## Evidence Table

<table>
<thead>
<tr>
<th>Clinical Area:</th>
<th>Photodynamic laser therapy for Barrett's esophagus.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keywords:</td>
<td>Barrett's esophagus, photodynamic therapy, porfimer.</td>
</tr>
</tbody>
</table>

### Study Type: Case series.

### Study Aim: To evaluate the long-term effectiveness of photodynamic therapy (PDT) and acid suppression therapy, supplemented with focal Nd: YAG laser photoablation of residual Barrett’s mucosa for the treatment of Barrett’s esophagus with dysplasia or early stage cancer.

### Outcomes
- **Primary:** Survival, and response to treatment.

### Design
- **Number of subjects:** N=103 patients.
- **Method of subject selection (inclusion/exclusion criteria):** Patients with histologically proven Barrett’s dysplasia or early adenocarcinoma, and who were not candidates for, or refused surgery, were included in the study. In patients with endoscopic abnormalities, only those with lesions staged T1, N0, M0 by EUS and CT were included in the study.
- **Consecutive patients?** Yes.
- **Description of study population:** The study included patients referred for PDT in a cancer center in Knoxville, TN. Their age ranged from 33 to 83 years with a mean of 65 ± 10 years, and the majority (79.6%) were men. Initially 80 (77.7%) patients were histologically diagnosed with high-grade dysplasia (HGD), 14 (13.6%) with low-grade dysplasia (LGD) and 9 (8.7%) with early stage carcinoma.
- **Intervention:** Patients were administered porfimer sodium 2 mg/kg intravenously. 48 hours later, 630 nm laser light was endoscopically delivered to the esophageal lumen using a cylindrical diffuser or a windowed esophageal-centering balloon. A follow-up endoscopy was performed at 48 hours to determine if additional light was needed. 3-6 months after the procedure, patients with residual Barrett’s mucosa <1.5 cm in diameter underwent one to four ND:YAG laser photoablations. Those with lesions ≥2 cm were re-treated with PDT. All patients were maintained on omeprazole 20 mg twice daily (the dose was doubled if the pH was <4.0) for the first three months then maintained at once daily. Other proton pump inhibitors could also be used at an equivalent dose.
- **Source of outcome data (e.g. patient self-report, doctor report, lab results):** Patients underwent follow-up endoscopy at one week, 3, 6, 9, and 12 months after the procedure, then annually to evaluate healing and obtain biopsy specimens.


- **Length of follow-up:** Mean follow-up was 50.7 ± 20.6 months (range, 2-122) months for all patients, and 58.5 ± 12.9 months (range 41-122 months) for the 82 patients who completed the study.
- **Completeness of follow-up:** 82/103 (79.6%) patients were followed up throughout the study, but all 103 patients had at least two months of follow-up.

### Validity
- **Is the study type appropriate for the question(s) being asked?** No, A RCT would have been more appropriate.
- **Were patients similar with respect to baseline characteristics?** There was some variability, but all patients met eligibility criteria.
- **Was the intervention and other aspects of patient care similar for all patients (or for all patients in a defined subgroup)?** Patients who did not respond to the initial PDT received additional treatment.
- **Was the process of observation likely to affect the outcome?** No.
- **Did an objective observer assess outcomes and were outcome measurements consistent?** Yes.
- **Were frequency of follow-up and follow-up duration appropriate?** Yes. However, the follow-up duration varied among patients (range 2-122 months).
- **Was completeness of follow-up sufficient?** Almost 80% of the patients were followed up throughout the study.
Conclusions regarding validity of methods:
This case series was prospective and there were clear eligibility criteria. However like all case series it is subject to biases. It also lacked a control or comparison group. Patients who did not respond to PDT were given other treatments; and thus the outcome may not evaluate the effect of PDT per se.

Results:
Survival rates (according to Kaplan –Meier estimate for survival curves for 120 months).

For patients with:
- Low grade dysplasia (LGD) 92.9%
- High grade dysplasia (HGD) 80.0%
- Cancer 66.7%

These rates were 92.9%, 77.5%, and 44.4% respectively when patients lost to follow-up were treated as treatment failures.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>LGD n=80</th>
<th>LGH n=14</th>
<th>Cancer n=9</th>
<th>Total N=103</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment success, No (%)</strong></td>
<td>52 (65%)</td>
<td>13 (92.9%)</td>
<td>4 (44.4%)</td>
<td>79 (76.7%)</td>
</tr>
<tr>
<td>No dysplasia, no Barrett’s</td>
<td>43 (53.8%)</td>
<td>10 (71.5%)</td>
<td>3 (33.3%)</td>
<td>56 (54.4%)</td>
</tr>
<tr>
<td>No dysplasia with Barrett’s</td>
<td>19 (23.7%)</td>
<td>3 (21.4%)</td>
<td>1 (1.1%)</td>
<td>23 (22.3%)</td>
</tr>
<tr>
<td><strong>Treatment failure, No (%)</strong></td>
<td>17 (21.3%)</td>
<td>1 (7.1%)</td>
<td>5 (55.6%)</td>
<td>23 (22.3%)</td>
</tr>
<tr>
<td>Persistence of disease</td>
<td>2 (2.5%)</td>
<td>0</td>
<td>0</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Progression of disease*</td>
<td>1 (1.2%)</td>
<td>0</td>
<td>0</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td>Death</td>
<td>7 (8.8%)</td>
<td>1 (7.1%)</td>
<td>5 (55.6%)</td>
<td>13 (12.6%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>7 (8.8%)</td>
<td>0</td>
<td>0</td>
<td>7 (6.8%)</td>
</tr>
<tr>
<td><strong>Lost to follow-up: (No (%))</strong></td>
<td>1 (1.2%)</td>
<td>0</td>
<td>0</td>
<td>1 (1.0%)</td>
</tr>
</tbody>
</table>

* Progressed to cancer. According to the text 6 of the 80 HGD patients developed carcinoma (this was counted among patients who died or underwent surgery)
p =0.026 for difference among three groups, p= 0.235 between LGD and HGD, p=0.012 between LGD and cancer, and p=0.028 between HGD and cancer.

Length of Barrett’s mucosa was reduced by a mean of 6.92 ± 4.56 cm (range 1-22cm)

Adverse effects:
Esophageal stricture: 30%  (this was more with two PDT treatments [50%] vs. one PDT treatment [18%])

Authors’ Conclusions
The authors concluded that porfimer PDT treatment supplemented with focal Nd:YAG laser photoablation, and continuous treatment with omeprazole reduces the length of Barrett’s esophagus, eliminates the high-grade dysplasia, and may reduce the development of carcinoma.
Reviewer’s Conclusions
This was a prospective case series of photodynamic therapy used for patients with Barrett’s dysplasia or early adenocarcinoma, who were not candidates for, or refused surgery. The study had some advantages: it had inclusion criteria, the patients were consecutive, it had a relatively long follow-up duration, and patients who died were lost to follow-up were treated as treatment failures. However, as all case series the study is subject to selection bias, and lacks a control or comparison group. Moreover, in this series the authors studied the effect of PDT treatment supplemented with focal Nd:YAG laser photoablation, and continuous treatment with omeprazole, and thus the long-term outcomes cannot be attributed solely to PDT.

Overall the results of the study show that PDT had a high success rate (no dysplasia with or without Barrett’s) of 76.7% after a long-term follow-up duration with a mean of $50.7 \pm 20.7$ months. This was more pronounced among patients with low-grade dysplasia who had a success rate of 93%. An important adverse event of the treatment was esophageal stricture experienced by 30% of the patients. This was more common among those who received two PDT treatments.