Asymptomatic esophageal varices should be endoscopically treated

Nib Soehendra MD

Endoscopic treatment has generally been accepted in the management of bleeding esophageal varices. Both the control of acute variceal bleeding and elective variceal eradication to prevent recurrent bleeding can be achieved via endoscopic methods. In contrast to acute and elective treatment, the role of endoscopic therapy in asymptomatic patients who have never had variceal bleeding remains controversial because of the rather disappointing results obtained from prophylactic sclerotherapy. Most published randomized controlled trials showed that prophylactic sclerotherapy had no effect on survival. In some studies, neither survival rate nor bleeding risk was improved. In this article, the author champions the view that asymptomatic esophageal varices should be endoscopically treated.

Key Words: Endoscopic treatment, Esophageal varices

Les varices œsophagiennes asymptomatiques doivent être traitées par voie endoscopique

RÉSUMÉ : Le traitement endoscopique est généralement accepté dans les cas de varices œsophagiennes hémorragiques. Il est possible d’obtenir par la méthode endoscopique une maîtrise de l’hémorragie variqueuse aiguë et une éradication élective des varices pour prévenir les récidives de saignement. Contrairement aux traitements urgents ou électifs, le rôle du traitement endoscopique chez les patients asymptomatiques qui n’ont jamais présenté d’hémorragies variqueuses demeure encore controversé à cause des résultats relativement décevants obtenus avec la sclérothérapie prophylactique. La plupart des essais cliniques randomisés et contrôlés publiés ont démontré que la sclérothérapie prophylactique n’exerçait aucun effet sur la survie. Lors de certaines études, ni le taux de survie, ni le risque hémorragique n’ont été amélioré. Dans le présent article, l’auteur défend l’opinion selon laquelle il faut traiter par voie endoscopique les varices œsophagiennes asymptomatiques.

Endoscopic treatment has generally been accepted in the management of bleeding esophageal varices. Both the control of acute variceal bleeding and elective variceal eradication to prevent recurrent bleeding can be achieved via endoscopic methods. Endoscopic obliteration therapy using the tissue glue Histoacryl (B Braun, Melsungen, Germany) is the best method for controlling acute variceal bleeding and for eradicating large fundic varices. For the initial eradication of esophageal varices, endoscopic band ligation appears to be superior to conventional sclerotherapy because of its lower procedural morbidity. But varices tend to recur more frequently after band ligation than after sclero-

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TABLE 1
Prospective controlled trials: Rates of variceal bleeding and bleeding-related mortality

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Follow-up (months)</th>
<th>First variceal bleeds (%)</th>
<th>Deaths from variceal bleed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paquet (12)</td>
<td>36</td>
<td>6</td>
<td>0</td>
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<tr>
<td>Witzel et al (13)</td>
<td>25</td>
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<tr>
<td>Santangelo et al (14)</td>
<td>13</td>
<td>30</td>
<td>9</td>
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<td>Piai et al (15)</td>
<td>18</td>
<td>42</td>
<td>7</td>
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<td>Sauerbruch et al (16)</td>
<td>22</td>
<td>28</td>
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<td>Russo et al (17)</td>
<td>17</td>
<td>0</td>
<td>15</td>
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<td>Pötzi et al (18)</td>
<td>10-36</td>
<td>29</td>
<td>34</td>
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<td>Kobe et al (19)</td>
<td>45</td>
<td>30</td>
<td>73</td>
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<td>VA (20)</td>
<td>23</td>
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<td>16</td>
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<td>Triger et al (21)</td>
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<td>De Francis et al (22)</td>
<td>24</td>
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<td>35</td>
</tr>
<tr>
<td>Koch et al (23)</td>
<td>55</td>
<td>7</td>
<td>44</td>
</tr>
</tbody>
</table>

*The bleeding-related mortality rate was higher in the treated group than the controls. C: Control; ES: Endoscopic sclerotherapy; VA: Veterans Affairs Cooperative Variceal Sclerotherapy Group

Cost of Variceal Bleeding Prophylaxis

In a recent study by Teran et al (6), a Markov model was used to estimate the cost-effectiveness of variceal bleeding prophylaxis with propranolol, sclerotherapy and shunt surgery. The analysis was based on data from the literature published mostly until the early 1990s. The incidence of variceal bleeding, mortality due to variceal bleeding, total mortality, life expectancy and quality-adjusted life expectancy were analyzed, and the three predictive bleeding risk factors – Child’s class, size of varices and presence of red signs – were considered.

The study found that propranolol is the only cost-effective form of prophylactic therapy for preventing initial variceal bleeding in cirrhotic patients, except for patients with Child’s class A with small varices. Prophylactic sclerotherapy caused significantly higher cumulative costs than propranolol due to the higher incidence of bleeding episodes (between US$6,000 and US$11,000 for five years, depending on the patient’s bleeding risk). Based on data from three meta-analyses, the relative reduction of bleeding risk with sclerotherapy was 30% (7,9); it was 50% with propranolol (7,8,10).

Weighing the benefit of prophylactic sclerotherapy and the risk of bleeding if varices are untreated, one should also consider the risk of sclerotherapy. Sclerotherapy is a user-dependent endoscopic method that may carry considerable procedural complications including bleeding (mainly from sclerotherapy induced ulcers), esophageal stricture, mediastinitis and perforation. According to a meta-analysis of seven studies of elective sclerotherapy, complications of sclerotherapy occurred in 35% of patients, with 12% of patients having esophageal strictures, 7% pneumonia, 13% bleeding and 4% perforation (11). The mean procedure-related mortality reported in the literature is approximately 1%.

SCLEROThERAPY

The results of sclerotherapy regarding long term eradication and prevention of bleeding vary among studies. The incidence of first variceal bleeding following prophylactic sclerotherapy reported in 12 controlled studies ranged from 0% to 39% (mean follow-up times from 13 to 61 months). The rates of variceal bleeding-related deaths ranged from 0% to 18% (12-23). In three studies (14,20,21), the bleeding-related mortality rate was even higher in the treated group than the control (Table 1). It is likely that sclerotherapy-induced ulcers were partly responsible for the higher bleeding rates.

There is no doubt that physician expertise influences the results of sclerotherapy. In our previous controlled trial on prophylactic sclerotherapy comprising two periods (23), the complication rate in the first period, between 1980 and 1982, was 20% (bleeding from sclerotherapy-induced ulcers, stricture and perforation); in the second period, between 1985 and 1989, it was only 2.5% (one stricture in 40 patients).

Another possible influencing factor is the sclerosant used. In a meta-analysis study, Fardy and Laupacis (24) found heterogeneity when the trials were pooled in subgroups based on the sclerosant used. Trials using polidocanol (Kreussler; Wiesbaden, Germany) showed a highly significant benefit in prophylactic sclerotherapy in terms of overall mortality compared with results from trials using sodium tetradecyl. It remains unclear whether injection technique and treatment protocol may also influence the results of sclerotherapy.

ENDOSCOPIC VARICEAL LIGATION

Since the beginning of the 1990s, endoscopic therapy of esophageal varices has significantly evolved. Today, endoscopic variceal ligation (EVL) has replaced sclerotherapy as the initial method of choice in the elective treatment of esophageal
varices. Sclerotherapy remains as an adjuvant measure for achieving long term eradication in cases where residual vari-
ces are refractory to EVL. Both the complication rate and
the rebleeding rate have been reported to be lower for EVL
than for sclerotherapy in several clinical trials. In those
studies, the rebleeding rates for EVL ranged from 20% to
36%, whereas rates for sclerotherapy were between 27% and
53% (25). Owing to the lower rebleeding rate, prophylactic EVL
may be beneficial in patients with asymptomatic esophageal
varices.

In three recent controlled studies, the results favoured en-
doscopic prophylaxis using EVL. Sarin et al (26) studied the
efficacy and safety of EVL for primary prophylaxis of varical
bleeding in patients with high risk varices. Esophageal vari-
ces were obliterated by EVL in 3.2±1.2 sessions within
4.9±2.2 weeks. Three patients in the EVL group (8.6%) and
13 in the control group (39.4%) bled during a mean follow-
up of 14.1±5.0 months (P<0.01). The cumulative probabil-
ity of the patients remaining free from bleeding was higher in
the EVL group than in controls (P<0.01). Bleeding-related
mortality was significantly lower in the EVL group versus the
control group (2.9% versus 15.2%). The overall mortality rate
was 11.4% in the EVL group and 24.2% in the control
group. The difference was, however, not statistically signifi-
cant.

In another controlled study, Lo and Lai (27) reported
similar results in terms of varical bleeding (7.7% versus
22%) and mortality rate (11% versus 24%). No significant
complications occurred in the EVL group except for two
cases of EVL-induced ulcer bleeding.

Lay et al (28) randomly assigned 126 cirrhotic patients
with high risk esophageal varices to either prophylactic liga-
tion using the Stiegmann-Goff single ligator or no treat-
ment. Their results also showed that prophylactic ligation
significantly reduced the rates of variceal bleeding (19% ver-
sus 60%) and overall mortality (28% versus 58%). Ten per
cent of patients in the EVL group died of hepatic failure;
only 2% died of esophageal hemorrhage. In this study,
Child’s class A patients benefitted more than those with ad-
vanced disease from the prophylactic variceal banding.

Prophylactic EVL is justified because of its low complica-
tion rate and capability of reducing the risk of variceal bleed-
ing. With the multiple band ligation devices, endoscopic
variceal banding has become easier and safer. More studies
are needed to reproduce the encouraging results of the three
controlled trials.

The efficacy of prophylactic EVL needs to be weighed
against the risk of first variceal bleeding. We now know more
about the risk factors for bleeding. Patients in Child’s stage C
with large varices and red signs on the varices are more likely
to bleed. Whether the incidence of first variceal bleeding
can be significantly reduced by ligation therapy, particularly
in patients at high bleeding risk, is unknown. However, pa-
tients with decompensated liver disease are more likely to
die from the first bleeding episode. For this subgroup of pa-
tients, any prophylactic treatment modality must therefore
provide safety in terms of treatment-induced bleeding.

There have been some reservations about the use of band
ligation alone in Child’s stage C patients with coagulopathy,
due to relatively high risk of bleeding from ligation-induced
mucosal necrosis (29). The combined use of obliteration
therapy using tissue glue (30) and EVL in Child’s stage C pa-
tients with large varices should therefore be discussed.

Comparative studies with beta-blockers are also war-
ranted in order to demonstrate whether band ligation can
achieve a reduction in bleeding episodes and mortality.

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Asymptomatic esophageal varices and endoscopic treatment

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