Photodynamic Laser Therapy for Tracheobronchial Cancer (early stage cancer)

Clinical Area: Photodynamic laser therapy for tracheobronchial cancer (early stage cancer)
Keywords: photodynamic therapy, early stage lung cancer

Study Type: Case Series
Study Aim: To evaluate the effectiveness and safety of photodynamic therapy (PDT) with photofrin II in centrally located early-stage lung cancer.

Outcomes
• *Primary*: Rate of complete response
• *Secondary*: Survival, toxicity

Design
• *Number of subjects*: n=54 patients (n=64 carcinomas) entered into study; n=51 patients evaluated (3 were later determined to be ineligible)
• *Method of subject selection (inclusion/exclusion criteria)*: histologically proven lung cancer with endoscopically recognized superficial thickening or protrusion; all lesions located in the subsegmental or larger bronchi; lesions with clear visibility of the distal tumor margins or roentgenographically occult lesions; no metastasis in hilar and mediastinal lymph nodes; no distant metastasis; performance status (PS) of 0 to 2; arterial oxygen pressure tension (PaO2) greater than 60 mm Hg.
• *Consecutive patients?* Not specified.
• *Description of study population*: Median age=69 years (range=47-79); 48 male/3 female; 61% squamous cell.
• *Intervention*: Topical anesthesia was used for “almost all” of the procedures. Patients received 2 mg/kg photofrin II intravenously, 48 hours before light irradiation. The light sources were either an argon dye laser or an excimer dye laser, wavelength=630 nm. Initial bronchoscopy was performed 2-4 days after PDT for clean up. Bronchoscopy and endoscopic, cytologic and histological examination were done every week for 1 month after PDT. Thereafter, examinations occurred at 2 to 3 month intervals after confirmation of a complete response. Patients who did not have a complete response or who developed local recurrence were given other therapy such as surgery or radiation therapy.
• *Source of outcome data (e.g. patient self-report, doctor report, lab results)*: Clinical and radiological data.
• *Length of follow-up*: Median follow-up=20.2 months (range, 7.4-40.3).
• *Completeness of follow-up*: 49/51 (96%) eligible patients were available for tumor response. Completeness of long-term follow-up is not known.

Validity
• *Is the study type appropriate for the question(s) being asked?* No, to determine treatment efficacy, there should be a control or comparison group.
• *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)?* Yes. Patients who did not respond to treatment 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?* Not known.
• *Were frequency of follow-up and follow-up duration appropriate?* Yes.
• *Was completeness of follow-up sufficient?* Yes, for immediate post-treatment follow-up. Unknown for long-term follow-up.
Conclusions regarding validity of methods:
This case series was prospective and there were clear eligibility criteria. As a case series, it is subject to selection and observation biases. The authors did not mention whether patients were consecutive and there was no control or comparison group. Patients who did not respond to PDT were given other treatments; therefore, the follow-up data do not evaluate PDT alone.

Results

Tumor response* (n=59 assessable carcinomas in 49 patients)

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>50</td>
<td>84.8</td>
<td>73.0-92.8</td>
</tr>
<tr>
<td>Partial response</td>
<td>6</td>
<td>10.2</td>
<td>--</td>
</tr>
<tr>
<td>No change</td>
<td>3</td>
<td>5.0</td>
<td>--</td>
</tr>
</tbody>
</table>

*Complete response (CR)=no tumor observable by biopsy and/or brushing cytology for at least 4 weeks, and no visible tumor by chest roentgenographically for at least 4 weeks; partial remission (PR)=reduction in tumor volume >50% but with the cancer still present on biopsy or brushing for at least 4 weeks after therapy; No change (NC)= reduction in tumor volume <50% and the cancer still present at biopsy or brushing.

Of the 50 carcinomas that had a CR after initial PDT:

5 (10%) had local recurrence outside the photoradiated field; there was no metastasis of hilar and mediastinal lymph nodes.

Tumor response by tumor size (n=59 carcinomas)

<table>
<thead>
<tr>
<th>Tumor size (mm)</th>
<th>No. carcinomas</th>
<th>CR</th>
<th>PR</th>
<th>NC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>≤20-&gt;10</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>≤10-&gt;5</td>
<td>12</td>
<td>11</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>≤5</td>
<td>33</td>
<td>33</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Survival (n=51 eligible patients)

At the end of the median follow-up time of 20.2 months. 45 (88.2%) were alive, 6 had died.

Overall survival was estimated to be 50% after 40 months (from Kaplan-Meier curve). Note: Patients who did not have a complete response after PDT received other treatments (surgery or radiation therapy); survival at 40 months reflects PDT and subsequent treatments.

Data from approximately 38 (75%) of patients who dropped out or were lost to follow-up were missing at the 40 month follow-up.

Authors’ Conclusions

“PDT with photofrin II has an excellent effect on patients with centrally located early-stage lung cancer who have limited tumor invasion extending over a small (≤1 cm) area.

Reviewer’s Conclusions

This was a prospective case series of photodynamic therapy in patients with early lung cancer. A large proportion of patients had complete response following PDT therapy; the rate of complete response was higher with smaller tumors. 5 patients (10%) who had a complete response experienced local recurrence. After a median follow-up time of 20.2 months, 45 (88.2%) of the 51 eligible patients were alive. Patients who did not have a complete response or who experienced recurrence had other treatments so long-term outcomes cannot be attributed solely to PDT. There was no control or comparison group with which to compare clinical outcomes.