

An outcome of Surgically Treated Head and Neck Cancer in one of the tertiary Referral Center in the East Coast of Malaysia: A 6-year Retrospective Analysis

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Abstract

Background: Surgical management of head and neck cancer is undoubtedly challenging, and we would like to see the outcome of managing such cases at one of the tertiary referral center in the East Coast of Malaysia.

Methods: A 6-year retrospective analysis of surgically treated head and neck cancer cases in Hospital Tengku Ampuan Afzan (HTAA) Kuantan, Pahang was conducted.

Results: The total number of patients reviewed was 55 and mean age of the patients was 59 years (SD 12). The larynx was the most common surgically treated site (29.1%), followed by the oral cavity (16.4%) and the paranasal sinuses (14.5%). Majority of the patients presented with stage III (32.8%) and stage IV (41.8%) cancer. Post-operative local complications (23.6%) and wound breakdown was identified as the most common cause (20%). Low hemoglobin level prior to surgery was associated with anemia after surgery ($P = 0.007$) and prolonged hospital stay ($P = 0.030$). Tumor recurrence was observed in 21.8% of the cases. Advanced stage tumor had more percentage of positive margin than early stage tumor i.e., 23% in early stage versus 58% in advanced stage ($P = 0.050$).

Conclusion: Surgical management of head and neck cancer in this center has an acceptable outcome.

Keywords: head and neck cancer, surgery, complications, recurrence

Introduction

Head and neck cancer is a broad term, which comprises epithelial malignancy involving upper aerodigestive tract such as paranasal sinus, nasal cavity, oral cavity, pharynx, larynx, and salivary gland. A total of 18 219 new cancer cases were diagnosed among Malaysians in the year 2007 and the report indicates that head and neck cancer contributed 10% (1826) of the cases (1). Despite this significant number of cases being reported, only few articles were published concerning head and neck cancer, and majority focused on nasopharyngeal carcinoma (NPC) as it was the most common head and neck cancer in Malaysia (2–8). A PubMed search revealed very limited literature on surgically treated head and neck cancer in Malaysia (9–11). Various options for the treatment of head and neck cancer are available including surgery, radiotherapy,

chemotherapy or any combination of them (12). However, not all these facilities were available in most of the tertiary referral centers in Malaysia, particularly radiotherapy and reconstructive surgery. Site, grade, and stage of the primary tumor as well as patient's age and general medical condition are among the factors that influence the choice of treatment. In Malaysia, the location of patients from a tertiary referral center and the availability of radiotherapy and reconstructive surgery were also an important aspect in the choice of treatment. With this retrospective analysis, we would like to see the outcome in terms of complications and tumor recurrence of the surgically treated head and neck cancer in one of the tertiary referral centers in the east coast of Malaysia. The data obtained can be used as future reference in treating these challenging cases.

Materials and Methods

Hospital Tengku Ampuan Afzan (HTAA) is a 673-bedded tertiary center, which received referral from majority of district hospitals within the state of Pahang and from southern part of its neighboring state Terengganu. A list of patients who were previously untreated (except for two NPC cases) and underwent surgical management for head and neck cancer in HTAA from January 2002 until December 2007 was obtained from the record book in the operation theater. All operated cases with confirmed malignant head and neck cancer were included in this study except for thyroid malignancy. This was because at our center, majority of thyroid malignancy was managed by the general surgeon. Between this period of data collection, two head and neck surgeons were involved in treating the patients, and in most of situations, they worked together as a single team. Patients with pathological T3 or T4 tumor, close tumor margin (≤ 5 mm), perineural or lymphatic or vascular invasion, and positive nodal disease (pN1-3) will be sent for radiotherapy or combination of chemoradiotherapy. However, the decision for the treatment will be in the jurisdiction of the oncologist at the respective center. Most of the patients received post-operative radiotherapy or chemoradiotherapy at the oncology unit in Hospital Kuala Lumpur, which was located approximately 250 km from HTAA. Some may have undergone radiotherapy or chemoradiotherapy either at the oncology unit in Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM) (approximately 270 km from HTAA) or at Hospital Universiti Sains Malaysia (HUSM) (approximately 360 km from HTAA).

Apost-operative complication was defined “as any deviation from the ideal post-operative course that is not inherent in the procedure and does not comprise a failure to cure” (13); we divided post-operative complications into local and systemic. Most of the cases received intravenous rocephine as prophylaxis, which was administered once the patient was under general anesthesia and continued as a daily dose till post-operative day 5. According to the World Health Organization, anemia was defined as any hemoglobin level of $< 13\text{g/dL}$ for men and $< 12\text{g/dL}$ for women (14). Data concerning the characteristics of the patients, tumor site, stage, histopathological (HPE) result, and the modalities of reconstruction were obtained through retrospective reviews of the medical records.

A total of 86 patients underwent surgical management for head and neck cancer within the

mentioned period and this brought to an average of 14 cases a year. However, because of improper filing and documentation system, 25 folders were unable to be traced, while six folders did not have complete data for significant review and analysis. Of the 86 patients, record files of only 55 (64%) patients were retrieved either from the ear, nose, and throat (ENT) clinic or the HTAA Record Department. The remaining 31 files were unable to trace because the hospital has adopted the Arkib Negara Act 2003, which states that any file, which is inactive (either the patient had passed away or defaulted follow-up) and has no historical value, will be disposed (15). The estimated average duration of follow-up for all patients was three years. There was one case of incomplete data on the duration of hospital stay and hemoglobin levels. Analysis of surgical margin was possible in only 46 cases because of the lack of information on the histopathological records of the remaining nine patients. The data were entered and analysed using SPSS 15.0 (SPSS Inc., Chicago, Illinois). Age was expressed as mean (standard deviation). Other variables were expressed as frequency (%). Chi-square test was used for statistical analysis. Because of the small sample size, Fisher’s exact test was used to evaluate any association between hemoglobin levels and duration of hospital stay as well as between tumor recurrence and TNM staging. For all analyses, P values of < 0.05 (two tails) were considered significant.

Results

Demographic characteristic and locations of head and neck cancer

Table 1 showed the demographic characteristic and locations of head and neck cancer cases, which have been surgically treated at HTAA from January 2002 until December 2007, based on age, gender, ethnicity, and tumor site. The age ranged from 27 to 84 years, with mean age being 59 years (SD 12). Male patients were 3.2-fold more common than the females. Malays contributed to the largest number of cases, followed by Chinese, and only small number of Indians were included in this study. For cancers in the upper aerodigestive tract, cancer of the larynx, oral cavity, and paranasal sinuses were among the top three cancers that were surgically treated at our center. Meanwhile, only small number of cases from hypopharynx, oropharynx and nasopharynx were treated surgically. Other cancer sites which were not in the upper aerodigestive tract included the salivary gland (9.1%), skin (7.3%), temporal bone (7.3%), thyroglossal duct (1.8%), and cervical

lymph node (1.8%).

HPE result, TNM staging, and types of flap reconstruction

Squamous cell carcinoma constituted the most common HPE result as illustrated in Table 2. Advanced stage tumor (stage III and IV) clearly outnumbered early stage tumor (stage I and II). There were different types of flap reconstructions, which have been performed as part of the surgical management of head and neck cancers. The two most commonly utilised myocutaneous flaps were pectoralis major (PM) and trapezius flap. Between these two, pectoralis major flap reconstruction was the most favored procedure by our surgeons and constituted 72.7% of the cases. It was used for reconstruction in oral cavity cancer (two cases); hypopharyngeal cancer (two cases); and one each for laryngeal, salivary gland, temporal bone, and thyroglossal duct malignancy.

Table 1: Demographic characteristic and locations of head and neck cancer

| | n | % |
|-------------------|------------|----------|
| Age (years) | 59 (27–84) | (SD 12)* |
| Gender | | |
| Male | 42 | 76.4 |
| Female | 13 | 23.6 |
| Ethnicity | | |
| Malay | 33 | 60.0 |
| Chinese | 18 | 32.7 |
| Indian | 4 | 7.3 |
| Tumour Site | | |
| Nasopharynx | 2 | 3.6 |
| Paranasal sinuses | 8 | 14.5 |
| Oropharynx | 2 | 3.6 |
| Hypopharynx | 3 | 5.5 |
| Larynx | 16 | 29.1 |
| Oral Cavity | 9 | 16.4 |
| Salivary Gland | 5 | 9.1 |
| Cutaneous | 4 | 7.3 |
| Malignancy | | |
| Temporal bone | 4 | 7.3 |
| Thyroglossal Duct | 1 | 1.8 |
| Unknown primary | 1 | 1.8 |

* Mean (Standard Deviation).

Hemoglobin levels

There was a significant relationship between hemoglobin levels of the patient before surgery and the development of anemia after surgery ($P < 0.05$) (Table 3). Ten patients (18.5%) with low hemoglobin levels developed anemia after the surgery. Patients (24.5%) with normal hemoglobin levels prior to the surgery only required a week of hospital stay compared with those with low hemoglobin levels ($P < 0.05$). However, there was no significant relationship between hemoglobin levels and wound infection.

Complications

Post-operative local complications were observed in 23.6% of the cases, while 50.9% of the patients experienced systemic complications (Table 4). Wound infection and wound breakdown were the most common type of local complications, with one case of hematoma

Table 2: HPE result, TNM staging and types of flap reconstruction

| | n | % |
|---------------------------------------|----|------|
| HPE Result | | |
| Squamous Cell Carcinoma | 42 | 76.4 |
| Adenocarcinoma | 2 | 3.6 |
| Mucoepidermoid | 1 | 1.8 |
| Adenoid Cystic | 2 | 3.6 |
| Basal Cell Carcinoma | 6 | 11.0 |
| Papillary Carcinoma | 1 | 1.8 |
| Carcinosarcoma ex Pleomorphic Adenoma | 1 | 1.8 |
| TNM Staging | | |
| Stage I | 7 | 12.7 |
| Stage II | 7 | 12.7 |
| Stage III | 18 | 32.8 |
| Stage IV | 23 | 41.8 |
| Flap Reconstruction | | |
| Pectoralis Major Flap | 8 | 14.5 |
| Trapezius Flap | 3 | 5.5 |
| Local Skin Flap | 7 | 12.7 |
| No Flap Reconstruction Done | 37 | 67.3 |

and fistula respectively (Table 5). Both cases of hematoma and fistula were conservatively treated and did not require surgical intervention. Post-operative fever and anemia were the two most common systemic complications observed in our study. Other systemic complications include hypotension, electrolyte imbalance, and sepsis. There was one case of sepsis in which the patient was diagnosed to have cutaneous malignancy and underwent tumor resection with local myocutaneous pedicle flap. He developed high grade temperature, and vital signs and

blood investigation results indicated sepsis few days after surgery. Furthermore, he had wound breakdown, which was conservatively treated and sepsis resolved with intravenous antibiotics. None of the patients died of any post-operative complications.

Tumor recurrence

At the time the data was collected, there were 21.8% of patients who developed tumor recurrence and 70% of them had a positive surgical margin (Table 6 and 7). Patients (66.7%) that developed

Table 3: Haemoglobin status and its association

| | Haemoglobin Status | | | | P |
|------------------------|--------------------|------|--------|------|--------------------|
| | Low | | Normal | | |
| | n | % | n | % | |
| Anemia | | | | | |
| Yes | 10 | 18.5 | 3 | 5.6 | 0.007 ^a |
| No | 14 | 25.9 | 27 | 50.0 | |
| Wound Infection | | | | | |
| Yes | 6 | 11.1 | 5 | 9.3 | 0.539 ^a |
| No | 19 | 35.2 | 24 | 44.4 | |
| Hospital Stay | | | | | |
| 1 week | 4 | 7.5 | 13 | 24.5 | 0.030 ^b |
| 2 weeks | 6 | 11.3 | 6 | 11.3 | |
| 3 weeks | 5 | 9.4 | 5 | 9.4 | |
| 4 weeks | 6 | 11.3 | 0 | 0.0 | |
| > 1 month | 2 | 3.8 | 6 | 11.3 | |

^a Chi Square Test.

^b Fisher's Exact Test.

Table 4: Types of complication

| | n | % |
|-------------------------------|----|------|
| Local Complications | | |
| Yes | 13 | 23.6 |
| No | 42 | 76.4 |
| Systemic Complications | | |
| Yes | 28 | 50.9 |
| No | 27 | 49.1 |

Table 5: Details of complication

| | n | % |
|-------------------------------|----|------|
| Local Complications | | |
| Wound Infection/ Breakdown | 11 | 20.0 |
| Hematoma | 1 | 1.8 |
| Fistula | 1 | 1.8 |
| Systemic Complications | | |
| Post-operative Fever | 16 | 29.1 |
| Anemia | 13 | 23.6 |
| Sepsis | 1 | 1.8 |
| Electrolyte Imbalance | 2 | 3.6 |
| Hypotension | 3 | 5.5 |

recurrence were in the advanced stage group (stage III and IV). Advanced stage tumor had more percentage of positive margin than early stage tumor i.e., 23% in early stage versus 58% in advanced stage ($P = 0.05$). Tumor recurrence was identified in 33.3% of patients who received post-operative chemoradiotherapy. Patients who were positive for neck nodes were 58% and out of this only 15.6% developed tumor recurrence.

Discussion

Over period of 6 years, this center managed an average of 14 cases per year, which was approximately one case per month. This relatively small number of cases may reflect the small size of the population in Kuantan and the neighboring district with an estimated population of 698 104 (16). In addition, it may be because of the lack of

awareness regarding head and neck cancer signs and symptoms among the population of this region. A study on oral cavity cancer awareness indicated moderate awareness among the adult population attending the School of Dental Sciences, University Sains Malaysia, Kelantan (17). This was partly evidenced by the higher number of cases that presented in the late stage in this study. Furthermore, reluctance to accept surgery as one of the treatment modalities, particularly in the exposed area of head and neck and strong belief in traditional treatments, may contribute to the lower number of cases in this study. Majority of the population in Pahang state are Malays, followed by Chinese, Indians, and others (16). This variation in ethnicity explained the difference in head and neck cancer prevalence among the different races in this study, and a majority was observed among Malays (58.7%), followed by Chinese (34.8%) and Indians (6.5%). In our 6-year retrospective study, the larynx was the most common surgically treated site, which attributed 34.8% of the cases, followed by the oral cavity (19.6%) and paranasal sinuses (17.4%). Despite the development of early voice hoarseness in laryngeal cancer, a substantial number of patients presented late with 31% in stage III and 44% in stage IV at the first encounter. This

Table 6: Tumour recurrence

| | n | % |
|------------|----|------|
| Recurrence | | |
| Yes | 12 | 21.8 |
| No | 43 | 78.2 |

Table 7: Tumour recurrence and its association

| | Recurrence | | | | P |
|--------------------|------------|------|----|------|--------------------|
| | Yes | | No | | |
| | n | % | n | % | |
| Surgical Margin | | | | | |
| Free | 3 | 6.5 | 21 | 45.7 | 0.159 ^a |
| Not Free | 7 | 15.2 | 15 | 32.6 | |
| TNM Staging | | | | | |
| Stage 1 | 3 | 5.5 | 4 | 7.3 | 0.599 ^a |
| Stage 2 | 1 | 1.8 | 6 | 10.9 | |
| Stage 3 | 4 | 7.3 | 14 | 25.5 | |
| Stage 4 | 4 | 7.3 | 19 | 34.5 | |
| Positive Nodes | | | | | |
| Yes | 5 | 9.1 | 27 | 49.1 | 0.190 ^b |
| No | 7 | 12.7 | 16 | 29.1 | |
| Chemo-radiotherapy | | | | | |
| Yes | 6 | 10.9 | 18 | 32.7 | 0.615 ^b |
| No | 6 | 10.9 | 25 | 45.5 | |

^a Fisher's Exact Test.

^b Chi Square Test.

justified a more aggressive treatment for laryngeal cancer cases in our study with 81% (n = 13) requiring total laryngectomy with neck dissection and the remaining were treated with conservative laryngeal surgery (vertical partial laryngectomy). The higher incidence of laryngeal cancer in this study was in agreement with national data that cancer of the larynx was the second most common head and neck cancer in Malaysia (1); this could be explained by the fact that smoking habit was rampant among our population; a better socioeconomic status could be the reason for lifestyle. A local study revealed that a 1% increase in real income increased cigarette consumption by 1.46% (18).

Betel nut chewing, which has long been associated with the etiology of oral cavity cancer was also common in our population mainly among Malay and Indian females (1,19,20). However, from the total number of patients with oral cavity cancer, 67% were Malay, 33% were Chinese, and none were Indian. Apart from the low number of Indian population in this part of Malaysia, another reason could be the reluctance to accept surgery among the Indian patients or they may present late with an advanced disease, whereby only palliative treatment is possible. In our study, all oral cavity cancer presented late and majority of the cases were in those > 50 years. However, in one case, the patient presented with stage III tumor as early as 27 years. He underwent total glossectomy, total laryngectomy, left radical neck dissection, right selective neck dissection, and pectoralis major myocutaneous flap. Our approach was aggressive in this patient in view of his relatively young age and operable tumor, based on clinical and radiological assessment. Although he completed the radiation therapy, he developed recurrence of the primary tumor and presented with pathological fracture of left mandible and eventually died.

Despite the higher incidence of NPC mainly among the Chinese in our country (1,4), limited indication for surgery contributed to lower number of NPC cases (n = 2) encountered in our study. The only two cases presented were primary tumor recurrence after months of completion of radiotherapy, treated with nasopharyngectomy.

Squamous cell carcinoma was the most common histopathological diagnosis in this study representing 82.6% of total patients, and this was comparable with international data (21,22). Most of the patients were in stage III and IV (78.2%) when first observed, which was almost similar with a study conducted in Penang Hospital in the West Coast of Malaysia (23). The data from these

two states indicate that majority of our Malaysian patients were in the late stage (stage III and IV) at the first consultation with the head and neck surgeon compared with that in developed countries (24). A study conducted among NPC patients in Sarawak revealed that the reason for late presentation to the hospital is because of the patient's lack of knowledge, absence of pain, and perception of accepting traditional treatment as their first priority (25); this may be true for other types of head and neck cancer as well. For this reason, a head and neck cancer campaign and an outreach program is necessary to create awareness among our population, mainly in the district and remote area.

From a total of 55 patients, only 18 required reconstruction because of the surgical defect. The three most common flaps that were used in our center were PM myocutaneous flap (14%), trapezius myocutaneous flap (5.5%), and local skin flap (12.7%). In this retrospective study, all PM flaps were opted for in the advanced stage tumor (n = 4 for stage III and n = 4 for stage IV). This flap was an excellent option for head and neck reconstruction in the pharyngeal region apart from radial forearm free flap, free jejunal flap, and the gastric pull-up procedure (26-30). One of the reasons for PM flap preferences in this study was the unavailability of plastic and reconstructive unit expertise and facilities at our center. The second most common pedicle myocutaneous flap harvested was trapezius flap, which was used for temporal bone malignancies (two cases) and for salivary gland malignancy (one case).

Hemoglobin level is one of the factors that influenced prognosis and survival of head and neck cancer patients receiving post-operative chemoradiotherapy (31-33). In this study, low hemoglobin levels were significantly correlated with post-operative anemia and because of relatively large number of patients with post-operative anemia, in the future, emphasis on correcting anemia is crucial for those patients who required post-operative radiotherapy. In addition, low hemoglobin level significantly correlated with prolongation of hospital stay, and these may have adversely influenced the cost of head and neck cancer treatment at least in our hospital.

Complications were relatively common following surgical treatment mainly for advanced stage tumor in which a large surgical wound and prolonged operating time were the contributing factors (34,35). In addition, prior radiotherapy, pre-operative transfusion, and flap reconstruction were identified as factors that contributed to a significantly higher complication rate (36). In

our study, rate of wound infection was 20% and reported rate of wound infection following head and neck surgery according to literature were varied between 10% and 45% (34–39).

Tumor margin was regarded as an important prognostic factor for surgical management of head and neck cancer, particularly in the oral cavity (40). This was evidenced in this study and although the difference was not statistically significant, there were more percentage of patients with positive margin (31.8%) who developed recurrence compared with those with free tumor margin (12.5%). A relatively low percentage of tumor recurrence (21.8%) in our study may indicate that surgical management of head and neck cancers at our center was satisfactory and had an acceptable outcome. However, further study on the quality of life as well as survival analysis of these patients is necessary to thoroughly evaluate our approach and strategy in managing head and neck cancers in this center.

As Malaysia is moving toward the status of developed country by the year 2020, much is needed to be done in the area of health care services for his population, at least in this region of this country. The nearest available radiotherapy services are located very far, which makes it difficult for head and neck patients from this hospital to complete their management. A study on this aspect is required to thoroughly evaluate the impact of this drawback in managing head and neck cancer from this center. The main limitation identified in this study was a small number of cases. We believed that to get a larger sample size, multicenter study is ideal; however; this will involve higher costs. In addition, data filing is an important aspect that needs to be emphasised in this hospital and there is a need for a computerised data filing system. However, the Arkib Negara Act regarding the disposal of an old patient's record will hinder this effort, and to solve this issue higher authorities and political influences are probably required; a lot of invaluable patient's data could be lost, which it could be translated into invaluable research.

Conclusion

In conclusion, surgical management of head and neck cancer at this center has a satisfactory outcome in view of a relatively low percentage of recurrence and rate of wound breakdown. We recommend pre-operatively optimising the hemoglobin level, so that the incidence of post-operative anemia could be minimised. Managing advanced stage tumor requires special

consideration to achieve adequate surgical margin followed by chemo-radiation to reduce tumor recurrence. Further reduction in tumor recurrence would be minimised if there is no delay in receiving post-operative chemoradiotherapy and this justifies the need for an oncology center in this region in Malaysia.

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Conflict of Interest

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