RESEARCH
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ELECTIVE NECK DISSECTION VERSUS OBSERVATION IN THE MANAGEMENT OF SQUAMOUS CELL CARCINOMA OF TONGUE WITH CLINICALLY NODE NEGATIVE NECK- A SYSTEMATIC REVIEW

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Abstract
Background:
Early oral squamous cell carcinoma are reported to be about 90% of all the oral cancers especially in older individuals more specific to males. Though etiology is multifactorial it can be strongly related to tobacco and alcohol abuse other factors like Human papillomaviruses (HPV16-18), genetic factors and pre-neoplastic lesions also play a major role in the etiology of oral squamous cell carcinoma. There is no consensus in the literature for the treatment of early squamous cell carcinoma of the tongue (stages I–II); both an elective neck dissection as well as observation policy have their proponents in various centres' globally.
Aim: The systematic review aims to analyse if elective neck dissection or observation without neck dissection gives good prognosis for patients diagnosed with squamous cell carcinoma of the tongue in terms of recurrence rates and survival rates.
Materials And Methods: PROSPERO registration was obtained before beginning of the study. PROSPERO ID : CRD42023430920.PubMed/Medline, Cochrane and Google Scholar were searched comprehensively to identify relevant literature. Manual search was also done from the esteemed journals pertaining to the fields of Oral Surgery, Oral Pathology , Oral Medicine, Radiology, International Journal of Oral and Maxillofacial Surgery (IJOMS); and British Journal of Oral and Maxillofacial Surgery(BJOMS). Four studies were selected following PRISMA guidelines and inclusion criteria. All the included studies were retrospective studies. Literature abstracts and full text articles were analysed in this review. Two reviewers independently assessed the full text of included articles and extracted data items related to research questions. Further, quality of assessment of all the included studies was done with the Risk of bias assessment tools.
Results: Four studies were short listed and included in this review as per PRISMA guidelines. All the included studies were retrospective studies. The methodological quality of the studies was graded moderate to low. The outcome concerned the comparison between elective neck dissection and observation in the management of squamous cell carcinoma of the oral tongue with node negative neck clinically and to asses which one has the better prognosis. Based on results analysed from the included studies it can be concluded for lesions falling under T1 Category observation with out neck dissection can be a treatment of choice if only the treatment for primary tumour resections is in strict compliance with cancer surveillance protocol, while in cases of T2, T3 and T4 all the included studies showed that there less local recurrence rates and more survival rates in groups where elective neck dissection was done over observation group.
Conclusion: Based on the cumulative results obtained from the included studies, most of the authors concluded that in T1 lesions with no neck node involvement wait full watching and observation can be the treatment of choice. In T2, T3, T4 lesions with no neck involvement authors have advised to go for elective neck dissection as treatment of choice. Recent advances like Sentinal node biopsy can be used as a good diagnostic tool to evaluate for presence of

disease in the neck.More prospective clinical trails should be done to further evaluate the benefit of elective neck dissection done based on the reports obtained by sentinel lymph node biopsy in the treatment of early stages of SCC.
Keyword: Squamous Cell Carcinoma, Tumour, Oral Tongue, Node Negative, Early Lesion, Elective Neck Dissection, Observation

INTRODUCTION

Cancer is being identified as a leading cause of concern as the amount of morbidity and mortality associated with it is on an increasing trend. As per the study conducted by Bagan J, Sarrion G et al., out of all the cancers that affect the oral cavity, 90% of them are squamous cell carcinoma (1). As all tumors with epithelial origin metastasis occur predominantly through lymphatics rather than hematogenous spread, oral squamous cell carcinoma also being epithelial origin follows the same pattern. Squamous cell carcinoma of the oral cavity metastasis happens predominantly to the lymph nodes of the neck. Metastasis to the neck is considered as the regional metastasis and this regional metastasis is considered as one of the most important factors which decides the treatment plan and also it is one of the most important prognostic factors(2). Compared to all other subsites, oral tongue has a very unpredictable way of exhibiting metastasis. According to Pimenta Amaral et al even early oral tongue lesions exhibit skip metastasis(3). Skip metastasis is a phenomenon in which there is direct lateral nodal involvement without central nodal involvement. Normally involved lymph nodes which develop disease in them turn out to be stony hard in consistency and easily identified upon simple palpation, but one cannot be completely assured that the disease is absent in the neck if there are no clinically palpable lymph nodes. As far as present day scenario radiological confirmation with CT, MRI, ultrasound and positron emission tomography is being done to confirm absence of neck involvement(4). Although screening of clinically N0 neck by ultrasound, CT, MRI, or positron emission tomography (PET) can help with the detection of some of the non palpable nodal disease, what about those micro metastases that are seen in majority of the cases which if left untreated will lead to poor prognosis due to formation of metastatic lesions in the neck, and will be needing another surgery which will reduce the quality of life of the patient. According to Brugere et al.,1996; Khafif et al., 1991; Okamoto et al., 2002 the recurrence rate in the observed N0 neck is 23.7% to 42%(5)(6) . According to Young et al., approximately 25% of all clinically occult metastases are too small to be detected using any of the imaging techniques which are currently in clinical use(7).Ultrasound guided FNAC carried by an experienced clinician and a cytopathologist is the most accurate diagnostic method but still micro metastasis is not detected in this test.More accurate tests like sentinel node biopsy have proven to be better diagnostic test to rule out occult metastasis.Prospective randomized studies would be valuable to further evaluate the benefit of elective neck dissection determined by sentinel lymph node biopsy in the treatment of early stages Squamous cell carcinoma of the tongue(8)(9).

This systematic review was carried out to compare elective neck dissection and observation in the management of squamous cell carcinoma of tongue with clinically node negative neck and to assess which one has the better prognosis.

RESEARCH QUESTION

Which one of the following ,elective neck dissection or observation without neck dissection will give better prognosis for patients with early stage squamous cell carcinoma of tongue?

PICO Analysis

P Patients with early stages of squamous cell carcinoma of tongue
I Elective neck dissection
C Observation without neck dissection
O Recurrence and survival rate

MATERIALS AND METHODS:

The systematic review was enrolled in PROSPERO before beginning the study. PROSPERO ID: CRD42023430920.The Systematic review was conducted by following the methods of Cochrane systematic review and reported according to the guides lines put forward by Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Guidelines.

INCLUSION CRITERIA:

Types of studies -Randomized clinical trials , retrospective studies, prospective studies.

Types of Participants –

Patients with squamous cell carcinoma of tongue confirmed with biopsy and node negativity confirmed radiologically.

Types of Intervention

Elective neck dissection

Types of Comparison

Observation or wait full watching without neck dissection

Types of Outcome Measures

- Recurrence rates
- 5 years actuarian Survival rates

EXCLUSION CRITERIA:

The following studies were excluded,

- Case reports / Case series
- Literature review articles
- Animal model studies
- In vitro studies
- Studies which do not meet the inclusion criteria
- Literatures which were originally in non English language and cannot be translated by the reviewer.

Search strategy and sources

The final data which was collected for this study was performed according to PRISMA guidelines. Electronic data base search was performed using PubMed, Scopus, Cohrane , web of sciences and Google Scholar. Search terms used to achieve maximum data were: (‘‘well differentiated squamous cell carcinoma’’ OR ”ulceroproliferative lesion” OR “malignancy” OR “ “Tumor” OR ‘‘Cancer’’ OR ‘‘SCC’’ OR “Carcinoma”) AND (‘‘Tongue’’ OR ‘‘oral tongue’’OR “ muscular tongue “OR ‘‘mobile tongue’’) AND (‘‘T1 lesion’’ OR ‘‘T2 lesion’’ OR ‘‘early stage lesion ’’) AND (‘‘elective neck dissection’’ OR ‘‘END’’, ‘‘neck dissection’’ OR ‘‘no neck treatment’’ OR ‘‘observation’’ OR ‘‘wait and watch’’) AND (‘‘node-negative

neck" OR "N0 neck") as MeSH terms. Figure 1 shows the Screenshot of Google scholar search.

We used free-text terms to search the following journals"

- British Journal of Oral and Maxillofacial Surgery (BJOMS)
- Journal of Oral and Maxillofacial Surgery (JOMS)
- Journal of Cranio Maxillofacial Surgery
- Journal of oral oncology
- journal of otorhinolaryngology
- Journal of head and neck oncology

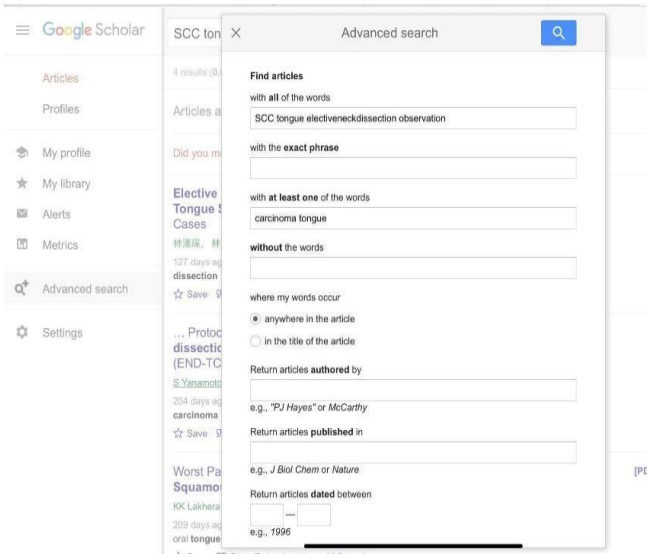


Figure 1-Screenshot of Google scholar search

The Figure 2 shows the Screenshot of PubMed search.

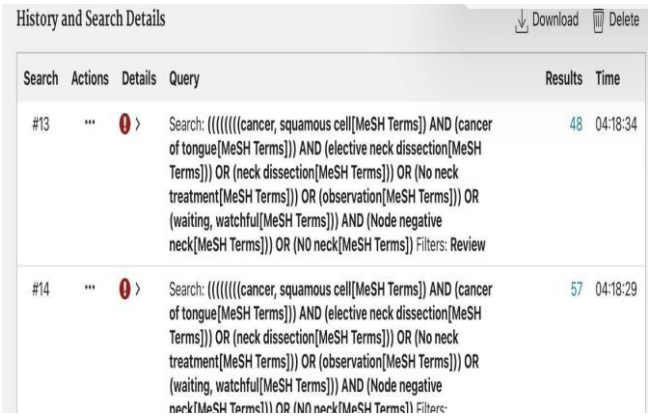


Figure 2-Screenshot of PubMed search

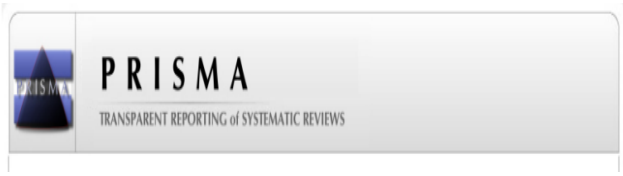
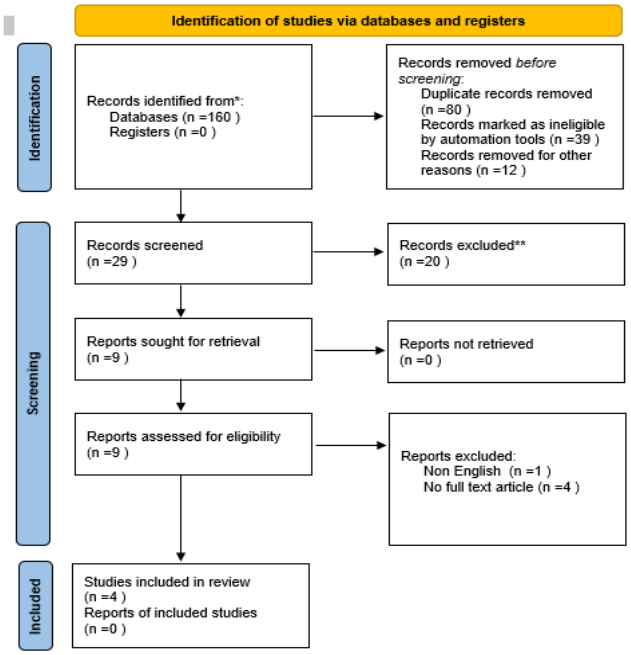


Figure 3: PRISMA 2020 Flow Diagram



** Records excluded were manually excluded as those studies included the patients who went for pre operative radio/chemotherapy.

Study screening and Selection

Based on the set of inclusion and exclusion criteria which were predetermined, the titles and the abstracts of the studies that were analysed for relevance independently by two review authors (Dr. Ruthvik, Prof. Dr. Murugesan K). Conflicts involving inclusion of the studies were resolved by discussion over the same. Abstracts of selected articles were reviewed independently. No articles were excluded after reading the abstract. Full text English language articles were retrieved for four studies which were found relevant for the study.

Data Extraction

Data extraction for general characteristics of studies and variables of outcome was done in Table 2 (General characteristics of the study). For each included study the following data was recorded: Author, Year, Study Type, Total sample size, study groups, interventions, method of evaluation, statistical test used for analysis, results and inference. We grouped and analysed studies based on the effect of two stage and single stage palatoplasty in Speech, Maxillary growth and Fistula formation.

TABLE: 1 Table of variables:

S.NO	VARIABLES OF INTREST
1.	Recurrence rate
2.	5 year actuarial disease free survival rate

RISK OF BIAS IN INCLUDED STUDIES (Table 2)

The study can be categorized into "high risk","moderate risk" and "low risk". If in the below mentioned table it did not record yes in more than three or three main categories it is considered as " high risk", if if two of the main sub headings didn't record yes it is considered as moderate risk and if all the four categories did not record yes then it is considered as "low risk". Blinding of follow up was considered adequate. Risk of bias and Quality

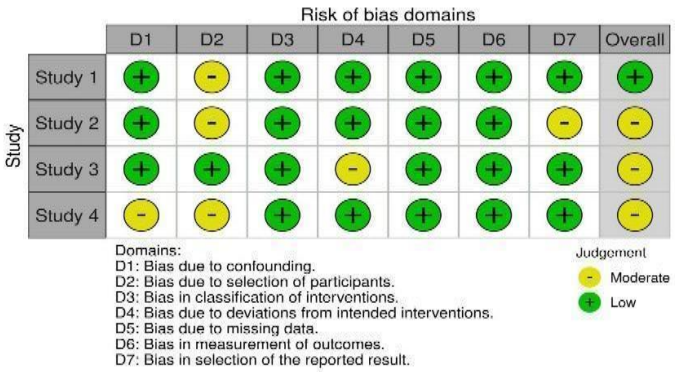
assessment was assessed using a software called Review Manager.

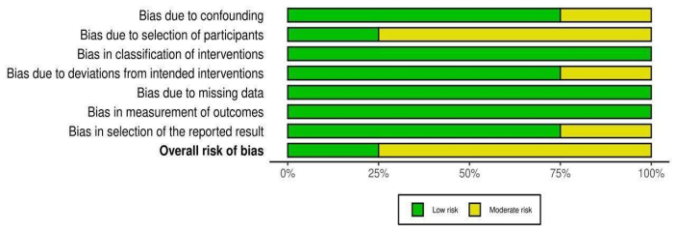
Table 2: Risk of bias

STUDY	RANDOMIZATION	ALLOCATION CONCEALED	ASSESSOR BLINDING	DROPOUT DESCRIBED
Giovanni Dell et al	Yes	No	Yes	Yes
Young chang lim et al	No	No	No	None
Anthony powing yuen et al	Yes	No	Yes	Yes
Zhien feng et al	No	No	No	None

The Figure 4 represents the Risk of bias

Figure 4: Risk of bias





According to

RESULTS:

Search results (Figure 3)

Electronic search from the data base was carried out using pre-determined keywords in the Search engines- PubMed, Cochrane and Google Scholar which yielded a total of 160 articles. 131 study record were removed before screening. 29 records were screened and then 25 records were excluded after reading titles. Four titles were identified from the search.

Figure 5: Study population

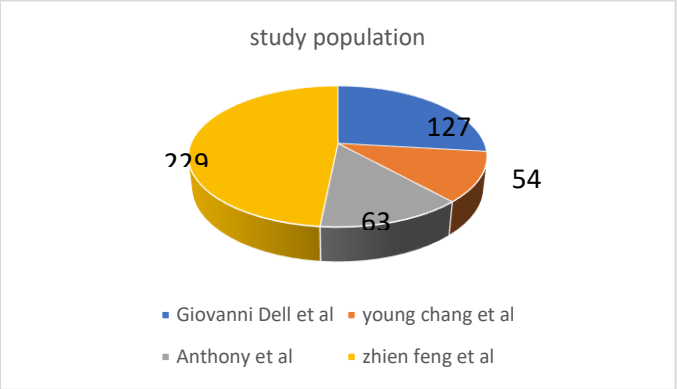


Table 3: characteristics table

S.No	Author/ year	Study design	Sample size /age	Groups	Method of evaluation	Results
1.	Giovanni Dell et al	Retrospective Study design	Total sample 127 with mean age of 52	66 patients in a group in which elective neck dissection was done. 61 patients in the group where only observation without neck dissection was opted.	Chi square test along with student t test for categorical data and	No statistical significance between END and observation group in T1N0 lesions
2.	Young chang lim et al	Retrospective Study design	Total sample size with mean age of 53	25 patients in a group in which elective neck dissection was done. 29 patients in the group where only observation without neck dissection was opted.	Chi square test for categorical data and Kaplan meier method compared using the log rank test	No statistically significant survival benefit between END and observation groups.
3.	Anthony powing yuen et al	Retrospective Study design	Total sample size 63 with mean age of 57 years	33 patients in a group in which elective neck dissection was done. 30 patients in the group where only observation	Fisher exact test for categorical data and life table method and Wilcoxon statistics	There is statistical siginificance showing reduced regional

				without neck dissection was opted.	for actuarial survival rates.	recurrence and recurrence related mortality
4.	Zhien feng et al	Retrospective study design	Total sample size of 229 patients with mean age of 55	156 patients in a group in which elective neck dissection was done. 73 patients in the group where only observation without neck dissection was opted.	students T test for categorical data and life table method and Wilcoxon statistics for actuarial survival rates.	In T1 lesions no significant difference is observed between 2 groups while in T2 lesions there is significant difference between recurrence rate and survival rate showing END as better treatment option

INTERPRETATION OF RESULTS (table 3 and figure 5):

4 retrospective studies included in this systematic review.

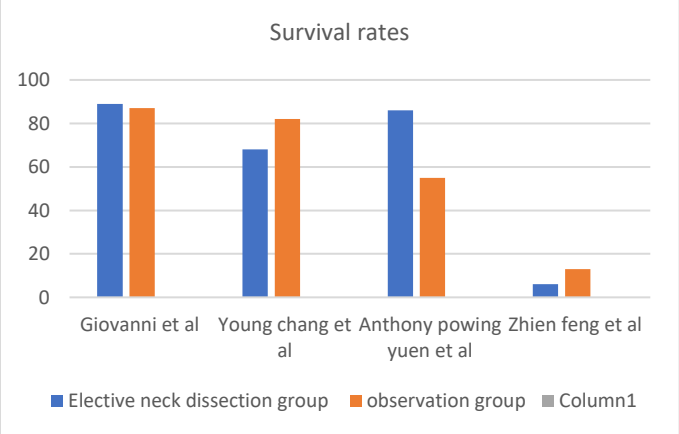
According to *Giovanni Dell et.,al* T1 tumours with depth of invasion less than or equal to 4mm wait full watching is preferred treatment option while in T2 lesion with depth of invasion more than 4mm elective neck dissection is preferred treatment option.

According to *Young chang et .,al.* there is no survival benefit that is statistically significant for patients who underwent elective neck dissection rather than observation. Thus observation of N0 neck for the treatment of early tongue carcinoma may not be harmful.

According to *Anthony powing yuen et.,al* elective neck dissection found to reduce regional recurrence rate and eventual regional recurrence related mortality. This study suggests elective / selective neck dissection is a treatment strategy of choice for stage I ,II carcinoma of the tongue.

According to *Zhien Feng et.,al* there is no significant difference in elective neck dissection over observation in recurrence rate and survival rate. While T2 lesion there is significant difference between recurrence rate and survival rate (figure 6 and table 4-5).

Figure 6: Survival rates and recurrence rates of included the studies



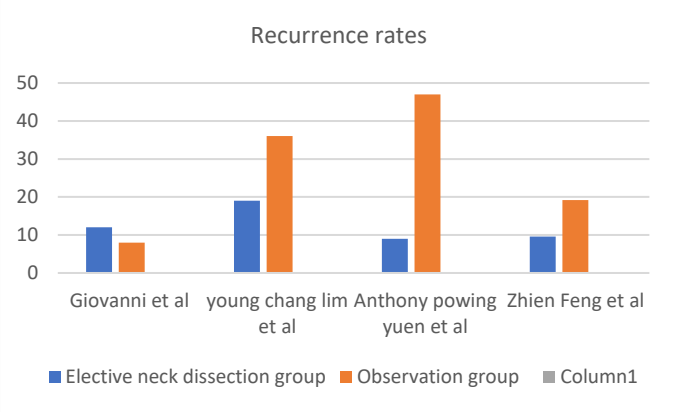


Table 4: Survival rates of included the studies

	Elective neck dissection group	Observation group
Giovanni et al	89%	85%
Young Chang lim et al	68%	82%
Anthony powing Yuen et al	85%	54%
Zhien Feng et al	86%	72%

Table 5: Recurrence rates of included studies

	Elective neck dissection group	Observation group
Giovanni et al		
Young Chang lim et al		
Anthony powing Yuen et al		
Zhien Feng et al		

DISCUSSION

The main goal of treatment of squamous cell carcinoma of the oral cavity is to eliminate the entire lesion surgically along with 2 cm of clinically healthy or normal tissue. As we all know that all epithelial originated tumours have lymphatic spread and primary surgery alone will not suffice in cases where there is proper evidence of lymphatic infiltration. When it is about the oral cavity squamous cell carcinoma the lymphatic spread is mostly to the cervical lymph nodes(10).Sub-mental , sub-manbibular, jugular group of the lymph nodes are graded into level I to level V are in main focus. Along with primary surgery, neck dissection of the nodes is also an important part of surgical treatment for better prognosis(11). Lymph node involvement is generally confirmed initially by clinical palpation, all the involved nodes turn round in shape and become stony hard on palpation. It is not always necessary that clinically absence indicates actual absence of the nodal spread in the neck. Radiographic confirmation is generally practiced as of now in most of the centers. Generally in cases of early lesions like T1 and T2 lesions there is N0 (no neck nodal involvement), but there have been reported cases of local recurrence in the neck even though there is no nodal involvement confirmed by the radiographic analysis. This kind of local recurrence is mainly seen in cases of squamous cell carcinoma of the tongue. As SCC of the tongue exhibits spik metastasis its is very difficult to clinically find out such kind of metastasis. Apart from size of the lesions it has been proved that depth of invasion also determines the prognosis of the disease in terms of metastasis. It has been seen that lymph node metastasis increases as the depth of tumour increases more than 4mm(12). Surgical treatment of these neck involved patients include neck dissection in which all the lymph nodes along with fibrofatty tissues are removed. Based on the levels of neck nodes removed and structures along with them which are removed or preserved there are various types of neck dissections. Mostly in lesions with clinical node involvement and primary lesion at oral cavity selective and modified radical neck dissection is mostly practiced. When there is a neck involvement along with the primary lesion there is no much confusion with the treatment plan involved, confusion happens when there is primary lesion in the oral cavity but no clinical or radiological evidence of the neck involvement(13). Many centers across the globe follow different surgical protocols in such cases. Some centers believe in waitfull watching without performing neck dissection while some centers believe that performing elective neck dissection gives a better outcomes interms of recurrence rates as well as disease free survival period. In this review based on the existing literature we have come to a conclusion that in T1 and T2 lesions with limited depth of invasion observation without any neck dissection gave good prognosis and also better quality of life. Where as in lesions with T3 and T4 clinical category even without neck node involvement (N0) elective neck dissection gave better prognosis in terms of recurrence rates and disease free survival rates.Yu et al. in 2006 reported a survival rate of 5 years in 100% after elective neck dissection, versus 68,7% of survival in patients that were only observed (14).

CONCLUSION

Based on the cumulative results obtained from the included studies , most of the authors concluded that in T1 lesions with no neck node involvement wait full watching and observation can be the treatment of choice. In T2 lesions with no neck involvement authors have advised to go for elective neck dissection as treatment of choice.Prospective randomized studies would be worthwhile to further evaluate the benefit of elective neck dissection informed by sentinel lymph node biopsy in the treatment of early stage SCC.

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