RECURRENCE OF ORAL CANCER FOLLOWING TREATMENT IN AN INSTITUTIONAL SET UP - A RETROSPECTIVE ANALYSIS OF THE ASSOCIATED FACTOR

Sindhu Priya Kuppusamy Sundara Murthy¹, Dr. Mahathi. N², Dr. Suresh

Abstract

Incidence of cancers of the oral cavity is increasing and has replaced laryngeal cancer as the most frequently occurring cancer in the head and neck area. Routine follow up is must for a period of 6 months to 1 year after treatment. Current guidelines advocate a follow-up period of at least 5 years to evaluate the time of recurrence following the treatment of oral cancer. Data samples required for study were taken from hospital records. All the collected data were cross verified and compiled together in an excel sheet. Compiled data were statistically analysed in SPSS software. In this study, a total of 51 patients with oral cancer had undergone treatment. 74.51% of patients reported back without any recurrence after a follow-up period of 6 months to 1 year. On associating recurrence with age it was noted that the recurrence was more in higher age groups p value of 0.025. Recurrence was common in males than females with p value of 0.025 (<0.05). To conclude, the majority of the patients in the study had no recurrence following treatment in the above follow-up period.

Keywords: Laryngeal cancer, Recurrence, Tumour.

Introduction

Head and neck squamous cell carcinoma are the 6^{th} most common malignancies in the world. The oral cavity is the most common subsite and makes upto 3% of all cancer cases worldwide. Oral squamous cell carcinoma has poor prognosis and in case of relapse with mortality rates upto $92\%^{1,2,3}$.

Surgery is the preferred treatment for squamous cell carcinoma. Despite great progress in chemotherapy and radiotherapy, the prognosis of OSCC is poor due to aggressive local invasion and metastasis, leading to recurrence⁴.

After curative treatment of primary tumour, recurrence rates range from 7 - 47.7% have been reported. Even though significant improvements in diagnostics and treatment modalities were made, tumour relapse is one of the major problems. Upto 86% of all recurrent tumours recur in the first 2 years after treatment^{5,6}.

¹ Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical sciences (SIMATS), Saveetha University, Chennai - 77, India, Email ID: <u>151501024.sdc@saveetha.com</u>

² Corresponding author: Reader, Department of Oral and Maxillofacial surgery, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical sciences (SIMATS), Saveetha University, Chennai - 77, India, Email ID: mahathin.sdc@saveetha.com

³ Reader, Department of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical sciences (SIMATS), Saveetha University, Chennai - 77, India, Email ID: suresh@saveetha.com

The incidence, recurrence and mortality rate of OCC are increasing. Monitoring the trends in OCC is essential for optimised prevention, treatment, and surveillance care for the growing group of patients, therefore in order to slightly improve the survival rates⁷.

Previously our team had conducted numerous clinical trials⁸⁻¹¹ and lab animal studies¹²⁻¹⁹ and in-vitro students²⁰⁻²² over the past 5 years. Now we are focusing on epidemiological surveys. The aim of this study is to evaluate the time of recurrence following the treatment of oral cancer in a private hospital.

Materials and method

All the data of patients who underwent treatment for oral cancer and returned with recurrence of oral cancer were taken for the study as a sample. The study setting was a university setting. Exclusion criteria was case sheets with incomplete data and those patients who did not come for follow up visits when called.

Data was collected from case sheets of patients who reported during the months of October 2019 and March 2020 from the hospital record management system where all the records of patients regarding their medical and dental history and treatment done are stored. Cross verification was done to avoid bias by another examiner. To avoid missing any data, photographic evaluation was done.

All the relevant data were retrieved and tabulated in excel sheet. Later, it was statistically analysed by IBM SPSS statistics, using the Chi-Square test. Independent variables are the total number of treated patients and dependent variables are recurrence of oral cancer.

Results

The study consisted of a total of 51 patients, among which 34 patients were males, and 17 patients were females. All the 51 patients had undergone treatment for oral cancer, among which 12 patients had recurrence of oral cancer and 39 had no recurrence. The percentage of patients with recurrence is 25.49% and without recurrence is 74.51% (Fig.1). 5.88% from 46-60 and 19.61% from >60 age groups had recurrence. 19.61% from 30-45, 21.57% from 46-60 and 33.33% from >60 age groups had no recurrence with p value of 0.025 (<0.05) (Fig.3). 15.69% of males had recurrence and the rest 56.86% had no recurrence. The number of females who had recurrence of oral cancer were 9.80% and without was 17.65% with p value of 0.025 (<0.05) (Fig.2). The percentage of recurrence that occurred within 1-2 months was 58.33%, within 3-4 months was 25% and after more than 5 months was 15.62% (Fig.4).

Discussion

In the present study, a higher percentage of patients did not have recurrence of oral cancer.

In a study by Bo wang, 32.7% of patients had recurrence. Chi square test showed that in the T-stage, degrees of differentiation were important factors of recurrence. The 2- and 5- year survival rates were lower in patients with recurrence than in those without^{23,24}. Factors that influence the recurrence of OSCC have been explored in recent years. Ebrahim et al and Camisasca have analysed patient's clinico pathological data, including tumour sites, clinical and pathological stages, invasion mode and perineural invasion. They concluded that tongue cancer and poor differentiation contributed to recurrence after surgery²⁵.

Vasquez et Al reported recurrence rate of 44.9% in 118 patients. The important factors were co-morbidities rate, degree of tumour differentiation and stage. In another study, it suggested that when the treatment involved only surgery, the recurrence rate was higher. When combined with chemotherapy and radiotherapy, complete tumour resection with various flaps reduces tumour recurrence, suggested by Bo Wang^{26,27}.

Vincente et Al followed up to 98 patients with OSCC, the mortality rate 47% in patients with flap repair and 67% in patients without flap repair. Capote et Al suggested careful removal of lymph nodes with primary resection of tumours. Because the OSCC might metastasize into the sternocleidomastoid muscle lymph groups, these should be removed during surgery. The recurrence rate in their study was 32.7%. Lopez Rodriguez et al reported that preoperative radiotherapy and chemotherapy for OSCC at N2-N3 stage can completely control neck lymph node metastasis^{28,29}.

In the present study, the reason for the low recurrence rate of 25.49% is highly due to combination therapy of surgery and chemotherapy and radiotherapy.

This study could be further improved by increasing the sample size and checking at a molecular level using biomarkers to predict the recurrence and prognosis of oral cancer.

Conclusion

Oral squamous cell carcinoma is a commonly occurring oral cancer and it is associated with significant mortality and morbidity. The purpose of this study was to evaluate the recurrence of oral cancer following treatment in order to provide better prognosis and quality of life. In our study, the majority of the patients did not have recurrence and it was found to be statistically significant that the majority of people had recurrence within 1-2 months following treatment.

AUTHORS CONTRIBUTION First author, Sindhupriya performed the data collection by reviewing patient details, filtering required data, analysing and interpreting statistics and contributed to manuscript writing.

Second author, Dr.Mahathi contributed to conception of study title, study design, analysed the collected data, statistics and interpretation and also critically revised the manuscript.

Third author, Dr. Suresh. V participated in the study and revised the manuscript. All the three authors have discussed the results and contributed to the final manuscript.

ACKNOWLEDGMENT This research was supported by Saveetha Dental College and Hospital. We thank the department of Oral Medicine, Saveetha Dental College for providing insight and expertise that greatly assisted this research.

CONFLICT OF INTEREST The authors declare that there

is no conflict of interests.

References

- 1. Bagan JV, Scully C. Recent advances in Oral Oncology 2007: epidemiology, etiopathogenesis, diagnosis and prognostication. Oral Oncol [Internet]. 2008 Feb;44(2):103–8. Available from: http://dx.doi.org/10.1016/j.oraloncology.2008.01.008
- van Dijk BAC, Brands MT, Geurts SME, Merkx MAW, Roodenburg JLN. Trends in oral cavity cancer incidence, mortality, survival and treatment in the Netherlands. Int J Cancer [Internet]. 2016 Aug 1;139(3):574–83. Available from: http://dx.doi.org/10.1002/ijc.30107
- 3. Rogers SN, Brown JS, Woolgar JA, Lowe D, Magennis P, Shaw RJ, et al. Survival following primary surgery for oral cancer. Oral Oncol [Internet]. 2009 Mar;45(3):201–11. Available from: http://dx.doi.org/10.1016/j.oraloncology.2008.05.008
- 4. Johnson FE, Maehara Y, Browman GP, Margenthaler JA, Audisio RA, Thompson JF, et al. Patient Surveillance After Cancer Treatment [Internet]. Springer Science & Business Media; 2013. 538 p. Available from: https://play.google.com/store/books/details?id=ZcZDAAAAQBAJ
- 5. McGarry GW, Mackenzie K, Periasamy P, McGurk F, Gatehouse S. Multiple primary malignant tumours in patients with head and neck cancer: the implications for follow-up. Clin Otolaryngol Allied Sci [Internet]. 1992;17(6):558–62. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2273.1992.tb01718.x
- 6. Curtis RE. New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000 [Internet]. U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2006. 492 p. Available from: https://play.google.com/store/books/details?id=z28dJN3EdAYC
- 7. Coviello V, Boggess M. Cumulative Incidence Estimation in the Presence of Competing Risks. Stata J [Internet]. 2004 Jun 1;4(2):103–12. Available from: https://doi.org/10.1177/1536867X0400400201
- 8. Jesudasan JS, Wahab PA, Sekhar MM. Effectiveness of 0.2% chlorhexidine gel and a eugenol-based paste on postoperative alveolar osteitis in patients having third molars extracted: a randomised controlled clinical trial. British Journal of Oral and Maxillofacial Surgery. 2015 Nov 1;53(9):826-30.
- 9. Santhosh Kumar, M.P., RAHMAN R. Knowledge, awareness, and practices regarding biomedical waste management among undergraduate dental students. Asian J Pharm Clin Res. 2017;10(8):341-5.

- 10. Christabel A, Anantanarayanan P, Subash P, Soh CL, Ramanathan M, Muthusekhar MR, Narayanan V. Comparison of pterygomaxillary dysjunction with tuberosity separation in isolated Le Fort I osteotomies: A prospective, multi-centre, triple-blind, randomized controlled trial. International journal of oral and maxillofacial surgery. 2016 Feb 1;45(2): 180-5.
- 11. Marimuthu M, Andiappan M, Wahab A, Muthusekhar MR, Balakrishnan A, Shanmugam S. Canonical Wnt pathway gene expression and their clinical correlation in oral squamous cell carcinoma. Indian Journal of Dental Research. 2018 May 1;29(3):291.
- 12. Packiri S, Gurunathan D, Selvarasu K. Management of paediatric oral ranula: a systematic review. Journal of clinical and diagnostic research: JCDR. 2017 Sep;11 (9):ZE06
- 13. Santhosh Kumar, M.P. Relationship between dental anxiety and pain experience during dental extractions. Asian J Pharm Clin Res. 2017;10(3):458-61.
- 14. Patil SB, Durairaj D, Kumar GS, Karthikeyan D, Pradeep D. Comparison of extended nasolabial flap versus buccal fat pad graft in the surgical management of oral submucous fibrosis: a prospective pilot study. Journal of maxillofacial and oral surgery. 2017 Sep 1;16(3):312-21.
- 15. Rao TD, Santhosh Kumar, M.P. Analgesic Efficacy of Paracetamol Vs Ketorolac after Dental Extractions. Research Journal of Pharmacy and Technology. 2018;11(8): 3375-9.
- 16. Abhinav RP, Selvarasu K, Maheswari GU, Taltia AA. The patterns and etiology of maxillofacial trauma in South India. Annals of maxillofacial surgery. 2019 Jan;9(1): 114.
- 17. Santhosh Kumar, M.P., Snena S. Knowledge and awareness regarding antibiotic prophylaxis for infective endocarditis among undergraduate dental students. Asian J Pharm Clin Res. 2016;9: 154-9.
- 18. Santhosh Kumar, M.P. The emerging role of botulinum toxin in the treatment of orofacial disorders: Literature update. Asian J Pharm Clin Res. 2017;10(9):21-9.
- 19. Rahman R, Santhosh Kumar, M.P. Knowledge, attitude, and awareness of dental undergraduate students regarding human immunodeficiency virus/acquired immunodeficiency syndrome patients. Asian J Pharm Clin Res. 2017;10(5):175-80.
- 20. Santhosh Kumar, M.P., Sneha S. Knowledge and awareness regarding antibiotic prophylaxis for infective endocarditis among undergraduate dental students. Asian J Pharm Clin Res. 2016;9: 154-9.
- 21. Patturaja K, Pradeep D. Awareness of Basic Dental Procedure among General Population. Research Journal of Pharmacy and Technology. 2016;9(9): 1349-51.
- 22. Jain SV, Muthusekhar MR, Baig MF, Senthilnathan P, Loganathan S, Wahab PA, Madhulakshmi M, Vohra Y. Evaluation of three-dimensional changes in pharyngeal airway following isolated lefort one osteotomy for the correction of vertical maxillary excess: a prospective study. Journal of maxillofacial and oral surgery. 2019 Mar 8;18(1):139-46.
- 23. Pagh A, Grau C, Overgaard J. A longitudinal study of follow-up activities after curative treatment for head and neck cancer. Acta Oncol [Internet]. 2015 May;54(5):813–9. Available from: http://dx.doi.org/10.3109/0284186X.2015.1028591
- 24. Wang B, Zhang S, Yue K, Wang X-D. The recurrence and survival of oral squamous cell carcinoma: a report of 275 cases. Chin J Cancer [Internet]. 2013 Nov;32(11):614–8. Available from: http://dx.doi.org/10.5732/cjc.012.10219
- 25. Lindenblatt R de CR, Martinez GL, Silva LE, Faria PS, Camisasca DR, Lourenço S de QC. Oral squamous cell carcinoma grading systems--analysis of the best survival predictor. J Oral Pathol Med [Internet]. 2012;41(1):34–9. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0714.2011.01068.x
- 26. Ebrahimi A, Clark JR, Zhang WJ, Elliott MS, Gao K, Milross CG, et al. Lymph node ratio as an independent prognostic factor in oral squamous cell carcinoma. Head Neck [Internet]. 2011 Sep;33(9):1245–51. Available from: http://dx.doi.org/10.1002/hed.21600
- 27. Vázquez-Mahía I, Seoane J, Varela-Centelles P, Tomás I, Álvarez García A, López Cedrún JL. Predictors for tumor recurrence after primary definitive surgery for oral cancer. J Oral Maxillofac Surg [Internet]. 2012 Jul;70(7):1724–32. Available from: http://dx.doi.org/10.1016/j.joms.2011.06.228
- 28. de Vicente JC, Rodríguez-Santamarta T, Rosado P, Peña I, de Villalaín L. Survival after free flap reconstruction in patients with advanced oral squamous cell carcinoma. J Oral Maxillofac Surg [Internet]. 2012 Feb;70(2):453–9. Available from: http://dx.doi.org/10.1016/j.joms.2011.02.020
- 29. Farhat Yaasmeen Sadique Basha, Rajeshkumar S, Lakshmi T, Anti-inflammatory activity of Myristica fragrans extract . Int. J. Res. Pharm. Sci., 2019 ;10(4), 3118-3120 DOI: https://doi.org/10.26452/ijrps.v10i4.1607
- 30. Capote A, Escorial V, Muñoz-Guerra MF, Rodríguez-Campo FJ, Gamallo C, Naval L. Elective neck dissection in early-stage oral squamous cell carcinoma—does it influence recurrence and survival? Head & Neck: Journal for the Sciences and Specialties of the Head and Neck [Internet]. 2007;29(1):3–11. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/hed.20482

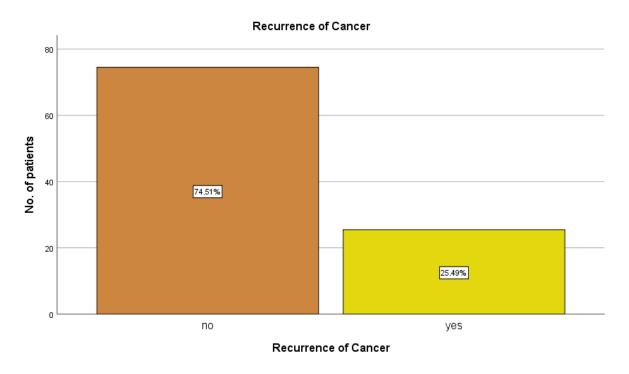


Fig.1 Bar graph represents the percentage of patients with and without recurrence of cancer. X-axis represents the patients with and without recurrence and Y-axis represents the number of the patients. From the graph is evident that the percentage of patients with recurrence was 25.49% (yellow bar) and without recurrence was 74.51% (brown bar).

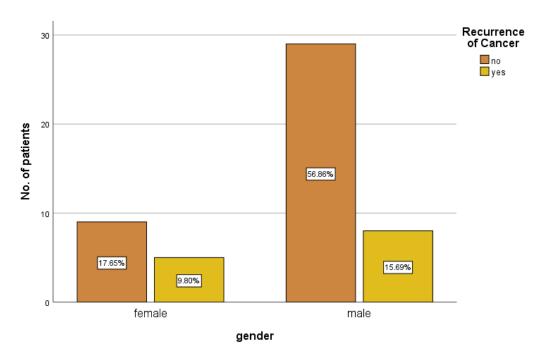


Fig.2 Bar graphs represent the association between gender and recurrence of oral cancer after treatment. X-axis represents the gender of patients. Y-axis represents the number of patients either recurrence after treatment. More males (15.69%) than females (9.80%) had recurrence of oral cancer (yellow bar). Chi-square test was

done and the association was found to be statistically significant. Pearson's Chi-square value: 0.303, DF:2, p value: 0.025(<0.05), proving that more males had recurrence than females.

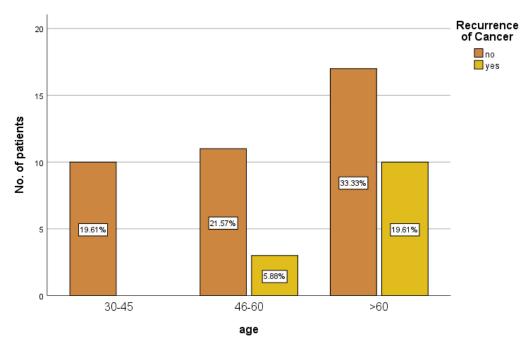


Fig.3 Bar graphs represent the association between age and recurrence of oral cancer after treatment. X-axis represents the age of patients. Y-axis represents the number of patients with recurrence. Majority of patients who had recurrence of oral cancer (19.61%) were above 60 years of age. Chi-square test was done and the association was found to be statistically significant. Pearson's Chi-square value: 0.327, DF:2, p value: 0.025(<0.05), proving that recurrence of oral cancer is common in older age groups.

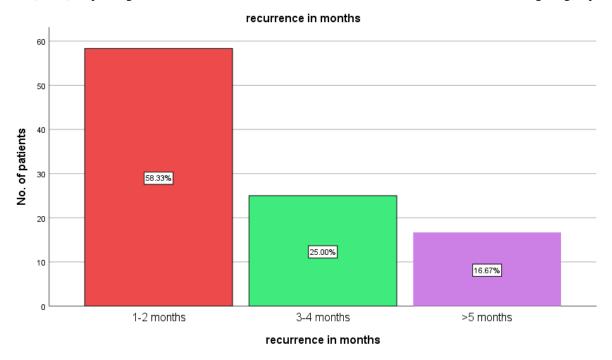


Fig.4 Bar graph represents the time period of recurrence and the number of patients in each category. X-axis represents the time period of recurrence in months. Y-axis represents the number of the patients with recurrence. The percentage of patients with recurrence within 1-2 months is 58.33% (pink bar), within 3-4 months is 25% (green bar) and more than 5 months is 16.67% (purple bar).

Legend of graphs

Graph 1	Percentage of patients with recurrence of cancer
Graph 2	Gender association with recurrence of cancer
Graph 3	Age association with recurrence of cancer
Graph 4	Time of recurrence in months