Results of Multidisciplinary Therapy of Squamous Cell Carcinoma of the Buccal Mucosa at Srinagarind Hospital, Thailand

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Objective: *Review the clinical presentation and treatment of buccal carcinoma and compare it to the results of treatment as per survival rate.*
Material and Method: *The authors reviewed the medical records of newly diagnosed seen between 1995 and 2005 at the Division of Plastic Surgery and the Department of Radiotherapy, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University. Patients previously treated elsewhere or those whose lesions secondarily involved the buccal mucosa were excluded.*
Results: *The authors reviewed the medical records of 107 buccal carcinoma patients (94 females and 13 males) averaging 67 years of age. The 5-year survival rates of patients with Stage I (5.6%), II (6.5%), III (12.1%), and IVa (75.7%) were 67%, 43%, 47%, and 26%, respectively. A combined modality treatment (surgery and radiation or chemotherapy) was used to treat the advanced stage (III and IV) patients. The rate of incomplete therapy was high (47.78%). In the group that completed the protocol (i.e., neoadjuvant, surgery, and post operative radiation), there were five patients for whom the 5-year survival seemed higher than the patients who followed the standard treatment of surgery and post-operative radiation but it was not statistically significant.*
Conclusion: *The treatment of buccal carcinoma requires a multidisciplinary team approach because most of the patients are elderly and present with an advanced stage. If treatment continues through to completion of the protocol, the survival rate would increase.*

Keywords: *Buccal carcinoma, Survival rate*

J Med Assoc Thai 2010; 93 (11): 1262-7
Full text. e-Journal: *http://www.mat.or.th/journal*

Squamous cell carcinoma is the most common malignancy of the upper aerodigestive tract[1]. This structure includes the lip, oral cavity, nasopharynx, oropharynx, and hypopharynx. The buccal mucosa is part of the oral cavity that includes the epithelial lining of the inner surface of the lips and the oral surface of the cheeks to the line of attachment of the mucosa superiorly and inferiorly at the alveolar ridge of the upper and lower jaws. Its posterior limit is the attachment at the retromolar trigone.

At Srinagarind Hospital, the cancer center for Northeast Thailand, oral cavity cancer remains one of the top five cancers reported for both sexes[2]. A non-healing ulcer is the common presentation of the oral cavity cancer but different survival rates and treatment modalities depend on the location of the primary tumors. At the early stage, buccal cancer is characterized by a painless lesion, the nature of which makes patients unconcerned until they have difficulty chewing or swallowing, trismus, neck pain or altered speech and breathing problems. At this stage, the cancer is advanced and sometimes results in unresectable tumor.

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Local control at the early stage includes a single modality of either surgery or radiotherapy. At the advanced stages (III or IVa), surgery, radiation therapy, and/or chemotherapy are the combined managements required[3]. However, the choice of treatment depends on the resectability of the cancer, performance status and any co-morbidities.

The authors' aim was to describe the nature of disease and the results of treatment at Srinagarind Hospital, Khon Kaen University, Thailand.

Material and Method

The authors reviewed the database between 1995 and 2005 for all new patients with cancer of the buccal mucosa. The data included sex, age, staging, treatment, follow-up information, and survival rate. A questionnaire was sent to the family and civil registry of patients who were lost to follow-up. Patients previously treated elsewhere or those whose lesions secondarily involved the buccal mucosa were excluded.

Statistical analysis

STATA (version 10) was used to create a database and to perform statistical analysis. Statistical analysis included descriptive statistics on age, sex, site of lesions, primary treatments, and adjuvant treatments. Overall survival rate and respective curves comparison were evaluated using the Kaplan-Meier method. The hazard ratio and 95% confidence interval (95% CI) were used to determine the significance of the difference between the estimates for each treatment subset.

Results

One hundred seven patients were included in the present study, and were mostly (87.9%) female. Furthermore, all of the females had a history of betel nut chewing. The median age was 67 years and 39 patients (36.44%) were older than 70.

The dominant side of the cancer was on the left. Cancer was co-morbidities with two of the patients (*viz.*, hepatoma and colon cancer) (Table 1). Six (5.6%), 7 (6.5%), and 13 (12.1%) cases were Stage 1, 2, and 3, respectively. Stage IVa was the predominate stage with 81 (75.7%) cases and the one patient in stage IV had a bilateral tumor.

The treatment given depended upon the stage of the disease and the patient's status. The treatment of choice for early stage cancers (I and II) was surgery or radiation alone; while a combined therapy was needed for advanced stage cancers (III and IV) (Table 2).

The standard treatment was a minimum of surgery and post-operative radiation. Neoadjuvant chemotherapy was the accepted protocol. Incomplete therapy was indicated if the treatment was surgery alone or neoadjuvant chemotherapy alone or surgery and chemotherapy without radiation. The ratio of incomplete therapy was high (47.87%). In the group treated with radiation alone, the purpose of the treatment was palliation.

Among patients who have undergone surgery, a wide excision and neck dissection were the standard treatment for advanced stage cancer. Reconstruction depended on the remaining tissue and the general condition of the patient. Most of the

Table 1. Demographic data

Stage	Number	Side		Gender	
		Right	Left	Male	Female
I	6 (5.6%)	1	5	1	5
II	7 (6.5%)	3	4	2	5
III	13 (12.1%)	4	9	1	12
IV	81 (75.7%)	32	50	9	72
Total	107 (100%)	40	68	13	94

Table 2. Overall survival in each treatment protocol

Stage	No.	Sx	5Y	Sx, Rt	5Y	Sx, C	5Y	Sx, Rt, C	5Y	Rt	5Y	C	5Y	No Tx
I	6	5	80%	1	100%									
II	7	4	75%	2	50%					1	0%			
III	13	3	67%	4	75%			1	100%	3	0%	2	0%	
IVa	81	13	39%	18	50%	12	42%	7	43%	15	0%	15	0%	1

Sx = surgery; Rt = radiation; C = chemotherapy; Tx = treatment; 5Y = 5 years survival rate

Table 3. Surgical treatment

Stage	No.	Wide excision	Neck dissection	Mandibulectomy		Partial maxillectomy	Reconstruction		
				Segment	Marginal		Skin graft	Local flap	Free flap
I	6	6	1 (SOH)				1	3	1
II	7	6	4 (SOH)				1	3	1
III	13	8	6 (RND)					7	1
IV	81	49	49 (RND)	8	8	6	3	23	23

SOH is supraomohyoid neck dissection. RND is radical neck dissection

Table 4. Overall survival and staging

Stage	No.	3Y survival	5Y survival
I	6	84%	67%
II	7	43%	43%
III	13	54%	47%
IVa	81	36%	26%

reconstructions required either a local or free flap (Table 3).

The 3- and 5-year survivals were higher for early stage cancers and depended upon the treatment protocol (Table 2, 4-6 and Fig. 1-4). One patient in stage IV was septic at admission and died without any definitive treatment for buccal carcinoma.

Table 5. Comparison of each treatment to the standard treatment (of surgery and post-operative radiation) in all stages

Treatment	Hazard ratio	Standard error	p-value	95% confidence interval	
Sx	1.117	0.448	0.783	0.508	2.453
Sx, C	1.391	0.617	0.457	0.583	3.320
Sx, C, Rt	0.743	0.422	0.601	0.244	2.261
Rt	6.304	2.398	0.000	2.991	13.289
C	12.470	5.194	0.000	5.512	28.211

Sx = surgery; Rt = radiation, C = chemotherapy

Table 6. Comparison of each treatment to the standard treatment (of surgery and post-operative radiation) in advance stages

Treatment	Hazard ratio	Standard error	p-value	95% confidence interval	
Sx	1.165	0.498	0.720	0.504	2.695
Sx, C	1.194	0.530	0.689	0.500	2.850
Sx, C, Rt	0.987	0.515	0.981	0.355	2.743
Rt	5.674	2.177	0.000	2.675	12.035
C	11.152	4.666	0.000	4.911	25.323

Sx = surgery; Rt = radiation, C = chemotherapy

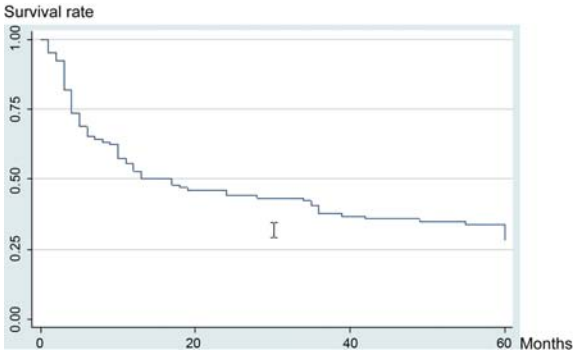

Fig. 1 5-year overall survival as per Kaplan-Meier survival estimates for all stages

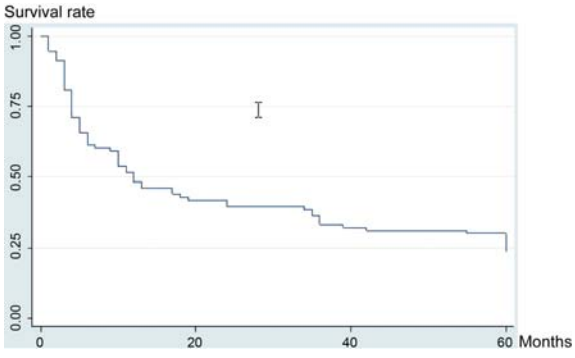

Fig. 2 5-year overall survival as per Kaplan-Meier survival estimates for advanced stages

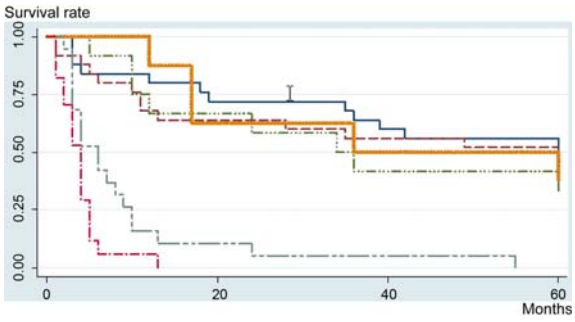

Fig. 3 5 years overall survival in each treatment protocol for all stages

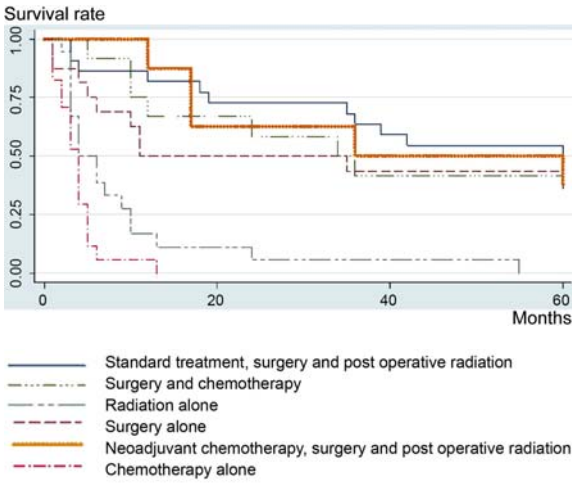

Fig. 4 5-year overall survival in each treatment protocol for advanced stages

Discussion

Worldwide, cancer of the head and neck is relatively uncommon compared with other tumor locations and two-thirds of the deaths occur in men[4]. The risk factors are alcohol and tobacco, both of which act as local irritants to the mucosa[5]. By contrast in Northeast Thailand, these are among the top five cancers and highest among woman because of habitual betel nut chewing. The dominant side of these tumors is the left side. The cause is unknown but may be from the betel nut chewing pattern as most of the people were right side chewers. After crushing the betel nut, it is sucked from the left cheek where mucosal irritation is greatest.

Early detection and appropriate treatment of buccal cancer are associated with a high rate of cure. Data for 5-year survival of the early stage range from 57.7% to 100% and of the advanced stage range from 0% to 78%[6-11]. In the present study, survival depended on the stage and specific treatment and might be best accomplished using the combined therapy. The respective 5-year survival for Stage 1 to 4 was 67%, 43%, 47%, and 26%. Formerly, surgery and radiation had a role for the locally-advanced stage. From the mid-1970s, as part of a combined modality treatment, chemotherapy is used to improve the cure rate[12,13], including for advanced stage, making some operable that were not[7,11,14-18]. Pignon et al in a meta-analysis evaluating the use of chemotherapy in squamous cell carcinoma of the upper aerodigestive tract concluded better results occur when chemo-therapy is used concurrently with radiotherapy[19].

At Srinagarind Hospital, neoadjuvant chemotherapy was started for cancer of the buccal mucosa, which increased operability of formerly inoperable cancers. However, this is only a preliminary protocol. The total subject for this group was 34 patients and 15 were lost to follow-up during the neoadjuvant therapy: the 5-year survival time was 0%. Twelve patients did not receive post-operative radiation after completing the neoadjuvant therapy and surgery. In this group, the 5-year survival time was 42%. In the group that completed the protocol (*i.e.*, neoadjuvant chemotherapy, surgery, and post operative radiation) there were five patients for whom the 5-year survival seemed to be higher than the patients who followed the standard treatment of surgery and post-operative radiation but the difference was not statistically significant.

The toxic effects of chemotherapy included anorexia, vomiting, hemolytic-uremic syndrome, neutropenia, thrombocytopenia, stomatitis, xerostomia, and diarrhea[14,20,21], but this regimen is usually well tolerated. The most serious side effect is death[22]. At Srinagarind Hospital, the toxic effects of chemotherapy were not different from published information. However, this group of patients is frequently elderly and has signs of malnutrition, poor socioeconomic status, and low education, all of which seem to contribute to a high rate of complications, side effects, and loss to follow-up.

In the poorest patients, palliative radio-therapy was the treatment of choice as it was better than incomplete neoadjuvant chemotherapy, with respect to both survival and side effects. If the criteria used to select the appropriate treatment for each patient were better, the survival rate might be improved or at least the end-of-life quality would be better.

The future treatment plan may be the combination of induction chemotherapy before tumor resection and followed by concurrent chemo-radiotherapy for improved local control, quality of life with organ preservation, disease-free, and overall survival rates. The patients may, however, suffer from severe treatment-related toxic effects. Therefore, it will be important to prepare the patient with good nutrition, health education, and evaluation using Karnofsky's classification. To avoid loss to follow-up and incomplete treatment, more health education may help to overcome poor education and low socio-economic status.

Acknowledgements

The authors wish to thank Mr. Bryan Roderick Hamman for assistance with the English-language presentation of the manuscript.

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ผลของการรักษาผู้ป่วยมะเร็งเยื่อบุกระพุ้งแก้ม แบบสหสาขาในโรงพยาบาลศรีนครินทร์

กมลวรรณ เจนวิถีสุข, พลากร สุรกุลประภา, บวรศิลป์ เชาวน์ชื่น, วรชัย ตั้งวรพงศ์ชัย, มณเฑียร เปสี, ศรีชัย ครุสันธิ์, จันทร์ศรี ศุภอดิเรก

วัตถุประสงค์*: เพื่อศึกษาผลของการรักษาผู้ป่วยมะเร็งเยื่อบุกระพุ้งแก้มแบบสหสาขาในโรงพยาบาลศรีนครินทร์*

วัสดุและวิธีการ*: ทำการศึกษาเวชระเบียนผู้ป่วยมะเร็งเยื่อบุกระพุ้งแก้มที่เข้ารับการรักษาในโรงพยาบาลศรีนครินทร์ โดยหน่วยศัลยศาสตร์ตกแต่ง ภาควิชาศัลยศาสตร์ และหน่วยรังสีรักษา ภาควิชารังสีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ระหว่างวันที่ 1 มกราคม พ.ศ. 2538-31 ธันวาคม พ.ศ. 2548*

ผลการศึกษา*: มีผู้ป่วยมะเร็งเยื่อบุกระพุ้งแก้ม ที่ได้รับการรักษาทั้งหมด 107 ราย เป็นเพศหญิง 94 ราย และเพศชาย 13 ราย โดยมีอายุเฉลี่ยที่ 67 ปี แบ่งเป็นมะเร็งระยะที่หนึ่ง ร้อยละ 5.6 ระยะที่สองร้อยละ 6.9 ระยะที่สามร้อยละ 12.1 และระยะที่สี่ร้อยละ 75.7 โดยมีอัตรารอดชีพที่ 5 ปี ของระยะที่ 1 ถึง 4 คือร้อยละ 67 ร้อยละ 43 ร้อยละ 47 และร้อยละ 26 ตามลำดับ การรักษาผู้ป่วยในระยะที่สามและสี่ เป็นการให้การรักษาร่วมในด้านการผ่าตัด การให้รังสีรักษา และ/หรือ การให้ยาเคมีบำบัด อย่างไรก็ตามมีผู้ป่วยร้อยละ 47.78 ที่ไม่ได้รับการรักษาครบถ้วนตามแผนที่วางไว้ ส่วนในกลุ่มที่ได้รับเคมีบำบัดนำร่อง ตามด้วยการผ่าตัดและการฉายแสงมีแนวโน้มของการรอดชีพสูงกว่าการผ่าตัดและการฉายแสง แต่ยังไม่พบว่ามีนัยสำคัญทางสถิติ*

สรุป*: การให้การรักษาผู้ป่วยมะเร็งเยื่อบุกระพุ้งแก้ม จำเป็นต้องได้รับการดูแลรักษาแบบสหสาขา เนื่องจากผู้ป่วยส่วนใหญ่เป็นผู้ป่วยสูงอายุ และเป็นมะเร็งในระยะที่สามและสี่ซึ่งมีความรุนแรงของโรคสูง หากสามารถให้การรักษาแบบสหสาขาได้ครบถ้วนตามแผนที่วางไว้จะสามารถเพิ่มอัตรารอดชีพให้แก่ผู้ป่วยได้*