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Review Article

Elective neck dissection vs. Sentinel node biopsy for oral squamous cell carcinoma: Systematic review and Meta anaylsis

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ABSTRACT:
Introduction: The sentinel node biopsy concept has been gaining approval in the head and neck cancer literature and several pilot studies have been published. Hence in the present study we aimed to systematically assess the diagnostic accuracy of sentinel lymph node biopsy (SLNB)and the elective neck dissection(END) in patients with squamous cell carcinoma of the oral cavity and oropharynx. **Material and methods**: A systematic literature review was done using MEDLINE from 1980 to 2014 by combining oral cavity and oropharyngeal SCC keywords with sentinel node biopsy keywords. We comprised diagnostic accuracy studies which used neck dissection as a reference test for the sentinel node biopsy. Study characteristics and measures of accuracy were extracted. Diagnostic accuracy was calculated. **Results:** A total of 35 studies (1121 patients) were included. The pooled sensitivity, specificity, positive likelihood ratio (LR+), negative likelihood ratio, diagnostic odds ratio, positive predictive value, negative predictive value and accuracy were 93%, 100%, 35.89%, .12%, 282.7%, 100%, 97% and 97.8%, respectively. **Conclusions**: High sensitivity, negative predictive value and accuracy of SLNB support its role as a valid diagnostic technique to correctly stage cN0 patients with OCSCC and OPSCC.
Key words: Sentinel Node Biopsy, Elective Neck Dissection, Oral Squamous Cell Carcinoma.

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INTRODUCTION

Oral cavity and Oropharyngeal squamous cell carcinoma (OCSCC and OPSCC) are cheifly due to the widespread use of tobacco and alcohol.[1] The chief prognostic factor is the presence of cervical lymph node metastases, which can decrease the 5-year survival rates to lower than 50%.[2] Staging of the neck by palpation and imaging techniques are not sensitive enough in detecting micrometastases resulting in a high incidence of occult metastases in the neck.[3] These techniques are based cheifly on size criteria, with nodes smaller than 10 mm not generally considered suspicious. However, nodes as small as 2.0 mm can contain micrometastatic disease[4] and therefore there is still a 20–30% incidence of occult nodal metastasis in necks categorized as N0.[5] Exact staging of the N0 neck is therefore vital in handling this type of cancer. In SCC of the oral cavity and oropharynx, the cheif options for the treatment of the N0 neck are elective neck dissection, radiation

therapy, or a combination of the two.[6] Presently accepted management policies are that patients with greater than 20% chance of subclinical metastases, based on the anatomic site and the size of the primary tumor, should undergo elective neck dissection (END).[7] However, such a policy might still over treat up to 80% of patients, and ENDs carry with them an associated morbidity.[8] Because of the need to accurately stage the neck and to treat only those most likely to benefit from therapy, much interest has arisen in sentinel lymph node biopsy (SLNB). The validity of the concept of SLNB is based on the fact that tumor cells will spread from the primary site to a single node or group of nodes (the sentinel nodes), before progressing to the remainder of the lymph nodes[9,10] Hence in the present study we aimed to systematically evaluate the diagnostic accuracy of sentinel lymph node biopsy and the elective neck dissection in patients with squamous cell carcinoma of the oral cavity and oropharynx.

MATERIAL AND METHODS

Online data was collected from the search engines of EBSCO, Pubmed, Google Scholar, Scopus. The study articles were collected that from 1980 to 2014. Two reviewers independently checked the data collected and disputes resolved by consensus. The study was conducted with reference to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), Meta-analysis of Observational Studies in Epidemiology guidelines, and the Cochrane Handbook for Systematic Reviews of Interventions. We excluded case reports. The random effect model incorporated the heterogeneity of the studies into the analysis of the overall efficacy. The fixed effect model assumed that data came from a single study that is, assuming no inter-study heterogeneity.[13] Statistical heterogeneity among studies was evaluated by the Cochran Q statistic (considered significant for p values <0.10) and the I^2 test. Likelihood ratios are metrics that are calculated using a combination of sensitivity and specificity values. The positive likelihood ratio (LR+) is defined as the ratio of sensitivity/ (1 — specificity), whereas the negative likelihood ratio (LR—) is defined as the ratio of specificity/(1 sensitivity). When a diagnostic test has absolutely no discriminating ability, both likelihood ratios equal 1. Meta analysis of the collected data was conducted using the software: Meta-Disc version 1.4.[14]

RESULT

Out of the 525 relevant studies 35 original articles were finalized. The overall cohort totaled 1121 patients. In these studies at least one sentinel node was detected in almost all patients and a sentinel node biopsy could thus be performed in all patients. The pooled sensitivity of SLNB versus END is 93%. There is a significant heterogeneity between the sensitivities of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies as the p value of chi- square test was 0.06 (<0.1) and I^2 index was 28.1% (25–50%) (Fig. 1). The pooled specificity is 100%. There is no significant heterogeneity between the specificities of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies as the p value of chi square test was 1.0000 (>0.1) and I^2 index was 0.0% (0–25%) (Fig. 2). The pooled Positive Likelihood Ratio is 35.89. There is no significant heterogeneity between the Positive Likelihood Ratios of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies as the p value of chi-square test was 0.999 (>0.1) and I^2 index was 0.0% (0–25%) (Fig. 3). The pooled Negative Likelihood Ratio is 0.12. There is no significant heterogeneity between the Negative Likelihood Ratio of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies as the p value of chi-square test was 0.433 (>0.1) and I^2 index was 2.1% (0–25%) (Fig. 4). The pooled Diagnostic Odds Ratio is 282.73 (denoting high validity of the test). There is no significant heterogeneity of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies as the p value of chi- square test was 0.996 (>0.1) and I^2 index was 0.0% (0–25%)(Fig. 5).

Figure 1 Forest plot showing the sensitivities (Random Effect Model) of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies.

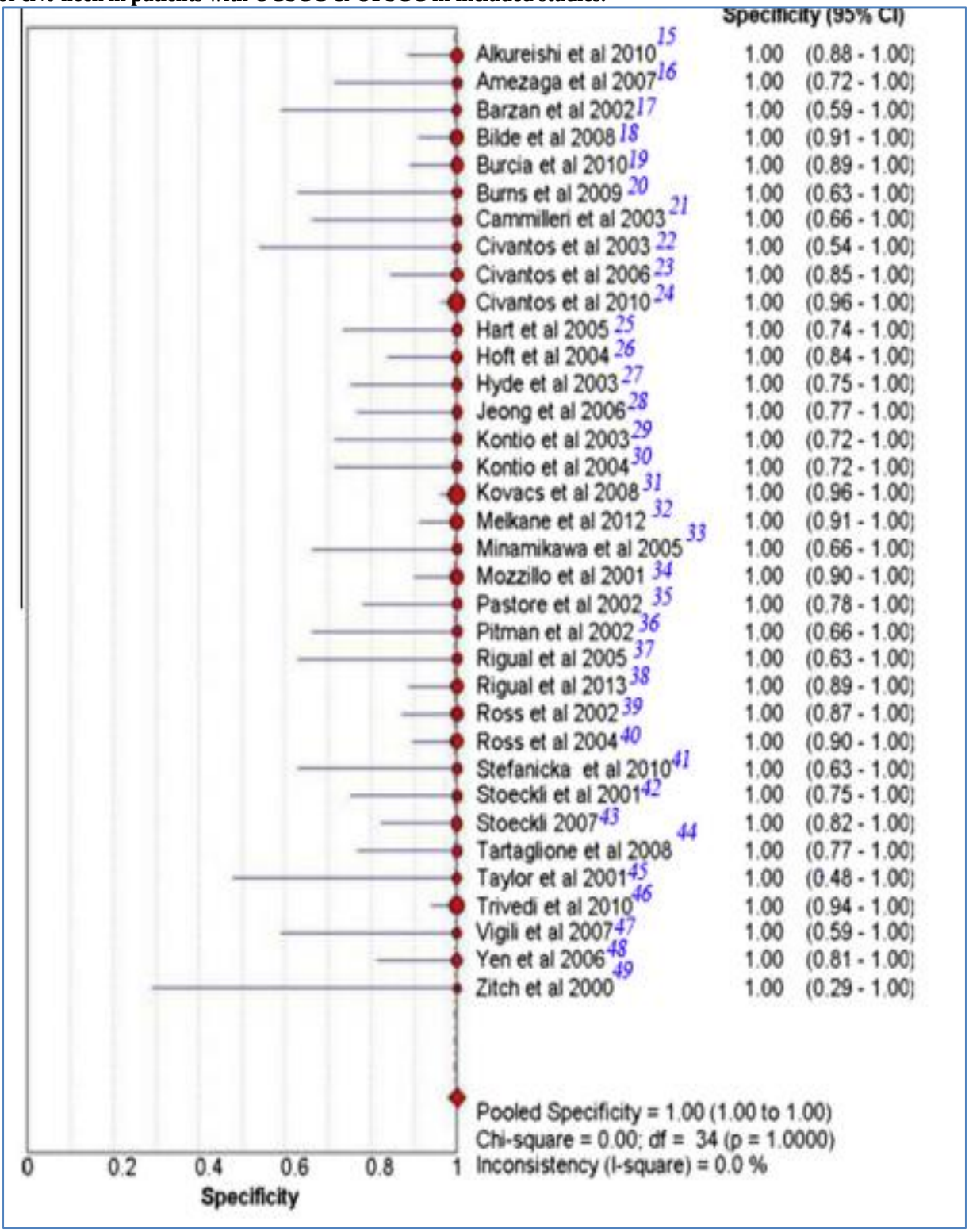


Figure 2 Forest plot showing the specificities (Fixed effect model) of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies.

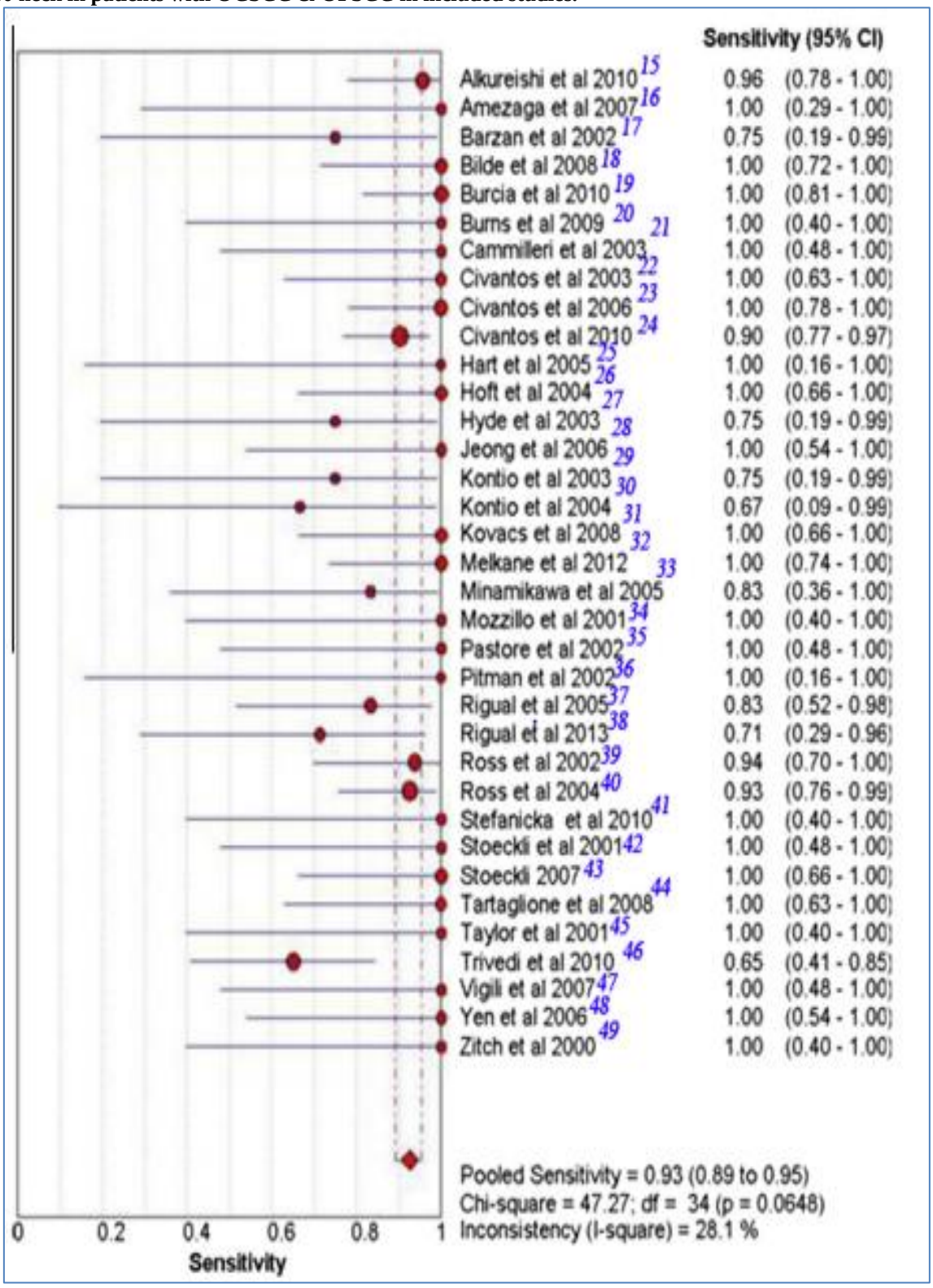


Figure 3 Forest plot showing the Positive Likelihood Ratios (Fixed effect model) of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies.

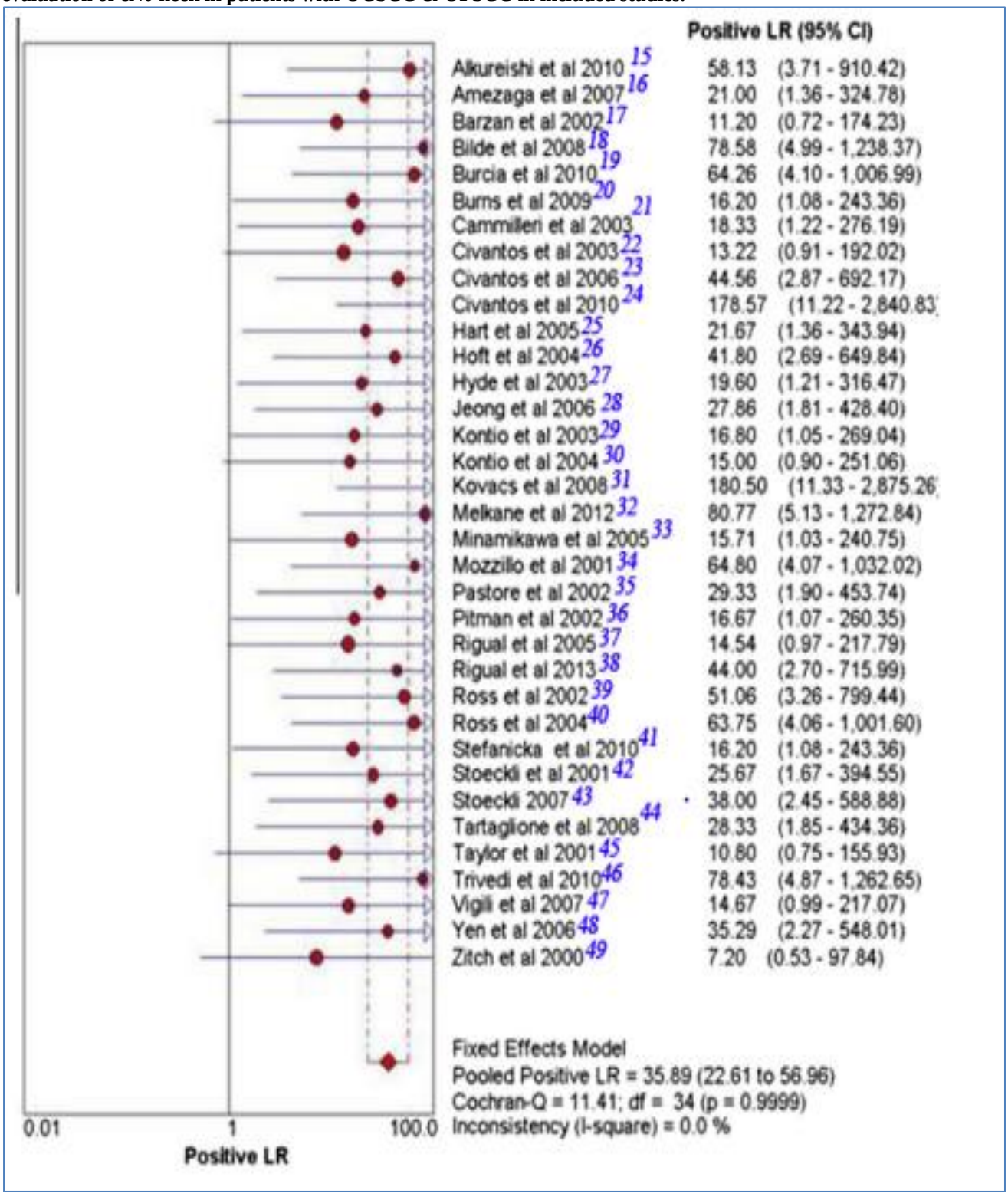


Figure 4 Forest plot showing the Negative Likelihood Ratios (Fixed effects model) of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies.

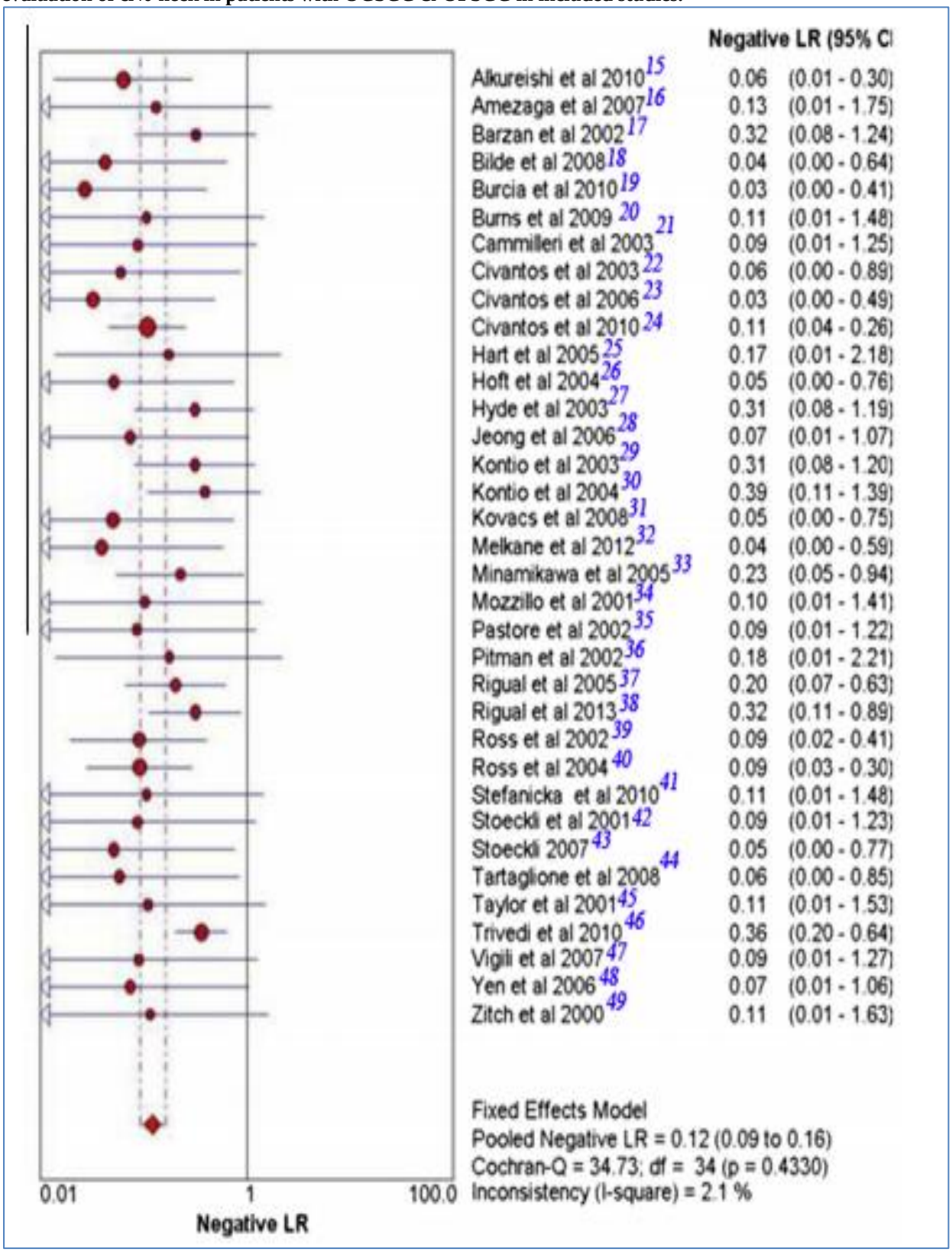
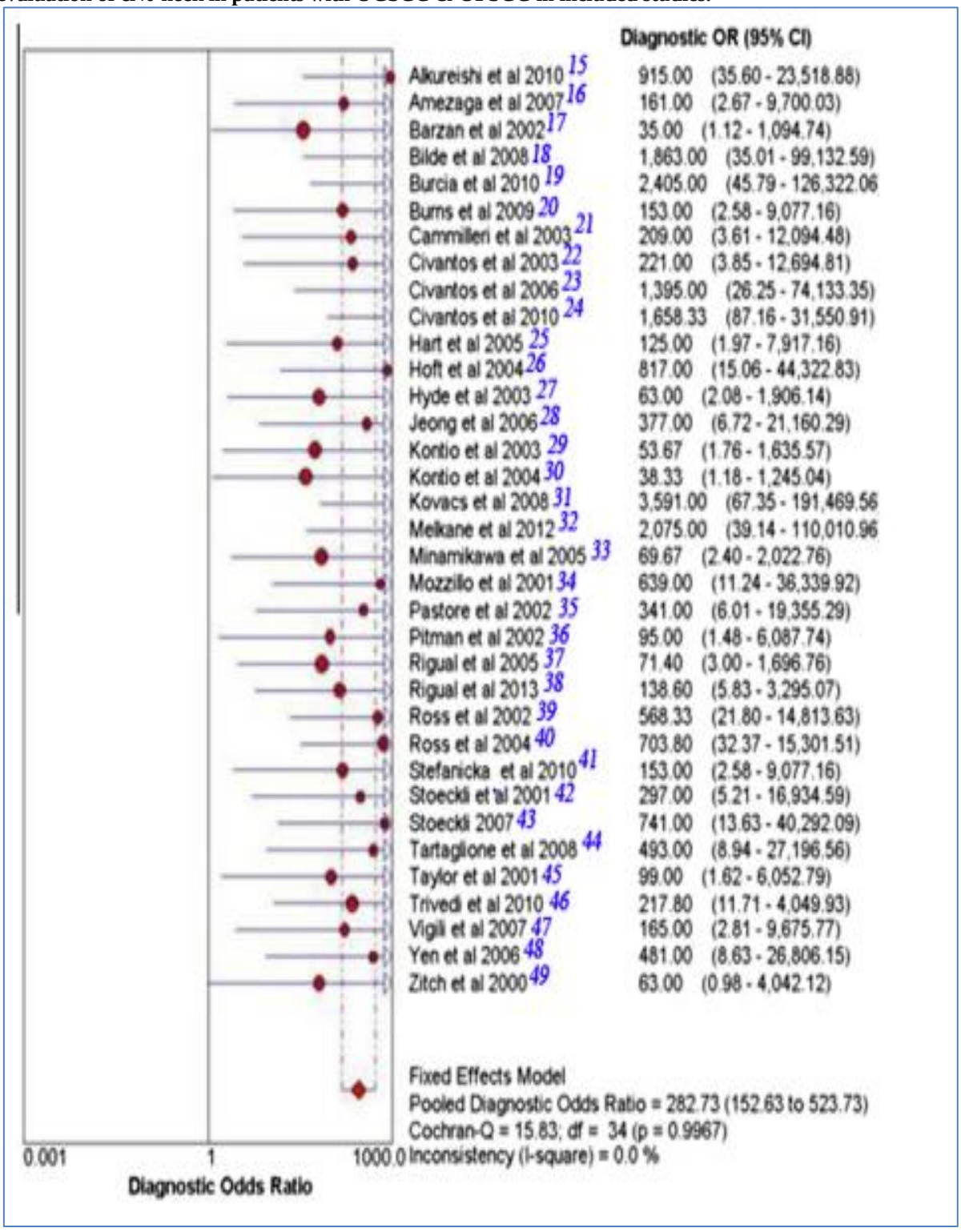


Figure 5 Forest plot showing the Diagnostic Odds Ratios (Fixed effects model) of SLNB versus END in evaluation of cN0 neck in patients with OCSCC & OPSCC in included studies.



DISCUSSION

Although diagnostic tools have developed significantly, we have no effective procedures available to identify hidden metastatic disease in the cervical lymph nodes of patients with OSCC and OPSCC. The incidence is situated at around 30%, a high percentage, and the presence of regional disease is the cause of the death of one of every two patients.[15-40] The application of SNB has been demonstrated to be very useful in melanoma and breast cancer[15-39] and for this reason we have studied its application in primary OCSCC and OPS- CC, through Meta analysis of 35 studies, in an attempt to determine if SLNB is a useful technique in the

diagnosis of regional metastasis. It must be noted that all articles in this study have 100% specificity (Fig. 2) and positive predictive value because there are no false-positive cases in this scenario. However, false negative results can have several causes including uneven radionuclide injection, obscuring of sentinel lymph nodes by the radioactive signal of the primary tumor, and lymphatic obstruction by gross tumor, resulting in redirection or unpredictable lymphatic flow and were defined as skip metastases or jump metastases.[8] Our results were concordant with the diagnostic meta-analysis of Govers et al. 2013 (21 studies comprising 847 patients of cT1/T2N0 oral cavity and oro-pharyngeal squamous cell carcinoma)[43] and Paleri et al. 2005 (19 studies comprising 301 patients of oral cavity and oropharyngeal squamous cell carcinoma)[54] who reported a pooled sensitivity of 0.94 (0.90–0.97) and 92.6 (85.2–96.4), respectively. In the present study, the pooled Positive Likelihood Ratio of SLNB is 35.89 (Fig. 3). This means that a person with cN0 neck having metastatic lymphadenopathy is about 36 times more likely to have a positive test than a person with cN0 neck who has not got metastatic lymphadenopathy in cases of OCSCC and OPSCC. On the other hand, the pooled Negative Likelihood Ratio of SLNB is 0.12 (Fig. 4), indicating that the probability of having a negative test for individuals with metastatic lymphadenopathy in cN0 neck is 0.12 times of that of those without metastatic lymphadenopathy in cN0 neck of patients with OCSCC and OPSCC. In the present study, the pooled Diagnostic Odds Ratio of SLNB is 282.73 (>1) (Fig. 5). This means that for the SLNB the odds for positivity among cN0 neck of subjects with metastatic lymphadenopathy is nearly 283 times higher than the odds for positivity among cN0 neck of subjects without meta- static lymphadenopathy. The present study revealed generally high quality scores of the included studies; suggesting that most of included studies presented enough information overall and satisfied most of the requirements established. However most of studies had a suboptimal design in regard to the blinding method (Item 11) as the interpretation of the histopathological examination results of the neck dissection specimen was done with the knowledge of the SLNB histopathological results.[48,49] There is no significant heterogeneity between the specificity, Positive Likelihood Ratio, Negative Likelihood Ratio and Diagnostic Odds Ratio in the included studies (Figs. 2–5), while there was a significant heterogeneity between the sensitivity in the included studies (Fig. 1) and this was the reason to adapt a random effect model for data pooling.[55]

To the best of our knowledge, this is the largest meta-analysis of SLNB in patients with oral cavity and oro-pharyngeal SCC.

CONCLUSIONS

The results of this diagnostic meta-analysis demonstrate that sentinel node biopsy appears to be a sensitive method in the detection of neck metastases in cN0 neck of OCSCC and OPS- CC that could suggest its utility in the management process. Multi-center prospective randomized double blind controlled trials comprising larger patient cohorts comparing the roles of SLNB versus END in evaluation of cN0 neck in patients with OCSCC and OPSCC are required.

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