Detection of Metastatic Cervical Lymphnode

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Abstract

This was a cross sectional study conducted in Dhaka Dental College Hospital and Shaheed Suhrawardy Hospital for a period of two years starting from July 2003 to June 2005. The main objective of the study was to assess the accuracy of detection neck nodal metastasis by physical and contrast enhanced computed tomography against nodal biopsy after surgery.

Pattern of primary site of tumor revealed that highest percentage were in the retromolar trigone (23.5%) followed by cheek (21.6%), alveolar mucosa and vestibule (13.7%), tongue (13.7%) floor of the mouth (7.8%), lower lip (5.9%), hard palate (5.9%), facial skin (3.9%), upper lip (2.0%) and soft palate (2.0%). Clinical staging indicated that highest percentage had stage IV tumor (49.0%) followed by stage III (23.5%), stage I (15.7%) and 11.8% had stage II tumor. Imaging staging of the tumor indicated that highest percentage had stage IV tumor (45.1%) followed by stage III (39.2%) stage I (13.7%) and stage II (2.0%). Histopathological staging tumor support that highest percentage classified as stage IV tumor (45.1%) followed by stage III (39.2%), stage I (13.7%) and stage II (2.0%). Comparative analysis of clinical, imaging and histopathological staging of tumor were done. The sensitivity, specificity, positive predictive value, negative predictive value and predictive accuracy of the clinical staging were 75.6%, 60.05, 88.6%, 37.5% and 72.5% respectively.

Key word: *Neck node metastasis, cervical nodal metastasis.*

Introduction

Cancer is the second major cause of death after heart disease worldwide.[1] The most common oral cancer is squamous cell carcinoma. Oral cancer in Bangladesh showed tobacco as main aetiological factor.[2]

A malignant tumor always invades the surrounding structures. It eventually enters the channels like the lymphatics and blood vessels and group of cells are carried to the other parts where it sets up as anabolic spread, is called metastasis. If it is in lymph node is called nodal metastasis[4].

The tumor can metastasise in ipsilateral and/or contralateral or bilateral neck nodes. As the tumor grows within a node. it enlarges and becomes indurate and rounded. The tumor eventually extends though the capsule of the lymph node and invades the surrounding structures, extension through the neurovascular bundle is relatively common and results its fixation.

Rationale of treating Squamous cell carcinoma which has metastasized to regional lymph nodes is based on the fact the treatment of primary disease and lymphatic metastasis of the neck.

Neck metastasis by a oral squamous cell carcinoma is firm statement of its aggressive malignant nature and its advanced condition. Understanding of adjacent nodal anatomy and its advanced condition. Understanding of adjacent nodal anatomy and detection of neck metastatic disease is crucial for its management. Studies of the Head neck cancer death shows that approximate 25% of uncured patients have recurrence at the primary site. About 50% succumb to invasion and compression from uncontrolled lymphatic or soft tissue spread in the neck and about 25% die with distant metastasis.

Once dissemination to regional lymph nodes take place, the probability of 5 years survival, regardless of the treatment rendered, reduce to nearly one half of that seen in early staged patients[3] The survival rate is then 5% in patient who previously underwent surgery and have a recurrent neck metastasis. Therefore first detection of metastasis then the control of neck metastasis is one of most important aspects in successful management of oro-facial squamous cell carcinoma. Knowledge of the basic principles of oncology and expertise in patient assessment and in individual specialty are essential for staging work up of the patients and treatment selection and integrated interdisciplinary collaboration. The mortality rate from all cancers in the United States fall 2.6% between 1991-1995. Of interest in that the highest decline in the mortality arte (9.6%) occurred in patients with head neck cancer due to improvement of detection of neck nodal metastasis[4].

Once the neck has suspicious metastatic disease, then for adequate treatment and evaluation of neck is important. Preoperatively there are many options for neck evaluation. As follows:

Physical examination (PE)
Contrast- enhanced Computed Tomography (CECT)
Magnetic Resonance imaging (MRI)
Ultrasonogram
2-Fluoro-2-deoxy-glocose (FDG) Positron Emission Tomography
(FDG-PET) etc.
Among them contrast enhanced computed Tomography (CECT) is the most common modality employed to assess the cervical lymphatic metastasis.

Tumor can grows in the lymphatics between a primary and the draining lymph nodes. It cannot be detected by any of the above-mentioned methods5. But till today though some investigator claiming PET gives overall appreciating result for detection of neck nodal metastasis. There are no ideal method for identification of metastatic neck disease. Therefore false positive and false negative is not uncommon. Adequate management cannot standardize if not all precaution is taken for more accurate detection of metastattoc mecl mpdes/

A large number of patients with oro-facial squamous cell carcinoma come to Dhaka Dental College Hospital seeking treatment. PET facilities are not available in Bangladesh. We used to do Physical Examination (Neck palpation) and Contrast Enhanced Computer Tomography (CECT) for detection of neck metastasis. Yet we do not know the accuracy of them individually or combined.

In the view of above, this study so as to determine the appropriate cost effective tool for accurate detection of neck metastasis, which help us in the process of decision making for saving and decrease the suffering of million's life.

Hypothesis:
Detection of metastatic cervical lymph nodes CT scan is complementary to physical examination.

Objectives
General : Accurate detection of metastatic cervical lymph node for management of squamous cell carcinoma.

Ultimate: Choice of investigation for more accurate detection of Neck nodal metastasis for third world country like Bangladesh.

Specific: Pre-operative staging of the orofacial cancer.

By physical examination (eTNM)

Patients and methods
      (i)   Study type
                 Prospective cross sectional study
      (ii)   Study population:
                 Patient admitted into in patient department with Oro-facial squamous cell carcinoma irrespective of age sex and occupation
      (iii)   Sampling technique:
                 Consecutive patient attending in in-patient department with Oro-facial squamous cell carcinoma.
      (iv)   Estimated sample size:
                 Total number of patients were 51. Initially a total of 80 patients were included of the study. Finally 51 patients complete all steps of procedure of the study.
      (v)   Place and duration of work:
                 Study place: ENT department & in-patient department, Dhaka Dental College Hospital, Dhaka, Bangladesh.
                 Period of study: July'03 to June'05.

(vi)   Recruitment procedure:

Among all the patient attended to in-patient department of OMS department study subjects were recruited on the basis of inclusion and exclusion criteria's:

  (a) Patient criteria for inclusion -
- All patient with Oro-facial squamous cell carcinoma
- Primary tumor previously not operated upon
- As staging system has been diverse for malignant tumor, within salivary gland it is not include here.

  (b) Patient criteria for inclusion -
- The patient who got Neo-adjuvant chemotherapy
- Anterior radiotherapy
- Recurrent squamous cell carcinoma
- Time expend more than 7 days after CT scan
- Who don't under went surgery for neck disease
- Infected primary lesion
- Change of T-value after imaging

(vii)   Operational definition used for each variable:

  (a) Parameter to be recorded (variables) -

1. Clinical parameter:
   - (i)   Primary site and clinical type
   - (ii)   T-value
   - (iii)   Neck examination - Number of + ve node
   - (iv)   Criteria for +ve node in physical examination:
     - (a) Greater than 1 cm in diameter
     - (b) Hard and fixed consistency than normal node
     - (c) Spherical in configuration rather than flat and ovoid

2. The N-category relates on the regional lymph node metastasis (N-classification on the basis of clinical status of node).

3. TNM classification based on American Joint Committee on cancer (AJC, 1988).

4. Stage staging of the tumor and its metastases was based on the international union against cancer (UICC, 1992).
   - (a) Investigation - Contrast enhanced computed topography (CECT)
   - (b) Contrast used - Lopamiro (lopamidol) - 300 Bracco milan, Italy. The contrast used 100ml (2 ml/kg body weight at the rate 1.0 ml/second IV for 1 minutes.

Patients anatomic landmark used for site of lymph node are previously mentioned in literature review.

1. Number of visible nodes
2. Number Parameter to be recorded (variables) -

Criteria of +ve node

(a)   A ill defined irregular bordered mass
(b)   Non enhancing mass in the nodal area greater than 1.5 cm for sub-mandibular; jugulo diagastric node, greater than 1.0 cm for all other nodes, greater than 0.8 cm for retropharygeal nodes.

(c)   Grouping of 3 or more nodes in 6-15 mm area
(d)   Central necrosis evidence with decrease density
(e)   Central necrosis evidence with decrease density
(f)   Dirty fat appearance with or extrandal spread

Nodal metastasis were assessed using classification of the Union International Centre le cancer (UICC). Here in cervical lymph nodes are leveled and sub-classified into 12 region CT contain above mention criteria.

(c)   Histopathological examination:
Shortly after the final physical examination CT studies radical surgery of the primary tumor and selective or modified radical or radical neck dissection was performed median time interval between the studies and the surgical procedure was 5 days.

Specimen collection:
Specimen is collected on a wide mouth container after neck dissection filled with 10% form saline with 3 times more volume of specimen.

Labeling transpiration:
Patient's name with age, sex registration number clearly written on and transported to laboratory with a biopsy data sheet.

Biopsy data sheet:
The sheet is composed off particulars of the patient, containing brief medical history/CT finding/clinical finding/clinical diagnosis specimen orientation and tag identification etc.

Post operative specimen biopsy is done after different type of neck dissection for identification of anatomical alignment or orientation steronocleidomastoid muscle and/or part of mandible are used as affixed land mark. The nodes or area of beside this the are interest is specified in specimen is by used of sutures to tag as important coordinated landmark.

All lymph nodes palpated or found after specimen sectioning were examined mocroscopically in the pathological laboratory. The lymph nodes were embedded in paraffin. Then 3 to 5 micromol serial section were prepared from every paraffin block and stained with hematoxylin-eosin.

Metastases detected in the neck dissection specimens were analyzed according to the compartments of the neck level and subclass of node and the histopathologic findings of the neck dissection specimens were compared.

Data collection methods and quality control measure (Diagnosis of a node)

During CT scan to prevent overlap of anatomical structures and head movements advised to restricted. The CT image were analyzed using a check list visually by two observes at the same time. Disagreements were solved by consensus the number and location of position nodes assessed.

(i)   Data collection (Research instruments):
A standardized structured research instrument was used to collect necessary information on of the study subject.

(a)   Which include general scheme of case taking. General scheme includes (i) History taking, (ii) Physical examination, (iii) Special investigation, (iv) Clinical diagnosis, (v) Treatment (surgical), (vi) Progress during post operative period, (vii) Follow-up and (viii) Termination.
(b)   Contrast enhanced CT scan, physical examination of neck and histopathological finding of nodes in surgical specimen after different type of neck dissection were recorded in a checklist

(ix)   Procedure followed (Relation of dissected nodes to PE & CT scan):
Topographical correlation between dissected nodes and CT scans or physical examination was performed by using a reporting system as previously described. At surgery, the lymph nodes were excised in block along with the adjacent reference structure to move easily ascertain the spatial relationship between the excised nodes and surrounding structure, such as muscles salivary gland and veins. The size of the node are also used to compare with the results of CT and physical examination surgeons and together compare the examination results the excision nodes that matched those on CT scan and physical examination were then examine histopathologically.

(x) Method used for data processing and analysis:
After data has been collected, researcher will needed to process it values are expressed as eman + standard deviation (SD). Data are expressed in terms of sensitivity (the number of metastatic nodes at imaging and histology), specificity (the number of non-metastatic nodes at imaging and histology and the number of non-metastatic nodes in histology), accuracy and positive (the number of metastatic nodes at imaging and histology and the number of metastatic node at imaging) and negative predictive (the number of non-metastatic nose at imaging and histology and the number of non-metastatic nodes at imaging).

(ix) Approval from the concern authorities:

The patient was informed and explained nature of the study about importance and objectives.

Results and Observations

the mean age of the patients was 51.1 ± 10 years. The mean age of the male patients was 49.42 ± 10.2 years and the female patients was 52.7 ± 9.9 years. Analysis revealed no statistically significant mean age difference between male and female patients. Among the ale patients, highest percentage were in the age group, 40-49 years (37.5%) followed by 50-59 years (33.3%), 60 years and above (16.7%) and less than 40 years (12.5%) whereas among the female patients highest percentage were in the age group 50-59 years (29.6%) and equal percentage were also in the age group of years and above (29.6%) followed by 40-49 years (25.9%) and lowest in the age group less than 40 years (14.8%).

Table-I

Distribution of the patients by site of primary tumour

Sites of involvement tumour	Frequency	Percent
Retromolar trigone	12	23.5
Cheek	11	21.6
Alveolar mucosa and vestibule	7	13.7
Tongue	7	13.7
Floor of the mouth	4	7.8
Lower lip	3	5.9
Hard palate	3	5.9
Facial skin	2	3.9
Upper lip	1	2.0
Soft palate	1	2.0
Total	51	100.0

Table 1 shows the pattern of primary site of tumour. it was found that highest percentage were in the retromolr trigone (23.5%) followed by cheek (21.6%), alveolar mucosa and vestibule (13.7%), tongue (13.7%), floor of the mouth (7.8%), lower lip (5.9%), hard palate (5.9%), facial skin (3.9%), upper lip (2.0%) and soft palate 2.0%.

Table-II

Relationship between clinical and histopathologial staging of tumour

| Clinical stage | Histopathological stage | | | | Total | |
| | Positive | | Negative | | | |
	Count	%	Count	%	Count	%
Positive	31	75.6	4	40.0	35	68.6
Negative	10	24.4	6	60.0	16	31.4
Total	41	100	10	100	51	100

Sensitivity - 75.6%
Specificity - 60.0%
Positive predictive value - 88.6%
Negative predictive value - 37.5%
Predictive accuracy - 72.5%

It was found that sensitivity, specificity, positive predictive value, negative predictive value and predictive accuracy of the clinical staging were 75.6%, 60.0%, 88.6%, 37.5% respectively.

Table-III
Relationship between clinical and histopathologial staging of tumour

| Clinical stage | Histopathological stage | | | | Total | |
| | Positive | | Negative | | | |
	Count	%	Count	%	Count	%
Positive	37	90.2	5	50.0	42	82.4
Negative	4	9.8	5	50.0	9	17.6
Total	41	100	10	100	51	100

Sensitivity - 90.2%
Specificity - 50.0%
Positive predictive value - 88.1%
Negative predictive value - 55.6%
Predictive accuracy - 82.4%

The sensitivity, specificity, positive predictive value, negative predictive value and predictive accuracy of the CT scan were 90.2%, 50.0%, 88.1%, 55.6% and 82.5% respectively.

It was found that sensitivity, specificity, positive predictive value, negative predictive value and predictive accuracy of the clinical staging were 75.6%, 60.0%, 88.6%, 37.5% respectively.

Table-II
Relationship between clinical and histopathologial staging of tumour

| Clinical stage | Histopathological stage | | | | Total | |
| | Positive | | Negative | | | |
	Count	%	Count	%	Count	%
Positive	31	75.6	4	40.0	35	68.6
Negative	10	24.4	6	60.0	16	31.4
Total	41	100	10	100	51	100

Sensitivity - 75.6%
Specificity - 60.0%
Positive predictive value - 88.6%
Negative predictive value - 37.5%
Predictive accuracy - 72.5%

It was found that sensitivity, specificity, positive predictive value, negative predictive value and predictive accuracy of the clinical staging were 75.6%, 60.0%, 88.6%, 37.5% respectively.

Table-IV
Comparison between clinical and imaging staging of tumour in relation with histopathological

Parameters	Clinical staging	Imaging
Sensitivity	75.6%	90.2%
Specificity	60.0%	50.0%
Positive predictive value	88.6%	88.1%
Negative predictive value`	37.5%	55.6%
Predictive accuracy	72.5%	82.4%

Comparative analysis of clinical staging and CT scan indicated that the sensitivity and specificity were better in clinical staging compared to CT scan, but overall accuracy was better in CT scan (82.4%) than clinical staging (72.5%). Which is not statistically significant (P>0.05).

Discussion
The presence of cervical lymph node metastasis in SCC of the Oro-facial region will often change the extent of surgical treatment or radiotherapy and others. For instance in Dhaka Dental College and Hospital, the SCC of the oral cavity having T1 No Mo criteria is treated with only local resections of the tumour alone and watchful follow-up is

instituted for the neck. If metastatic lymph node is found the treatment consist of resection of the primary tumour and a supraomohyoid or modified radical neck dissection etc.

The increase size or structural changes in the lymph node is consider as a symptom of metastatic disease. Though in general the surgeon largely depends on palpation to assess the presence of metastatic lymph modern techniques that would allow better assessment of the presence of the cervical metastatic lymph nodes. Some author conclude that CT is superior to palpation in detecting or excluding or excluding metastatic neck disease preoperatively with advancement of the 3rd generation high resolution CT scanner is available now.

It is well known that palpation is an inaccurate technique to stage cancer in the neck. It is not clear from previous studies number of times of the examination or palpation of each neck14. Palpation is a subjective method of detection of cervical metastatasis. It is totally operator (examiner) and/or experience dependent. If the skill in repeated examination of neck improve then physical examination become competitive with advances of CT scan. In the study we palpate each neck at least three times between admission and operation.

If the same neck is examined time to time it improve the clinical finding of that individual neck. As in general palpation has no hazard and inexpensive can repeat bed side. But it is assume that multiple palpation may encourage the further extension of metastasis by passive movement of lymph. So it must be done carefully and precise way.

The limitation of this research was that the T-value of the disease for specific tumour was always kept constant in both clinical and imaging CT to increase focus on metastatic lymph node and if changes we omit the patient. In our present research total number of the patient was 14 in clinical stage-I and stage-II. But after imaging there are only (&+1) 8 patient in the stage (stage 1 + stage II) which was formed similar after histopathology. This means contrast enhanced CT scan can up stage significant number of patients. Though in the study stage change of the tumour only depends on N-classification as the patients were MO for distant metastasis.

Though improvement of contrast CT scan bears more predictive value. It is very operator dependant process as IV contrast >50 ml needs to be given rapidly in bolus and then immediately scan the neck. It must be done swiftly and accurately and if delay contrast can not given optimal result. In Bangladesh the procedure is done reluctant mood so result may be poor. Besides this slice thickness is usually taken 5 mm so node may total image those less than 5 mm in diameter.

The number of section examined per node and the use of immuno-histochemical which is need for intense scrutiny were not done to exclude metastasis from synchronous lesion.

Finally the data open the challenge of superiority of contrast CT scan as its predictive value 88.1% which is less that found in physical examination.

Physical examination shows high sensitivity (75.6%) and specificity (60%) reported in this article only have a limited clinical value as they were calculated per lymph node and probably a majority of the metastatic lymph nodes were palpable as a consequence, the sensitivity would have been lower if the study had been limited to an no-neck population.

It is the most important drawback of the study that CT scan of metastatic node may mimic a benign node, CT or MR imaging stages a clinically N+neck with hyperplastic nodes reaching specificity of 75-86% 26. But here CT specificity is 50% only. It is due to technical fault that mention above because contrast wash away. In the study we did not go for surgery just after CT scan. Metastasis may occur in the period between CT scan and surgery. Histopathologic diagnosis is therefore necessary for the final diagnosis before treatment by surgery or radiotherapy. So FNAC must needed to be done before critical decision of the different type of radical neck dissection.

Imaging technique like CT, MRI and sonography are more accurate than palpation14. In our study we found that difference between the CECT scan and physical examination is not statically significant. In dictating importance of repeated palpation method.

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