When and How to Scope in Portal Hypertension

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When and How to Scope in Portal Hypertension

• Why to scope?

• When to scope?

• How to scope?
Incidence of Variceal Bleeding in The Placebo-treated Control Groups of RCTs of Primary Prophylaxis With β-blockers

Average incidence of bleeding: 24%

Small studies (< 50 patients)
Large studies (>50 patients)
Risk of Bleeding Increases with Variceal Size, RWM and Child Class

(Data from NIEC N Engl J Med 1988;319:983-989)

Bosch J, J Hepatol 2006;45:174-177

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30 Days or 6 Weeks Mortality in Bleeding Cirrhotic Patients

D’Amico G and de Franchis R Hepatology 2003;38:599-612

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Why to scope

- Due to the frequency and severity of variceal bleeding, diagnosing portal hypertension is extremely important.
- The best tool to measure portal hypertension is the Hepatic Vein Pressure Gradient (HVPG).
- However, at present, HVPG measurement cannot be done routinely.

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Why to scope

• **Upper GI endoscopy** is far more widely available than HVPG measurement and is appropriate, since the size of varices is related to the risk of bleeding.

• In addition, endoscopy allows the identification of other potentially bleeding lesions related to portal hypertension, such as gastric varices and portal hypertensive gastropathy.
When and How to Scope in Portal Hypertension

- Why to scope?
- When to scope?
- How to scope?

identification of patients with varices
Prevalence of Esophageal Varices in 3122 Cirrhotic Patients

Mean Prevalence 58.7%


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When to scope

Identification of patients with varices

- There are no satisfactory non-endoscopic indicators of the presence of varices *
- Endoscopic screening is still the best practice to detect varices *
- All cirrhotic patients should be screened for esophageal varices by endoscopy at the time of diagnosis of cirrhosis §

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§ de Franchis R J Hepatol 1996;25:390-394
* de Franchis R J Hepatol 2005;43:167-176

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When and How to Scope in Portal Hypertension

- Why to scope?
- When to scope?
- How to scope?

Monitoring the appearance and growth of varices
Development of “New” Esophageal Varices in Cirrhotic Patients

Annual incidence of varices

- Median 7.5%

Pagliaro L et al. in Portal Hypertension Blackwell 1994;

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Progression of Variceal Size From Small to Large in Patients With Liver Cirrhosis

One-year progression of varices

Median 12%

Pagliaro L. et al. in Portal Hypertension; Blackwell 1994:72-92
Merli M et al. J Hepatol 2003;38:266-272
When to scope
Timing of follow-up endoscopies

• In deciding the timing of follow-up endoscopy, we must first decide which level of risk (i.e. what proportion of patients bleeding before starting prophylactic treatment) we are willing to accept.

• If we set this level at 10%, then patients with no varices at baseline can be re-endoscoped at 3-years intervals.

de Franchis R. J Hepatol 2000;33:846-852

de Franchis 2007
When to scope
Timing of follow-up endoscopies

• For patients with small varices at baseline, the current recommendations are that follow-up endoscopy should be performed at 1-2 years intervals in compensated patients, adopting the shorter interval for patients with alcoholic cirrhosis, with more severe impairment of liver function and with endoscopic risk signs.

de Franchis R. J Hepatol 2000;33:846-852
When and How to Scope in Portal Hypertension

• Why to scope?

• When to scope?

• How to scope?
How to scope

• The systematic application of these recommendations generates a considerable burden for endoscopy units.

• In addition, the adherence of patients to screening programs may be hampered by the fact that EGD is perceived as unpleasant, may require conscious sedation, may lead to decreased work productivity, and has a small but not insignificant risk of complications.
How to scope

• The esophageal videocapsule provides a less invasive approach to visualizing the esophagus

• Advantages include:
  – elimination of the need for conscious sedation
  – minimally invasive nature of the test
  – ability to pursue normal daily activities following the procedure
  – probability of being more readily accepted by patients as compared to standard EGD
Applications of capsule technology for the study of esophageal varices

PillCam ESO capsule

- Specially designed capsule
- Size 11 x 26 mm
- 2 CMOS imagers
- 14 images per second
- Special ingestion procedure
- Battery life: 20 min. (disposable)
Given Pillcam ESO

7 frames/sec. for each camera

Dimensions:
Height: 11 mm
Width: 26 mm
Weight: 3.7 gr
Duration of capsule batteries: 20 min’
Appearance of esophageal varices on capsule endoscopy
# Pilot studies with the PillCam ESO capsule for esophageal varices

<table>
<thead>
<tr>
<th></th>
<th><strong>Eisen</strong> (International)</th>
<th><strong>Lapalus</strong> (France)</th>
<th><strong>Groce</strong> (U.S.A.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nº patients</td>
<td>32</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Varices classification</td>
<td>Japanese classification</td>
<td>Unspecified</td>
<td>Japanese classification</td>
</tr>
<tr>
<td>Overall agreement</td>
<td>96.9%</td>
<td>84.2%</td>
<td>80.9%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100.0%</td>
<td>81.25%</td>
<td>78.0%</td>
</tr>
<tr>
<td>Specificity</td>
<td>88.9%</td>
<td>100.0%</td>
<td>83.0%</td>
</tr>
<tr>
<td>PPV</td>
<td>95.8%</td>
<td>100.0%</td>
<td>78.0%</td>
</tr>
<tr>
<td>NPV</td>
<td>100.0%</td>
<td>57.1%</td>
<td>83.0%</td>
</tr>
<tr>
<td>LR +</td>
<td>9.1</td>
<td></td>
<td>4.6</td>
</tr>
<tr>
<td>LR -</td>
<td>0.0</td>
<td></td>
<td>0.26</td>
</tr>
<tr>
<td>Patients preference</td>
<td>CE &gt; EGD</td>
<td>95.3%</td>
<td>90.0%</td>
</tr>
</tbody>
</table>


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PillCam ESO for esophageal varices
Multicenter International study

• Blinded comparison of EGD and esophageal capsule endoscopy for the screening and surveillance of esophageal varices in patients with portal hypertension

• 11 Centers, in the U.S.A. (7), Europe (3), and Israel (1)

• 288 patients

• Pre-test probability of EV: 62.5%

PillCam ESO for esophageal varices
Multicenter international study
Methods: grading of varices

EGD Grading*
- **F0** = no varices
- **F1** = < 33% of radius of esophagus
- **F2** = > 33% and < 66% of radius of esophagus
- **F3** = > 66% of radius of esophagus
- +/- presence of red spots

PillCam ESO Grading
- **C0** = no varices
- **C1** = small varices (< 25% of circumference of the capsule picture frame)
- **C2** = large varices (> 25% of circumference of the capsule picture frame)
- +/- presence of red spots

*The Italian Liver Cirrhosis Project J Hepatol 1987;4:93-98

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PillCam ESO for esophageal varices
Multicenter international study
PillCam ESO grading of varices

C0

C1

C2
### PillCam ESO for esophageal varices
#### Multicenter international study

#### Patients characteristics

<table>
<thead>
<tr>
<th>Nº patients ; (Sex: M/F)</th>
<th>288; (183/105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening/ surveillance (N°)</td>
<td>195/93</td>
</tr>
<tr>
<td>Etiology of portal hypertension (%)</td>
<td></td>
</tr>
<tr>
<td>- HBV Cirrhosis</td>
<td>8.9%</td>
</tr>
<tr>
<td>- HCV Cirrhosis</td>
<td>35.0%</td>
</tr>
<tr>
<td>- Alcoholic cirrhosis</td>
<td>20.0%</td>
</tr>
<tr>
<td>- Alcohol + HBV or HCV cirrhosis</td>
<td>13.3%</td>
</tr>
<tr>
<td>- Other (Budd Chiari, PVT, etc.)</td>
<td>22.8%</td>
</tr>
<tr>
<td>Child-Pugh Class (%)</td>
<td></td>
</tr>
<tr>
<td>- A</td>
<td>68.8%</td>
</tr>
<tr>
<td>- B</td>
<td>25.4%</td>
</tr>
<tr>
<td>- C</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

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### Comparison of EGD and PillCam ESO Detection of Esophageal Varices

<table>
<thead>
<tr>
<th>Capsule Endoscopy</th>
<th>Traditional Endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>152</td>
</tr>
<tr>
<td>-</td>
<td>13</td>
</tr>
<tr>
<td><strong>165</strong></td>
<td><strong>Overall agreement 85.8%</strong></td>
</tr>
</tbody>
</table>

- **Positive likelihood ratio:** 7.0
- **Negative likelihood ratio:** 0.18
- **Overall agreement:** 85.8%
- **Kappa value:** 0.733

**Pre-test probability of EV:** 62.5%

**Post-test probability of EV:** 93.0%

<table>
<thead>
<tr>
<th>Capsule Endoscopy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>84%</td>
<td>88%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
<td></td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td></td>
<td></td>
<td></td>
<td>77%</td>
</tr>
<tr>
<td>NPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Comparison of EGD and PillCam-ESO Grading of Esophageal Varices**

<table>
<thead>
<tr>
<th>PillCam Grade</th>
<th>EGD Grade</th>
<th>F0</th>
<th>F1</th>
<th>F2/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0</td>
<td>95</td>
<td>24</td>
<td>4</td>
<td>123</td>
</tr>
<tr>
<td>C1</td>
<td>11</td>
<td>70</td>
<td>13</td>
<td>94</td>
</tr>
<tr>
<td>C2</td>
<td>2</td>
<td>7*</td>
<td>62</td>
<td>71</td>
</tr>
</tbody>
</table>

Overall agreement 79%

Kappa value = 0.675

*A second EGD performed after 5 weeks showed large varices*
Comparison of EGD and PillCam ESO
Distinguishing medium-large from small-no varices

<table>
<thead>
<tr>
<th></th>
<th>EGD</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0-F1</td>
<td>200</td>
</tr>
<tr>
<td>F2-F3</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>217</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>PillCam</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0-C1</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>217</td>
</tr>
</tbody>
</table>

Overall agreement 91%
Kappa value = 0.766

Pre-test probability of large EV: 27.4%
Post-test probability of large EV: 85.0%

Sensitivity: 78%   PPV 87%   Likelihood ratio + 19.5
Specificity: 96%   NPV 92%   Likelihood ratio - 0.2

Comparison of EGD and PillCam ESO

Patients preference evaluation

- 2 questionnaires:
  - Pre-procedure perception
    - anxiety for the procedure and for pain during the procedure
      Significantly better for capsule endoscopy
  - Post-procedure satisfaction
    - Ease of swallowing/insertion,
    - Pain and discomfort during and after the procedure,
    - Preferred procedure,
    - Overall convenience,
    - Missed time from work
      Significantly better for capsule endoscopy
Capsule endoscopy: conclusions

- Capsule endoscopy is somewhat inferior to conventional EGD in diagnosing the presence and grading the size of varices.
- However, it appears to be more patient-friendly, and this might increase patients’ adherence to screening programs.
- For the time being, capsule endoscopy appears to be a suitable alternative to EGD in patients unable or unwilling to undergo conventional endoscopy.
• Whether capsule endoscopy will ultimately replace conventional endoscopy as the first line tool to detect and grade varices will depend on the results of appropriately designed cost-effectiveness analyses.
When and How to Scope in Portal Hypertension
Take home messages

• All cirrhotic patients should undergo screening upper GI endoscopy at the time of diagnosis of cirrhosis.

• Patients with compensated disease and without varices at screening endoscopy should undergo surveillance endoscopy at 2-3 years intervals.

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Patients with **small varices** at screening endoscopy should undergo surveillance endoscopy at **1-2 years** intervals; the interval should be **1 year** for patients with **alcoholic cirrhosis**, with more **severe impairment** of liver function and with **endoscopic risk signs**.
• At the present time, capsule endoscopy can be proposed as an alternative to EGD for patients unable or unwilling to undergo upper GI endoscopy.
Acknowledgements

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