Original Article

Squamous Cell Carcinoma of Head and Neck in Vajira Hospital: The Outcomes in a Real-World Practice

Bandidwattanawong C, MD[1], Chalongphobsinchai S, MD[1], Tantiwattana T, MD[2]

[1] Division of Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Navamindradhiraj University, Bangkok, Thailand

[2] Division of Radiation Oncology, Department of Radiology, Faculty of Medicine, Navamindradhiraj University, Bangkok, Thailand

Background: Squamous cell carcinoma of the head and neck (SCCHNC) is the fifth most common cancer in Thailand. Even though the multi-modality treatment including surgery, radiotherapy, and chemotherapy is the standard practice, the survival outcomes are not impressive.

Objective: The primary objectives were to determine the overall survival (OS) and 3-year OS of all patients with SCCHNC and as analysis according to the primary site of the primary tumor. The secondary objectives were progression-free survival (PFS), outcomes of induction chemotherapy (IC), prevalence of serious toxicities from treatments, and independent factors of survival.

Materials and Methods: Retrospective analyses were conducted in patients who had SCCHNC confirmed by histology with complete details of staging and treatment, excluding nasopharyngeal carcinoma, carcinoma of the salivary glands, carcinoma of paranasal sinuses, and cutaneous squamous cell carcinoma.

Results: There were 216 eligible patients. OS of all participants was 24.1 months (IQR 14.3 to 50.1). At the median follow-up of 51.49 months, 3-year OS was 52.2% (95% CI 45 to 95). The patients with primary tumor site at the glottic larynx had the longest OS of 45 months (IQR 21.2 to 64.8). The patients with primary sites at the oral cavity (OS 20.1 months, IQR 13.4 to 45.8), oropharynx (OS 20.05 months, IQR 12.4 to 48.5), hypopharynx (OS 23.3 months, IQR 13.3 to 44.6), and supraglottic or transglottic larynx (OS 25.15, IQR 19.55 to 37.8) had nearly equally worst OS. Stratified by primary site of tumor, the investigators found that PFS of patients with glottic larynx was the longest (23.6 months, IQR 17.5 to 53.4). On the other hand, PFS of patients with supraglottic or transglottic laryngeal cancer, oral cavity cancer, oropharynx, hypopharynx was only 11.35 months (IQR 5.8 to 28.65), 12.5 months (IQR 6.2 to 31.3 months), 13.2 months (IQR 6.3 to 27.8), and 15.1 (IQR 8.9 to 29.3), respectively. The IC did not improve the patients' outcomes. Thirty patients (22.4%) had serious (grade 3 to 4) adverse effects from definitive treatment, mostly from severe mucositis. The primary sites at the oral cavity and hypopharynx, T4 diseases, and failure to primary definitive treatment were the independent predictors of early deaths.

Conclusion: Due to the very late stage at presentation, the OS of the participants was only two years. The primary sites at the oral cavity and hypopharynx, T4 diseases rather than the composite TNM staging, and failure to primary definitive treatment were the independent prognostic factors of short survival.

Keywords: Squamous cell carcinoma of the head and neck, Multi-modality treatment, Outcomes, Survival

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Correspondence to:

Bandidwattanawong C.

Division of Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Navamindradhiraj University, Vajira Hospital, 681 Samsen Road, Vajiraphayaban Subdistrict, Dusit District, Bangkok 10300, Thailand.

Phone: +66-2-2443467, **Fax**: +66-2-6687061

Email: chanyootmd@gmail.com

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Squamous cell carcinoma of the head and neck (SCCHNC) is the fifth most common cancer in Thailand according to the Thailand National Cancer Institute Tumor Registry[1]. Most patients are the elderly heavy smokers and live in urban area. Overall survival (OS) among these patients were quite short. Puapermpulsiri et al[2] reported SCCHNC cases in Vajira Hospital and found that most patients presented with locally advanced to advanced diseases such as large cervical lymph nodes or impending upper airway obstruction and were precluded from surgery with curative intent. The five-year survival among the American patients were only 56% in patients with oral cavity (OC) and oropharyngeal cancers and

41% in patients with laryngeal cancer[3]. Standard of care for a patient with early stage (AJCC stage I to II) is definitive surgery with post-operative adjuvant radiotherapy (RT) or chemoradiotherapy, strongly indicated for positive margin. For the locally-advanced disease (AJCC stage III, Iva, and IVb), either surgery, if amenable, or definitive chemoradiotherapy are the options. Surgery or re-irradiation, if amenable, is also reserved as a salvage treatment for a highly-selected residual disease or loco-regional recurrence after definitive chemoradiotherapy[4]. Definitive concurrent RT with cisplatin is the most widely accepted treatment for patients with locally advanced disease[5]. Concomitant anti-epidermal growth factor receptor (EGFR) monoclonal antibody cetuximab with RT are usually reserved for platinum-ineligible cases[4]. The novel RT techniques like intensity-modulated radiotherapy (IMRT) and altered fractionation also add modest clinical benefits in terms of improved locoregional control and less long-term toxicities[6]. To enhance treatment outcomes beyond concurrent chemoradiotherapy (CCRT) in locally advanced SCCHNC, clinical trials tried to compare induction chemotherapy (IC) with no induction treatment. Platinum-and-5-fluorouracil (PF) combination was shown to lead to nearly 54% complete response rate when used as the induction treatment[7] and was used as the comparative regimen in clinical trials. Based on the MACH-NC meta-analysis, PF improved the 5-year survival significantly but marginally compared to no IC[4]. Adding a taxane (TPF regimen) further improved response rate and survival compared to PF. Nevertheless, TPF induction is still controversial because more recent studies comparing TPF versus PF as the induction treatment prior to the standard-of-care concomitant RT with cisplatin failed to demonstrate survival benefit[8]. Most of the patients with SCCHNC needs multi-disciplinary approach. The present study intended to explore the outcomes of Thai SCCHNC patients in the real-life situation of limited resources.

Materials and Methods

After being approved by the Committee of Medical Research Ethics of Navamindradhiraj University (COA no.35/2559), the investigators retrieved the patients' clinical data from the electronic and written databases. The participants included SCCHNC patients aged 18 years or older who attended Vajira Hospital between January 1, 2005 and December 31, 2015 and had complete detailed clinical data including full results of ENT examination, histopathology, imaging studies, and treatments. The investigators used ICD-10 codes of C10 (malignant neoplasm of oropharynx), C13 (malignant neoplasm of hypopharynx), C14 (malignant neoplasm of OC), and C32 (malignant neoplasm of larynx) to extract the data. Due to different prognosis, the investigators subdivided malignant neoplasm of larynx into carcinoma of the glottic larynx and supraglottic or transglottic larynx. The patients with nasopharyngeal carcinoma, carcinoma of the salivary glands, carcinoma of paranasal sinuses, and cutaneous squamous cell carcinoma were excluded. Only patients with complete details of treatments and follow-ups were explored. Participants were followed from the date of diagnosis as indicated in the official pathological reports to the date of death. The data were censored on December 31, 2016. Dates of death were confirmed and determined from the Ministry of Internal Affair Census Database. The exact date of cancer recurrence or metastasis was the date indicated on the official radiological report of recurrence or metastasis. If not available, the date indicated first on the medical record confirming recurrence or metastasis was used. The investigators collected the baseline characteristics of patients including age at diagnosis, gender, primary tumor site, degree of tumor differentiation, overall stage (AJCC 7th edition)[9], tumor stage (T), nodal stage (N), smoking history, and modality of primary definitive treatment. The primary tumor site was classified as OC, oropharynx (OP), hypopharynx (HP), glottic larynx (G), and supraglottic or transglottic larynx (SG/TG). The modality of primary definitive treatment was classified as surgery (S), surgery with adjuvant radiotherapy or chemoradiotherapy (S→RT/CCRT), IC, and definitive chemoradiotherapy (IC→CCRT). The investigators also included the duration of RT session and response to primary definitive treatment as a potential prognostic variable. "Prolonged time to completion of RT course" was defined as the time to completion of RT session that was delayed for more than two weeks as expected. "Failure to primary definitive treatment" was defined as the presence of residual disease or disease progression or death up to six months after the date of diagnosis, no matter if it was determined by clinical examination or imaging studies and confirmed by biopsy or in agreement with the multi-disciplinary team. Only the participants who had finished the primary definitive treatment were determined. "Response to primary definitive treatment" was defined as no evidence of progression of disease or death at six months after the

date of diagnosis. The date of diagnosis was the day the pathological result was officially reported. Either computed tomography (CT) or magnetic resonance imaging (MRI) scans of the whole neck with contrast were obtained prior to commencing treatment and within two to three months after finishing definitive treatment. Further metastatic workups were optional, if clinically indicated. The positron emission tomography (PET)-CT scan was not compulsory. External RT, if indicated was used with conventional fractionation and technique. All the patients who were indicated for RT received conventionally fractionated RT. Neither intensity modulated nor intensity guided RT was applied. The adverse events during treatment were graded according to the CTCAE version 2.0[10]. The response to chemotherapy and RT was evaluated by RECIST criteria version 1.1[11].

Objective

The primary objectives were to assess the OS and 3-year OS of all participants and as stratified by the primary site of the tumor. The OS was measured as the time from the initial diagnosis to the date of death from any cause. The secondary objectives were to determine progression-free survival (PFS) of all patients and stratified by the primary site of the tumor, effect of IC on patients' OS, prevalence of serious adverse events (grade 3 to 4) during definitive treatment, and independent factors of survival. The PFS was measured from the date of initial diagnosis to the date of recurrence (local, loco-regional, or distant) or death whatever occurred first.

Statistical analysis

Based on the study by Shirai et al, at least 101 subjects were required to determining survival outcomes[12]. Each baseline characteristic and descriptive data were reported in number and percent. PFS and OS were reported in months and interquartile range (IQR). The 3-year OS was reported in percent and 95% confidence interval. The Kaplan-Meier method was used to calculate the cumulative proportion surviving and to plot survival curves. The log rank test was used to compare time to event (PFS and OS) functions. Any variables with significant p-value of 0.05 level in univariate analysis model were included into the final multivariable Cox proportional hazards model to determine the independent factors of survival. Statistical analyses were performed using Stata software, version 14 (StataCorp. 2015. Stata Staistical Software: Release 14. College Station, TX: StataCorp LP).

Results

Between January 1, 2005 and December 31, 2015, there were 356 patients with any kinds of head and neck cancers, however, only 216 patients met the eligible criteria with complete details of medical treatments and follow-ups. Table 1 shows the baseline characteristics of patients. The median age at diagnosis was 58.8 years (IQR 23.7 to 85.7). Most of them were male (182, 84.3%) and smokers (173, 80.1%). The most common primary site was OP (66, 30.6%). The other sites included OC (50, 23.2%), glottic larynx (45, 20.8%), HP (31, 14.3%), and SG/TG (24, 11.1%). Most of them had stage IVa (95, 44.0%) and had moderately-differentiated squamous cell carcinoma histology (114, 52.8%). Most of them received CCRT as the primary definitive treatment (70, 32.4%). Fifty-four patients (25%) received IC and then definitive CCRT. Forty-seven patients (21.8%) received definitive surgery with either adjuvant RT or CCRT. Thirty-one patients (14.3%) received only RT as the definitive treatment and all these patients had glottic laryngeal cancer. Only eight patients (3.7%) received only surgery as the definitive treatment and all these patients had early OC cancer.

At the median follow-up of 51.49 months, the OS of all participants was 24.1 months (IQR 14.3 to 50.1) and 3-year OS was 52.2% (95% CI 45 to 95). The patients with primary tumor site at glottic larynx had longest OS of 45 months (IQR 21.2 to 64.8). On the contrary, patients with primary sites at OC (OS 20.1 months, IQR 13.4 to 45.8), OP (OS 20.05 months, IQR 12.4 to 48.5), HP (OS 23.3 months, IQR 13.3 to 44.6), and SG/TG (OS 25.15, IQR 19.55 to 37.8) had nearly equally worst OS (Figure 1). Stratified by primary site of tumor, the investigators found that the PFS of patients with glottic larynx was longest (23.6 months, IQR 17.5 to 53.4). On the other hand, PFS of patients with SG/TG laryngeal cancer was only 11.35 months (IQR 5.8 to 28.65). PFS among patients with OC cancer, OP, and HP were 12.5 months (IQR 6.2 to 31.3 months), 13.2 months (IQR 6.3 to 27.8), and 15.1 (IQR 8.9 to 29.3), respectively (Figure 2).

The most commonly-used concomitant chemotherapy with RT was cisplatin (80, 55.9%). Less commonly-used agents were carboplatin/5-FU (59, 41.3%) and cetuximab (4, 2.8%). All the patients who received cetuximab had chronic kidney disease. IC regimens were either cisplatin/5FU or cisplatin/5-FU/paclitaxel. The response rate of IC was dramatically high (72.2%) with minimal rate of serious toxicities (grade 3 to 4) (7.4%). The most serious adverse events during IC were severe oral mucositis (3, 5.5%) and

Table 1. Baseline characteristics of patients with squamous cell carcinoma of head and neck

Characteristics	Patients n (%)
Age (year); median (IQR)	58.8 (23.7 to 85.7)
Sex	
Male	182 (84.3)
Famale	34 (15.7)
Site	
Oral cavity	50 (23.1)
Oropharynx	66 (30.6)
Hypopharynx	31 (14.4)
Supraglottic/transglottic larynx	24 (11.1)
Glottic larynx	45 (20.8)
Differentiation	
Well	42 (19.4)
Moderately	114 (52.8)
Poorly	21 (9.7)
Unknown	39 (18.1)
Smoking	
No	23 (10.6)
Yes	173 (80.1)
Unknown	20 (9.3)
T stage	
1	32 (14.8)
2	51 (23.6)
3	53 (24.5)
4	80 (37.1)
N stage	
0	93 (43.0)
1	35 (16.2)
2	68 (31.5)
3	20 (9.3)
AJCC TMN stage	
I	23 (10.6)
II	25 (11.6)
III	39 (18.1)
IVa	95 (44.0)
IVb	34 (15.7)
Modality of definitive treatment	
Surgery	8 (3.7)
Surgery and adjuvant RT/CCRT	47 (21.8)
Definitive RT	31 (14.3)
Definitive CCRT	70 (32.4)
Induction CMT→RT/CCRT	54 (25.0)
Palliative care	6 (2.8)
PFS	
<6 months	39 (18.1)
≥6 months	177 (81.9)

T stage=tumor stage; N stage=nodal stage; AJCC TMN stage=composite stage based on American Joint Committee on Cancer, 7th edition; RT=radiotherapy; CCRT=concurrent chemoradiation; CMT=chemoradiation; PFS=progression-free survival; IQR=interquartile range

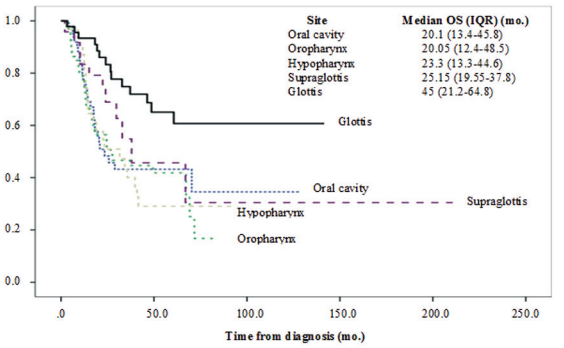

Figure 1. Shows overall survival (OS) stratified by primary site of tumor.

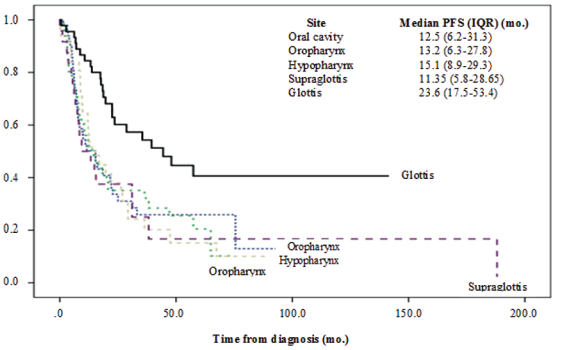

Figure 2. Shows progression-free survival (PFS) stratified by primary site of tumor.

severe anemia (1, 1.9%). Most of the participants (136, 73.9%) finished RT on time (within 7 to 9 weeks). Only a quarter of participants had prolonged time to complete RT course. Thirty patients (22.4%) had serious (grade 3 to 4) toxicities during CCRT. Fourteen patients (10.4% of all participants) had

Table 2. Predictors of overall survival among patients with squamous cell carcinoma of head and neck

	Death from all causes (univariate analysis)			Death from all causes (multivariate analysis)		
	HR	95% CI	p-value	HR	95% CI	p-value
Site						
Glottis	Reference			Reference		
Oral cavity	2.41	1.26 to 4.61	0.008	2.07	1.06 to 4.05	0.033
Oropharynx	2.72	1.47 to 5.03	0.001	1.94	0.98 to 3.84	0.056
Hypopharynx	2.9	1.47 to 5.72	0.002	2.37	1.63 to 4.80	0.017
Supraglottic/transglottic	1.9	0.86 to 4.18	0.114	1.19	0.51 to 2.75	0.69
T stage						
T1-T3	Reference			Reference		
T4	2.41	1.65 to 3.51	<0.001	2.91	1.63 to 5.18	<0.001
N stage						
N0-N1	Reference			Reference		
N2-N3	1.8	1.24 to 2.62	0.002	1.5	0.82 to 2.74	0.19
AJCC TNM stage						
Stage I-III	Reference			Reference		
Stage IVa-IVb	2.19	1.45 to 3.31	<0.001	0.66	0.30 to 1.45	0.3
Induction CMT						
No	Reference			Reference		
Yes	2.29	1.15 to 2.60	<0.001	1.32	0.81 to 2.16	0.26
Duration of RT						
Complete	Reference			Reference		
Incomplete/prolong	1.8	1.15 to 2.81	0.01	1.26	0.80 to 2.02	0.32
PFS						
≥6 months	Reference			Reference		
<6 months	3.73	2.48 to 5.62	<0.001	2.82	1.77 to 4.53	<0.001

HR=hazer ratio; CI=confidence interval; T stage=tumor stage; N stage=nodal stage; AJCC TMN stage=composite stage based on American Joint Committee on Cancer, 7th edition; RT=radiotherapy; CCRT=concurrent chemoradiation; CMT=chemoradiation; PFS=progression-free survival

severe oral mucositis. Seven (5.2%) patients had severe electrolyte imbalances. The toxicities during definitive RT (without concomitant chemotherapy) were less common. Severe oral mucositis occurred in three patients (6%) and severe electrolyte imbalances happened in only one patient (2%). The investigators found that response to primary definitive treatment was as high as 89.9% (177 patients). The rest had confirmed residual disease or progression or death up to six months after the diagnosis as defined as failure to primary definitive treatment. All the patients with failure to primary definitive treatment had either confirmed residual disease or progression at loco-regional site. Only one patient had confirmed second primary adenocarcinoma of lung.

The univariate analysis revealed that the primary tumor site, advanced T stage, advanced N stage, advanced TNM AJCC staging, IC, prolonged time to RT completion, and failure to primary definitive treatment were the prognostic factors of early death. However, the multivariate analysis demonstrated that primary sites at OC and HP, T4 disease, and failure to primary definitive treatment were the independent predictors of short survival (Table 2).

Regarding the role chemotherapy in palliative setting, a platinum plus 5-FU (51.3%) and carboplatin plus paclitaxel (30.8%) were the most commonly used regimens. A platinum plus 5-FU and cetuximab was rarely prescribed (2.5%). The response rate of the first line regimen was 35.9%. One-third of the patients had stable disease response, and the rest had progressive disease. The OS after palliative chemotherapy was quite short at only 8.7 months.

Discussion

SCCHNC is one of the most fatal cancers. Most

of the patients with unresectable locally advanced diseases usually die within three to five years after diagnosis. Multi-modality management is the standard of care for such patients. The results from the present study showed that response to primary definitive treatment and severe adverse event rates were comparable to the international reports. Nevertheless, the OS was quite short. One of the explanations was probably because most of the patients (77.8%) had advanced stage (AJCC stage III, IVa and IVb) at the time of presentation. In comparison with the result from a real-life practice in Italy reported by Cadoni et al[13], the percentage of patients with stage III, IVa, IVb was 54.2%. The investigators demonstrated that primary sites at OC and HP, T4 disease, and failure to primary definitive treatment were the independent poor prognostic factors of survival. Regarding the primary tumor sites, the investigators' result was in accordance with the Italian report[13]. They found that 5-year OS at HP was 50%, OC 49%, OP 54.8%, and larynx (63.4%). The investigators' multivariate analysis revealed that primary sites at OC and HP were the independent sites of the worst prognosis. The patients with early OC cancer (AJCC stage I to II) are usually treated with curative surgery with excellent outcomes. However, the results among patients with more locally advanced diseases (AJCC stage III) are not impressive. Such patients usually succumb to loco-regional recurrences after curative resection alone. Most of them require adjuvant treatment. Moreover, salvage surgery is not amenable in most cases. Either re-irradiation or chemotherapy slightly prolong survival. Therefore, no effective curative treatment is existed for advanced OC patients with failure to primary definitive treatment or unresectable loco-regional recurrence. Multi-disciplinary treatment for OC patients with more advanced diseases (AJCC stage IVa and IVb) also fails to improve curability. The investigators found that even though IC and concurrent chemo-radiation improved treatment response, it did not translate to significantly improved curability. Neither salvage surgery nor re-irradiation led to long-term remission. Both were limited to palliative intent. The participants with primary tumor at HP usually presented at later stages. The reason would be the fact that HP tumor tends to progress into more advanced T stages before symptoms such as odynophagia, upper airway obstruction, and hoarseness of voice develop. The richness of lymphatic drainage at this site also explains why the HP patients usually present with bulky nodal metastasis. Moreover, most of the HP patients are the heavy smokers. Based on the anatomy and pathogenesis, HP cancer is most deleterious. The investigators found that the participants with advanced HP cancer (AJCC stage IVa and IVb) never lived beyond two years after definitive combined modality treatment. The investigators found that glottic larynx was the site of best prognosis. Most of such patients usually present with easily noticeable symptom like hoarseness of voice, even at the early stage. True glottic larynx is also devoid of lymphatics. Both surgery and RT or definitive CCRT are equally effective in terms of survival. Either modality can be obtained as the salvage treatment with curative intent. Regarding the staging, the investigators revealed that only advanced T stage was the significant prognostic factor. On the other hands, the N stage and the composite AJCC staging were not the independently prognostic factors. Magnano et al[14,15] found that the extent of tumor invasion was the independent factor that determined the chance of nodal metastasis. The T stage was also the independent factor of survival among patients with OP and HP cancers[16]. However, T stage seemed not to be a perfect tool to define extent of tumor. Depth of tumor invasion was the better predictor especially among patients with OC. Tumor diameter was also the better prognostic factors among patients with OC and OP cancers[17] and larynx[18]. Tumor volume was the more precise predictor among patients with SG[19]. Regarding the N stage, Valle-Zapico et al[20] demonstrated that the number of involved lymph nodes was not the independent factor when it was adjusted to other pathological factors. Extracapsular nodal invasion was instead the independent factor of short disease-free interval and survival[21-23]. Non-sentinel lymph node metastasis was also reported as the better prognostic factor[24]. Low-lying cervical node metastasis (to level IVa and IVb) was interestingly the better predictor of adverse outcomes compared to nodal size[25]. The investigators did not include the pathological factors like extracapsular extension and lympho-perineural invasion in the survival analysis because all the patients with high risk pathological factors always received adjuvant chemoradiotherapy if it was not contraindicated.

According to the investigators' analysis, the tumor differentiation was not the independent prognostic factor. Most of the pathologists have used the system of determination of the degree of tumor differentiation established by Broders[26]. Many studies agreed that the tumor differentiation was not the independent factor because patients with poorly differentiated tumors also had more advanced

AJCC staging[27]. The novel "Invasive Cell Grading System"[28] would be the better prognostic factor; however, it is rarely used[28-30].

The investigators used the PFS within six months after diagnosis as the definition of failure to primary definitive therapy. According to the routine practice in Vajira Hospital, imaging studies were done prior to primary definitive treatment and 8 to 12 weeks after finishing RT. To biopsy the suspicious residual disease in either primary site or node was not routinely practiced. Symptomatic residual disease or obvious progression up to six months after the diagnosis as determined by ENT examination or follow-up imaging studies in agreement with the multi-disciplinary care team (MDT) was unquestionably proper for the declaration of residual disease or progressive disease. Biopsy was done only in a doubtful case. The investigators demonstrated that the failure to primary definitive treatment was the significant bad prognostic factor of survival. This notion would be explained by the fact that salvage surgery, salvage neck dissection, or re-irradiation never resulted in long-term remission.

Smoking is one of the established predictors of survival outcomes among patients with SCCHNC. Ang et al[31] reported that more-than-10 pack per year smoking was associated with shorter survival in OP patients treated with definitive RT. Furthermore, Browman et al[32] also found that patient who were still smoking while receiving RT led to more adverse outcomes compared to patients who had already quitted smoking. The investigators showed that smoking was associated with poor survival outcome only in univariate analysis. The investigators could not determine a participant's smoking habit precisely as a result of the limitation of the retrospective analysis. Alcohol-used disorder in patients with SCCHNC was also an adverse survival factor[33]. The investigators noticed that many SCCHNC patients who developed alcohol-used disorder during hospitalization were not systematically reported in medical reports.

The investigators recorded the time to finishing radiation course as a potential prognostic factor. Alden et al[34] and Shaikth et al[35] revealed that longer time to finishing RT than expected was the predictor of shorter survival no matter the patients receiving conventional or altered fractionation RT. Interestingly, the investigators found that prolonged time to complete radiation course (more than two weeks as expected) was a significant prognostic factor in univariate analysis, but it failed to demonstrate in multivariate analysis. However, the investigators' study had not enough power to test this hypothesis.

The p-16 is the surrogate marker of HPV-driven OP cancer. The p-16 status was not yet routinely determined in Vajira Hospital during the period the participants were treated. Ang et al demonstrated that p-16 status was one of the independent good prognostic factors among OP patients regardless of smoking and nodal status[31]. The investigators found that the participants with OP cancer had grave prognosis comparable to the ones with non-glottic laryngeal cancers. It could be deduced that the prevalence of HPV-driven OP cancer was possibly low.

The investigators did not demonstrate the benefit of IC as a predictor of improved outcome. Presumably, most of the patients receiving IC suffered from either very advanced disease (stage IVa and IVb) or very symptomatic locally-advanced disease who needed immediate treatment while waiting for initiation of definitive RT. A meta-analysis by Budach et al[36] reported the doubtful survival benefit of IC. The investigators suggest that IC is still investigational. Routine prescription of IC is not recommended, even though its response rate is very high. Therefore, IC would be indicated only for a patient with symptomatic bulky disease who requires urgent palliation. The investigators found that gastrostomy and prophylactic tracheostomy could be avoided in such patients who responded dramatically after the first few cycles of induction treatment.

Due to the retrospective design, the investigators had to exclude patients with incomplete data. The investigators could not determine the dose density of chemotherapy used during concomitant treatment that would affect the outcomes. The investigators also lacked the p-16 status that would be the potential prognostic marker. Nevertheless, the investigators demonstrated the outcomes of the usual practices done in Thailand and in the developing world. It would reflect overall national outcomes that are still scarce of data. The investigators' results could be referred and benchmarked in future studies.

Conclusion

The investigators demonstrated the worse OS and 3-year OS among SCCHNC patients treated in Vajira Hospital compared to other parts of the world. The primary sites at OC and HP, T4 stage, and failure to primary definitive treatment predicted the adverse survival.

What is already known to this topic?

Multi-modality treatment is the standard of care

for locally advanced SCCHNC. The toxicities are not different from the literatures. Most of them are manageable.

What this study adds?

Most of the Thai patients manifest at very late stage of diseases. Even though multi-modality treatment is accessible, the outcomes are still not impressive. The outcomes and prognostic factors are useful for further clinical trials in Thailand.

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Conflicts of interest

The authors declare no conflict of interest.

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