An overview of the treatment of oesophageal varices: recommendations for the best approach in our patients

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Abstract
Oesophageal variceal rupture is the commonest cause of upper gastrointestinal bleeding in central Sudan. In 90% of patients, it is secondary to schistosomal portal hypertension. The majority of these patients are young and their disease is characterized by a benign course compared to cirrhosis. However, a major cause of death in these patients is acute variceal bleeding. The current treatment for oesophageal varices in our patients is endoscopic therapy and the beta blocker propranolol. Surgery is reserved for failures of this therapy. Endoscopic centers and vasoactive drug therapy are not readily available in the endemic areas. A more appropriate and cost-effective approach is required. This communication is a literature overview that attempts as much as possible to provide evidence based recommendations for the most suitable approach in our patients in the areas of primary prophylaxis against a first variceal bleed, treatment of acute variceal bleeding, and secondary prophylaxis against variceal rebleeding, especially for those with schistosomal portal hypertension.

Keywords: oesophageal varices, treatment, schistosomiasis, cirrhosis

Introduction
Over the last two decades endoscopic therapy and beta blockade have emerged as the treatment of choice for oesophageal varices in the Sudan(1,2). This, in part, was due to the marked decline in the prevalence of schistosomiasis following the extensive mass treatment campaign and preventive measures implemented by the Blue Nile Health project by the WHO from 1980 to 1990(3). “Primary prophylaxis” to prevent a first variceal bleed in our patients includes beta blockade, in the
form of propranolol, and to a limited extent, endoscopic therapy in high risk varices. The main treatment for acute variceal bleeding is resuscitation, vasoactive therapy when and where available, and endoscopic sclerotherapy. The current measures for “secondary prophylaxis” to prevent rebleeding take the form of long-term endoscopic sclerotherapy and propranolol. The role of surgery has declined and currently is reserved for failure of endoscopic therapy in the majority of our central hospitals.

Following cessation of the Blue Nile Health Project, the prevalence of schistosomiasis has risen from 6% in 1989 to about 55% in 2005 in the endemic areas of Gezira and Managil, which had a population of 5.5 million in the 2005 census. The disease was found to have spread beyond these areas. During the schistosomiasis pandemic of the 1980’s, periportal fibrosis was found in about 18% of patients in the affected areas. Of these patients, 60% had portal hypertension with oesophageal varices. In 2008, in a special referral center for acute upper gastrointestinal bleeding in the capital Khartoum, it was found that bleeding oesophageal varices formed 77% of all causes. The main cause for oesophageal varices in these patients was schistosomal periportal fibrosis forming 90%. A small proportion was due to viral cirrhosis. Viral hepatitis is becoming a serious health hazard in the Sudan. The reported prevalence of positive HBsAg in some regions ranges between 5% and 7% and HCV around 2%.

Methods
An extensive search of Pub Med from 1960 to date was made. Emphasis was laid on articles of Cochrane database systematic reviews, meta-analytic studies, randomized controlled trials, prospective and retrospective open trials in that order; in addition to other related studies on the treatment of oesophageal varices in both cirrhosis, in which there is an abundance of literature, and in particular schistosomal periportal fibrosis. Selection was made of the most relevant studies addressing the natural history and treatment of oesophageal varices in both diseases. The selected articles on treatment included 2 Cochrane database studies, 7 meta-analysis, 17 randomized trials (7 on schistosomal varices), 33 prospective studies (26 on schistosomal periportal fibrosis), and other relevant studies on disease prevalence, natural history, and hemodynamic changes after surgical treatment.

Natural history
In cirrhosis, 30% of patients with asymptomatic oesophageal varices will bleed within the first year of diagnosis. The 6 weeks mortality is about 25-30%. Untreated patients surviving a bleed have a 1-2 year risk of rebleeding of about 60% and a risk of death of about 40-50%. However, in the developed world, with modern therapy, acute bleeding mortality has declined to 20% at 6 weeks. Schistosomal portal hypertension pursues a more benign course. Only 15% of patients with asymptomatic varices are expected to bleed over a span of 6 years and these harbor high risk varices. Following a primary
bleed, 50% will rebleed within one year. The majority of patients survive repeated episodes of rebleeding over many years, but without treatment 60% will rebleed of whom 20% will die within 4 years\(^\text{16}\). Longitudinal field studies in Sudan and Brazil have shown that the mortality from variceal bleeding in schistosomiasis is about 11/100/year\(^\text{17}\) and 5/100/year\(^\text{18}\) respectively.

Primary prophylaxis against a first variceal bleed
In cirrhosis, the use of beta blockade has failed to prevent development of varices\(^\text{19}\). In schistosomiasis, it has been shown that the antischistosomal drug praziquantel given to patients living in the endemic areas prevented development of periportal fibrosis and hence varices\(^\text{20}\).

In cirrhosis, once oesophageal varices develop their size progresses at the rate of 5-12% per year\(^\text{19}\) or 12% at one year and 31% at 3 years\(^\text{21}\). Merkel et al found that patients with small varices treated with nadolol had significantly lower progression to large varices (11% at 3 years) than patients randomized to receive placebo (37% at 3 years)\(^\text{22}\).

In schistosomiasis, it was shown that praziquantel can reverse or reduce sonographically proven periportal fibrosis in a significant number of patients\(^\text{20,23,24}\). The effect is apparent in the second year after treatment. However, Ruiz-Guevara et al from Brazil have shown that in advanced periportal fibrosis the effect of the drug is contradictory\(^\text{25}\). In addition, Berhe et al’s study from Ethiopia\(^\text{24}\) have shown that the drug does reduce fibrosis in advanced cases. A recent study by Rahoud et al have suggested that regression, progression and stabilization of PPF after praziquantel therapy is controlled by gender, age, grade of fibrosis, and possibly inherited factors\(^\text{26}\). More randomized studies in this field are required to elucidate the mechanism and validate the efficacy of praziquantel in reducing or reversing periportal fibrosis, and the factors that influence its action. For the moment, there is adequate evidence to suggest that its use is of definite benefit in a significant proportion of patients with schistosomal periportal fibrosis.

Beta blockade in the form of propranolol was shown to be effective in preventing a first variceal bleed in cirrhotic patients with low risk asymptomatic varices\(^\text{27,28}\). In schistosomiasis, as the probability of bleeding in low risk varices is extremely low\(^\text{15}\), praziquantel should be used as it may reverse or reduce periportal fibrosis in a substantial portion of patients. In addition (to its effect on periportal fibrosis - delete), a field study has shown that it reduces the prevalence of varices\(^\text{29}\). Two yearly endoscopic monitoring should be considered for patients with low risk schistosomal varices.

In cirrhotic patients, with high risk varices the choice is between endoscopic band ligation which has been shown to reduce the risk of a first bleed, bleeding mortality and overall mortality\(^\text{30}\), or beta blockade. The latter is more cost-effective\(^\text{31}\). In schistosomiasis beta blockade and praziquantel would form a less expensive choice than endoscopic therapy. High risk factors in cirrhosis include large varices (>5mm), at least one red color sign, and severe liver disease\(^\text{32}\). In schistosomal varices additional factors include grade 2 and 3 periportal fibrosis, thrombocytopenia, and a splenic longitudinal diameter more than 11 cm\(^\text{15,33,34}\).

Endoscopic sclerotherapy for primary prophylaxis did not reduce the risk of a first variceal bleed or improve survival in cirrhotic subjects\(^\text{35,36,37,38}\). It gave way to endoscopic band ligation as a better alternative with less adverse effects\(^\text{39}\). The use of endoscopic therapy in primary prophylaxis has not been studied in patients with schistosomal varices.

Acute variceal bleeding
In addition to resuscitative and the general recognized measures, patients with acute
variceal bleeding should be offered immediate vasoactive therapy to lower portal pressure and arrest bleeding. Vasoactive therapy should be given before endoscopic therapy and should be maintained for 3-5 days afterwards\(^{40}\). Terlipressin (triglycyl lysine vasopressin; glypressin), is the best option. In a systematic review by Ioannou et al\(^{41}\) it was shown to be the only drug that reduces the mortality of an acute variceal bleed. Once the patient is stabilized, endoscopic therapy should be instituted.

A Cochrane database systematic review by D’Amico et al\(^{42}\) which included 17 clinical trials, involving 1,817 patient, has shown that there is no convincing evidence to support the use of emergency sclerotherapy for variceal bleeding as the first, single treatment when compared with vasoactive drugs. In addition, it demonstrated that vasoactive drugs may be safe and effective whenever endoscopic therapy is not promptly available and seem to be associated with less adverse events than emergency sclerotherapy. Furthermore, the study has shown that combined vasoactive drugs and endoscopic therapy is superior to either intervention alone. This treatment successfully arrests variceal bleeding in over 90% of patients.

In the choice of endoscopic therapy, meta-analysis have shown that endoscopic band ligation is superior to endoscopic sclerotherapy as it was associated with lower rates of rebleeding, lower rates of complications, fewer endoscopic sessions in a shorter period of time, and a lower mortality\(^{39}\). However, in situations like ours sclerotherapy in the initial acute setup is the cheaper modality.

Failure to arrest bleeding by the above measures can be dealt with initially by balloon tamponade followed by repeat endoscopic therapy. Failure leaves no option, but to proceed to either emergency surgery, or to Transjugular Intrahepatic Portal Systemic Shunt (TIPSS). Transjugular Intrahepatic Portal Systemic is not available in underdeveloped settings. Emergency surgery takes the form of devascularisation without stapled transection in schistosomal patients, which is more suited to our underdeveloped settings\(^{43,44}\). In cirrhosis, the distal splenorenal shunt is advocated\(^{45}\). Emergency surgery carries a high mortality. In advanced settings TIPSS, which is a total shunt, is very effective in arresting bleeding in cirrhotic patients and forms an excellent bridge to liver transplantation\(^{46}\).

Secondary prophylaxis: prevention of rebleeding

Following successful treatment of an acute variceal bleed, all patients should be offered secondary prophylactic treatment to prevent rebleeding. The options include pharmacologic therapy, endoscopic therapy, and surgery.

Pharmacologic therapy

Propranolol reduced the rebleeding rate by 40%, and improved survival by 20% in cirrhotics\(^{47}\). In patients with schistosomal portal hypertension propranolol significantly reduced the rebleeding rate, and improved survival\(^{48}\). Propranolol reduces variceal pressure and wall tension\(^{49}\). However, in cirrhotic patients, it reduces the portal pressure by only 20%, or <12mmHg, and this is achieved in only 10-30% and 10-15% respectively\(^{50}\). Combination drug therapy in the form of the non-selective beta blocker nadolol, and isosorbide-5-mononitrate has emerged as a superior treatment compared to propranolol alone in secondary prophylaxis against rebleeding\(^{51}\). Isosorbide-5-mononitrate reduces further the portal pressure in cirrhotic patients by reducing the intrahepatic resistance\(^{52}\). The combined effect of both drugs was shown to enhance portal pressure reduction and thus is more effective in preventing rebleeding\(^{52,53}\). Combination drug therapy has not been studied in patients with schistosomal varices.
Endoscopic therapy
Long term endoscopic sclerotherapy as a single modality of treatment is falling out of favor. Krige et al[54] in a long-term study of 287 patients with cirrhosis treated by endoscopic sclerotherapy, in the period 1982 to 2001, had shown high rates of rebleeding at 36.2%, high rates of recurrence of varices after eradication at 53% with a rebleeding rate of over 50%. There was no survival advantage for sclerotherapy in the long term. Madonia et al[55] in a prospective cohort study in 2000 found a 41% rate of variceal recurrence after obliteration in 139 cirrhotic patients within 1 year with 33% mortality. Their patients required a mean of 10 endoscopic sessions and 6 hospital admissions with an estimated cost of US dollars 7,154 per patient during the first two years of therapy.

Studies of endoscopic sclerotherapy for secondary prophylaxis in patients with schistosomal varices show the same high rates of variceal rebleeding and, in some, a significant mortality[3,56,57,58,59,60,61]. Follow-up in these studies ranged from 2 to 5 years (Table 1).

<table>
<thead>
<tr>
<th>Author, year [reference]</th>
<th>Follow-up</th>
<th>Rebleeding</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bessa, 1985[56], 20 patients</td>
<td>Mean 18.4 months Study period 31 months</td>
<td>43.3%</td>
<td>25%</td>
</tr>
<tr>
<td>El Zayadi,1988[57], (*RCT): SCL versus Control), 118 patients</td>
<td>22 months</td>
<td>36% SCL group</td>
<td>14.3%, SCL group</td>
</tr>
<tr>
<td>Cordiero,1992[58], 50 patients</td>
<td>Mean 2 years Study period 5 years</td>
<td>28.1%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Al Karawi, 1996[59], (SCL in Schisto and others)</td>
<td>Mean 40 months Study period 5 years</td>
<td>Schisto 42% Early: 20% Late: 22%</td>
<td>Schisto 24%</td>
</tr>
<tr>
<td>El Sayed, 1996[60], (RCT: SCL versus SCL + Propranolol), 200 patients</td>
<td>2 years</td>
<td>38.6% SCL group versus 14.6% combination group</td>
<td>12% in both groups</td>
</tr>
<tr>
<td>Dowidar, 2005[61], (RCT: SCL versus SCL + Propranolol), 40 patients</td>
<td>2 years</td>
<td>25% SCL group versus 13.3% combination group</td>
<td>(Full Article could not be retrieved)</td>
</tr>
<tr>
<td>Mudawi, 2007[62], 118 patients (28% of patients lost for follow up)</td>
<td>Mean 12 months Study period 2 years</td>
<td>32%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

*RCT: Randomized controlled trial. SCL = Sclerotherapy. Schisto = schistosomiasis.

Gasim et al from Sudan[2], reported a clinical trial on long term endoscopic sclerotherapy in 1,070 patients treated over a span of 10 years. However, they lost 56.8% of their patients for follow-up. Thus it would be difficult to draw definite conclusions on the long term outcome of endoscopic sclerotherapy for secondary prophylaxis in schistosomal patients. Because of its higher incidence of side effects and rebleeding, sclerotherapy has been replaced by endoscopic band ligation[62]. The meta-analysis conducted by Laine et al[39] in 1995 has shown that long term endoscopic band ligation is superior to sclerotherapy in secondary prophylaxis against rebleeding in cirrhotic subjects. The evidence for this in patients with schistosomal periportal fibrosis has not as yet been satisfactorily answered.
Only one randomized trial from Brazil compared the two modalities\(^{(63)}\). It showed no difference between the two in outcomes.

**Pharmacologic therapy versus, or with endoscopic therapy**

On evaluating the evidence on drug therapy versus endoscopic therapy some important outcomes were obtained. A meta-analysis by D’Amico et al in 1995 has shown that endoscopic sclerotherapy is superior to propranolol in preventing rebleeding in cirrhotic portal hypertension\(^{(64)}\). More recent randomized trials have shown that combination beta blockade plus nitrites was superior to beta blockers alone\(^{(53)}\) and to endoscopic sclerotherapy\(^{(65)}\). The same does not hold true for endoscopic band ligation. A meta-analysis by Ding et al\(^{(66)}\) in 2009, evaluating randomized trials from 1980 to 2007, have shown that the combination beta blockers + isosorbide mononitrate is as effective as endoscopic band ligation in the prevention of variceal rebleeding. A multicenter randomized trial reported in 2009 demonstrated that adding endoscopic band ligation to pharmacologic combination therapy did not alter outcomes of recurrent bleeding, the need for rescue surgery, or mortality, and that it was associated with more adverse events\(^{(67)}\). Thus the evidence suggests that either can be used alone in cirrhotic patients.

The use of the combination drug therapy nadolol + isosorbide-5-mononitrate against, or with, endoscopic therapy was not studied in patients with schistosomal varices. However, single drug therapy (propranolol) with endoscopic sclerotherapy was tested against endoscopic sclerotherapy therapy alone in two randomized trials from Egypt. It showed conflicting results. Elsayed et al in 1996 have shown that endoscopic sclerotherapy plus propranolol is more effective than sclerotherapy alone in preventing rebleeding\(^{(68)}\). However, Dowidar et al in 2005 showed no difference between the two treatment modalities in either rebleeding or survival\(^{(61)}\). A recent randomized trial in non-cirrhotic portal hypertension, published in 2010 by Sarin and his co-workers\(^{(68)}\), have shown that the beta blocker propranolol is not different from endoscopic band ligation in secondary prophylaxis after a first variceal bleed.

These conflicting results have been reasonably settled by a recent meta-analysis published in December 2010 addressing the use of endoscopic therapy plus beta blockers without the addition of nitrites\(^{(69)}\). It included trials on patients with alcoholic cirrhosis, viral cirrhosis, and schistosomal periportal fibrosis from 1950 to 2012 [Medline]. The analysis showed evidence that endoscopic therapy plus beta blockers used from the onset is superior to endoscopic therapy alone in terms of recurrent bleeding at 6, 12, and 24 months, and lesser mortality at 24 months. Furthermore, the analysis showed that endoscopic band ligation beta blocker combination was superior to that of endoscopic sclerotherapy beta blocker (Table 2).

### Table 2: Outcome of sclerotherapy and band ligation each alone and in combination with beta blockade in secondary prophylaxis: meta-analysis (1950-2009) including patients with alcoholic and viral cirrhosis, and schistosomal periportal fibrosis, by Funakoshi et al, 2010\(^{(69)}\).

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Rebleeding</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerotherapy</td>
<td>39.2%</td>
<td>17.2%</td>
</tr>
<tr>
<td>Sclerotherapy and beta blockade</td>
<td>25.4%</td>
<td>13.7%</td>
</tr>
<tr>
<td>Band ligation</td>
<td>39.5%</td>
<td>21.8%</td>
</tr>
<tr>
<td>Band ligation plus beta blockade</td>
<td>17.2%</td>
<td>13.3%</td>
</tr>
</tbody>
</table>

However, it must be noted that pharmacologic therapy and endoscopic therapy, alone or in combination, are associated with high rates of rebleeding, adverse effects, and a variable mortality in cirrhotic subjects\(^{(39,54,64,65)}\), and in those with schistosomal periportal fibrosis\(^{(56,57,58,59,60,61)}\).
The role of surgery in prevention of variceal rebleeding

In cirrhosis, dissatisfaction with total shunts in the west led to the development of the distal splenorenal shunt (DSRS) by Warren and his colleagues\(^{(70)}\). Encephalopathy was the main problem after the operation and can reach up to more than 20%\(^{(71)}\). However, the technical improvements in the operation by splenopancreatic disconnection, and division of the greater and lesser omenta have significantly reduced the incidence of encephalopathy after the operation\(^{(72,73)}\). Orozco et al\(^{(74)}\) in 21 years of follow-up after the operation in cirrhotic patients had a 5% operative mortality, 5% rate of encephalopathy, and 6% rebleeding rate. However, what is remarkable is that their patients attained 65% survival rate at 15 years, which is similar to survival after liver transplantation in end stage liver disease\(^{(75)}\). Furthermore, it has been shown that DSRS is not associated with increased morbidity or mortality in future liver transplantation and as such the operation is the preferred method of treatment in well compensated cirrhotic patients\(^{(76)}\). The extensive devascularisation and transection procedure of Sugiura from Japan\(^{(77)}\) had excellent results in terms of rebleeding and mortality in good risk patients, however, it precludes future liver transplantation due to extensive adhesions. The only option for poor risk Child’s C cirrhotic patients is non surgical therapy for bleeding till liver transplantation, a modality which is beyond the capabilities of under developed settings.

In schistosomal portal hypertension, the choice is between DSRS and the simpler operation of splenectomy and oesophagogastroscopic devascularisation (SOGD)\(^{(78)}\). DSRS produced good results in patients with schistosomal portal hypertension\(^{(79,80)}\). Although the operation carries a very low rate of variceal rebleeding, yet it is associated with a significant degree of encephalopathy when compared to splenectomy and oesophagogastroduodenal devascularisation (SOGD)\(^{(81)}\). Hassab had a 7% rate of recurrent bleeding at 10 years after SOGD\(^{(82)}\). However, other clinical trials have shown high rates of variceal rebleeding after the operation averaging 23.5%\(^{(80,81,83,84)}\). Despite this it has been shown that the operation is associated with very good long-term survival rates\(^{(81,82,86,87)}\). Raia and his colleagues\(^{(88)}\) from Brazil, in a randomized trial compared SOGD to DSRS and to the total proximal splenorenal shunt. They have shown that SOGD was associated with zero encephalopathy and carried the best survival rates at a mean follow-up of 7 years. The longest follow-up period of 25 years after the operation was attained by Kelner et al’s study\(^{(86)}\). They had a late mortality of 8.38%. Table 3 shows the outcome of surgery in bleeding schistosomal varices. The benefits of SOGD can be attributed to the hemodynamic changes after the operation. Variceal pressure is significantly reduced\(^{(89)}\), and the hyperdynamic state observed preoperatively is corrected\(^{(90)}\). In addition, the portal flow is reduced by 27% in the immediate postoperative period, and by 37% within the first to second year of follow-up; remaining stable after that, without deterioration in hepatic function\(^{(91)}\).

The high rate of recurrent variceal bleeding after SOGD have been addressed by salvage\(^{(81,84,85)}\), and prophylactic sclerotherapy\(^{(87,92,93)}\) (Table 4). Superior results were obtained in these studies in terms of recurrent bleeding and survival when compared to SOGD alone. Sakai et al have shown that previous surgical treatment for portal hypertension in patients with mansonic schistosomiasis greatly benefits treatment of rebleeding oesophageal varices by endoscopic sclerotherapy\(^{(94)}\). They were able to control variceal rebleeding in 97.3% of their patients. This can be attributed to the lowered portal...
pressure and flow after the operation\(^{(88,91)}\). On the other hand, endoscopic band ligation was also shown to be of great value when combined with SOGD. Oi et al\(^{(95)}\) randomized 135 cirrhotic patients to receive endoscopic band ligation alone, SOGD alone, or a combination SOGD and endoscopic band ligation. They found the rate of recurrence of varices to be 83\%, 30\%, and 8\% respectively over a 3 years follow-up period. The cost-effectiveness of SOGD plus endoscopic therapy can only be maximized if we can select patients who are at risk of developing recurrent varices and rebleeding. Ferraz et al have shown that patients with grade 1 periportal fibrosis are significantly less prone to develop variceal rebleeding than those with grades 2 and 3 after SOGD\(^{(91,96)}\).

<table>
<thead>
<tr>
<th>Modality of surgery</th>
<th>Follow-up</th>
<th>Early mortality</th>
<th>Variceal Rebleeding</th>
<th>Encephalopathy</th>
<th>Late mortality or survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOGD Hassab(^{(82)})</td>
<td>10 years</td>
<td>7%</td>
<td>None</td>
<td>5% overall mortality</td>
<td></td>
</tr>
<tr>
<td>Elmasri and Hassan(^{(83)}) 1982: 113 patients</td>
<td>8 years</td>
<td>4.9%</td>
<td>20%</td>
<td>None</td>
<td>23.4%. (10.1% from variceal rebleeding 9.7% from hepatic failure)</td>
</tr>
<tr>
<td>SOGD Kelner(^{(86)}) 1992: 358 patients</td>
<td>25 years</td>
<td>3.07%</td>
<td>11.58%</td>
<td>None</td>
<td>8.38%</td>
</tr>
<tr>
<td>SOGD Conceicao(^{(87)}) 2002:102 patients</td>
<td>16 years</td>
<td>9.9%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other operations, and, compared to SGOD

<table>
<thead>
<tr>
<th>DSRS. Bessar(^{(79)}) 1987: 20 patients</th>
<th>16 months</th>
<th>10%</th>
<th>None</th>
<th>None</th>
<th>Survival 85%</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSRS. Ezzat(^{(80)}) 1998: 60 patients</td>
<td>Median 37 months</td>
<td>1.7%</td>
<td>6.7%</td>
<td>5.1%</td>
<td>Survival at 5 years 88%</td>
</tr>
<tr>
<td>DSRS SOGD (RCT) Ezzat(^{(81)}) 1990: 219 patients (41% SPPF, 59% Mixed SPPF / Cirrhosis)</td>
<td>Mean 82 Mean 78 months</td>
<td>3.3%</td>
<td>3.1%</td>
<td>5.7%</td>
<td>18.7%</td>
</tr>
</tbody>
</table>

| PSRS DSRS SOGD (RCT) Raia\(^{(88)}\) 1994: 90 patients | Mean 85.7 months | 24.1\% no difference between the three groups | 39.3\% | 42.9\% | 14.8\% | 7.1\% Overall mortality |

SOGD= Splenectomy and oesophagogastroduodenal devascularisation. DSRS= Distal splenorenal shunt. PSRS= Proximal splenorenal shunt (total shunt). SPPF=Schistosomal periportal fibrosis. (RCT)= Randomized Controlled Trial.

\(\text{\textcopyright this is the highest mortality encountered. During this study, from Sudan, vasoactive drugs and sclerotherapy were not available. The high death rate from hepatic failure indicates poor liver status in these patients.}\)
Table 4: impact of endoscopic therapy after SOGD in schistosomal varices.

<table>
<thead>
<tr>
<th>Modality of endoscopic therapy</th>
<th>Follow-up period</th>
<th>Early mortality</th>
<th>Variceal Rebleeding</th>
<th>Encephalopathy</th>
<th>Late mortality or survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLAVAGE SCL SOGD</td>
<td>12 years (1980-1992)</td>
<td>4.2% (none from variceal rebleeding)</td>
<td>23.6% (Before SCL)</td>
<td>zero</td>
<td>4.4% Late mortality (2.2% due to rebleeding and hepatic failure)</td>
</tr>
<tr>
<td>Elimam (84), 2012: 190 patients (trial 1980-1990)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SALVAGE SCL SOGD</td>
<td>6 years: 111 SOGD followed for 3 years</td>
<td>2.2% (266 splenectomy none from bleeding varices)</td>
<td>12% Before SCL</td>
<td>none</td>
<td>No late mortality in 111 patients at 3 years</td>
</tr>
<tr>
<td>PROPHYLACTIC SCL</td>
<td>Mean 30 months</td>
<td>14.5% after SCL</td>
<td>Zero</td>
<td>5.4% global mortality</td>
<td></td>
</tr>
<tr>
<td>Ferraz (92), 2001: 111 patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROPHYLACTIC SCL or EBL</td>
<td>Mean 116.4 months (1990-2009)</td>
<td>2%</td>
<td>14.5% after endoscopic therapy</td>
<td>zero</td>
<td>Less than 5 years: 1.3% (unrelated 1.3%) 5-15 years: no mortality</td>
</tr>
<tr>
<td>Makdissi (93), 2010, 153 patients 97 patients followed for 5 to 15 years</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

SOGD = Splenectomy & oesophago gastric devascularisation. SCL = Endoscopic Sclerotherapy. EBL = Endoscopic band ligation. (RCT) = Randomized controlled trial.

However, a more accurate and reliable method to evaluate the risk of rebleeding have been developed by Ferreira and his colleagues using Doppler flow studies (97). They studied 146 patients before and after SOGD at 1, 2, 5, and 10 years with Doppler portal flow studies. The method successfully predicted variceal progression and rebleeding at the first postoperative year. The critical threshold flow was found to be 15.5 cm/sec. Patients with portal flow at this value or above should be included in the endoscopic program for eradication of recurrent varices.

One of the major problems of SOGD in our patients is post splenectomy sepsis and malaria (83, 84, 85). As a routine, polyvalent pneumococcal vaccine and vaccination against haemophilus influenzae and neiseria meningitides should be given preoperatively (83). In addition, patients should receive antimalarial prophylaxis for life in regions endemic for the disease like Sudan.

**Recommendations**

**Primary prophylaxis:**

**Schistosomiasis**

- No varices:
  - Praziquantel.
- Low risk varices:
  - Praziquantel.
  - Endoscopic and ultrasound follow up at 2 yearly intervals.
- High risk varices:
  - Propranolol + Praziquantel.

**Cirrhosis**

**Low risk varices:**

- Propranolol.
- Endoscopic follow up at yearly intervals.

**High risk varices:**

- Combination beta blockade and nitrites or
- Endoscopic band ligation.

**Acute variceal bleeding**

- Resuscitation.
- Terlipressin (glypressin) should be promptly started before during and after endoscopy and endoscopic therapy for 3 to 5 days.
- Endoscopic sclerotherapy is cheaper than band ligation.
- Balloon tamponade for failures followed by endoscopic sclerotherapy.
• Oesophagogastric devascularisation for failures of the above therapy.
• There is an imperative need to improve blood bank services, and avail the drug terlipressin, and the modified Blakemore Sengstaken tube in the small hospitals and health centers in the endemic areas to allow transport of patients to endoscopic therapy centers.

Secondary prophylaxis:

Schistosomiasis

• Good risk patients: Splenectomy and oesophagogastric devascularisation followed by selective endoscopic band ligation based on portal blood flow parameters during follow-up in the first year.
• Preoperative: Vaccination against pneumococci, neisseria meningitides, and haemophilus influenzae. Antimalarial prophylaxis for life.
• Failures of surgery: beta blocker plus endoscopic band ligation.
• Bad risk patients: long term beta blocker from onset plus endoscopic band ligation.

Cirrhosis

Good risk patients:
• The distal splenorenal shunt, or
• Long term endoscopic band ligation + propranolol (in case of lack of expertise).
Bad risk patients:
• combination drug therapy in the form of beta blockers + isosorbide-5-mononitrate, or
• Endoscopic band ligation and beta blocker from onset.
• Liver transplantation in end stage disease.

In conclusion, the choice of the best approach to the treatment of oesophageal varices in our patients depends upon the availability of the therapeutic modalities, their cost, and the associated morbidity and mortality. Treatment must be tailored to suite the prevalent circumstances. The drug praziquantel should be given its due consideration in patients with schistosomal periportal fibrosis with or without varices. In the area of primary prophylaxis for high risk varices in schistosomiasis the combination of praziquantel and propranolol is probably as good as, and a cheaper alternative, to endoscopic band ligation. In acute variceal bleeding the availability of blood bank services, vasoactive drugs, and balloon tamponade at the local level to allow transfer to endoscopy centers are of crucial importance. In secondary prophylaxis against variceal rebleeding in schistosomiasis the best option is surgery in the form of SOGD followed by prophylactic selective endoscopic therapy based on portal blood flow parameters. It provides a better quality of life and is more cost effective in the long run. Combined endoscopic therapy + beta blockers should be reserved for failures of surgery and for poor risk patients. We strongly recommend multicenter randomized trials in our patients to test and compare the available treatment modalities.

References


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