

# Evaluation of the Role of Neck Dissection in Patients with Verrucous Squamous Cell Carcinoma of the Oral Cavity: A Cohort Study

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## ABSTRACT

**Introduction:** Verrucous Carcinoma (VC), a well-differentiated Squamous Cell Carcinoma (SCC), commonly presents in the oral cavity, accounting for 2-16% of oral carcinomas. Though rare, it poses a challenge in establishing a pathological diagnosis, even in adequate biopsies, as 20% of Oral Cavity Verrucous Carcinoma (OVC) contains concomitant SCC. VC is primarily treated by surgery, similar to oral SCC. The role of neck dissection in oral SCC is well-established, but there is limited data on VC.

**Aim:** To evaluate the role of neck dissection in the management of OVC. It also aimed to evaluate the clinicopathological demographics of OVC and identify predictors for survival outcomes.

**Materials and Methods:** A retrospective cohort study was conducted using medical records of 2312 patients with oral carcinoma treated from January 2010 to December 2020 at Department of Surgical Oncology, Malabar Cancer Centre, Kannur, Thalassery, Kerala, India, a tertiary cancer centre under the Government of Kerala. Among 116 patients identified with VC, 49 patients met the inclusion criteria. The collected data was analysed using Statistical Package for Social Sciences

(SPSS) version 20.0. The primary outcomes were overall survival rate and disease-free survival rate. Kaplan-Meier curves were constructed based on the survival data and compared using the log-rank test.

**Results:** The mean age of the entire population was 62.8 years, with an age range of 40-90 years. Among the 2312 patients who underwent surgery for oral carcinoma, 49 (2.11%) patients were diagnosed with VC based on the final histopathology report. The majority of patients were diagnosed with early-stage disease on histopathological examination 36/49 (73.5%). A total of 34 patients received neck dissections, of which 13 patients (38.3%) had palpable nodes on presentation. All patients were node negative (PNO). On univariate analysis, neck dissection was not found to be a predictor of mortality or locoregional recurrence. There was no significant difference in overall survival rate ( $p=0.160$ ) or disease-free survival rate ( $p=0.67$ ) when comparing patients who underwent primary resection with neck dissection to those whose necks were kept under observation.

**Conclusion:** The OVC has an excellent prognosis, and surgery remains the mainstay of treatment. The decision on neck dissection and the extent of neck dissection should be judiciously made based on the surgical approach and the procedure's morbidity.

**Keywords:** Kaplan-meier curves, Oral cavity verrucous carcinoma, Verrucous carcinoma

## INTRODUCTION

Verrucous Carcinoma (VC), a well-differentiated SCC, commonly presents in the oral cavity, accounting for 2-16% of oral carcinomas [1,2]. Though rare, it poses a challenge in establishing a pathological diagnosis, even in adequate biopsies, as 20% of OVC contains concomitant SCC [3]. It has a predilection for the elderly with a male preponderance. Ackerman described this tumour in 1948 as a variant of SCC with an exophytic growth pattern [4]. VC is usually slow-growing with an excellent prognosis and is usually treated with a single modality treatment in the form of surgery [3,5].

Oral cancer is the most common cancer in India among men (11.28% of all cancers), with the most common histology being SCC, and survival rates ranging from 30% to 80%. OVC is primarily treated similarly to oral SCC, with surgery remaining the mainstay of treatment for this disease. Primary tumour resection ranges from simple wide local excision to composite resection, depending on the stage of presentation. The role of neck dissection and the extent of neck dissection remain under debate [3,5]. Due to the rarity of the disease and the low chance of nodal metastasis, the role of prophylactic neck dissection in clinically node-negative cases, as well as the extent of neck dissection in clinically positive nodes, remains unclear. The low incidence of OVC has resulted in a lack

of literature guiding the management of the disease. Despite the high prevalence of oral cancer, there is limited data from the Indian subcontinent on VC to guide the extent of surgery and adjuvant treatment [3]. Most studies have focused on the clinicopathological profile of the patients [1,4]. The present study primarily aimed to evaluate the role of neck dissection in OVC. Since surgery is the only available modality for the treatment of this disease, the debate on the extent of surgery, especially for transorally resectable lesions, remains significant. Additionally, the authors aimed to evaluate the clinicopathological demographics and predictors for survival outcomes, with a focus on locoregional control.

## MATERIALS AND METHODS

A retrospective cohort study was conducted on 2312 patients with oral carcinoma over an 11-year period, from January 1, 2010, to December 2020, at Department of Surgical Oncology, Malabar Cancer Centre, Kannur, Thalassery, Kerala, India, a tertiary cancer centre under the Government of Kerala. The study was conducted after obtaining permission from the Institutional Review Board (IRB No: 0835).

**Inclusion and Exclusion criteria:** Only patients who received surgery as the primary modality were included for analysis. Patients

with recurrent cancers and those who had received prior treatment for head and neck malignancies were excluded. Patients with co-existent SCC along with VC were also identified and excluded to ensure homogeneity.

### Study Procedure

Forty-nine patients who fulfilled the inclusion criteria were included for the final analysis. The clinicopathological parameters included for analysis were age at diagnosis, sex, habits, co-morbidities, primary site and subsite, presence of nodal and distant metastases, clinical stage, pathological stage, extent of surgery, neck dissection and its extent, lymph node involvement, adjuvant therapy, recurrence, and survival. The patients were staged based on the 7<sup>th</sup> edition guidelines of the American Joint Committee on Cancer for oral carcinoma [6].

### STATISTICAL ANALYSIS

The collected data was analysed using SPSS version 20.0. The primary outcomes were overall survival rate and disease-free survival rate. Kaplan-Meier curves were constructed based on the survival data and compared using the log-rank test.

### RESULTS

There were 49 (2.11%) patients diagnosed with VC based on the final histopathology report. Out of these, 25 were males (51%) and 24 were female patients (49%). The mean age of the entire population was 62.8 years, with an age range of 40-90 years. The incidence of tobacco chewing was 82%. On presentation, the most common epicenter was the Buccal Mucosa, with 30 patients (61.2%), followed by the oral tongue with 11 patients (26.5%), the lower alveolus with 6 patients (12.2%), and the lip with 2 patients (4.1%) [Table/Fig-1].

Variables	n (%)
Age	62.86 (40-90)
Sex	Male 25 (51%)
	Female 24 (49%)
Subsite	Lip 2 (4.1%)
	Tongue 11 (26.5%)
	Alveolus 6 (12.2)
	Buccal mucosa 30 (61.2)
Stage	I 16 (32.7)
	II 20 (40.8)
	III 13 (26.5)
	IV 0
Extent of surgery	Without ND 15 (30.6)
	With ND 34 (69.4)
Radiotherapy	Adjuvant RT 5 (10.2)
	No adjuvant RT 44 (89.8)

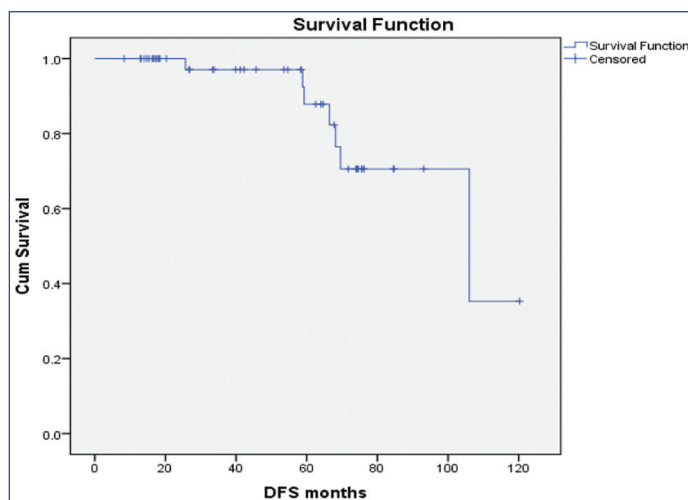
**[Table/Fig-1]:** Clinicopathological demographics of the patients with Oral Verrucous Carcinoma (OVC).  
ND: Neck dissection; RT: Radiotherapy

A total of 116 patients (5.01%) were reported to have a verrucous growth pattern on initial biopsies, of which 49 patients were included for the analysis. Among them, 36 patients had co-existing SCC, while the rest showed dysplastic lesions.

In terms of clinical presentation, 12 patients (24.4%) presented with early-stage disease (Stage-I: 3 patients, Stage-II: 9 patients), while 37 patients (75.5%) presented with advanced-stage disease (Stage-III: 26 patients, Stage-IV: 11 patients). On histopathological examination, 16 patients (32.7%) were reported to be in Stage-I, and 20 patients (40.8%) were in Stage-II. Thirteen patients had Stage-III disease (26.5%), while no patients had Stage-IV disease [Table/Fig-1]. A total of 73.4% of patients (36 patients) were clinically node-negative. Among the 34 patients who received neck dissections,

13 patients (38.3%) had palpable nodes on presentation. Patients with advanced T stage on presentation (21 patients, 61.76%) also underwent neck dissection as a part of their treatment. None of the patients had positive nodes or lymphovascular or perineural invasion on the final histopathology. Out of the 49 patients, 41 (83.67%) had clear margins, while 8 patients (16.32%) had close margins, and no patients had positive margins. Adjuvant radiotherapy was recommended for 5 patients (10.2%) after tumour board consensus.

The median follow-up period was 58 months, with a recurrence rate of 14% (7 patients). The overall survival rate for five years was 87.6%, and the disease-free survival rate for five years was 83%, with most of the recurrences being local [Table/Fig-2]. Four patients with local recurrence could be salvaged, while the remaining patients declined surgery for the same.



**[Table/Fig-2]:** Disease free survival for the patients -83% with a recurrence rate of 14%.

Univariate analysis showed that only age was a significant factor affecting the overall survival rate, as shown in [Table/Fig-3]. Patients' age, sex, stage of the disease, neck dissection, and adjuvant radiotherapy were found to be not significant predictors of overall survival rate or disease-free survival rate on univariate analysis [Table/Fig-3].

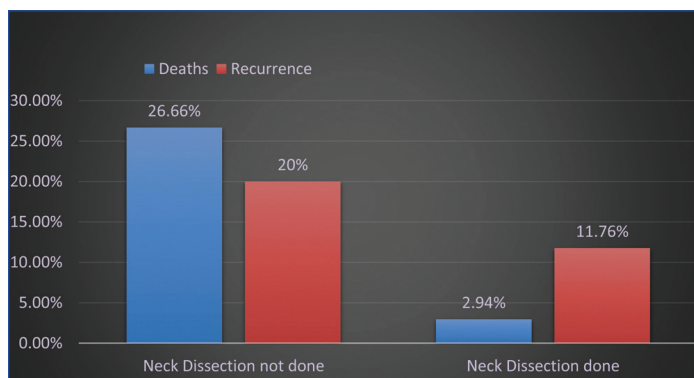
Characteristics	Univariate analysis	
	OS (log rank p)	DFS (log rank p)
Age	0.029 (1032-1.772)	0.992 (0.929-1.077)
Sex	0.928 (0.178-6.633)	0.598 (0.29-3.25)
Primary site	0.316 (0.447-12.129)	0.418 (0.509-5.043)
Neck dissection	0.197 (0.026-2.116)	0.680 (0.261-7.83)
Stage	0.30 (0.183-1.70)	0.223 (0.684-5.106)

**[Table/Fig-3]:** Types of implant used for internal distraction plating in distal radius fractures.

### The Role of Neck Dissection

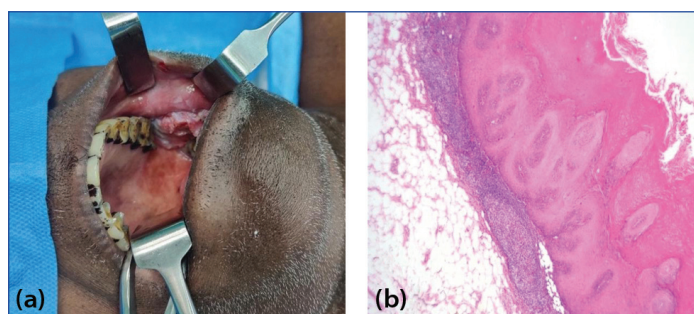
A total of 13 patients had clinically palpable nodes on presentation (cN+), while 36 patients did not have any palpable nodes (cN0). Out of the 34 patients who received neck dissection as part of their surgery, all were pN0 on the final histopathology report, indicating no positive nodes. A total of 15 patients underwent only primary tumour resection, and the neck was kept under observation with clinical follow-up. On analysing the oncological outcomes using univariate analysis, neck dissection was not found to be a predictor for both overall survival and disease-free survival. There were no deaths due to the disease. In terms of recurrences, there were no nodal recurrences in both groups. The local recurrence rate for patients who received neck dissection was 34 (11.78%), while it was 15 (20%) for patients who did not undergo neck dissection. Among the patients who underwent neck dissection, 34 (97.06%)

were alive, whereas 15 (73.33%) of the patients who did not undergo neck dissection were alive [Table/Fig-4].



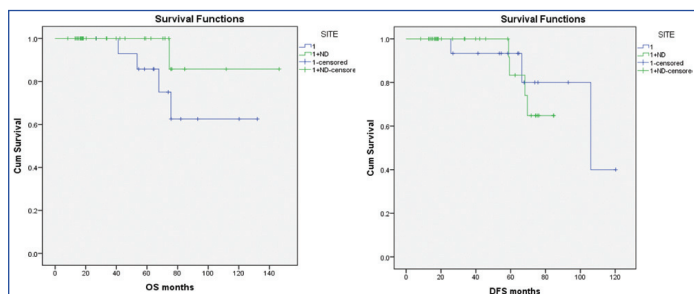
**[Table/Fig-4]:** Number of deaths observed in the group with neck dissection done vs the group without neck dissection.

Grossly, VC appears as an exophytic tumour with a warty, white or red surface and may show keratin-filled clefts [Table/Fig-5a]. On cut sections, it exhibits a flat, well-defined pushing interface with the underlying tissue [Table/Fig-5b]. Microscopically, VC is characterised by a well-differentiated exophytic and endophytic squamous epithelial proliferation that is broad-based, with marked surface keratinisation and keratin plugging. There is even stromal invasion with well-defined pushing borders, extending below the level of adjacent epithelium.



**[Table/Fig-5]:** Gross verrucous appearance of the tumour on the left. Microscopy shows well-defined pushing borders with lymphoplasmacytic inflammatory response along the interface. H&E stained section shows exophytic and endophytic components (10x).

When comparing the overall survival rate between the two groups (neck dissection arm vs. no neck dissection), there was no statistical difference, with a p-value of 0.160. The same observation was obtained when comparing these groups for disease-free survival, with a p-value of 0.679 [Table/Fig-6].



**[Table/Fig-6]:** Overall Survival rate and Disease free Survival rate: Neck Dissection (green) versus No Neck Dissection (blue line): showed no significant difference.

## DISCUSSION

The VC is classified as a well-differentiated non metastasising SCC [7]. Oral SCC (OSCC) is the 16<sup>th</sup> most common cancer worldwide and the most common cancer among males in India [2]. The 2022 World Health Organisation (WHO) section on OSCC has been updated and includes a dedicated section on VC, highlighting the fact that the oral cavity is the most common location in the head and neck, and its clinical and histological features are distinct from

conventional SCC [7]. OVC is rare, accounting for 2-16% of oral carcinomas [7,8]. In the present study data, 2.11% of patients were diagnosed with VC based on the final histopathology report among those who underwent treatment for oral cancer.

The VC predominantly occurs in males, with a higher incidence in older age groups, particularly in the sixth decade [7]. The mean age of our population was 62.8 years, consistent with the literature, with a range of 40 to 90 years [5,9]. In our analysis, age was a significant predictor of the overall survival rate (p=0.02) on univariate analysis, although it did not show the same significance for disease-free survival. As detailed in the analysis by Alonso JE et al., outcomes tend to be poorer in older age groups due to other causes of death unrelated to the disease [5]. Although there was only a slight predominance of males in our data (51% male, 49% female), this finding aligns with previously published population-based analyses [5,9].

Published series on OVC have shown that the most common epicenter is the buccal mucosa, followed by the alveolus and oral tongue [3,5]. The present study data also corroborated these findings, with the buccal mucosa being the most common subsite (61.2%). This supports the association with tobacco chewing, as the incidence of tobacco chewing in our population was 82%. Lesions in the buccal mucosa and alveolus may be detected later compared to those in the oral tongue and other subsites, as they tend to be slow-growing and usually painless [5]. However, the subsite was not found to be an independent predictor of overall survival or locoregional recurrence, despite conflicting evidence in the literature [3,5].

The VC presents as a broad-based exophytic tumour with a warty keratinised surface and specific architecture [2]. It can be locally aggressive, and in some series, bone erosion has been reported [3,4,10]. VC lacks substantial cytological features of malignancy and is characterised by slow lateral spread and pushing invasion [7]. Among the 116 patients suspected to have VC, only 49 had a confirmed diagnosis of OVC after surgical resection.

In the present series, a majority of the patients presented with advanced stage disease (75%). This could be attributed to the slow-growing and painless nature of the tumour, leading patients to ignore the symptoms. Histopathological examination revealed a down-staging, with 73.5% of patients having early-stage tumours and 26.5% having Stage-III disease. No patients had a Stage-IV disease, and stage was not found to be a significant predictor of mortality or disease recurrence, consistent with earlier series [1,5].

Histopathologically, a lymphoplasmacytic inflammatory response can be seen along with a sharply defined stroma-epithelial interface and coalesced bulbous rete [7]. VC lacks substantial cytologic features of malignancy, and the well-defined pushing borders limit the diagnosis on small biopsies, posing a challenge for physicians and pathologists. Thorough sampling of the specimen is necessary to make the diagnosis of VC and to rule out co-existing SCC, which is difficult on small biopsies as it limits the detailed examination of the epithelium and underlying stroma [7,11].

Surgery remains the mainstay of treatment for all patients. The limitations of the initial biopsy in establishing a definite diagnosis make it challenging to decide on the extent of surgery for the primary tumour, neck dissection, and adjuvant treatment. The main challenges lie between hybrid VC and verrucous hyperplasia [7,11]. All patients underwent wide local excision with 1 cm margins, following the guidelines for Oral Squamous Cell Carcinoma (OSCC). Patients with close margins on final histopathology received adjuvant radiotherapy after consensus from the tumour board, taking other risk factors into consideration. Although VC can be locally aggressive and erode bones, such instances are rare, prompting surgeons to consider more conservative approaches, such as marginal mandibulectomy, whenever possible [3].

The role of elective neck dissection has been undoubtedly established in the management of OSCC, with an absolute disease-free survival benefit of 32-52% [12,13]. On presentation, 38.3% of patients with OVC had palpable nodes, and 34 patients (69.3%) underwent neck dissection as a part of their treatment [Table/Fig-1]. The extent of neck dissection ranged from supraomohyoid neck dissection to modified radical neck dissections for those with clinical suspicion of nodes on presentation. On final histopathological examination, all patients were found to be node-negative (pN0), consistent with the literature [1,3,9,14]. On univariate analysis, neck dissection was not found to be a predictor of mortality or locoregional recurrence [Table/Fig-3]. There was no significant difference in the overall survival rate ( $p=0.160$ ) or disease-free survival rate ( $p=0.67$ ) when comparing patients who received neck dissection with those who were kept under observation [Table/Fig-6].

In line with the literature, all recurrences (14%) were local (7), with no nodal recurrence observed. This raises questions about the necessity of neck dissection in the context of OVC. Clinical judgement often leans towards performing neck dissection, especially in cases with aggressive presentation or palpable nodes [3]. The dilemma arises when there is a co-existing OSCC, as the initial biopsy may not be representative, and the final histopathology report may indicate a hybrid OVC. Published literature also supports considering a more conservative approach to neck management [1,3,9,10].

The VC has an excellent prognosis, with an overall five-year survival rate ranging from 77-86%. Our data shows that 89.8% of patients were alive, with 6.1% alive with the disease at the time of analysis. The overall five-year survival rate was 87.6%, and the five-year disease-free survival rate was 83%. The significance of neck dissection lies in the fact that many of these patients are long-term survivors, and neck dissection can have a significant impact on their functional quality of life. The morbidity associated with neck dissection becomes more prominent in light of the excellent survival rates.

The VC may serve as a precursor to SCC, and approximately 20% of oral cavity VC cases contain concomitant SCC. The diagnostic challenges posed by the initial biopsy often prompt surgeons to adopt an aggressive approach. It would be prudent to consider selective neck dissection, limited to supraomohyoid levels, where the neck can be approached for primary resection or reconstruction. Neck dissection can be considered as a second-stage procedure in cases where primary resection can be performed with less morbidity. The role of sentinel lymph node biopsy is emerging in the context of OSCC, and the extent of neck dissection can be determined based on frozen section analysis, where the neck can be explored for primary resection or reconstruction.

## Limitation(s)

The present study is limited by its retrospective nature and the small number of patients available for comparison between both groups, which is attributed to the rarity of the disease.

## CONCLUSION(S)

The OVC has an excellent prognosis, and surgery remains the mainstay of treatment. Adequate surgical resection with wide margins has been proven to yield better oncological outcomes. The decision regarding neck dissection and the extent of neck dissection should be made judiciously, taking into account the surgical approach and the morbidity associated with the procedure.

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