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ECOG 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. This study aimed to assess pre- and post-treatment ECOG changes in Malaysian oral cavity carcinoma (OCC) patients undergoing various treatments. We conducted a 12–36 month longitudinal observational study with 63 squamous cell carcinoma patients, evaluating ECOG perfomance, medical history, symptoms, sociodemographics, clinical details, and treatment modalities (surgery, surgery + radiotherapy (RT), or surgery + chemotherapy & RT (CCRT)). Oral cavity carcinoma 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-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 score performance in patients post-CCRT, as well as RT. These results highlight the need to provide OCC patients with specialized interventions and support, especially while they are undergoing chemotherapy-induced radiotherapy (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 (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). Oral cavity carcinoma 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 oral cavity carcinoma (Linton *et al.*, 2021).

The genesis of oral cavity carcinoma 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 oral cavity carcinoma, 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 postoperative radiation and chemotherapy is important as the treatment of oral cavity carcinoma, 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 oral cavity carcinoma 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 (ECOG) Performance Score performance status which could provide a valuable tool to assess the functional status of cancer patients, including those with oral cavity carcinoma, 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 performance status, treatment modalities, demographics, and clinical factors in Malaysian oral cavity carcinoma patients. Through this comprehensive analysis, we aim to enhance our understanding of the role of ECOG performance status and its interaction with demographics and clinical factors in guiding treatment decisions and predicting outcomes in Malaysian oral cavity carcinoma patients.

MATERIAL AND METHODS

Ethics 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 oral cavity carcinoma 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 oral cavity carcinoma. 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 radiation therapy (RT) or concurrent chemoradiotherapy (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 contextualized with ongoing developments in the field of oral cavity carcinoma treatment.

In the staging of oral cavity carcinoma, 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 (Tumor Stage) describes the size and extent of the primary tumor. It ranges from T1, indicating a tumor ≤2 cm, to T4, where the tumor has extended beyond the oral cavity or invaded adjacent structures. T4 tumors 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 tumor (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 oral cavity carcinoma (Edge *et al.*, 2010)	Recurrent oral cavity cancer Age > 20 Screening failure Mental compromise Medical unfitness Stage IVc

Evaluation of Performance Status

The ECOG Performance Status 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 Performance Status (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.

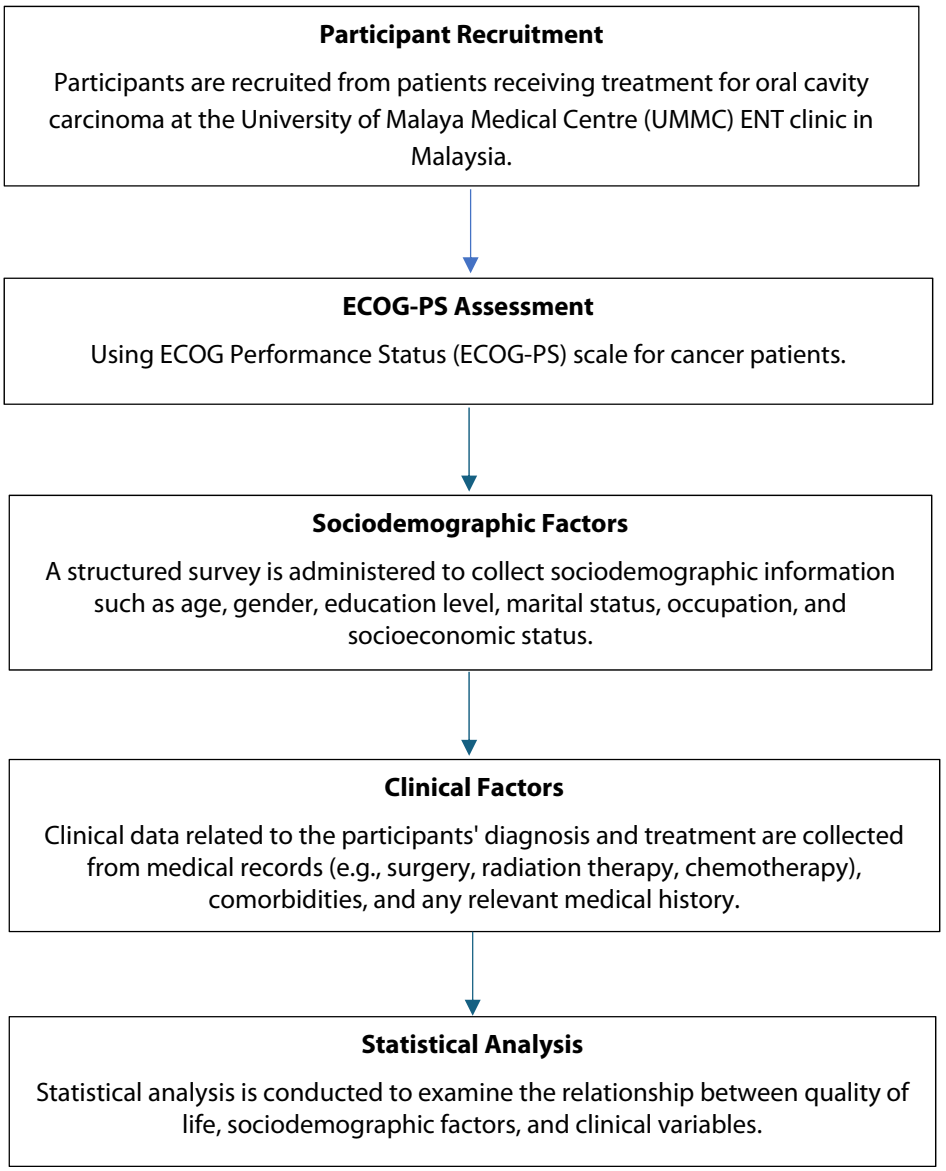

Fig. 1 The flowchart provides a step-by-step description of the data collection process.

Statistical Analysis

SPSS version 19.0 (SPSS Inc, USA) as 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 3 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 socio-demographic 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 oral cavity carcinoma occurred among the Chinese (41%) and Indians (38%), followed by Malay (14%) and the others (8%). 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 our study. Additionally, oral cavity carcinoma occurs at the highest frequency between 51 to 60 years (27%) as well as 61 to 70 years (25%).

As for the clinical data, majority of the patient's tumour was seen in the tongue (52%), followed by buccal (24%) and lower alveolar (11%). Other subsites were less commonly associated, with lower gingiva at 5%, upper alveolar (3%), upper gingiva (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.

Table 2 Socio-demographic and clinical data distribution

Demographic Data	Frequency (n)	Percent (%)
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	52%
Upper gingiva-alveolar	2	6%
Buccal	15	24%
Lower gingiva-alveolar	7	16%
Floor of mouth	1	2%
Histopathological Grade		
Well Differentiated	20	32%
Moderately Differentiated	43	68%
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%

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 patients had underwent surgery alone, 41 had underwent surgery, and post-operative RT and 14 patients had underwent 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.

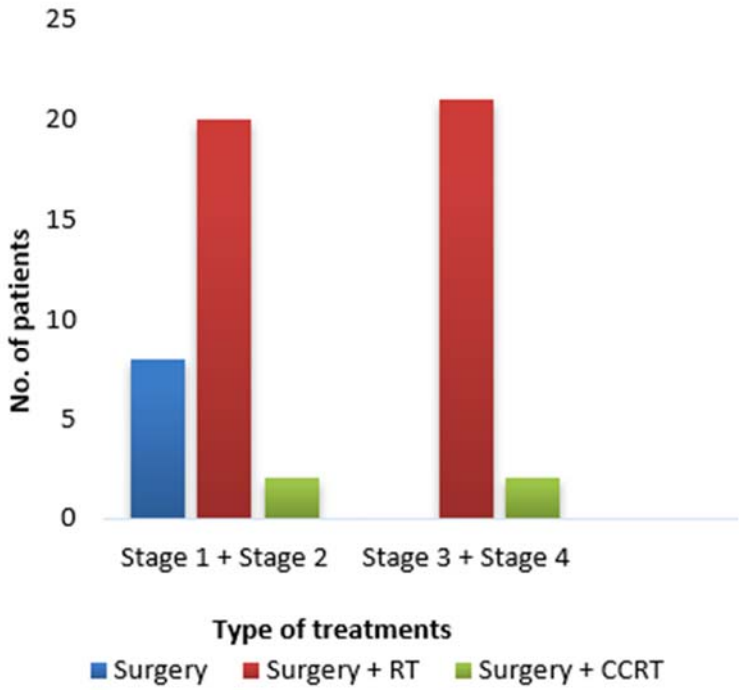

Fig. 2 Distribution of treatment modalities among patients with different disease severity

This suggests that in present study population, adjuvant radiotherapy following surgery is a commonly employed treatment approach for oral cavity carcinoma. 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 scores and our 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 score. 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	0.031
31-40	0.25 ± 0.46	
41-50	0.93 ± 0.69	
51-60	1.00 ± 0.56	
61-70	0.75 ± 0.70	
71-80	1.66 ± 1.11	
81-90	2.93 ± 1.39	
Ethnicity		
Chinese	0.35 ± 0.56	0.583
Indian	1.11 ± 0.27	
Malay	0.45 ± 1.03	
Others	0. 32 ± 0.57	

While gender and ethnicity did not exhibit statistically significant associations with ECOG scores, age group did. This suggests that age may play a crucial role in determining the baseline ECOG scores within our study population (Amri *et al.*, 2023). Furthermore, when the baseline ECOG 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 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 optimize 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	0.001
Stage 2	0.62 ± 0.42	
Stage 3	0.88 ± 0.52	
Stage 4	0.57 ± 0.48	
T Stage		
T1	1.45 ± 0.71	0.041
T2	1.52 ± 0.58	
T3	1.27 ± 0.72	
T4	2.68 ± 1.13	
N Stage		
N0	3.95 ± 1.41	0.040
N1	0.67 ± 0.58	
N2	1.43 ± 0.29	
N3	1.48 ± 1.05	

A comparison of ECOG 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 score for patients who received surgery and CCRT compared with the other 2 arms of treatment at 6 month post-treatment, with a p value of < 0.05. The significant deterioration in ECOG 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).

Table 5 Comparison of ECOG-PS difference between treatments, Surgery +RT 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

There was 3-year overall survival (OS) rate among patients who received either surgery only, surgery with RT or surgery with CCRT (Fig. 3). The OS of those who underwent surgery alone is the highest, followed by those who underwent surgery with RT, and lastly those who underwent surgery with CCRT, which recorded 3-year OS 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).

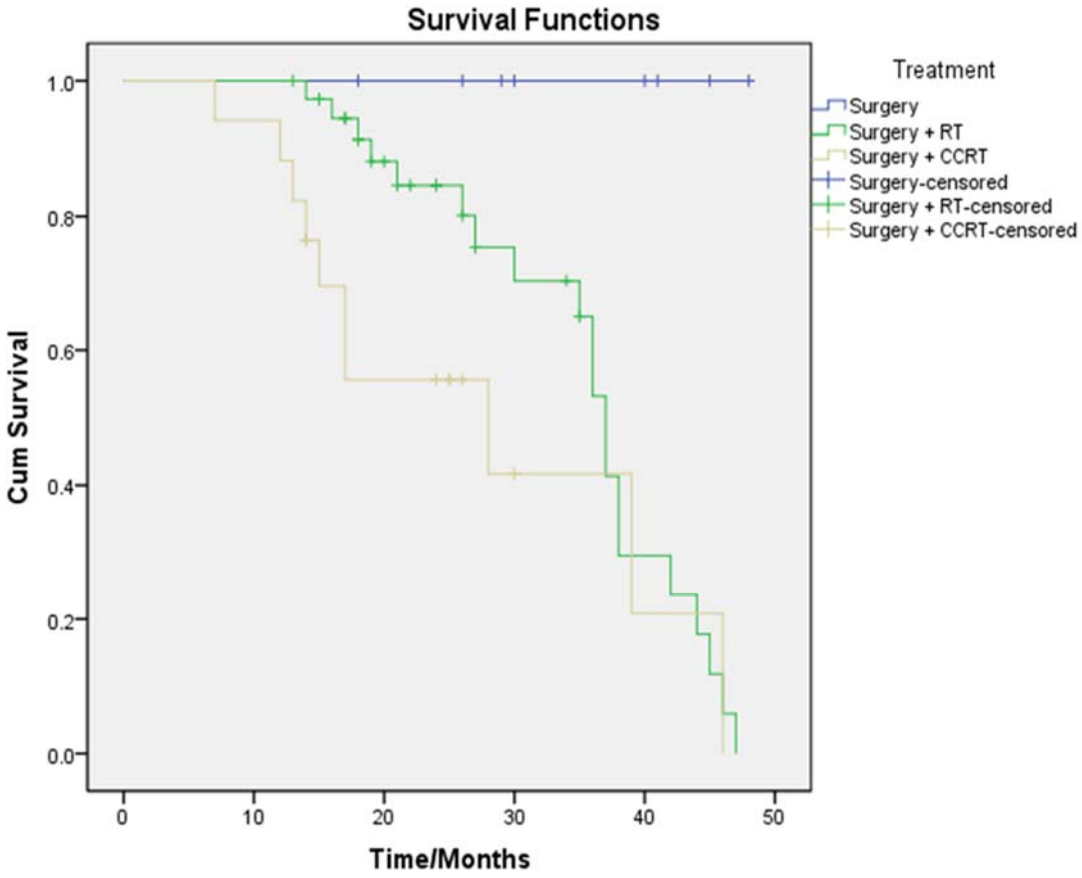

Fig. 3 Kaplan-Meier actuarial analysis showing the overall survival (OS) of patients receiving three different treatment modalities.

DISCUSSION

The majority of the oral cavity cancer (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 oral cavity carcinoma 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). The traditional outcome measures of treatment efficacy, such as tumour recurrence and survival time, are often meaningless to the patient. 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 (RT) (Woor *et al.*, 2015). In certain cases, chemotherapy is combined with radiotherapy (concurrent chemoradiation, CCRT) or administered before the primary treatment (neoadjuvant chemotherapy) to enhance the treatment outcomes (Woor *et al.*, 2015). Our results showed that patients in the CCRT arm had poorer outcomes compared to those in the RT-only arm, with significant deterioration of the ECOG-PS score after 3 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 RT-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 oral cavity carcinoma treatment. Recent studies, as cited in this manuscript, have corroborated some of our findings, and our results contribute to a deeper understanding of ECOG performance in oral cavity carcinoma, particularly in Asian countries, in light of the evolving research landscape.

Poor oral health outcomes and limited access to knowledge on preventing oral cavity carcinoma 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 toward minimizing 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 generalizability of the findings may be limited to similar demographic and clinical settings. Future studies should explore the mechanisms by which tumor 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 (RT) and concurrent chemoradiotherapy (CCRT) may increase overall survival rates. These therapies are linked to a significant decline in functional status following treatment, as indicated by the ECOG scores. Age is found to be a significant influence in determining initial ECOG scores, emphasizing the need of customized treatment plans that take into account unique patient characteristics. In order to address treatment-related impairments and maximize 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 minimize functional decline while preserving or enhancing survival benefits.

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