Management of the clinically negative neck (N0) of supraglottic laryngeal carcinoma: a systematic review


CRD summary
This review concluded that neck dissection for clinically negative supraglottic laryngeal carcinoma did not appear superior to radiotherapy, combined therapy or a wait-and-see policy in terms of survival. This review was carried out using robust methodology. The authors’ conclusions were appropriately cautious given poor-quality included trials, a small number of included studies and the limited evidence available.

Authors' objectives
To answer the question: among patients with clinically negative supraglottic laryngeal carcinoma, were survival and occurrence of neck metastases significantly different between patients that received neck dissection and those that had another therapeutic treatment?

Searching
Published trials in any language were identified through a search of MEDLINE, EMBASE, The Cochrane Library and Cochrane Central Register of Controlled Trials (CENTRAL) to 2006. References lists of relevant studies were searched. Search terms were reported.

Study selection
Studies that reported management of initial supraglottic cancer in patients treated for clinically negative supraglottic laryngeal carcinoma of squamous epithelium were eligible for inclusion. Patients were eligible for inclusion regardless of size, site and histological grade of the primary carcinoma. Studies were required to compare neck dissection with another therapeutic procedure: radiotherapy; neck dissection plus radiotherapy; or a wait-and-see (conservative) approach. Results were required to present survival data in the form of time-to-event analysis and include patient assessments annually for at least three years. The primary outcomes were five-year disease-specific survival (DSS), five-year overall survival and five-year neck disease-free survival. Secondary outcomes included site of recurrence. Most (75%) tumours in included studies were in the early stage (T1/T2).

Two reviewers independently selected studies for inclusion. Disagreements were resolved through discussion.

Assessment of study quality
Methodological quality was assessed by two independent reviewers based on recommendations of Group for Meta-Analysis of Observational Studies in Epidemiology (MOOSE) and Cochrane Handbook for Systematic Reviews of Interventions.

Data extraction
Two independent reviewers extracted general characteristics, procedural data and outcome data into standard data extraction forms. Authors of included studies were contacted to provide missing data.

Methods of synthesis
The studies were combined using a narrative synthesis supported by tables.

Results of the review
Six studies (n=792) were included in the review. Overall study quality was poor. All included studies were retrospective. Sample sizes ranged from 38 to 385 patients. Specific problems with study quality were: inclusion of retrospective studies that were underpowered to detect clinically important differences; subjective allocation of patients to treatment groups; lack of intervention protocols; and lack of reporting of diagnostic or follow-up procedures.

Neck dissection versus neck radiotherapy: Neck DSS rate was reported in two studies and was not significantly
different between patients who underwent neck dissection compared to radiotherapy. The rate difference in one study was 9.4% (95% CI -4.6 to 23.8) and in the other was -10.8% (95% CI -31.0 to 4.3). Overall survival was reported in one study with survival rates of 55% in the neck dissection group (95% CI 31 to 79) and 71% in the radiotherapy group (95% CI 61 to 81). There were no statistically significant differences.

**Neck dissection versus combined therapy (dissection plus radiotherapy)**: One study investigated DSS rate and found no differences between patients who underwent neck dissection 75.5% (95%CI 66.3 to 83.8) and patients who underwent combined therapy 66.9% (95% CI 58.8 to 74). Neck disease-free survival rate and site of neck recurrence did not differ between groups.

**Neck dissection versus the conservative approach**: DSS rate was reported in one study with survival rates of 75.5% in the neck dissection group (95% CI 66.3 to 83.8) and 79.9% in the wait-and-see group (95% CI 69.6 to 87.2); these rates were not different between groups (rate difference -4.4%, 95% CI -16.0 to 8.3).

**Overall survival rate (reported in two studies)**: One study reported 64% overall survival in the neck dissection group and 50% in the wait-and-see group (p<0.05). The other study reported 46.4% (95% CI 29.5 to 64.2) survival in the neck dissection group and 50% (95% CI 23.7 to 76.3) in the wait-and-see group; these rates were not statistically significant (rate difference -3.6%, 95% CI -34.9 to 28.2).

Neck disease-free survival rate and site of neck recurrence did not differ significantly between patients who received neck dissection and those who had a conservative approach in any of the three studies.

**Authors’ conclusions**
The authors concluded that neck dissection was not superior to radiotherapy, combined therapy or a wait-and-see policy in terms of survival and control of neck disease; further studies were necessary to provide more reliable conclusions.

**CRD commentary**
This review addressed a clear question supported by appropriate inclusion criteria. Relevant databases were searched, but it appeared that no attempts were made to identify unpublished studies. Publication bias was not considered in the report. Suitable methods were used throughout the review process to minimise risks of reviewer error and bias. Study quality was evaluated, but full results of the quality assessment were not presented. The decision to present included studies narratively and not to pool studies in a meta-analysis was appropriate given the heterogeneity between studies. This review was carried out using robust methodology. The authors’ conclusions were appropriately cautious given poor-quality included trials, a small number of included studies and limited evidence available.

**Implications of the review for practice and research**
**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that well-designed prospective studies were needed to provide more reliable answers to the debatable issue of management of clinically negative supraglottic laryngeal carcinoma.

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