Original Article

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Diagnostic Accuracy of Computed Tomography and Clinical Examination in the Assessment of Mandibular Invasion of Oral Squamous Cell Carcinomas.

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ABSTRACT:

Introduction: Computed tomography **(**CT) scan precisely shows soft and hard tissues in the same test hereby determines the lesion extension, involvement of regional node as well as of bone. Current study was aimed to evaluate the efficacy of clinical examination and CT to assess mandibular invasion in oral squamous cell carcinoma.

Materials and methods: This cross-sectional study was conducted at Dhaka Dental College Hospital from July, 2016 to July, 2017 among conveniently selected 35 patients of histologically confirmed squamous cell carcinoma which was close to the mandible. The patients underwent proper clinical examination. CT scan was performed; preoperative staging and treatment plan was formulated according to the status of bone invasion. After mandibulectomy, the resected specimens were sent for histopathology. The findings from clinical examination and CT were then correlated with the gold standard, postoperative histopathology.

Results: Clinical examination accurately detected 22 cases to have bone invasion and 8 cases with no bone invasion. It also gave 2 false positive and 3 false negative results. On the other hand CT accurately detected 24 cases to have bone invasion and 9 cases with no bone invasion. It provided one false positive and one false negative result. However, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of clinical examination were 88%, 80%, 91.67%, 72.73%, 85.71% respectively ($p = 0.0002$) and of CT were 96%, 90%, 96%, 90%, 94.28% respectively ($p < 0.0001$). Clinical examination and CT were found sensitive enough and have an acceptable range of specificity as primary investigative modalities. CT scan outperforms clinical examination in terms of sensitivity, specificity, NPV, and accuracy.

Conclusion: CT scan imaging is the method of choice for planning treatment in advanced oral squamous cell carcinoma. This study reveals how a CT scan can provide additional diagnostic value to detect bone invasion.

KEYWORDS: clinical examination, computed tomography, diagnostic accuracy, mandibular invasion, oral squamous cell carcinoma

INTRODUCTION

Oral squamous cell carcinoma (OSCC) representing 90% of oral cancer cases in Bangladesh[1] often exhibits bone invasion crucial for treatment planning and outcome. The recent studies claimed direct extension into mandible[2] with invasion pattern being erosive, mixed or infiltrative. Whatever the route of entry or pattern of invasion, whether invasion of mandible affects the survival rate or not is confusing among different studies.[3–5] Inability to detect bone invasion may lead to inadequate resection, resulting in recurrence and regional or distant metastasis; while over treatment impairs the quality of life. Depending on tumour size and the proximity to mandible the incidence of mandibular invasion ranges from 12% to 56%.[6–8] Carcinoma involving mandible has high recurrence (70%) and low the survival (26%).[9] Conversely, many mandibles are sacrificed without histological evidence of invasion. Preserving the mandible to enhance quality of life ensuring local control is essential. Therefore, accurate preoperative evaluation of mandibular invasion is imperative.

Various imaging modalities, including plain radiograph, cone-beam computed tomographic scan (CBCT scan), magnetic resonance imaging (MRI), bone scintigraphy (BS), single photon emission computed tomographic scan (SPECT scan) are employed to asses mandibular invasion but none can predict mandibular invasion with 100% reliably, each carrying inherent limitations.[10] A study compared bone scintigraphy and computed tomography (CT) with clinical assessment and histopathologic findings. Results indicated CT's

specificity (78%) surpassed bone scanning's (47%).[8] Clinical examination exhibited high sensitivity (82%) and specificity (87.5%) in predicting bone invasion, supported by CT findings.[11] Clinical examination & orthopantomograms (OPGs) were deemed sufficiently sensitive as primary investigative modalities.[12]

Plain radiograph has limitation to detect early invasion; particularly in visualizing the midline area.[13] MRI and SPECT often yield false positive result and frequently overestimates the tumour invasion extent.[14,15] Bone scintigraphy while sensitive, lacks specificity.[16] Nevertheless CBCT fails to accurately represent the soft tissues structure & lesion and offers limited correlation with Hounsfield Unites for standardized bone density quantification.[17]

Shaha (1991) advocated for clinical examination as the best method for mandible evaluation.[18] CT scans, accurately displaying both soft tissue and bone structures, offer advantages over other techniques, aiding lesion extension determination, nodal involvement assessment, and bone involvement detection[11] surpassing MRI and bone scintigraphy in diagnosing mandibular erosion. CT results compare favourably and are superior to the reported diagnostic accuracy of MRI & BS in detecting mandibular erosion.[19] It is economically advantageous[20] and, in tandem with clinical examination, ensures comprehensive preoperative bone invasion detection, preventing unnecessary mandible loss.[21] Current study aims to evaluate clinical examination and CT efficacy in OSCC mandibular invasion assessment to optimize treatment outcomes and enhance quality of life.

MATERIALS AND METHODS

This observational study, conducted between July 2016 and July 2017 at Dhaka Dental College and Hospital, included 35 patients with histologically proven squamous cell carcinoma located in close proximity to the mandible. Approval was obtained from the Ethical Committee of Dhaka Dental College, and patients were enrolled based on specific criteria, excluding those in advanced stages, debilitated, elderly (above 80 years), or receiving new adjuvant chemo-radiotherapy. After admission of the patient proper clinical examination followed by positive incisional biopsy report- a definitive treatment plan was decided. Clinical examination included the size and site of the lesion, fixity to skin or muscle, mobility of teeth within lesion, irregularities of bone, paraesthesia of lower lip, assessment of regional lymph nodes and distant metastasis.

Patients fit for surgery were included after obtaining written consent. Then CT scan was performed (by the Philips 3D-128 slice machine while thickness of sections was 0.30-2.00 mm) to determine the type of mandibulectomy required. Clinical staging was assessed based on CT scanning reports. All subjects provided informed consent. A data sheet was designed to record the demographic information along lesion details, CT scan and histopathology reports.

The data were analysed using SPSS version 16. The diagnostic validity of preoperative clinical examination & CT was compared against histopathology. Chi-square tests were used to assess agreement between clinical examination, CT scan, and histopathology for detecting bony invasion. Significance was considered at $p < 0.05$ with a 95% confidence interval. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of clinical examination and CT were calculated and presented in tables and graphs.

RESULTS

Among 35 patients 16 were male and 19 were female. Their mean age was 53.3 years (ranged from 30-80 years). The least affected groups (n=2, 5.71%) were between 30 years to 39 years of age and 70 years to 80 years, whether the most affected group (n= 14, 40.0%) were between 50 years to 59 years of age. Buccal mucosa & alveolar mucosa was the most frequently affected site, involved in 37.14% (Figure 1).

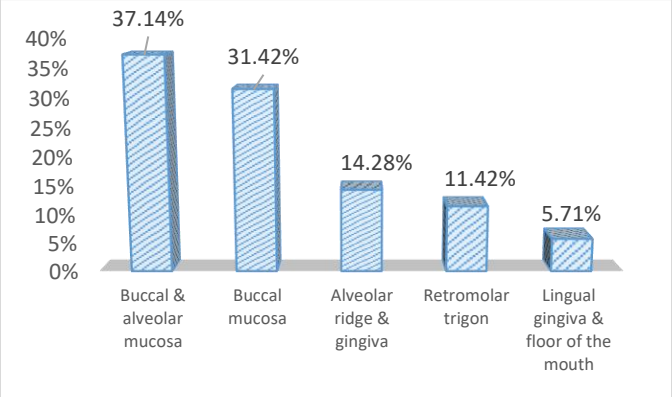

Figure 1: Distribution of site of lesions.

Among 54.28% respondents the size of the lesion varied from 2-4 cm while among 37.14% it was more than 4cm. Lesion was found to be fixed with the surrounding structures among 65.71%. Paraesthesia of the lower lip were absent in 94.28% cases. In 54.28% cases mobility of teeth within the lesion was present. Irregularities of bone were present in 34.28% case. The regional lymph nodes were palpable in 94.28% case (Table 1).

Table 1: Distribution of respondents by Clinical findings (n=35)

Characteristics	Frequency	Percentage
Size of the lesion		
0-2 cm	3	8.57
2-4 cm	19	54.28
>4 cm	13	37.14
Fixity to surrounding structures		
Free from bone/ muscle/ skin	12	34.28
Fixed with bone/ muscle/ skin	23	65.71
Paraesthesia of lower lip		
Present	2	5.71
Absent	33	94.28
Mobility of teeth within lesion		
Present	19	54.28
Absent	16	45.71
Irregularities of bone		
Present	12	34.28
Absent	23	65.71
Regional lymph node		
Not Palpable	2	5.71
Palpable	33	94.28

Regarding TNM staging there was no patient of stage I, 5.71% patients were in stage II while 28.57 % were in stage III. The maximum number of patients (65.71%) was in stage IV. Considering histopathological grading of OSCC out of 35 cases, 80.00% were well differentiated (G1), 17.14% were moderately differentiated (G2) and 2.85% were poorly differentiated (G3). This study did not find any patients of GX (grade could not be assessed) and G4 (Undifferentiated).

In this study, in clinical examination tumours were opined to be invading bone once there were clinical signs of tumour fixation to the bone, abnormalities of bone contour, teeth mobility inside the lesion or subjective indicators of inferior alveolar nerve paraesthesia were noted. Histopathology detected bone invasion to be present in 25 cases and lacking in 10 cases. According to clinical examination and CT scan bone invasion was present in 24 cases and in 25 cases respectively while absent in 11 cases and in 10 cases respectively.

According to histopathology of excised specimen to have bone invasion, 88% (22 cases out of 25) were detected by clinical examination to have so. Of the patients diagnosed with no bony invasion, 80% (8 cases out of 10) were also diagnosed similar by clinical examination (p=0.0002) (Table 2).

Table 2: Validity of bone invasion detected by clinical examination and histopathology

	Histopathology of excised bone		
Clinical examination	**Bone Invasion Present**	**Bone invasion Absent**	**Total**
Bone Invasion Present	22 (88%)	2 (20%)	24 (68.57%)
Bone Invasion Absent	3 (12%)	8 (80%)	11 (31.42%)
Total	25 (100%)	10 (100%)	35 (100%)

According to histopathology of excised specimen to have bone invasion, 96% (24 cases out of 25) were detected by CT scan to have so. Of the patients diagnosed with no bony invasion, 90% (9 cases out of 10) were also diagnosed similar by CT scan (p< 0.0001) (Table 3).

Table 3: Validity of bone invasion detected by CT scan and histopathology

	Histopathology of excised bone		
CT scan	**Bone Invasion Present**	**Bone invasion Absent**	**Total**
Bone Invasion Present	24 (96%)	1 (10%)	25 (71.43%)
Bone Invasion Absent	1 (4%)	9 (90%)	10 (28.57%)
Total	25 (100%)	10 (100%)	35(100%)

CT scan has higher sensitivity (96%) compared to clinical examination (88%) and also higher specificity (90%) compared to clinical examination (80%). Both methods have high PPV, with the CT scan having a slightly higher value (96% compared to 91.67% for clinical examination). CT scan has a higher NPV (90%) compared to clinical examination (72.73%), suggesting that a negative result from the CT scan is more reliable in ruling out the condition. Considering both true positives and true negatives, the CT scan has higher accuracy (94.28%) compared to clinical examination (85.71%), indicating that, overall, the CT scan provides more accurate diagnostic information (Table 4).

Table 4: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of Clinical examination and of CT scan

Parameters	**Clinical examination (Percentage)**	**CT scan (Percentage)**
Sensitivity	88	96
Specificity	80	90
Positive predictive value	91.67	96
Negative predictive value	72.73	90
Accuracy	85.71	94.28

DISCUSSION

Age of the participants of this study ranged from 30-80 years (mean age 53.3 years). Mostly affected (40.00%) age group was 50 years to 59 years and the lowest affected group was from 30 years to 39 years and 70 years and above. Rao et al[21] (2004) studied on 51 patients and found mean age of 53.4 which was quite equal to present study. In addition, these findings were also very much close to and consistent with the findings of other studies.[22,23]

The male: female ratio among the participants was 1:1.2. The female predominance of oral squamous cell carcinoma in our country may be due to they are confined to indoor activities and lack of recreation, habituated to betel quid chewing.[24]

Present study noticed buccal & alveolar mucosa as most frequently affected (37.14%) site and then buccal mucosa to be affected (31.42%) site. Molla and Hasan studied on 102 patients of OSCC and found buccal mucosa as the most common primary site and it comprised 35%.[25] Other study also showed buccal mucosa was the most predominant site.[26] In contrast, Iamaroon et al observed tongue to be the mostly frequent site.[27] The variations were may be due to the fact that in the later study 64.4% patients were smoker and only 50.2% were betel quid chewers, on the other hands, all most all patients of our country and in the subcontinent are betel quid chewers. The betel quids are habituated compressed against buccal mucosa and alveolar mucosa providing a direct access of carcinogens from the quid.[28] Chen et al (1999) showed that tongue was the most common site among patients without any oral habits; on the other hand, buccal mucosa was the overall predominant site and also for who consumed betel quid with or without smoking and/or alchohol.[29] Involvement of the alveolar ridge & gingiva was 14.28% and retro molar trigone alone was 11.42% in the present study.

Among our cases, 8.57% tumour was 0-2cm. in size, 37.14% was 2-4cm. in size and 54.28% was >4cm. in size. Although Uddin and Ahmed (2011) observed highest involvement was 2-4 cm, the percentage was less (48.6%) than present study. However, no plausible evidence was found whether size could be a predictor of bone invasion or not. [30]

Fixity of the lesion with surrounding structures was present among 65.71% patients and paraesthesia of lower lip was present among 5.71%. Clinical findings such as inferior alveolar nerve function

impairment or tumour fixation to the mandible lift up the suspicion of mandibular invasion.[31] Among the respondents 54.28% had mobility of teeth. Patients who are dentate may note loosening of teeth.[32] Irregularities of bone were present in 34.28% while most of the site of bone irregularities was mandibular alveolus. Lymph node involvement was also observed in this study although exploring their role in bone invasion was not within the purpose of this study.

About 65.71% respondents were of stage IV of carcinoma. Sadat et al (2012) studied in the same hospital and found stage IV to be the maximum number (55%).[33] In contrast to this study, Uddin & Ahmed[30] (2011) reported 68.5% were of stage III and only 14.3% in stage IV. The difference of two studies may be owing to the fact that in the present study staging a large number of patients was found to have skin involvement.

Regarding grading of the tumour, result of this study coincides with the study of Mamun (2012)[34]. Sadat et al[33] (2012) found 75.9% grade I tumour, 20.7% grade II, 3.4% grade III but no tumour of grade IV. Another study reported the highest (72%) findings of well differentiated carcinoma.[1] Several authors reported the similar findings.[22,27]

This study compared the clinical examination and histopathology report about mandibular invasion. Clinical examination showed 88.00% sensitivity that supports others report.[7,18,35–37] Clinical examination couldn't detect just three (12%) cases of bone invasion. Again in 20% cases of clinically decided positive for bone invasion were not histologically proven. Percentages of false positive results were high possibly due to the reactive alterations such as inflammation, fibrosis and new bone formation at the tumour-bone line giving the appearance of fixity of tumour to the mandible.[21] On the other hand clinical examination in 80.00% cases correctly detected the absent of bone invasion. Clinical examination appropriately detected 88% of cases of bone invasion backed by histopathological confirmation (sensitivity = 88%). Specificity, PPV, NPV and accuracy of clinical examination were 80%, 91.67%, 72.73% and 85.71% respectively. The results of present study were compared to the results of different studies conducted by different researchers (Table 5). PPV, NPV and accuracy of clinical examination in this study were 91.67%, 72.73% and 85.71% respectively but it could not be compared with other studies as the reviewed article had not shown PPV, NPV and accuracy.

Table 5: Results of clinical examination in different studies

Researcher	Year of publication	Sensitivity	Specificity
Albuquerque et al[11]	2009	82%	87.5%
Bahadur[6]	1990	82%	68%
Brekel et al[38]	1998	39%	100%
Brown et al [35]	2001	81%	66%
Close et al[39]	1986	82%	84%
Gilvert et al[7]	1986	88%	30%
Leipzig et al[36]	1985	94%	76%
Rao et al[21]	2004	96%	58%
Shaha* [18]	1991	-	-
Van cann et al[10]	2008	59.1%	73.9%
Zupi et al[37]	1986	83%	44%
In this study	2016	88%	80%

*Shaha reported the accuracy of clinical examination is 88% but did not mention sensitivity and specificity.

In present study specificity, PPV, NPV and diagnostic accuracy of CT scan were 90%, 96%, 90% and 94.28% correspondingly. The results of present study were compared to the results of different studies conducted by different researchers (Table 6).

Table 6: Results of CT scan in different studies

Researcher	Year	Total	Sensitivity	Specificity	PPV	NPV	Accuracy
Close et al[39]	1996	43	100%	97%	100 %	-	97.7%
Kalavrezos et al[8]	1996	60	78%	80%	89%	63 %	78.7%
Kushraj et al[40]	2011	15	75%	100%	100 %	78 %	-
Mukherji et al[19]	2001	49	96%	87%	89%	95 %	91.8%
Zupi et al[37]	1996	23	91%	96%	95.4 %	-	94%
In this study	2016	35	96%	90%	96%	90 %	94.28%

The study of Mukherji et al (2001) revealed same values for sensitivity (96%) as ours but different specificity (87%), PPV (89%) and NPV (95%)[19]. Study of Shaha et al (1991) depicted a lower accuracy (68%) for CT. The CT scan had some utility evaluating primary cancer and the neck nodes but limited definite value in terms of evaluating the mandible. The mandible is an uneven bone with changeable shapes throughout its configuration. In a mandibular CT scan it is very difficult to observe negligible invasion of the inner cortex.[18] According to Lane et al (2000) sensitivity was 50% while NPV was 61% summarizing CT as an imprecise technique.[41] Additionally, Brown et al (1994) reported 28% false negative rate for CT concluding a unsatisfactory predictability for identifying mandibular invasion.[35] However, weighing against these divisive results one should consider that the above mentioned studies acquired their images by 4-5 mm sections or failed to specify their CT technique.[18,35,41] Furthermore, there were some false positive cases which were due to the obscurities to differentiate the definite mandibular invasion from the bone loss resulting from periodontal diseases. On the other hand, there were fewer false positive cases when there was mandibular canal involvement because there were less dental artifacts at a greater distance. In contrast to this study Close et al (1986) found a better accuracy.[39] The accuracy of present study is equal to Zupi et al[37] (1996).

Sensitivity was better in present study than that of the studies of Brown et al and Lane et al[35,41] as the genuine true positive cases were higher in the present study than that of both of them, including more advanced stage cases. Nevertheless there was a case of false positive in the present study. Furthermore, while specificity rate was close to the findings of other studies fewer instances of early staging in the sample resulted in fewer cases of exact negative. It may be because patients in Bangladesh get surgical treatments at terminal stage. So, due to smaller true negative cases it would be impossible to acquire ample information on specificity from this study.

In this study sensitivity of CT was 96% with only one false negative case. So, it can be concluded that CT can assist detecting mandibular invasion and its results may facilitate the decision of mandibulectomy

whether needed or not though some (4%) false negative cases may lead to under treatment. CT's high sensitivity makes it clearly important to recognize the life threatening condition. On the other hand because of 90% specificity CT is not considered as an accurate diagnostic tool to identify bone invasion, especially in presence of periodontal diseases. So, decision depending solely on CT scan result may provide over treatment to the patient. More accurate result can be achieved from further study with a greater number of cases including early staging as the true negative cases were modest in the current sample. It is evident from the findings of this study and studies mentioned in table 6 that CT is a sensitive tool with an acceptable range of specificity. It is able to detect mandibular invasion precisely.

CONCLUSION:

Results of clinical examination and computed tomography scan suggested that they might be utilized as primary investigative approaches. All the instances of bone invasion were identified through the clinical examination and CT scans together. This let oral and maxillofacial surgeons to decide on mandibular resection based on definite invasion by OSCC.

LIMITATIONS:

1. Sample size was small and sampling technique was not randomized.
2. This study was not blinded.
3. The specimen was decalcified in nitric acid solution making it difficult to assess the extent of the invasion

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