TITLE: Proton Beam Therapy for the Treatment of Locally Advanced Adenoid Cystic Carcinoma: Clinical Effectiveness, Cost-Effectiveness, and Guidelines

DATE: 18 April 2016

RESEARCH QUESTIONS

1. What is the clinical effectiveness of proton beam therapy for the treatment of locally advanced adenoid cystic carcinoma?

2. What is the cost-effectiveness of proton beam therapy for the treatment of locally advanced adenoid cystic carcinoma?

3. What are the evidence-based guidelines regarding the use of proton beam therapy for the treatment of locally advanced adenoid cystic carcinoma?

KEY FINDINGS

Six non-randomized studies were identified regarding the clinical effectiveness of proton beam therapy for adenoid cystic carcinoma.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2011 and April 6, 2016. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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**SELECTION CRITERIA**

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Selection Criteria</th>
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<tr>
<td><strong>Population</strong></td>
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<tr>
<td>Adults with locally advanced adenoid cystic carcinoma (LAACC)</td>
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<tr>
<td><strong>Intervention</strong></td>
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<td>Proton beam therapy</td>
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<td><strong>Comparator</strong></td>
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<tr>
<td>Photon radiation therapy, including intensity modulated radiation therapy (IMRT) and RapidArc® Volumetric Arc Therapy (VMAT); Other treatments; No comparator</td>
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<td><strong>Outcomes</strong></td>
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<td>Q1. Clinical effectiveness (e.g., tumour reduction, elimination of the tumour, quality of life, survival, etc); Q2. Cost-effectiveness; Q3. Guidelines for use in LAACC</td>
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<tr>
<td><strong>Study Designs</strong></td>
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<tr>
<td>Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines</td>
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</table>

**RESULTS**

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

Six non-randomized studies were identified regarding the clinical effectiveness of proton beam therapy for adenoid cystic carcinoma. No relevant health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, economic evaluations, or evidence-based guidelines were identified.

Additional references of potential interest are provided in the appendix.

**OVERALL SUMMARY OF FINDINGS**

Six non-randomized studies\(^1\)\(^-\)\(^6\) were identified regarding the clinical effectiveness of proton beam therapy for adenoid cystic carcinoma. One non-randomized study\(^1\) reported on the outcomes of 16 patients with adenoid cystic carcinoma after receiving postoperative intensity-modulated proton therapy, with the majority of patients also receiving adjuvant chemotherapy. One patient experienced recurrence and died, while the remaining patients did not have evidence of disease at the end of the study (mean follow-up of 24.9 months). Four patients experienced grade 3 toxicities (oral mucositis and dermatitis) and one patient experienced grade 4 toxicity (optic nerve disorder).\(^1\)

The study by Linton et al.\(^2\) reported outcomes for 26 patients with head and neck adenoid cystic carcinoma after treatment with proton beam therapy; for initial disease treatment this rate was 93%, and for recurrent disease this rate was 57%. In this study, local control rates at two years were 95% for initial disease treatment and 86% for recurrent disease. The rate for distant metastasis was 25% at two years.\(^2\)
Two studies\textsuperscript{3,5} reported three year survival rates after treatment with proton beam therapy, for head and neck cancers, including adenoid cystic carcinoma. In the study by McDonald et al.\textsuperscript{3} the three year survival rate was 84.9%. This study\textsuperscript{3} also reported that the rate of temporal lobe radiation necrosis at three years was 12.4%. The survival rate was similar to the findings from the study by Morimoto et al.\textsuperscript{5} which reported a three year survival rate of 83%. In this study,\textsuperscript{5} 13 out of 25 patients with adenoid cystic carcinoma developed distant metastases; the local control rate at three years was 63%.

In the study by Frank et al.\textsuperscript{4} the outcomes for five patients with adenoid cystic carcinoma receiving active scanning proton therapy were reported. No patients in this study experienced treatment breaks or hospitalizations or treatment-related deaths (median follow-up of 28 months). The overall clinical complete response rate, which included ten patients with squamous cell carcinoma, was 93.3%.\textsuperscript{4}

The study by Takagi et al.\textsuperscript{6} compared outcomes of overall survival rate, progression-free survival rate, and local control rate at five years for 80 patients receiving either proton therapy or carbon ion therapy for adenoid cystic carcinoma. The authors did not find any significant differences between proton therapy or carbon ion therapy; the survival rate was 63%, the progression-free survival rate was 39%, and the local control rate was 75%.\textsuperscript{6}
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses
No literature identified.

Randomized Controlled Trials
No literature identified.

Non-Randomized Studies


Economic Evaluations
No literature identified.
Guidelines and Recommendations
No literature identified.

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APPENDIX – FURTHER INFORMATION:

Previous CADTH Reports


Health Technology Assessments – Adenoid Cystic Carcinoma Not Specified


Systematic Reviews

Uncertain If Intervention Specific for LAACC


Other Cancers


Non-Randomized Studies

Outcomes for Proton-Beam Therapy Not Specified


Evidence-Based Guidelines - Locally Advanced Adenoid Cystic Carcinoma Not Specified


Clinical Practice Guidelines – Uncertain Methodology


Reviews


Additional References