasis splenectomized, that those who had not been operated<sup>8</sup>. A randomized study of this author's group<sup>18</sup> of azygoportal disconnection with splenectomy + sclerotherapy versus sclerotherapy alone in schistosomiasis patients with previous bleeding, showed that there was no statistical significance in rebleeding between the two groups, but the patient who underwent sclerotherapy alone had chance twice more to have recurrence of gastrointestinal bleeding that patient who had been operated.

Other groups<sup>6,17,24</sup>, adopting methods without shunts, do not consider necessary to eradicate residual esophageal varices, except in rebleeding. Evangelista Neto et al.<sup>9</sup>, consider intra varicose pressure of 13 mmHg, achieved by ligation of the left gastric vein and splenectomy, secure for not indicate complementary sclerotherapy, since the varicose rupture occurs only from 20 mmHg. Opposite conduct of Sakay<sup>24</sup> and Ferreira et al.<sup>13</sup>, who consider the indices of 13 mmHg of varicose pressure or 15,5 cm/sec of the portal flow at Doppler as satisfactory for installation of treatment of esophageal varices, due to the high chance of bleeding. Below these indices eliminate the need of the varicose treatment because schistosomal portal hypertension appears to depend on hyperflow<sup>2</sup>. The safe cutoff of varicose pressure from which most patients would develop gastrointestinal bleeding has not been defined<sup>18</sup>. Sizable national experiences complemented the surgical treatment of varicose veins with sclerotherapy, because there is only esophageal bleeding if there are varices<sup>4,9,12,13,20,21,23,29,31</sup>.

The SLLGV + sclerotherapy in schistosomal portal hypertension is a similar method to other non-derivative surgical procedures as the rebleeding and mortality.

## CONCLUSION

Splenectomy associated with ligation of the left gastric vein reduces the degree and caliber of esophageal varices in all patients and if associated with sclerotherapy eradicates varices in 86%.

## REFERENCES

- Alves A. Critical analyses of my own experience in portal hypertension – varices ligation and splenectomy. In: Lima DR, Batista Neto J.(Ed). I Simpósio Alagoano de Hipertensão Portal e Esquistossomose Mansônica. Ed da Univ Fed de Alagoas 1987: 39-41.
- Arruda SMB, Barreto VST, Amaral FJ. Duplex sonography study in schistosomiasis portal hypertension: characterization of patients with and without a history of variceal bleeding. *Arq Gastroenterol* 2008; 45: jan/mar. Access: www.scielo.br in 10/25/2012. DOI: 10.1590/S0004-28032008000100003.
- Assef JC, Cápua Jr. A, Szutan LA. Treatment of recurrent hemorrhagic esophageal varices in schistosomotic patients after surgery; *Rev Assoc Med Bras* 2003; 49: 406-412.
- Bittencourt PL. Portal fibrosis and schistosomal portal hypertension: what is the best strategy for primary and secondary prevention of hemorrhage from esophageal varices. *Arq Gastroenterol* 2003; 40:1-3.
- Brazilian Society of Hepatology. Variceal bleeding consensus meeting report from the Brazilian Society of Hepatology. *Arq Gastroenterol* 2010; 47: 2 Apr/June. Access: www.scielo.br in 19/10/2012. DOI: 10.1590/50004-28032010000200017.
- Cápua Jr A, Szutan LA. Desconexão ázigo-portal e esplenectomia mais escleroterapia no tratamento da hipertensão portal. *Clin Bras Cir* 1995; 2: 231-42.
- Chaib AS, Lessa BS, Cecconello I, Félix VN, Chaib E. A new procedure for the treatment of bleeding esophageal varices by transgastric ázigo-portal disconnection. *Int Surg* 1983; 68: 353-356.
- Cordeiro F. Variceal sclerosis in schistosomotic patients: a 5-year follow-up study. *Gastrointest Endosc* 1990; 36: 475-478.
- Evangelista Neto J, Pereira FF, França ST, Amaral FJ, Brandt CT, Fonseca Neto OCL et al. Esplenectomia e ligadura da veia gástrica esquerda na esquistossomose mansônica: efeitos sobre pressão das varizes do esôfago e indicadores endoscópicos de risco de sangramento por varizes esofagogástricas. *Arq Bras Cir Dig* 2012; 25:1 Jan/Mar. Access: www.scielo.br, 21/11/2012. DOI:10.1590/50102-67202012000100010.
- Falcão D, Almeida SGF. Evolution of the treatment of the portal hypertension in Alagoas. *Rev Bras Cir* 1992; 82: 233-238.
- Ferraz AA, Bacelar TS, Silveira MJ, Coelho AR, Câmara Neto RD, de Araújo Jr. JG, Ferraz EM. Surgical treatment of schistosomal portal hypertension. *Int Surg* 2001; 86: 1-8.
- Ferraz AAB, Lopes EPA, Barros FMR, Sette MJA, Arruda SMB, Ferraz EM. Splenectomy plus left gastric vein ligation and desvascularization of the great curvature of the stomach in the treatment of hepatosplenic schistosomiasis. Postoperative endoscopic sclerosis is necessary? *Arq Gastroenterol* 2001; 38: 84-88.
- Ferreira F, Ribeiro M, Santos MF, Assef J, Szutan C. Doppler ultrasound could predict varices progression and rebleeding after portal hypertension surgery: lessons from 146 EGDS and 10 years of follow-up. *World J Surg* 2009; 33: 2136-2143.
- Gawish Y, El-Hammadi HA, Kotb M, Awad AT, Anwar M. Desvascularization procedure and DSRS. A controlled randomized Trial on selected haemodynamic portal flow pattern in schistosomal portal hypertension with variceal bleeding. *Int Surg* 2000; 85: 325-30.
- Kelner S, Silveira M, ed. Varizes do esôfago na esquistossomose mansônica. Recife: Editora Universitária da UFPE; 1997.
- Kelner S. Critical evaluation of schistosomiasis portal hypertension surgery. *Mem Inst Oswaldo Cruz* 1992; 87Suppl 4: 357-368.
- Lacerda CM, Freire W, Vieira de Melo PS, Lacerda HR, Carvalho GL. Splenectomy and ligation of the left gastric vein in schistosomiasis. The effect on esophageal variceal pressure measured by a non-invasive technique. *Keio J Med* 2002; 51: 89-92.
- Lacet CM, Batista Neto J, Wiszomirska RM, Ribeiro LT, Silva KCP, Oliveira FS, Sarmento CM, Balwani MCL, et al. Escleroterapia exclusiva ou associada à DAPE no tratamento da hipertensão portal esquistossomótica – Estudo prospectivo randomizado. *GED* 2007; 26 Supl 2: S3.
- Laosebikan AO, Thomson SR, Naidoo NM. Schistosomal portal hypertension. *J Am Coll Surg* 2005; 200: 795-752.
- Leonardi LS, Boin IFS, Brandalise NA, Andreollo NA, Callejas NF, Andrade RG, Pareja JC. Results of the ázigo-portal disconnection and splenectomy associated with sclerotherapy in schistosomiasis. *ABCD Arq Bras Cir Dig* 1988; 4: 99-103.
- Makdissi FF, Herman P, Pugliese V, De Cleve R, Saad WA, Cecconello I, D'Albuquerque LAC. Long-term results of esophagogastric devascularization and splenectomy associated with endoscopic treatment in Schistosomal Portal Hypertension. *World J Surg* 2010; 34: 2682-2688. DOI: 10.1007/soo268-010-0717-8.
- Malta P, Leal A, Falcão J, Santos P, Carvalho C, Malta J. Surgical treatment of brilliant portal hypertension and comparative study due to cirrhosis. *Rev Bras Angiol Cir Vasc* 1987; 17: 147-149.

23. Mendonça E. Critical evaluation of the surgical treatment of portal hypertension – Selective Portal decompression. In: Lima DR, Batista Neto J, eds. I Simpósio Alagoano de Hipertensão Portal e Esquistossomose Mansônica. Maceió: Ed da Universidade Federal de Alagoas; 1987: 43-4.
24. Menezes HL, Jucá MJ, Gomes EG, Brandt C, Araújo D. Avaliação endoscópica do grau das varizes esofagianas em pacientes esquistossomóticos submetidos à esplenectomia e ligadura da veia gástrica esquerda. *Rev Col Bras Cir* 2001; 28 Supl: 381.
25. Oliveira FS. Critical evaluation and results of esophagogastric devascularization + ligation or not varices associated to splenectomy In: Lima DR, Batista Neto J, eds. I Simpósio Alagoano de Hipertensão Portal e Esquistossomose Mansônica. Maceió: Ed da Universidade Federal de Alagoas; 1987: 33-8.
26. Paquet KJ. Prophylactic endoscopic sclerosing treatment of the esophageal wall in varices: a prospective controlled randomized Trial. *Endoscopy* 1982; 14: 4-5.
27. Raia S, da Silva LC, Gayotto LC, Forster SC, Fukushima J, Strauss E. Portal hypertension in schistosomiasis: a long-term follow-up of a randomized Trial comparing three types of surgery. *Hepatology* 1994; 20: 398-403.
28. Ramalho R. A hematêmese na hipertensão portal. *An Fac Med da Univ Fed de Alagoas* 1964; 1: 53-58.
29. Sakai P. Endoscopic esophageal varices sclerotherapy post-surgical treatment for portal hypertension in patients with hepatosplenic schistosomiasis. *Arq Gastroenterol* 2001;38: 81-3.
30. Santos ES, Rocha MD, Vilela RB, Lacet CMC. Portal Hypertension in Schistosomiasis Mansoni: Retrospective study of surgical treatment. *Rev Hosp Univ Ufal* 1995; 2: 9-14.
31. Silveira M, Kelner S, Silveira RK. Tratamento cirúrgico emergencial em varizes esofagogástricas sangrantes por esquistossomose: esplenectomia com ligadura da veia gástrica esquerda. *Clin Cir Bras* 2003; VIII(I): 235-245.
32. Voieta I, Queiroz LC, Andrade LM, Silva LCS, Fontes UF, Barbosa A Jr, Rezende V, Petroianu A, Andrade Z, Antunes CM, Lambertucci JR. Imaging techniques and histology in the evaluation of liver fibrosis in hepatosplenic schistosomiasis mansoni in Brazil: a comparative study. *Mem Inst Oswaldo Cruz* 2010; 105(4) July. Access: [www.scielo.br](http://www.scielo.br) in 10/25/2012. DOI: 10.1590/S0074-02762010000400011.
33. Wyszomirska RMAF, Lacet CC, Ribeiro LT, Nishimura NF, Mesquista MA, Batista Neto J, Oliveira F et al. Decrease of type collagen and TIMP-1 serum levels after splenectomy in patients with schistosomiasis mansoni. *Acta Tropica* 2006; 97: 301-308.