Sentinel node biopsy in squamous cell cancer of the oral cavity and oral pharynx: a diagnostic meta-analysis
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CRD summary
This review assessed the diagnostic performance of sentinel node biopsy in assessing the spread of oral and oropharyngeal cancer. The review was generally well conducted and clearly reported. However, the included studies were small and had a number of methodological flaws. The authors' conclusion, that sentinel node biopsy had shown high sensitivity in preliminary studies, is reasonable given the available data.

Authors' objectives
To assess the diagnostic performance of sentinel node biopsy to assess the spread of head and neck squamous cell carcinoma.

Searching
MEDLINE, EMBASE and conference proceedings (including Zetoc) were searched. Experts in the field were contacted and the bibliographies of articles obtained from electronic searches were screened for additional articles.

Study selection
Study designs of evaluations included in the review
No inclusion criteria for the study design were specified.

Specific interventions included in the review
Studies of sentinel node biopsy where the sentinel node was detected using established techniques and harvested surgically, and where standard histological assessment was used to determine nodal involvement, were eligible for inclusion. Nine of the 19 included studies used standard histological techniques: six used step-serial sectioning and four used immunohistochemistry.

Reference standard test against which the new test was compared
Studies where neck dissection was performed as the reference standard to assess nodal spread, irrespective of the result of sentinel node histology, were eligible for inclusion.

Participants included in the review
Studies of patients older than 16 years, with histologically proven head and neck mucosal squamous cell cancer, were eligible for inclusion. Three hundred and one patients with oral cavity primary tumours and 46 patients with oropharyngeal primary tumours were included; the site of the primary tumour was not specified for 20 patients.

Outcomes assessed in the review
The included studies were required to report sufficient data to calculate the sensitivity and specificity.

How were decisions on the relevance of primary studies made?
Two reviewers, who were blinded to the origin of the article, year of publication, journal and authors, independently assessed studies for inclusion based on the 'Methods' section of each paper. Any disagreements were resolved by re-review.

Assessment of study quality
Two reviewers, who were blinded to the origin of the article, year of publication, journal and authors, independently performed the quality assessment. Any disagreements were resolved by re-review. The quality of the included studies was assessed using an ordinal scale (described in full in the article), which included items for the following:
description of sentinel node detection method; description of histological technique; description of sampling technique for neck dissection; blinding of the pathologist to the diagnosis; description of the patient population; number of patients included. Study validity was also assessed, according to Cochrane recommended guidelines for diagnostic accuracy studies.

Data extraction
Two reviewers independently extracted the data using a predefined spreadsheet. Any disagreements were resolved by re-review. Demographic and tumour data were extracted, along with the numbers of true positives, false negatives, false positives and true negatives needed to calculate the sensitivity and specificity for each study.

Methods of synthesis
How were the studies combined?
A pooled sensitivity estimate was generated using the Clopper-Pearson method; confidence intervals (CIs) were generated by fitting a random-effects logistic regression model. All of the included articles had 100% specificity because, if a sentinel node was positive for disease, the neck was considered positive for disease regardless of whether any further deposits were found using other methods (i.e. there can be no false positives). One article had no true-positive or false-positive cases, therefore no sensitivity or specificity estimates were calculated for this study. Publication bias was assessed using funnel plots of sensitivity versus sample size.

How were differences between studies investigated?
The authors stated that clinical heterogeneity was not thought to be an issue, given the study populations, tests and reference standards in the included studies. Between-study heterogeneity in the sensitivity results was assessed by visual examination of a forest plot.

Results of the review
Nineteen articles, involving a total of 367 patients, were included in the analysis.

The method of sentinel node detection was well described in all but two studies, whereas approximately half of the studies did not clearly describe the histological method used to assess sentinel nodes and the number of nodes assessed (where reported in nine articles) varied widely. All of the included studies used a valid reference standard. Blinding was not done in any of the studies and there was no indication that verification bias had been avoided.

The pooled estimate for sensitivity was 0.926 (95% CI: 0.852, 0.964).

No significant publication bias was apparent.

Authors’ conclusions
Sentinel node biopsy has shown high sensitivity for oral and oropharyngeal squamous cell cancer in pilot studies, providing a basis for trials on its role in head and neck cancer.

CRD commentary
The review addressed a clearly stated research question, which was defined by appropriate inclusion criteria. A number of sources were searched for relevant studies, though the search strategies were not reported and it was unclear whether any language restrictions were applied. It was therefore difficult to judge the likely adequacy of the retrieval rate. Appropriate methods were used to minimise the potential for bias and error in the review process and these were clearly reported. The methodological quality of the included studies was assessed and a summary of the results reported, but methodological quality was not incorporated in the analysis.

The authors stated that 'clinical heterogeneity was thought not to be an issue'. However, the limited reporting of the characteristics of the included studies made this difficult to judge. Where characteristics of the test method were
reported, there appeared to be potentially significant between-study heterogeneity. The appropriateness of generating a pooled sensitivity value was assessed by visual examination of a forest plot, the interpretation of which is subjective. The authors’ conclusions noted the preliminary nature of their findings and were appropriate given the limitations of the available data.

**Implications of the review for practice and research**

**Practice:** The authors made no specific recommendations for practice.

**Research:** The authors stated that the results of their review provide a firm evidence base for two forthcoming, large trials in the field. They further stated that these trials should standardise the method for sentinel node biopsy, and they emphasised that the ultimate question remains whether the technique can improve survival and reduce morbidity.

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