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Review Article

2 - 5 Years Survival Rate of Patients Treated for Oral Squamous Cell carcinoma: A Systematic Review

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Abstract

Objective: The objective of this study is to comprehensively evaluate 2 - 5 years survival rate and local-regional control outcomes of patients with advanced stage OCSC, who underwent some kind of treatment.

Data Source: An extensive systematic literature search was performed using Pubmed, using combination of keywords like Squamous cell carcinoma, Survival rate, Oral, Malignancy, Cancer, Mortality rate, Death rate, Mouth, Face.

Study Eligibility Criteria

Inclusion Criteria: Studies that provide information about 2, 3 and 5 years survival rate of patients treated with oral squamous cell carcinoma.

Exclusion Criteria: Review articles, letter to editor, clinical trials.

Participant: Patient who underwent treatment for Squamous cell carcinoma.

Results: Through search strategy 2772 articles were yielded. After screening through title and abstracts, 268 articles remained. After removing duplicates 81 articles were obtained. Abstracts of all 81 articles were screened to get 37 free full text articles. Out of 37 article, 9 articles were selected after reading full text. 2 articles were selected from other sources. And thus 11 studies were finally used for this systematic review according to the eligibility criteria.

Conclusion: The study confirmed that oral cancer remains serious problem in terms of risk factors, delayed diagnosis and overall Survival rates. Overall survival rate also depends on the stage and grade of differentiation of the tumour.

Keywords: *Squamous Cell Carcinoma; Survival; Oral*

Introduction

Rationale

Oral carcinoma is the sixth most common cancer in the world and the most frequent cancers in the head and neck region [1]. Squamous cell carcinoma is the most frequent histological type in oral cavity [1]. The management of patients with locally advanced head and neck squamous cell carcinoma (HNSCC) has undergone several major paradigm shifts in the last 2 decades [2]. Despite improvements in treatment, the overall survival has not increased significantly for oral cancer over the past decades [1].

The most important prognostic factor is TNM staging. Survival also may be affected by patient co-morbidity, performance status, biological and histological parameters and treatment modality [1].

Conventional treatment for locoregionally advanced head and neck cancer has included either radical surgery and adjuvant radiotherapy or radiotherapy alone. Although progress has been achieved in radical surgical resection with reconstruction and use of postoperative radiotherapy/chemoradiotherapy, the 5-year survival rate has not improved substantially in recent years, remaining at 50% to 60% and even lower in patients with locally advanced lesions [4]. The overall 5-year survival rate is 62% in industrial countries, while in developing countries they hardly reached the rate of 30% [5]. The death rate associated with this cancer is particularly high not because it is difficult to detect or diagnose, but due to the cancer being routinely diagnosed late [5].

Surgery with radiotherapy is the most common practice and has been proven to improve locoregional control and overall survival of T1 or T2 stage SCCHN patients. While chemotherapy is recommended for T3, T4a, and T4b stages [7]. For patients with oral cavity squamous cell carcinoma (OCSCC) there is evidence that postoperative chemoradiation (CRT) can improve survival for high risk patients by approximately 6.5% but this is associated with additional morbidity [9].

Focussed Question

What is the % of patients with 2-5 years survival rate, following treatment of oral squamous cell carcinoma?

Objectives of the Study

1. To assess the literature regarding the 2 - 5 year survival rate of patients treated with oral squamous cell carcinoma.
2. To assess the disease free survival and locoregional control of the patients treated for oral squamous cell carcinoma.

Methods

Eligibility Criteria

Inclusion criteria

1. Literature written in English language were accepted.
2. Articles published between Jan 2012- Dec 2016.
3. Studies conducted worldwide.

Exclusion criteria

1. Reviews, abstracts, editorials, letters, and historical reviews were not included in the search.
2. Publication written in languages other than English.
3. Squamous cell carcinoma together with other kinds of tumours.
4. Studies that focused on other types of cancer.

PIO:

- **P:** Patients treated for Oral Squamous cell carcinoma.
- **I:** Radiotherapy and or chemotherapeutic agents.
- **O:** 5 years survival rate.

Information sources

Evidence from Internet sources were used in the satisfactory search of appropriate papers for the study. The National Library of Medicine (MEDLINE PubMed) and manual search using DPU college library resources. All the cross reference lists of the selected studies were screened for additional papers that could meet the eligibility criteria of the study.

The databases were searched up to and including December 2016 using the search strategy.

Search strategy for PubMed

1. Oral AND squamous cell carcinoma AND survival rate
2. Oral AND Malignancy AND survival rate
3. Oral AND cancer AND survival rate
4. Oral AND squamous cell carcinoma AND mortality rate
5. Oral AND Malignancy AND mortality rate
6. Oral AND cancer AND mortality rate

Sr. No.	Search strategy	Number of articles	Number of selected articles	After Duplicate Removal
1	Oral AND squamous cell carcinoma AND survival rate	76	43	21
2	Oral AND Malignancy AND survival rate	666	45	7
3	Oral AND cancer AND survival rate	670	43	00
4	Oral AND squamous cell carcinoma AND mortality rate	68	43	5
5	Oral AND Malignancy AND mortality rate	639	46	2
6	Oral AND cancer AND mortality rate	653	48	2
Total no of articles		2772	268	37

Study selection

Preliminary screening consisted of 2772 articles in total, out of which 11 articles were selected. The articles were screened independently by 4 reviewers. Initially the articles were screened on the basis of title. The selected articles were 268. Duplicates from 268 screened articles were removed to get 81 articles and abstract was made ready. As the second step, 81 abstracts were again screened to get 37 free full text articles. Out of 37 articles only 11 fulfilled the inclusion criteria. And thus 11 articles were selected for the study.

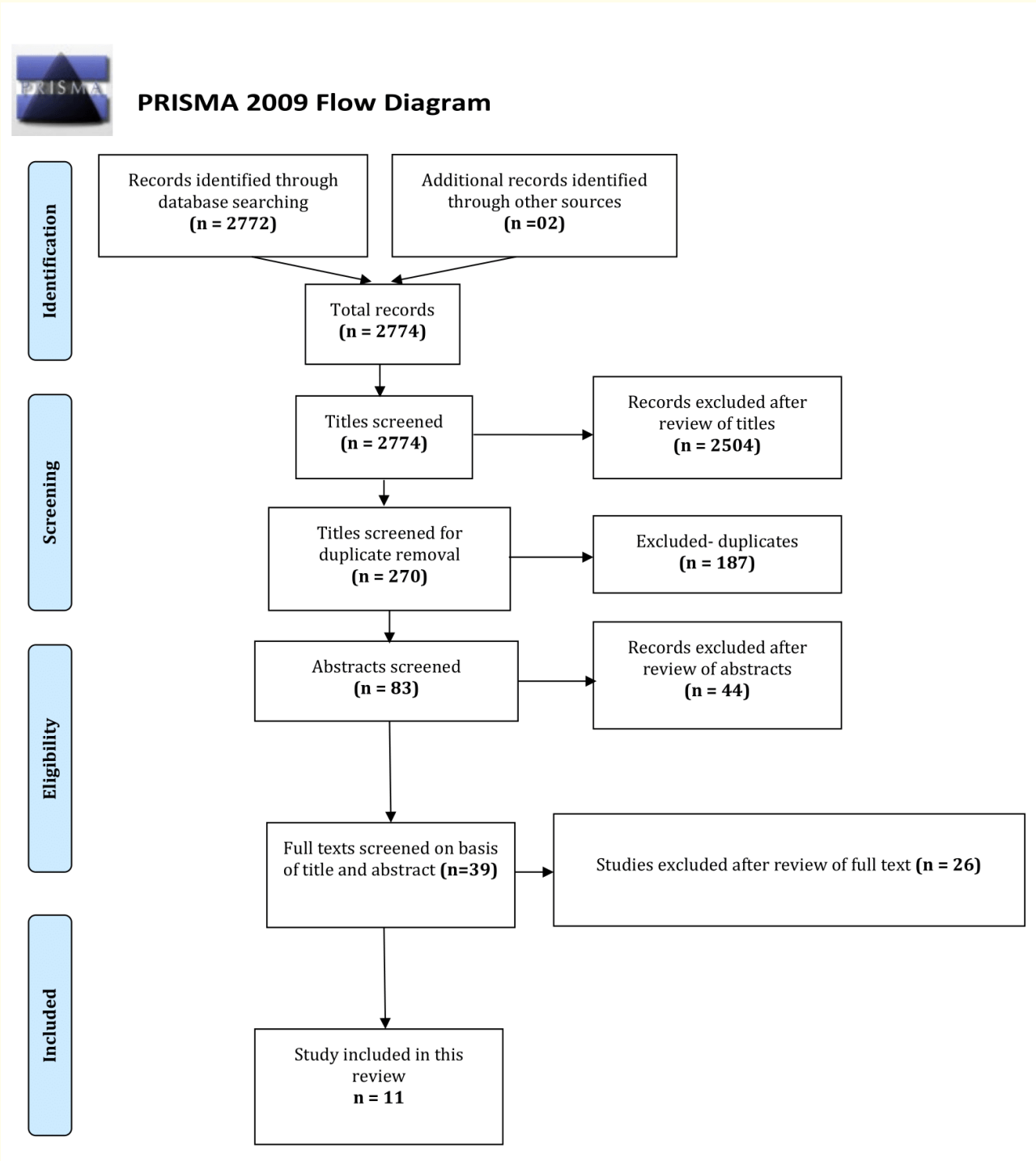
Data collection process

A standard pilot form in excel sheet was initially used and then all those headings not applicable for review were removed. Data extraction was done for one article and this form was reviewed by an expert and finalized. This was followed by data extraction for all the other articles.

Data items

The data items included were

1. Author - The name of the author
2. Location - The country in which the study took place
3. Year of publication - The year in which the study was published
4. Objective - why the study is being performed.
5. Study design - If the study was a control or a clinical trial.
6. Study duration - period during which the study was performed
7. Sample size - No of participants included in the study
8. Setting - Place where the study was conducted
9. Population - population from where the patients were selected.
10. Intervention - Radiotherapy and or chemotherapeutic agents.
11. Outcome- Result of the study
12. Side effects - any adverse drug reaction
13. Conclusion
14. Remark- comments of author



Discussion

Outcome of the patients with oral cancer is poor. The selection of treatment is according to tumour site, clinical stage, patient performance status, physician and patient preference. Survival remains the gold standard of treatment outcomes.

Presenting with an advanced stage lesion contributed to the result. Detecting in early stages offers the best chance of long-term survival. Surgery with radiotherapy is the most common practice and has been proven to improve locoregional control and overall survival of T1 or T2 stage SCCHN patients.

The role of chemotherapy in advanced cases remains to be defined. Elective neck dissection at the time of resection of the primary tumor confers an overall survival benefit in patients with early-stage, clinically node-negative oral squamous-cell carcinoma.

This study aimed at estimating 2 - 5 years overall survival rate of patients treated with oral squamous cell carcinoma. The high incidence, prevalence and mortality rate and low survival reported warranted the importance of the study.

Summary of Evidence

Larizadeh MF., *et al.* [2] studied total number of 69 patients with squamous cell carcinoma of the oral cavity that refused surgery or had unresectable tumour.

The patients with locoregionally advanced disease (57 patients with T3, T4 lesions and/or N+) induction chemotherapy following by concomitant chemoradiation was used. Induction chemotherapy consisted of 3 cycles of Cisplatin and 5-Flourouracil with or without Docetaxel. Weekly cisplatin was used in concomitant protocol.

Overall survival rates of 38% and 26% were observed at 2 and 3 years, respectively. The patients above 50 years had lower survival rate compared to younger patients. Overall survival was significantly reduced with advanced stage. Node positive patients had lower survival. Survival was better for T1/T2 lesions compared to T3/T4 tumors.

Harada H., *et al* [5] Study evaluated whether preoperative chemotherapy with S-1 and concurrent radiotherapy is feasible and efficacious in the treatment of advanced oral squamous cell carcinoma. All patients received a total radiation dose of 40 Gy, in once daily 2-Gy fractions, and received S-1 at 65 mg/m^2/day for 5 consecutive days, over 4 consecutive weeks with concurrent radiotherapy. Concurrent administration of S-1 and radiotherapy combined with surgery offers a well-tolerated method of successfully treating advanced oral squamous cell carcinoma.

Zhong LP., *et al.* [6] Conducted study to evaluate induction chemotherapy with docetaxel, cisplatin, and fluorouracil (TPF) followed by surgery and postoperative radiotherapy versus up-front surgery and postoperative radiotherapy in patients with locally advanced resectable oral squamous cell carcinoma (OSCC). Patients received two cycles of TPF induction (docetaxel 75 mg/m2 on day 1, cisplatin 75 mg/m^2 on day 1 and fluorouracil 750 mg/m^2 on days 1 to 5) followed by radical surgery and postoperative radiotherapy *(*54 to 66 Gy) versus up-front radical surgery and postoperative radiotherapy. The estimated 2-year OS was 68.2% and 68.8% in the control and experimental arms, respectively. The 2-year DFS was 63.6% and 62.2% in the control and experimental arms, respectively. Study failed to demonstrate that TPF induction chemotherapy improves survival compared with up-front surgery in patients with resectable stage III or IVA OSCC.

Albano PM., *et al.* [4] Studied Patient with squamous cell carcinoma of the oral cavity at the MMMH-MC between January 2003 and April 2012 were retrospectively reviewed. Treatment received was classified into radiotherapy, chemotherapy, a combination of 2 or more, or none at all.

Donato V., *et al.* [7] studied patients with oral cavity cancer treated with exclusive radiotherapy or concomitant chemoradiotherapy. Simultaneous integrated boost (SIB) in 30 fractions scheme was prescribed to all patients, using Helical Tomotherapy. Doses administered to primary tumour, oral cavity and positive lymph-nodes and negative lymph-nodes were 66 - 67.5 Gy, 60 - 63 Gy and 54 Gy, respectively. Chemotherapy (either carboplatin 100mg/m or cisplatin 80 mg/m was given intravenously every 3 weeks. The 1 and 2-year OS rate was 55.6%,

While the 1 and 2-year DFS rate was 75%. Concomitant radiochemotherapy or exclusive radiotherapy represents an important therapeutic option and a valid alternative to surgery, in patients affected by locally advanced and inoperable oral cavity carcinoma.

Chinn SB., *et al.* [8] conducted Retrospective cohort study, to evaluate the efficacy of an induction selection (IS) concurrent chemoradiation (CRT) protocol versus primary surgical extirpation in advanced oral cavity squamous cell carcinoma (OCSCC). OS at 5-years was 32% in the IS group and 65% in the surgical cohort. DSS at 5-years was 46% in the IS group and 75% in the surgical cohort. LRC at 5-years was 26% in the IS cohort and 72% in the surgical cohort. This cohort study strongly suggests that primary surgical extirpation with selective PORT/chemotherapy for adverse features results in better OS, DSS and LRC than an IS protocol.

Schneider I J C., *et al.* [10] studied 141 patients with oral cancer in a retrospective cohort study. 0verall 5 year survival was 33.3%.

Nguyen -Tan P H., *et al.* [9] studied the efficacy and toxicity of cisplatin plus accelerated fractionation with a concomitant boost (AFX-C) versus standard fractionation (SFX) in locally advanced head and neck carcinoma, patients were assigned to receive the experimental AFX-C or the control SFX. AFX-C consisted of 72 Gy in 42 fractions over 6 weeks with twice per-day irradiation for the last 12 treatment days, whereas SFX consisted of 70 Gy in 35 fractions over 7 weeks. Cisplatin dose was 100 mg/m^2 given once every 3 weeks for two cycles to patients on the AFX-C arm and for three cycles to patients on the SFX arm. When combined with cisplatin, AFX-C neither improved outcome nor increased late toxicity in patients with LA-HNC.

Ghosh S., *et al.* [1] studied the efficacy of concurrent chemoradiation using 40 mg/m^2 weekly cisplatin. This single institutional retrospective study included the data of 266 locally advanced head and neck cancer patients who were treated with concurrent chemoradiation using 40 mg/m^2 weekly cisplatin. The study showed the 3 year local control, locoregional control and disease free survival as 62.8%, 42.8% and 42.1% of the study patients. They concluded that the treatment of LAHNC with 40 mg/m2 weekly cisplatin based chemoradiation is effective and less toxic.

Iyer GN., *et al.* [3] conducted a study to compare concurrent chemotherapy and radiotherapy (CCRT) with surgery and adjuvant radiotherapy (RT) in patients with stage III/IV nonmetastatic head and neck squamous cell carcinoma. Total of 119 patients, 60 patients were randomized to primary surgery (S arm) and 59 patients were randomized to CCRT (C arm). Human papillomavirus status was tested in 75 patients, and only 3 were found to be positive. The median follow-up for surviving patients was 13 years. Analysis of the entire cohort demonstrated no statistically significant difference in overall survival and disease-specific survival (DSS): 5-year rates were 45% versus 35% for overall survival (P5.262) and 56% versus 46% for DSS (P5.637) for the S arm and C arm, respectively. This study conclude providing strong support for primary surgery as the main modality of treatment for the subsites

Tonchev K., *et al.* [5] the sites of oral cancer like tongue, floor of mouth, hard palate, retromolar trigone/area, upper gingiva, lower gingiva, buccal mucosa, lips), stages (I, II, III, IV) and degree of differentiation (well, moderately, poorly, undifferentiated) were recorded according to the TNM classification of carcinomas of the oral cavity. The overall 5-year survival rate was 36% while the disease-specific survival rate was 45%. The overall 5-year survival rate by stage was found to be as follows - stage I (67%), stage II (51%), stage III (33%), stage IV (15%).

Conclusion

Globally oral cancer represents an incidence of 3 percent (males) and 2 percent (females) of all malignant neoplasms, it has one of the lowest survival rates-50 percent, within a five-year period. World Health Organization reported oral cancer as having one of the highest mortality ratios amongst all malignancies.

The overall survival rate of patients treated for oral squamous cell carcinoma was different for different studies conducted in the period Jan2010 to Dec 2016.

The study confirmed that oral cancer remains serious problem in terms of risk factors, delayed diagnosis and overall Survival rates. Overall survival rate depended also on the stage and grade of differentiation of the tumor.

Though these studies are showing satisfactory results in 2 - 3 years, long term survival rate is questionable with current treatment modalities. Furthermore, studies are advised with modern techniques and newer drugs to increase survival rate of patients with oral cancer.

Further considering mortality and quality of life associated with current treatment modalities, question arises that are these treatment modalities justifiable?

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