Lifting versus Non-Lifting Sign for Prediction of Depth of Invasion of Early Colorectal Cancer

Y Ishiguro, Hirosaki National Hospital, Hirosaki, Japan
A Ishiguro, Narumi Hospital, Hirosaki, Japan
Y Uno, Tokedai Hospital, Sapporo, Japan

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Received 7 August 2012; Revision submitted 7 August 2012; Accepted 16 August 2012

Abstract

Submucosal (Sm) invasion by colorectal cancer can be classified as slight (depth of invasion < 1000 μm) or massive (depth of invasion > 1000 μm). Lesions classified as Sm1 and Sm2 are elevated in response to Sm injection, whereas lesions classified as Sm3 are not elevated. When Sm invasion is slight, there is negligible risk of lymphatic metastasis, and cure can be achieved by endoscopic resection alone. However, when Sm invasion is massive, the risk of lymphatic metastasis is substantial, increasing with the depth of invasion. The authors previously reported that a test based on lifting indicating Sm1 or Sm2 lesions would have a sensitivity of 83% and a specificity of 100%, whereas a test based on nonlifting indicating Sm3 lesions would have a sensitivity of 100% and a specificity of 83%. Here the evaluation of these two types of tumor, classified as lifting and nonlifting lesions, is demonstrated. This article is part of an expert video encyclopedia.

Keywords

Endoscopic mucosal resection; Methylene blue; Saline-assisted polypectomy; Standard endoscopy; Submucosal invasion; Video.

Video Related to this Article

Video available to view or download at doi:10.1016/S2212-0971(13)70168-7

Materials

• Endoscope: PCF TYPE 240I and CF-SV-L; Olympus Medical Systems, Tokyo, Japan.
• Injection needle: NM-400U Series; Olympus Medical Systems, Tokyo, Japan.

Background and Endoscopic Procedures

Saline-assisted polypectomy (SAP), also known as strip biopsy or endoscopic mucosal resection, is a technique in which saline solution is injected submucosally to elevate a lesion on a cushion of fluid, allowing flat lesions and broad-based sessile polyps to be removed completely and safely.1–3 Because the injected fluid separates the loose areolar tissue of the submucosa, the fluid accumulates in the submucosa, and a bleb forms beneath the lesion and lifts it. If substantial fibrosis is present in the submucosa, fluid injection does not separate the tissue, resulting in the nonlifting sign.4 Thus, fluid injection can help differentiate mucosal from invasive tumors. The authors previously examined the relationship between submucosal (Sm) invasion and lesion elevation induced by Sm injection in 60 patients with colorectal cancer with evidence of Sm invasion.5

Of the 60 lesions, 45 (75%) were classified as lifted and 15 (25%) as nonlifted. It was found that a test based on the assumption that lifting indicates invasion by Sm1 and Sm2 lesions had a sensitivity of 83% and a specificity of 100%. A test based on the assumption that nonlifting indicates invasion by Sm3 lesions had a sensitivity of 100% and a specificity of 83%.

The lifting of lesions is demonstrated in three cases, along with an explanation of how to classify the lesions as 'lifting' or 'nonlifting.'

Key Learning Points/Tips and Tricks

• To test the ‘lifting’ sign, inject 3–5 ml of a saline with some blue dye (e.g., methylene blue 0.05%) into the submucosa with a 23-gauge needle.
• Injections should be performed at 3–5 different sites approximately 2 mm from the edge of the lesion. Efficacy is not superior if injection volume exceeds 5 ml at a single site.
• Immediately after injection, evaluate the extent of elevation and classify the lesion as either ‘lifting’ or ‘nonlifting’; the normal mucosa around both types of lesion might be lifted. A slit between the lesion and the bleb indicates ‘nonlifting’ sign.

Complications and Risk Factors

Previous biopsy sampling or Sm injection might cause a false positive ‘nonlifting’ sign. Therefore, if forceps biopsy or
preinjection were performed previously, the lifting sign cannot be used to assess the indication for SAP.

**Scripted Voiceover**

<table>
<thead>
<tr>
<th>Time (min:sec)</th>
<th>Voiceover text</th>
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<tbody>
<tr>
<td>00:00</td>
<td>The extent of elevation of a lesion upon submucosal injection should be classified as lifting or non-lifting, as these features strongly correlate with the depth of invasion.</td>
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<tr>
<td>00:15</td>
<td>As shown in Figure A, lesions classified as sm1 (speak SM one) and sm2 are mostly elevated by fluid injection. This is called a positive 'lifting sign'.</td>
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<tr>
<td>00:28</td>
<td>As shown in Figure B, the dense fibrosis associated with invasive carcinoma, classified as sm3 prevents fluid infiltration through the submucosal connective tissue. Thus, there is no bleb formation and the lesion is not elevated. This is called a ‘positive non-lifting sign’.</td>
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<tr>
<td>00:52</td>
<td>The arrow points to a slit that developed between the lesion and the bleb.</td>
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<tr>
<td>01:00</td>
<td>This is our first case with a colorectal lesion. Inject 3–5 ml of diluted methylene blue into the submucosa with a 23-gauge needle. Injections should be made into 2 or 3 sites, each approximately 2 mm from the edge of the lesion. Always avoid puncturing the lesion. This lesion clearly shows a positive ‘lifting sign’. We can classify this tumor as lifting. Indeed after resection the specimen showed an invasion of the submucosa not deeper than 400 μm.</td>
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<tr>
<td>01:27</td>
<td>This is another case with a flat-type tumor suspicious for an early colorectal cancer. First, enhance demarcation of the lesion by some dye spraying, then inject fluid into the submucosal layer next to the lesion.</td>
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<tr>
<td>01:46</td>
<td>The lifting sign of this lesion is positive and we can proceed with endoscopic resection. The resection specimen showed a depth of invasion of 400 μm.</td>
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<tr>
<td>02:03</td>
<td>The third lesion is a pedunculated type tumor.</td>
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<td>02:10</td>
<td>Again we inject methylene blue into the submucosa, but the dense fibrosis associated with this invasive carcinoma prevents fluid infiltration through the submucosal connective tissue.</td>
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<tr>
<td>02:25</td>
<td>The normal mucosa around the tumor is lifted and forms a bleb. Here you see a slit that develops between the lesion and the bleb.</td>
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<tr>
<td>02:40</td>
<td>Therefore the lesion is classified as a non-lifting lesion and was removed surgically. Indeed maximum invasion depth was the muscularis propriae, corresponding to a T2 carcinoma.</td>
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</table>

**References**