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Eastern Cooperative Oncology Group Performance in Malaysian Oral Cavity Carcinoma: Treatment, Demographics and Clinical Factors

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ABSTRACT

Eastern Cooperative Oncology Group (ECOG) is gaining importance as a valuable outcome measure in the field of oral cavity carcinoma (OCC). This study aimed to assess pre- and post-treatment ECOG changes in Malaysian OCC patients undergoing various treatments. We conducted a 12–36 months longitudinal observational study with 63 squamous cell carcinoma patients, evaluating ECOG perfomance, medical history, symptoms, sociodemographics, clinical details, and treatment modalities (surgery, surgery + radiotherapy, or surgery + chemotherapy and radiotherapy [CCRT]). OCC patients aged 50–70 years are at risk for impaired quality of life (QOL) up to several years after diagnosis. The analysis of the association between baseline ECOG Performance Status (ECOG-PS) scores and demographic data revealed a statistically significant correlation only within the age group, demonstrating a *p*-value of 0.031. CCRT treatment has a more pronounced effect on patient performance status, with significant results in the 3-year overall survival rate and poor ECOG-PS score in patients post-CCRT, as well as radiotherapy. These results highlight the need to provide OCC patients with specialised interventions and support, especially while they are undergoing CCRT, to lessen the potential negative effects on their general well-being and quality of life.

Keywords: *Eastern Cooperative Oncology Group performance status; oral cavity carcinoma; quality of life; questionnaire*

INTRODUCTION

Globally, the prevalence of cancer in mouth and throat has been rising, and like the other countries, Malaysia also faces increasing rates of oral cavity carcinoma (OCC) (da Cunha *et al.*, 2023). GLOBOCAN 2018 prediction data shows an overall increase in the incidence and mortality of cancer of the lip and oral cavity by 2040 for most of

the South-East Asian countries (Bray *et al.*, 2018) and the incidence rates for Malaysia will increase by 106.6% (Gunjal et al., 2020). OCC is the 17th most common cancer in male and the 16th most common cancer in female according to the National Cancer Registry (Abllah *et al.*, 2019). It is interesting to note that there are unique trends in Malaysia, where the indigenous people of Sabah and Sarawak are the group that has the highest prevalence of OCC (Linton *et al.*, 2021).

The genesis of OCC is complicated and involves various factors, including but not limited to tobacco use, alcohol intake, chewing betel quid, and the presence of the human papillomavirus (HPV) (D'souza & Addepalli, 2018). According to Liu *et al.* (2021), the prognosis of the illness is affected by several variables, including the anatomic site, gender, diagnostic age, ethnic group, and type of therapy. Nonetheless, despite the general factors influencing OCC, Malaysia's unique social and cultural context can provide additional insights and affect how the disease is experienced and managed differently compared to other parts of the world.

Surgical resection is necessary for the best curative outcomes to maintain the high level of care, especially in the oral cavity site (Machiels *et al.*, 2020). However, it is important to examine the effects of surgery from a Malaysian perspective particularly on total tumour resection with free flap reconstruction, considering the cultural ideas about communication and beauty, as well as any potential effects on appearance, speech, and general function.

Additionally, the inclusion of post-operative radiation and chemotherapy is important as the treatment of OCC, yet the effectiveness of different treatment modalities and their impact on daily functioning and well-being remains uncertain (de Pauli Paglioni *et al.*, 2020). Comprehending the role that familial and community support networks play in the patient's journey and rehabilitation is crucial, especially in Malaysia where these networks are strong.

A careful balance must be struck when managing OCC between the goal of curing the disease and any potential effects on the patient's quality of life (QOL) (Ward *et al.*, 2022). In Malaysia, where cultural norms and personal expectations are paramount, it is imperative to comprehend the complex inclinations of cancer patients. There are numerous well-validated tools with which to measure the QOL of head and neck cancer patients and one of them is the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) which could provide a valuable tool to assess the functional status of cancer patients, including those with OCC, and its relation to QOL is significant (Lingappanoor *et al.*, 2019). The questionnaires are self-administered but with minimal assistance from a health-worker if necessary.

This study aims to elucidate the complex interplay between ECOG-PS, treatment modalities, demographics, and clinical factors in Malaysian OCC patients. Through this comprehensive analysis, we aim to enhance our understanding of the role of ECOG-PS and its interaction with demographics and clinical factors in guiding treatment decisions and predicting outcomes in Malaysian OCC patients.

MATERIAL AND METHODS

Ethical Approval

UM Medical Centre's Ethics Committee was responsible in approving the study (MECID.NO: 20155-1374). Participant confidentiality was ensured and no patient names had appeared in the instruments or publications. Compensation, within the budget of Otorhinolaryngology Department fund (UM.0000435/KWJ.AK), was provided in form of tokens.

Patients

Convenience sampling was used in the present study. This approach involved by selecting patients who were readily available and accessible for the study from those who were treated for OCC at a single centre, University of Malaya Medical Centre (UMMC) Ear, Nose, Throat (ENT) clinic between December 2013 and December 2017. Sample size calculation was based on a 95% power range using a one-tailed *t*-test estimated a group size of 63 (an effect size of 0.50) based on a hypothetical 50% detection rate of OCC. Patient recruitments were based on the inclusion and exclusion criteria (Table 1) and data was collected at baseline, one-month post-surgery, and three months post-RT/CCRT treatment. Baseline evaluations were conducted to gain a thorough understanding of the patient's features, disease stage, and general health. Evaluation of the initial post-operative results, including wound healing, functional recovery, and early problems, was possible up to one month after surgery. Furthermore, monitoring for late treatment-related adverse effects was made possible by the three-month mark following radiotherapy or CCRT, which was crucial in determining how well these treatments controlled the cancer. Although, the data for this study were collected between 2013 and 2017, but the publication of these findings has been delayed due to several important factors; including the need for extensive analysis to ensure robustness and accuracy, as well as the goal of aligning the publication with recent advancements by incorporating contemporary research findings into the discussion, thereby adding significant value to the manuscript and ensuring that the study's results are contextualised with ongoing developments in the field of OCC treatment.

In the staging of OCC, the disease is classified using the T Stage, N Stage, and Overall Stage to assess its progression and severity (Edge *et al.*, 2010). The T Stage (tumour Stage) describes the size and extent of the primary tumour. It ranges from T1, indicating a tumour ≤ 2 cm, to T4, where the tumour has extended beyond the oral cavity or invaded adjacent structures. T4 tumours have been divided into T4a (moderately advanced local disease) and T4b (very advanced local disease), leading to the stratification of Stage IV into Stage IVa (moderately advanced local/regional disease), Stage IVb (very advanced local/regional disease), and Stage IVc (distant metastatic disease) (Edge *et al.*, 2010). The N Stage (node stage) evaluates the extent of regional lymph node involvement. It ranges from N0, with no regional lymph node involvement, to N3, indicating extensive nodal involvement or metastasis to lymph nodes > 6 cm. The Overall Stage combines the T and N Stages, as well as additional factors such as distant metastasis, to determine the overall severity of the disease. This stage is classified from Stage 1, which involves a small tumour (T1) and no regional lymph node involvement (N0), to Stage 4, representing advanced local invasion (T4) or extensive regional lymph node involvement (N3), and may include distant metastasis. Each stage reflects the disease's progression, with Stage 1 being the earliest and Stage 4 representing the most advanced stage (Sambasivan *et al.*, 2021).

Table 1 Inclusion and exclusion criteria of patient recruitment

Inclusion criteria	Exclusion criteria
Patient age > 20 Diagnosed with OCC (Edge *et al.*, 2010)	Recurrent OCC Age > 20 Screening failure Mental compromise Medical unfitness Stage IVc

Evaluation of Performance Status

The ECOG-PS is a well-established tool used extensively in cancer research for assessing patient functional status (Quinn *et al.*, 2020). It has consistently demonstrated high validity and reliability across numerous cancer studies particularly in head and neck regions (Oswald *et al.*, 2020). In Malaysia,

it has been adapted to ensure cultural and linguistic relevance, maintaining its effectiveness and accuracy for Malaysian patients (Yahaya *et al.*, 2022). Five groups are identified by the ECOG-PS scale for cancer patients (Azam *et al.*, 2019): Normal activity is defined as 0, restricted or up to 50% of waking hours, bedridden or confined to a chair for more than 50% of waking hours, 100% bedridden, and 5 dead. OCC subjects were split into two groups in the current investigation based on their ECOG-PS scores (ECOG 0–1, good PS; and ECOG 2–4, bad PS). All OCC patients had their ECOG-PS scores evaluated at the time of diagnosis. The flow of data collection process was demonstrated in Fig. 1.

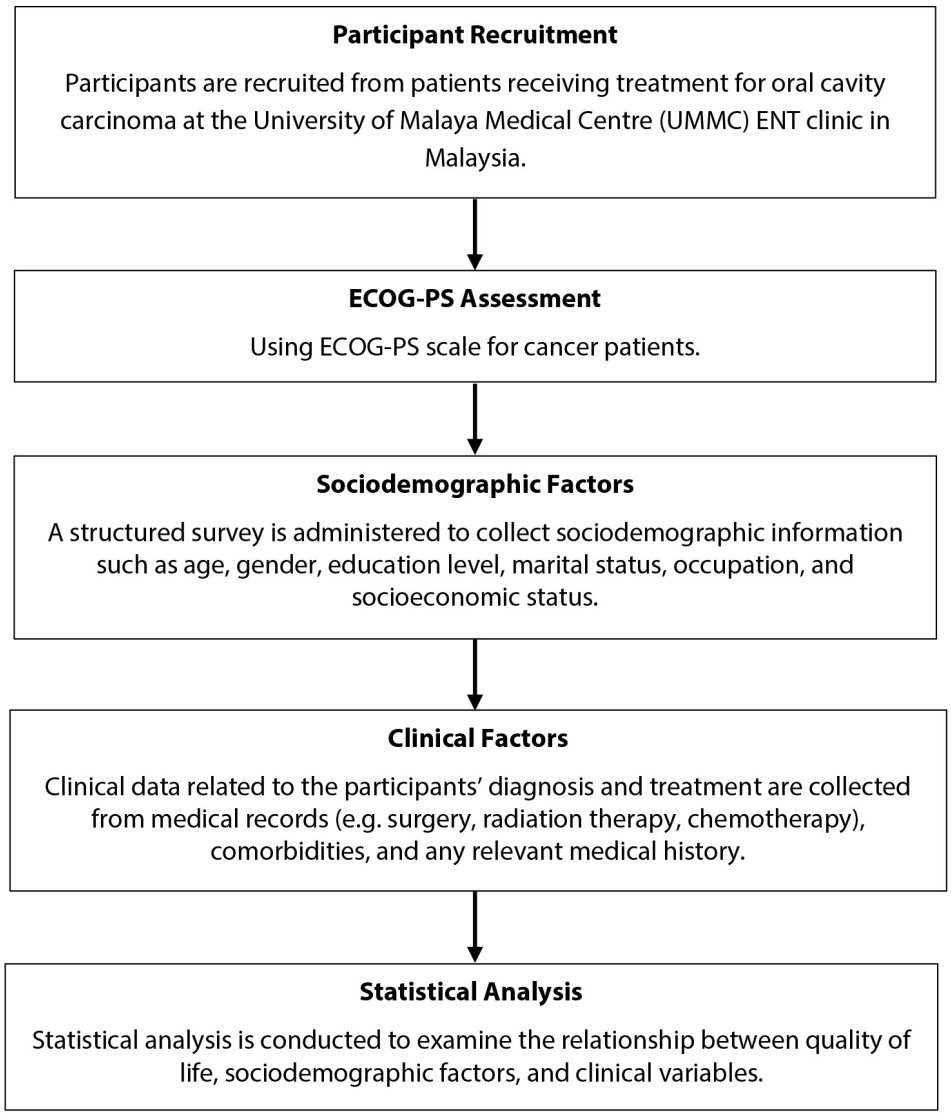

Fig. 1 The flowchart provides a step-by-step description of the data collection process.

Statistical Analysis

SPSS version 19.0 (SPSS Inc, USA) is used for statistical analysis. Bivariate analysis assessed associations, with significance tested using the chi-square test. ANOVA calculated the mean, and *t*-tests assessed the significance, with alpha set at 0.05. The study's follow-up time began at diagnosis, ending at death or last contact within three years. Overall survival rate served as the endpoint for disease control. Kaplan-Meier method plotted survival curves, and differences were compared using the log-rank test.

RESULTS

The sociodemographic and clinical data of the patients are presented in Table 2. A total of 63 patients were included in the present study. The highest incidence of OCC occurred among the Chinese (41%) and Indians (38%), followed by Malay (14%) and the others (7%). These results show almost similar occurrences among Chinese and Indian ethnicity. Knowing the distribution among different ethnic groups such as Chinese, Indian, Malay, and others helps to identify the populations at higher risk, allowing for targeted prevention and screening (Matos *et al.*, 2021). There were 24 males (38%) and 39 females (62%) reported in this study. Additionally, OCC occurs at the highest frequency between 51 to 60 years old (27%) as well as 61 to 70 years old (25%).

Table 2 Sociodemographic and clinical data distribution

Demographic data	Frequency (n)	%
Gender		
Male	24	38
Female	39	62
Age group		
21–30	1	2
31–40	5	8
41–50	8	13
51–60	17	27
61–70	16	25
71–80	14	22
81–90	2	3
Ethnic		
Malay	9	14
Chinese	26	41
Indian	24	38
Others	4	7
Tumour subsite		
Tongue	33	57
Upper gingiva-alveolar	2	3
Buccal	15	26
Lower gingiva-alveolar	7	12
Floor of mouth	1	2
Histopathological grade		
Well differentiated	20	32
Moderately differentiated	43	68

(*continued on next page*)

Table 2 (*continued*)

Demographic data	Frequency (n)	%
T Stage		
T1	12	19
T2	23	37
T3	16	25
T4	12	19
N Stage		
N0	42	67
N1	11	17
N2	10	16
N3	0	0
Overall stage		
Stage 1	11	17
Stage 2	19	30
Stage 3	13	21
Stage 4	20	32

As for the clinical data, majority of the patient's tumour was seen in the tongue (57%), followed by buccal (26%) and lower gingiva-alveolar (12%). Other subsites were less commonly associated, with upper gingiva-alveolar (3%) and floor of mouth (2%). The information about common tumour locations, commonly guides the clinical examinations and diagnostic priorities (Machiels *et al.*, 2020). The histological grade showed that most respondents tumour was moderately differentiated (68%), followed by well differentiated (32%), and there was no tumour which was poorly differentiated or undifferentiated.

The patients had an overall stage distribution of Stage 1 (17%), Stage 2 (30%), Stage 3 (21%), and Stage 4 (32%). These findings are significant in providing an insight into the disease's aggressiveness and potential prognosis (Soltani *et al.*, 2022). Most patients had presented with T2 (37%), followed by T3 (25%), T4 (19%), and T1 (19%). Among these patients, the majority had presented with N0 (67%), followed by N1 (17%) and N2 (16%).

The distribution of patients into the different treatment modalities are presented in Fig. 2. Among the recruited patients, 8 had undergone surgery alone, 41 had undergone surgery and post-operative RT, and 14 had undergone surgery and post-operative CCRT. In the present study, Stage 1 and Stage 2 were classified as the early-stage disease while Stage 3 and Stage 4 are the advanced stage disease.

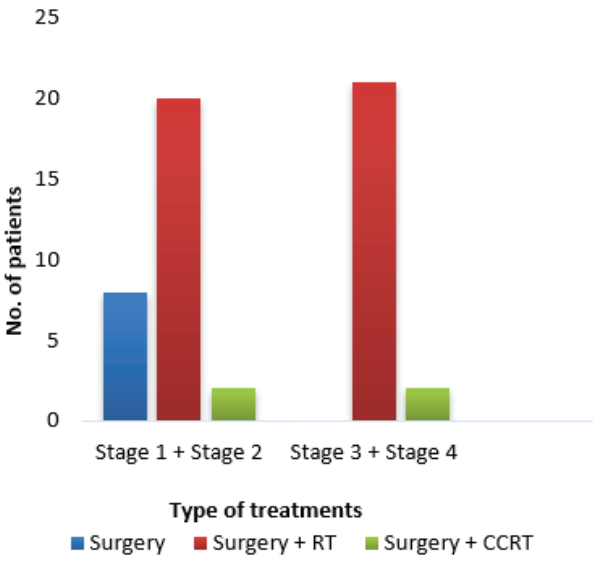

Fig. 2 Distribution of treatment modalities among patients with different disease severity.

This suggests that in present study population, adjuvant radiotherapy following surgery is a commonly employed treatment approach for OCC. This pattern may reflect the recognition of the importance

of adjuvant therapy in reducing the risk of disease recurrence and improving long-term outcomes after surgical resection (Hosni *et al.*, 2021).

The correlation between baseline ECOG-PS and the demographic data are presented in Table 3. The variables which were analysed included gender, age group, and ethnicity. These parameters are cross tabulated against the mean ECOG-PS. Among the demographic data, only the age group show statistically significant with a *p*-value of 0.031.

Table 3 Association between baseline ECOG-PS score against demographic data

Demographic variables	ECOG-PS mean score (SD)	*p*-value
Gender		
Male	0.13±0.35	0.405
Female	0.20±0.40	
Age		
21–30	0.36±0.50	
31–40	0.25±0.46	
41–50	0.93±0.69	
51–60	1.00±0.56	0.031
61–70	0.75±0.70	
71–80	1.66±1.11	
81–90	2.93±1.39	
Ethnicity		
Chinese	0.35±0.56	
Indian	1.11±0.27	0.583
Malay	0.45±1.03	
Others	0.32±0.57	

While gender and ethnicity did not exhibit statistically significant associations with ECOG-PS scores, age group did. This suggests that age may play a crucial role in determining the baseline ECOG-PS scores within our study population (Amri *et al.*, 2023). Furthermore, when the baseline ECOG-PS score is compared with clinical variables, there was a significant association between Overall Stage, T Stage and N Stage, as indicated in Table 4. The *p*-value for the overall stage was 0.001, and those for T Stage and N Stage were 0.041 and 0.040, respectively. Patients with higher ECOG-PS scores may have limited tolerance for aggressive treatments like surgery, chemotherapy, or radiotherapy (Chen *et al.*, 2024). In such cases, exploring alternative treatment options or implementing supportive care measures becomes essential to optimise outcomes.

Table 4 Association between baseline ECOG-PS score against clinical parameters

Clinical variables	ECOG-PS mean score (SD)	*p*-value
Overall Stage		
Stage 1	0.44±0.37	
Stage 2	0.62±0.42	0.001
Stage 3	0.88±0.52	
Stage 4	0.57±0.48	
T Stage		
T1	1.45±0.71	
T2	1.52±0.58	0.041
T3	1.27±0.72	
T4	2.68±1.13	
N Stage		
N0	3.95±1.41	
N1	0.67±0.58	0.040
N2	1.43±0.29	
N3	1.48±1.05	

A comparison of ECOG-PS score between the different treatment arms at baseline, during treatment and post-treatment is presented (Table 5). There was a significant deterioration in mean ECOG-PS score for patients who received surgery and CCRT compared with the other two arms of treatment at six month post-treatment, with a *p*-value of < 0.05. The significant deterioration in ECOG-PS scores post-treatment highlights the importance of long-term follow-up care for cancer patients. Monitoring patients' functional status beyond the acute treatment phase is crucial for detecting and addressing late effects or complications associated with treatment (Pennathur *et al.*, 2021).

There was a 3-year overall survival rate among patients who received either surgery only, surgery with RT or surgery with CCRT (Fig. 3). The overall survival of patients who underwent surgery alone was the highest,

Table 5 Comparison of ECOG-PS difference between treatments, surgery + radiotheraphy and surgery + CCRT

ECOG-PS	S + RT		S + CCRT		*p*-value
	Mean	SD	Mean	SD	
ECOG baseline	0.20	0.40	0.36	0.50	< 0.014
ECOG during treatment	0.93	0.69	1.00	0.56	0.229
ECOG post-treatment	1,661.00	1.11	2. 93	1.39	0.010

Note: S = Surgery; RT = Radiotheraphy

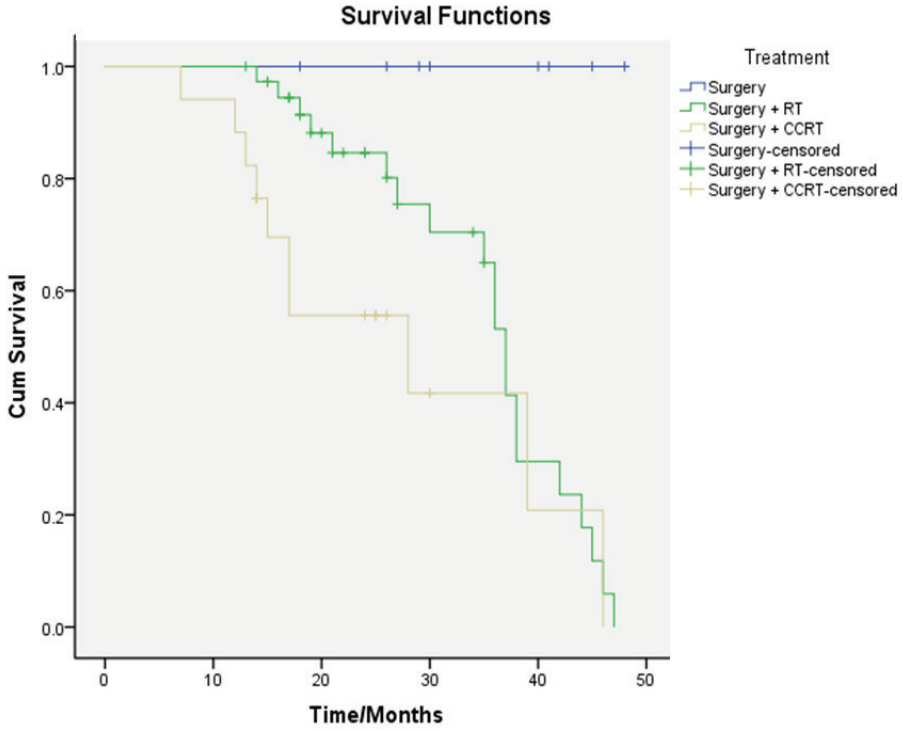

Fig. 3 Kaplan-Meier actuarial analysis showing the overall survival of patients receiving three different treatment modalities.

followed by those who underwent surgery with RT, and lastly those who underwent surgery with CCRT, with 3-year overall survival rates of 50%, 46.3%, and 42.9%, respectively. However, it was not statistically significant with a *p*-value of 0.81. Although the adjuvant treatments like RT and CCRT may improve survival outcomes, they could also lead to increased treatment-related toxicity or side effects, impacting patients' functional status in the long term despite the survival benefits (Zhu *et al*., 2024).

DISCUSSION

The majority of the OCC patients recruited in the present study were the Chinese, followed closely by the Indians. Based on the Malaysian National Cancer Registry data, the incidence of OCC is predominant among the Indian ethnic group (Ahmad *et al.*, 2021), where tongue cancers were among the 10th most common cancers among both genders (Sakr *et al.*, 2023). The underlying lifestyle habits, for example, betel quid chewing and smoking, may contribute to the high incidence of OCC among this specific ethnic group (Amarasinghe *et al.*, 2018). The present study did not show any significant

correlation between the baseline ECOG-PS and demographic parameters except for age due to poor stratification of patients with the different age groups (Liu *et al.*, 2020). Gender has also long been viewed as an important variable in affecting the change in QOL score. However, in the present study, it has been shown that there is no significance towards gender and ECOG-PS, as previously reported by Badola *et al.* (2023).

As for clinical parameters, we noticed a correlation between baseline ECOG-PS score with the severity of T Stage, N Stage and Overall Stage. Patient with more severe T Stage, N Stage and the Overall Stage has a poor ECOG–PS score (Janmunee *et al.*, 2021; Shrivastava *et al.*, 2024). Advanced T Stage and N Stage means bulkier primary tumour at the nodal enlargement. The extensive primary tumour will lead to local dysfunction such as difficulty in mouth opening (Pisani *et al.*, 2020). Systemic presentation such as loss of appetite and weight could be explained by the higher level of tumour necrosis factor such as interleukin-1 and interleukin-6 which are produced by the cancerous cells (Uz & Eskiizmir, 2021).

ECOG-PS assessment is particularly important in OCC because the disease and its treatment have such a profound impact on QOL (Lingappanoor *et al.*, 2019). The definition of successful treatment can often be different widely between patients and their doctors. Factors that patients use to measure success are not medical but only social, economic and cultural (Novirianthy *et al.*, 2023). Traditional outcome measures of treatment efficacy, such as tumour recurrence and survival time, are often meaningless to patients. What matters is the ability to return to pre-illness function. ECOG-PS assessment should be incorporated into clinical practice to identify the risk subgroup. In a study by Hammermüller *et al.* (2021), it has been shown that demographic parameters including sex, educational level, gender, marital status, and clinical characteristics such as the presence of feeding tube, severity, medical comorbidities were significant predictors of QOL in patients with head and neck cancer. These factors should be considered when treating patients and conducting studies in the future. Moreover, treatment-related morbidity is very often long-term, if not permanent. They consist of disfigurement, xerostomia, trismus, dysphagia, airway and speech disturbances, and shoulder dysfunction (Pingili *et al.*, 2021).

The standard of care for early-stage and locally advanced resectable lesions in the oral cavity is surgery followed by post-operative radiotherapy (Woor, 2015). In certain cases, chemotherapy is combined with radiotherapy (CCRT) or administered before the primary treatment (neoadjuvant chemotherapy) to enhance the treatment outcomes (Woor, 2015). Our results showed that patients in the CCRT arm had poorer outcomes compared to those in the radiotheraphy-only arm, with significant deterioration of the ECOG-PS score after three months post-treatment ($p < 0.05$). Comparison within each treatment arm also revealed worsening of the ECOG-PS score for both modalities, with the CCRT mean score poorer than the radiotheraphy-only arm, although this was not statistically significant during treatment. The mean ECOG-PS scores in both treatment arms deteriorated, which can primarily be attributed to the chronic side effects of radiation therapy, as patients in both arms received an equivalent dose of radiation ranging from 66 to 76 Gy (Bourbonne *et al.*, 2022; Zhu *et al.*, 2024). While the data were collected between 2013 and 2017, the insights gained remain pertinent given the advancements and current practices in the field of OCC treatment. Recent studies, as cited in this manuscript, have corroborated some of our findings, and our results contribute to a deeper understanding of ECOG-PS in OCC, particularly in Asian countries, in light of the evolving research landscape.

Poor oral health outcomes and limited access to knowledge on preventing OCC are potential consequences of some

circumstances, such as poorer income, lower education levels, and the existence of discomfort in the mouth, head, or neck. These factors may also have an impact on quality of life (Mathur *et al.*, 2019). A different strategy that could be used is improving the healthcare services. It is important to work towards minimising the societal disparities in oral healthcare access. Individuals with lower socioeconomic level should have priority in receiving preventive information and treatments from dental services, particularly those offered under the Family Health Strategy (FHS) (Ghanbarzadegan *et al.*, 2021). Dentists should also make sure that patients have enough time and resources to talk to them about their worries on their dental health and get the help they need. Furthermore, encouraging people to engage in oral self-examination and adopt healthy habits like giving up alcohol and tobacco usage might improve oral health outcomes and perhaps raise QOL scores (Raman *et al.*, 2023). Healthcare providers can offer direction and assistance in putting these strategies into effect.

However, the present study has several limitations. The sample may not be fully representative of the broader population, and there could be potential biases in patient selection. Additionally, the generalisability of the findings may be limited to similar demographic and clinical settings. Future studies should explore the mechanisms by which tumour burden affects ECOG-PS and investigate novel interventions to mitigate treatment-related toxicities. Longitudinal studies assessing long-term QOL outcomes and the impact of psychosocial support interventions are also needed. Research should continue to explore the disparities in healthcare access and develop strategies to improve oral health outcomes among lower socioeconomic groups.

CONCLUSION

The need to weigh the benefits of treatment against maintaining functional status is significant even though adjuvant therapies like radiotherapy and CCRT may increase overall survival rates. These therapies are linked to a significant decline in functional status following treatment, as indicated by the ECOG-PS scores. Age is found to be a significant influence in determining initial ECOG-PS scores, emphasising the need of customised treatment plans that take into account unique patient characteristics. In order to address treatment-related impairments and maximise patients' long-term functional results, it is imperative that patients get supportive therapies and long-term follow-up care. This is highlighted by the observed functional decline. The apparent discrepancy between treatment efficacy, as measured by survival outcomes, and functional status calls for further research to elucidate underlying mechanisms and refine treatment protocols, aiming to minimise functional decline while preserving or enhancing survival benefits.

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REFERENCES

Abllah Z, Juhari S, Pauzi NA, Han TM, Hassan H, Faizal GG (2019). Oral cancer awareness among patients attending University Dental Clinic in Kuantan, Pahang. *Mater Today Proc*, **16**(4): 2253–2261. https://doi.org/10.1016/j.matpr.2019.06.118

Ahmad WMAW, Ghazali FMM, Yaqoob MA, Alawthah GH, Srivastava KC, Shrivastava D *et al.* (2021). A comprehensive cross-tabulation analysis of oral carcinoma patients: A retrospective study of recent 7 years. *J Pharm Bioallied Sci*, **13**(Suppl 2): S1074–S1078. https://doi.org/jpbs.jpbs_105_21

Amarasinghe AAHK, Usgodaarachchi US, Johnson NW, Warnakulasuriya S (2018). High prevalence of lifestyle factors attributable for oral cancer, and of oral potentially malignant disorders in rural Sri Lanka. *Asian Pac J Cancer Prev*, **19**(9): 2485–2492. https://doi.org/10.22034/APJCP.2018.19.9.2485

Amri F, Belkhayat C, Yeznasni A, Koulali H, Jabi R, Zazour A *et al.* (2023). Association between pancreatic cancer and diabetes: Insights from a retrospective cohort study. *BMC Cancer*, **23**(1): 856. https://doi.org/10.1186/s12885-023-11344-w

Azam F, Latif MF, Farooq A, Tirmazy SH, AlShahrani S, Bashir S *et al.* (2019). Performance status assessment by using ECOG (Eastern Cooperative Oncology Group) score for cancer patients by oncology healthcare professionals. *Case Rep Oncol*, **12**(3): 728–736. https://doi.org/10.1159/000503095

Badola A, Mehta P, Mehra S, Sood S (2023). Epidemiology and survival analysis of head and neck cancer: Results from comprehensive care center in North India. *Oral Oncol Rep*, **6**: 100022. https://doi.org/10.1016/j.oor.2023.100022

Bourbonne V, Otz J, Bensadoun RJ, Dissaux G, Lucia F, Leclere JC *et al.* (2022). Radiotherapy mucositis in head and neck cancer: Prevention by low-energy surface laser. *BMJ Support Palliat Care*, **12**(e6): e838–e845. https://doi.org/10.1136/bmjspcare-2019-001851

Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*, **68**(6): 394–424. https://doi.org/10.3322/caac.21492

Chen P, Ding M, Li C, Long Y, Pan D, Ma L *et al.* (2024). Distinct experiences and care needs of advanced cancer patients with good ECOG performance status: a qualitative phenomenological study. *BMC Palliat Care*, **23**(1): 102. https://doi.org/10.1186/s12904-024-01425-3

da Cunha ARD, Compton K, Xu R, Mishra R, Drangsholt MT, Antunes JLF *et al.* (2023). The global, regional, and national burden of adult lip, oral, and pharyngeal cancer in 204 countries and territories: A systematic analysis for the global burden of disease study 2019. *JAMA Oncol*, **9**(10): 1401–1416. https://doi.org/10.1001/jamaoncol.2023.2960

de Pauli Paglioni M, Palmier NR, Prado-Ribeiro AC, Fregnani ER, Gavião MBD, Brandão TB *et al.* (2020). The impact of radiation caries in the quality of life of head and neck cancer patients. *Support Care Cancer*, **28**(6): 2977–2984. https://doi.org/10.1007/s00520-019-05171-8

D'souza S, Addepalli V (2018). Preventive measures in oral cancer: An overview. *Biomed Pharmacother*, **107**: 72–80. https://doi.org/10.1016/j.biopha.2018.07.114

Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti, Andy III (eds.) (2010). *AJCC Cancer Staging Manual, 7th Edn*. New York: Springer & American Joint Committee on Cancer (AJCC).

Ghanbarzadegan A, Balasubramanian M, Luzzi L, Brennan D, Bastani P (2021). Inequality in dental services: A scoping review on the role of access toward achieving universal health coverage in oral health. *BMC Oral Health*, **21**(1): 404. https://doi.org/10.1186/s12903-021-01765-z

Gunjal S, Pateel DGS, Lim RZS, Yong LL, Wong HZ (2020). Assessing oral cancer awareness among dental and medical students of a Malaysian private university. *Int Dent J*, **70**(1): 62–69. https://doi.org/10.1111/idj.12524

Hammermüller C, Hinz A, Dietz A, Wichmann G, Pirlich M, Berger T *et al.* (2021). Depression, anxiety, fatigue, and quality of life in a large sample of patients suffering from head and neck cancer in comparison with the general population. *BMC Cancer*, **21**(1): 94. https://doi.org/10.1186/s12885-020-07773-6

Hosni A, Chiu K, Huang SH, Xu W, Huang J, Bayley A *et al.* (2021). Non-operative management for oral cavity carcinoma: Definitive radiation therapy as a potential alternative treatment approach. *Radiother Oncol*, **154**: 70–75. https://doi.org/10.1016/j.radonc.2020.08.013

Janmunee N, Peerawong T, Rordlamool P, Bridthikitti J, Tangthongkum M, Kongkamol C *et al.* (2021). Tumor volume as a prognostic factor on the median survival in locally advanced oral cancer treated with definitive chemoradiotherapy. *Indian J Cancer*, [Advance online publication].

Lingappanoor S, Manupati GR, Meesala V, Yaragani P, Bachu B, Anchuri SS (2019). Assessment of quality of life of cervical cancer patients using ECOG-performance status scale. *J Cancer Tumor Int*, **9**(3): 1–8.

Linton RE, Daker M, Khoo AS, Choo DCY, Viljoen M, Neilsen PM (2021). Nasopharyngeal carcinoma among the Bidayuh of Sarawak, Malaysia: History and risk factors. *Oncol Lett*, **22**(1): 514. https://doi.org/10.3892/ol.2021.12775

Liu CJ, Lin SY, Yang CF, Yeh CM, Kuan AS, Wang HY *et al.* (2020). A new prognostic score for disease progression and mortality in patients with newly diagnosed primary CNS lymphoma. *Cancer Med*, **9**(6): 2134–2145. https://doi.org/10.1002/cam4.2872

Liu K, Lin C, Zhang L (2021). Novel prediction models for patients with oral squamous cell carcinoma at different anatomical sites. *J Oral Maxillofac Surg*, **79**(11): 2358–2369. https://doi.org/10.1016/j.joms.2021.06.023

Machiels JP, René Leemans C, Golusinski W, Grau C, Licitra L, Gregoire V (2020). Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHNS–ESMO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, **31**(11): 1462–1475. https://doi.org/10.1016/j.annonc.2020.07.011

Mathur R, Singhavi HR, Malik A, Nair S, Chaturvedi P (2019). Role of poor oral hygiene in causation of oral cancer—a review of literature. *Indian J Surg Oncol*, **10**(1): 184–195. https://doi.org/10.1007/s13193-018-0836-5

Matos S, Boakye EA, Crosby D, Sharma A (2021). Prevalence and factors associated with oral cavity and pharyngeal cancer screening in a rural population. *OTO Open*, **5**(4): 2473974X211065018. https://doi.org/10.1177/2473974x211065018

Novirianthy R, Syukri M, Gondhowiardjo S, Suhanda R, Mawapury M, Pranata A *et al.* (2023). Treatment acceptance and its associated determinants in cancer patients: A systematic review. *Narra J*, **3**(3): e197. https://doi.org/10.52225/narra.v3i3.197

Oswald LB, Lee JW, Argiris A, Webster KA, Forastiere AA, Cella D (2020). Validation of brief symptom indexes among patients with recurrent or metastatic squamous cell carcinoma of the head and neck: A trial of the ECOG-ACRIN Cancer Research Group (E1302). *Cancer Med*, **9**(23): 8884–8894. https://doi.org/10.1002/cam4.3506

Pennathur A, Brunelli A, Criner GJ, Keshavarz H, Mazzone P, Walsh G *et al.* (2021). Definition and assessment of high risk in patients considered for lobectomy for stage I non–small cell lung cancer: The American Association for Thoracic Surgery expert panel consensus document. *J Thorac Cardiovasc Surg*, **162**(6): 1605–1618. https://doi.org/10.1016/j.jtcvs.2021.07.030

Pingili S, Ahmed J, Sujir N, Shenoy N, Ongole R (2021). Evaluation of malnutrition and quality of life in patients treated for oral and oropharyngeal cancer. *ScientificWorldJournal*, **2021**: 9936715. https://doi.org/10.1155/2021/9936715

Pisani P, Airoldi M, Allais A, Aluffi Valletti P, Battista M, Benazzo M *et al.* (2020). Metastatic disease in head & neck oncology. *Acta Otorhinolaryngol Ital*, **40**(Suppl 1): S1–S86.

Quinn SE, Crandell CE, Blake ME, Bontrager AM, Dempsey AG, Lewis DJ *et al.* (2020). The correlative strength of objective physical assessment against the ECOG performance status assessment in individuals diagnosed with cancer. *Phys Ther*, **100**(3): 416–428. https://doi.org/10.1093/ptj/pzz192

Raman S, Shafie AA, Tan BY, Abraham MT, Chen Kiong S, Cheong SC (2023). Economic evaluation of oral cancer screening programs: Review of outcomes and study designs. *Healthcare (Basel)*, **11**(8): 1198. https://doi.org/10.3390/healthcare11081198

Sakr Y, Hamdy O, Eldeghedi M, Abdelaziz R, Med Sidi El Moctar E, Alharazin M *et al.* (2023). Shifting epidemiology trends in tongue cancer: A retrospective cohort study. *Cancers (Basel)*, **15**(23): 5680. https://doi.org/10.3390/cancers15235680

Sambasivan K, Sassoon I, Thavaraj S, Kennedy R, Doss G, Michaelidou A *et al.* (2021). TNM 8 staging is a better prognosticator than TNM 7 for patients with locally advanced oral cavity squamous cell carcinoma treated with surgery and post-operative radiotherapy. *Radiother Oncol*, **160**: 54–60. https://doi.org/10.1016/j.radonc.2021.04.003

Shrivastava N, Gautam S, Shrivastava S (2024). Head and neck carcinomas: Risk stratification study at an Indian tertiary care hospital. *Eur J Cardiovasc Med*, **14**(1): 1107–1111.

Soltani S, Ojaghi A, Qiao H, Kaza N, Li X, Dai Q *et al.* (2022). Prostate cancer histopathology using label-free multispectral deep-UV microscopy quantifies phenotypes of tumor aggressiveness and enables multiple diagnostic virtual stains. *Sci Rep*, **12**(1): 9329.

Uz U, Eskiizmir G (2021). Association between interleukin-6 and head and neck squamous cell carcinoma: A systematic review. *Clin Exp Otorhinolaryngol*, **14**(1): 50–60. https://doi.org/10.21053/ceo.2019.00906

Ward R, Kanani R, Romeed SA (2022). An audit into the timing of dental extractions pre-head and neck radiotherapy and the prevalence of osteoradionecrosis. *Br Dent J,* [Advance online publication]. https://doi.org/10.1038/s41415-022-3992-5

Woor DE (2015). National Comprehensive Cancer Network (NCCN) clinical practice guidelines for lung cancer screening. *Thoracic Surg Clin*, **25**(2): 185–197. https://doi.org/10.1016/j.thorsurg.2014.12.003

Yahaya NA, Abdullah KL, Ramoo V, Zainal NZ, Wong LP, Danaee M (2022). Effects of Self-Care Education Intervention Program (SCEIP) on activation level, psychological distress, and treatment-related information. *Healthcare (Basel)*, **10**(8): 1572. https://doi.org/10.3390/healthcare10081572

Zhu E, Wang J, Shi W, Jing Q, Ai P, Shan D *et al.* (2024). Optimizing adjuvant treatment options for patients with glioblastoma. *Front Neurol*, **15**: 1326591. https://doi.org/10.3389/fneur.2024.1326591