International Journal of Otolaryngology and Head & Neck Surgery, 2024, 13, 429-441
https://www.scirp.org/journal/ijohns
ISSN Online: 2168-5460
ISSN Print: 2168-5452

Diagnostic Role of Computerised Tomography in Mandibular Invasion among Patients with Oral Squamous Cell Carcinoma

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How to cite this paper: Singh, L., Singhal, P., Bansal, A., Tak, D., Saharan, R., Rawat, A., Singh, A., Anand, M., Bairwa, N.K., Nirwan, S., Singh, K., Sharma, A.K. and Yadav, R. (2024) Diagnostic Role of Computerised Tomography in Mandibular Invasion among Patients with Oral Squamous Cell Carcinoma. *International Journal of Otolaryngology and Head & Neck Surgery*, **13**, 429-441.
https://doi.org/10.4236/ijohns.2024.136037

Received: August 26, 2024
Accepted: October 12, 2024
Published: October 15, 2024

Abstract

Background: Oral cavity malignancy can result from surface epithelium, salivary glands, or submucosal soft tissue. Common symptoms may include non-healing ulcers, slurred speech, dysphagia, neck mass and pain which may indicate cortical invasion. Morbidity and quality of life have been seen to rise with mandibular excision in oral cavity squamous cell carcinoma. Therefore, in order to design the surgery appropriately, it is vital to be aware of the mandibular invasion prior to the procedure. Various researches have been focused on the accuracy of clinical examination and imaging technique in predicting tumour invasion of the mandible in oral malignancy. The goal of this study was to find a correlation between histological assessment, clinical examination, and computed tomography results in patients with mandibular involvement and oral cavity squamous cell carcinoma. Objectives: To determine the sensitivity, specificity, NPV and PPV of CECT and clinical diagnosis in patients with oral squamous cell carcinoma with mandibular invasion. Methods: A cross-sectional observational study was set out to review preoperative clinical and radiological assessment; and post operative histopathological finding of mandibular resection specimen in clinically evaluated and diagnosed cases of oral cavity squamous cell carcinoma (SCC) with mandibular invasion. Results: 43 individuals of oral cavity SCC with mandibular involvement were examined. 12 out of 28 mandibular resections had bone invasion, with numerous tumour entry sites being the most frequent mechanism of invasion, according to post-operative HPE. The positive predictive value (PPV) of contrast

enhanced computerised tomography (CECT) scans was 42.8%, as 28 individuals had invasions revealed; sensitivity is almost 100%; specificity is 48.3. Conclusion: Prioritizing the identification of mandibular invasion is essential to enhance the prognosis of patients with oral SCC. There is an urgent necessity to review the usefulness of radiology in the treatment of mandibulectomy. Combination of clinical and radiological examination increases sensitivity and specificity.

Keywords

Oral Squamous Cell Carcinoma, Mandibular Invasion, Mandibular Resection

1. Background

Oral cavity carcinoma is the eighth most common malignancy worldwide with an estimated incidence of 300,000 cases per year [1]. The unusual habit of chewing tobacco contributes to its significantly greater prevalence in Southeast Asian nations, particularly India. Males experience this condition more frequently than females, and the number of younger individuals is also increasing [2]. The extent of cancer spread is associated with prognosis and survival. The 5-year survival rate is 80% when the tumour is limited to the mucosa, but it decreases to 40% when the mandible is involved [3] [4].

The AJCC (American joint committee on cancers) 8th edition states that mandibular cortex involvement may upstage the tumour to IVa in squamous cell carcinoma of the mandibular alveolus, floor of mouth, gingivobuccal sulcus, buccal mucosa, or retromolar trigone [5]. Resection of the mandible is required in such cases, which not only increases mortality but also significantly hampers quality of life. Consequently, it is crucial to identify mandibular invasion prior to surgery to plan for surgical resection. This incursion can be infiltrative or erosive [6] [7]. There is currently no single definition for these concepts. On the other hand, the histological erosive pattern shows a broad pushing front with osteoclastic activity, while the infiltrative pattern has an uneven tumour front with projections that resemble fingers into the mandible and no discernible osteoclastic activity [8] [9].

Clinical examination is reliable in the majority of cases but has low sensitivity and specificity in detecting tumour invasion [10]. Currently, no one study has been able to predict mandibular invasion with any degree of precision. The following imaging techniques have been employed to identify bony involvement: orthopantomography, computed tomography, magnetic resonance imaging, bone scintigraphy, and Single photon emission computed tomography (SPECT) [11]. Thus, a combination of clinical and radiological assessments is required for accurate analysis of bone invasion. This study aimed to establish a correlation between histological assessment and clinical examination and computed tomography results in patients with mandibular involvement and oral cavity squamous cell

carcinoma.

2. Aim and Objectives

2.1. Aim

The aim of this validational type of observational study was to determine the diagnostic role of CECT and the clinical diagnosis of mandibular invasion in oral squamous cell carcinoma patients, with histopathological examination as the gold standard.

2.2. Objectives

- To determine the sensitivity of CECT and clinical diagnosis in patients with oral squamous cell carcinoma with mandibular invasion.
- To determine the specificity of CECT and clinical diagnosis in patients with oral squamous cell carcinoma with mandibular invasion.
- To determine the positive predictive value (PPV) of CECT and clinical diagnosis in patients with oral squamous cell carcinoma with mandibular invasion.
- To determine the negative predictive value (NPV) of CECT and clinical diagnosis in patients with oral squamous cell carcinoma with mandibular invasion.
- To determine the diagnostic efficacy of CECT and clinical diagnosis in patients with oral squamous cell carcinoma with mandibular invasion.

3. Methodology

3.1. Study Design

The present cross-sectional study was carried out after getting ethical clearance from the institution (146/MC/EC/2020) between March 2020 and November 2022 in the Department of Otorhinolaryngology and head and Neck Surgery at Sawai Man Singh Medical College and Hospital, Jaipur, Rajasthan, India.

3.2. Patient Selection

Patient with oral cavity squamous cell carcinoma showing mandibular involvement clinically or radiologically on computed tomographic scans or both who underwent primary surgical resection including marginal or segmental mandibulectomy were studied.

The inclusion criteria were as follows:

- Tumors of the gingivobuccal complex, alveolus, floor of the mouth, and retromolar trigone.
- Evidence of bone invasion clinically or on computed tomographic scans.
- Consented for mandibular resection surgery.
- Patients willing to participate in the study.

The exclusion criteria were as follows:

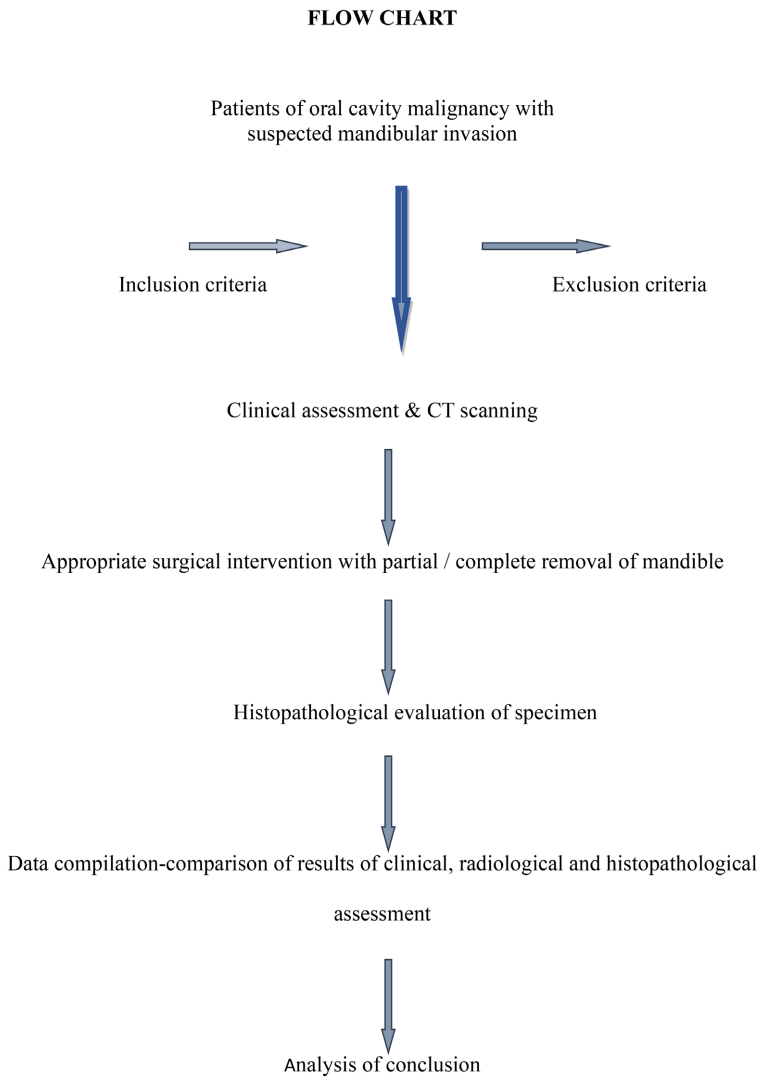
- Magnetic resonance imaging was the modality of choice for tongue carcinoma patients.

- Unresectable or T4b disease.
- Maxillary involvement.
- Involvement of the oropharynx.
- Recurrent disease.
- History of prior radiotherapy.
- Noncooperative and severely ill patients.

Overall, 53 patients with oral cavity carcinoma had mandibular involvement, 43 of whom fulfilled the inclusion criteria and were followed further.

3.3. Sampling Size & Sampling Technique

The sample size was calculated at 80% study power and 0.05α error as the sensitivity of CECT scans for detecting invasion of the mandible among oral cavity malignancy patients. All consecutive patients who fulfilled the inclusion and exclusion criteria were enrolled in the study until a sufficient sample size of 43 was achieved.



All eligible patients for the study were approached by the investigator himself and were informed of the nature and purpose of the study after providing informed consent. A detailed history was obtained, and a thorough clinical examination (local and systemic) was performed. CECT of the mandible performed for radiological assessment at Sawai Man Singh Hospital by an identified and qualified radiologist to minimize interobserver bias.

3.4. Preoperative Evaluation

The patient's full workup was completed after receiving the required consent. Questions concerning past medical or surgical history, persistent diabetes mellitus or hypertension, oral ulcers, dental pain, loosening of teeth, bleeding from the mouth, referred pain, and drug allergies were asked. Local examination included mouth opening, inspection and palpation of the oral ulcer, loosening of teeth, assessment of the ulcer margins, involvement of the gingivobuccal sulcus or alveolus, tenderness, bleeding, skin involvement or fixity to surrounding tissues. Preoperative computed tomographic scanning was then used to map and stage the illness. The 8th edition of AJCC, however, does not consider upstaging of the tumor if it is mere superficial cortical erosion, but in our study these cases were managed similarly to stage T4a. The results were confirmed by histopathology.

3.5. Surgical Planning

The decision was made intraoperatively by the operating surgeon in the majority of patients. The primary tumour was surgically removed from all included patients, with 2 cm safe margins maintained. Additionally, complete neck dissection, segmental mandibulectomy, or marginal/rim resection of the mandible, was performed, and the defect was rebuilt using vascularized pedicled flaps. The specimens were then sent for histopathological analysis.

3.6. Histopathological Examination (HPE)

Specimens were collected and transferred to the pathology laboratory in 10% neutral and buffered formalin. All specimens were reviewed and reported by an identified and qualified pathologist. Reporting of the primary tumor, neck dissection specimen and mandible were performed separately. The following parameters were studied microscopically:

- Presence or absence of mandibular involvement.
- Pattern of involvement: erosive or invasive (erosion was defined as extension of carcinoma beyond the periosteum in a broad pushing front characterized by scalloping of mandibular bone by osteoclasts mediating mandibular resorption, while invasion was defined as carcinoma extending into the cortical bone via finger like projections).
- Depth, height and length of mandibular bone involvement.
- Extent of involvement (cortex of the buccal or lingual side or both, marrow involvement).

- Routes of entry.
- Lymphovascular and perineural invasion.

3.7. Statistical Analysis

The resulting data were loaded into Microsoft Excel sheets to create master charts, which were documented on a prearranged study platform. These data were subjected to statistical analysis. Quantitative variables are displayed as the mean and standard deviation (SD) while qualitative factors are summarized as proportions and ratios. The sensitivity, specificity, NPV & PPV of CECT scans were calculated using standard formulae, with HPE as the gold standard. SPSS version 28.0 (Statistical package for social sciences) software was used for the statistical calculations.

4. Results

In this study, 43 individuals with mandibular involvement and oral cavity malignancy were examined. Of these, 7 (16%) were female and 36(84%) were male (M: F = 5.25:1) (Figure 1). The patient's ages ranged from 23 to 65 years (mean age = 40.2 years) (Table 1).

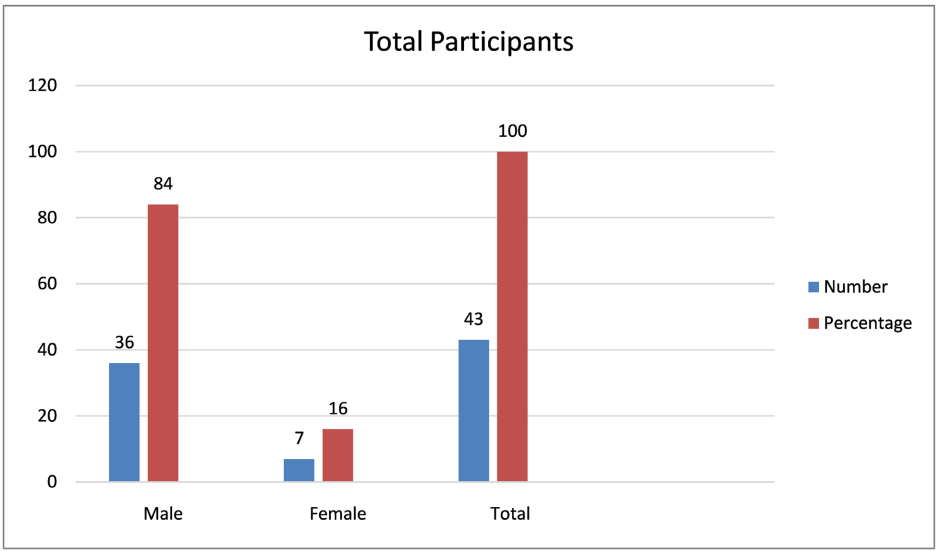


Figure 1. Number and percentage of male and female participants.

Table 1. Sociodemographic characteristics of the study participants.

Patient characteristics	
Age	23 to 65 years
Sex	M: F 5.2:1

In this study, buccal mucosa was most common site of involvement (14 cases) on clinical assessment and it was unfortunate to find that most of the cases we treated were at the advanced stage of disease (T4a) (Table 2).

CECT showed bone invasion in 28 patients (65.1%) (Table 3), out of which 21 cases underwent segmental mandibulectomy and rest were treated with marginal mandibular resection (Figure 2). Twelve out of 28 mandibular resections showed bone invasion on HPE (Table 4), with numerous tumor entry sites being the most frequent mechanism of invasion. The PPV of CECT scans was 42.8%, as, invasion was revealed in 28 individuals, the sensitivity was almost 100%, and the specificity was 48.3. CECT was 42.8% accurate in identifying mandibular invasion when HPE was taken into consideration as the gold standard diagnostic investigation. The PPV of the clinical examination was 57.14%, the sensitivity was almost 100% and the specificity was 70.96%.

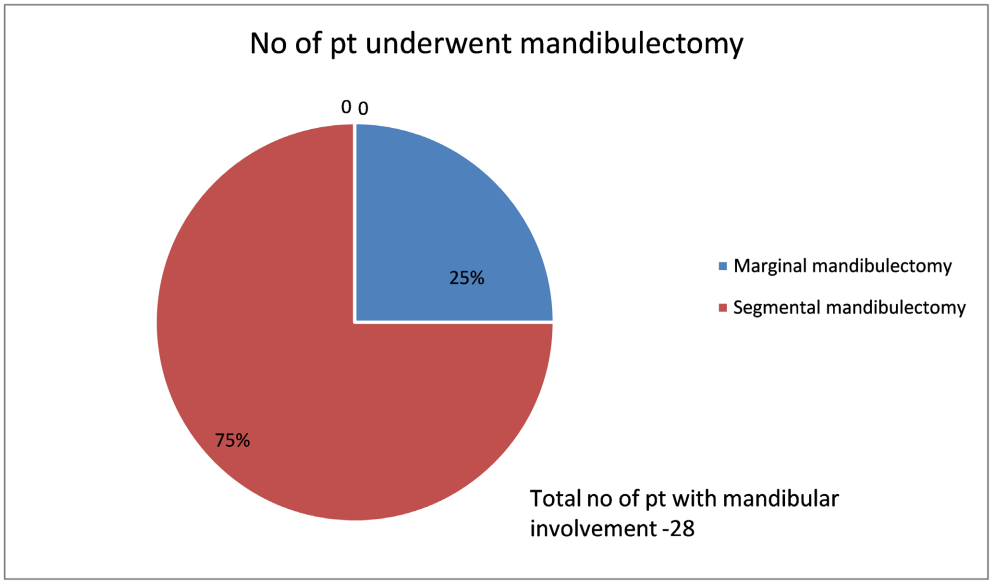


Figure 2. Pie chart showing the number of patients who underwent mandibulectomy.

Table 2. Clinical characteristics of study participants are tabulated.

Patient characteristics	
Tumor characteristics	Buccal mucosa: 14
• Subsite involved	Lower GBS: 08
	Lower alveolus: 07
	Floor of mouth: 05
• Clinical involvement of mandible	Retromolar triangle: 09
	21
T stage	
• T2	05
• T3	11
• T4a	24
Neck node involvement	39

Table 3. Pattern of mandibular bone involvement on CT scan and the type of mandibulectomy performed.

Mandibular bone involvement	28	65.1%
Type of mandibular resection	28	
• Marginal mandibulectomy	07	
• Segmental resection	21	

Table 4. Histopathological analysis of the tissues.

HPE assessment		
Grading of tumor		
• WDSCC	30	69.7%
• MDSCC	11	22.5%
• PDSCC	01	02.3%
Skin and subcutaneous tissue	18	41.8%
Lymphovascular/perineural/bone invasion		
• Bone invasion	12	27.9%
• Perineural invasion	03	6.9%
• Lymphovascular invasion	03	6.9%

5. Discussion

Squamous cell carcinoma of the oral cavity is one of the leading causes of morbidity and mortality worldwide. Cancers of the buccal mucosa, floor of mouth, lower alveolus, and retromolar trigonal region are often linked to direct extension of the mandible in an erosive or invasive way (the mandibular involvement pattern has a prognostic influence) [12]. The AJCC 8th edition states that an erosive pattern of involvement has a prognosis and survival comparable to that of no involvement, whereas an invasive pattern of involvement upstages the tumor. Thus, detection of mandibular bone invasion is of utmost importance in preoperative treatment planning for appropriate resection of the mandible.

Clinical examination alone is not sufficient to predict bony involvement and always requires imaging in the form of orthopantomogram, CECT, magnetic resonance imaging (MRI), SPECT, cone beam CT (CBCT) and bone scintigraphy. The choice depends upon a number of factors: surgeon preference, institutional availability, patient affordability and dental artifacts [13]. In a recent systematic review and meta-analysis, there was no discernible advantage between MRI and CECT for predicting mandibular bone invasion [14]. In 65.1% of our patients with oral squamous cell carcinoma, computed tomographic scans obtained before surgery were able to predict bone involvement. All mandibles exhibiting profound cortical invasion underwent segmental resection, whereas tumours adhering to the cortex, abutting the surface, or exhibiting only superficial cortical invasion underwent marginal mandibulectomy [15]. The remaining mandibular height

was taken into consideration and converted to segmental resection when the height was less than 1 cm. When a patient has advanced paramandibular disease, the operating surgeon prefers segmental resection since there is a greater risk of bone invasion because many tumor entry sites may go undetected on CECT imaging [16] [17]. In such cases, the risk of extra resection is greater than the risk of tumor recurrence.

De Angelis *et al.* reported that MRI had greater sensitivity and specificity (87.1% and 80.5%, respectively) than CECT in their radiological assessment of mandibular bone invasion. CECT had a sensitivity of 69.0% and a specificity of 79.6%. Their histopathological examination revealed more patients with mandibular invasion than detected by imaging while our study showed contrasting results. In our study, HPE assessment was positive for mandibular invasion in only 12 out of 28 resected specimens. Since the majority of patients who came to us are thought to be in an advanced stage with large mandibular invasion, these individuals should be more easily detected by CECT. However, mild mandibular cortical erosion can be difficult to detect in patients with modest tumor sizes. Our study has constraints as we did not include instances with early stage oral SCC to assess CECT sensitivity.

Rajan S. Patel *et al.* examined the effects of bone invasion and the extent of bone resection patients with oral carcinoma. They discovered that the most significant predictors of disease-specific survival were the extent of nodal disease (pathological nodal status and extracapsular spread), positive margins, pathologic T stage, and bone invasion; soft tissue margins in the presence of bone invasion appeared to be the single most significant predictor of outcome. Patients with gross mandibular invasion tend to have extensive disease (skin involvement, maxillary invasion, extracapsular lymph node extension etc.) whose reconstruction is difficult at times and the poor prognosis in such patients is due to advanced local disease rather than mandibular invasion alone.

In a comprehensive analysis of various imaging modalities used in the detection of head and neck cancer, the sensitivity of conventional CECT was shown to be 73% for mandibular invasion and 85% for bone marrow invasion. A minimum of marginal resection must be performed even on the smallest suspicion since early cortical erosion may be overlooked on CECT scans [18] [19]. Consequently, intraoperative clinical judgment is superior to imaging alone. For the individuals in our study, mandibular resection appeared unnecessary because over half of the resected tissues did not exhibit bony invasion. However, in patients in which there is a clinical mandibular abutment, we advise minimal resection rather than no resection.

As mandibular resection is highly dependent upon preoperative imaging, newer imaging modalities, such as cone beam CT and SPECT have gained wide popularity in the last decade. Among the available imaging modalities, CBCT has the highest diagnostic efficacy and SPECT has the highest sensitivity. Hakim *et al.* discovered that conventional CT had a superior negative predictive value and a

greater sensitivity for cortical invasion when identifying mandible invasion in oral SCC than CBCT and SPECT. Additionally, with significantly lower radiation exposure in CBCT, this invasion can be effectively ruled out preventing over resection of the mandibles [20]. Chauker *et al.* reported that Multi-detector CT had an accuracy of 83.3% in predicting mandibular invasion as well as the extent of invasion, with a mean underestimation of approximately one mm. The occlusal route appeared to be the predominant route of tumor entry in gingiva-buccal complex cancers in dentate patients. They suggested that in advanced tumours with paramandibular disease, mandibular conservation is contraindicated because of multiple routes of tumor entry involving larger portions of the cortex and medulla. Therefore, segmental resection seems to be the preferred approach for treating T3-4 tumours of the mandible, and the extent of resection should correspond to the adjacent soft tissue cut margins, thus avoiding unnecessary hemi mandibulectomies [21].

Compared to SPECT and bone scintigraphy, CBCT is becoming the preferred option due to its lower cost and radiation exposure [22] [23]. It is also more frequently used in oral surgery and dentistry, making it easier for doctors to interpret and explain the results. Additionally, the latter have higher false positive rates, which might lead to inappropriate resection of the mandible. However, CT and MRI show the highest specificity among all modalities, and MRI has greater sensitivity than CT but has the disadvantage of high false positivity due to periodontal inflammation.

It was unexpected that only 42.8% of patients had invasion on postoperative histology despite preoperative CT evidence of bone involvement, which raised questions about needless mandibular resection. Histology is the recognized gold standard; however, sampling mistakes can cause false positives from imaging, which could be false negatives from histology. The lack of serial sectioning and examination of an inadequate number of slices beneath the tumor could explain the negative results observed by histology. False positives from imaging might arise due to adjacent periodontal inflammation and prior biopsy. The current study was unable to determine the wide variation observed in the results and requires more research [24]. We need more accurate preoperative imaging modalities that show greater positive predictive value, and histological analysis can be improved by meticulous assessment of serial cut sections of the mandible by an experienced head and neck pathologist.

6. Conclusions

There is an urgent need to review the usefulness of radiology in the treatment of SCC of oral cavity warranting mandibular resection. The combination of clinical and radiological examination increases both the sensitivity and specificity.

This study has several limitations. First, MRI is required to determine the extent of soft tissue invasion, which limits the use of CECT for assessing bone invasion during treatment planning. Second, there was no comparison between the various

subsites for mandibular invasion. However, a large sample size study will be required to effectively conclude an association between radiological and histopathological features.

Declarations

- Ethics approval was taken from the institutional ethics committee (Sawai Man Singh Medical College, Jaipur, INDIA) (146/MC/EC/2020) and a written consent was taken from all the subjects/patients to participate in this study.
- All the subjects/patients consented to publish the data as well.
- All the datasets used and analysed in this study are available from the corresponding author on reasonable request.
- No funding was received for this study by any means.
- Authors' contribution: L.S.—Prime accreditation who did a thesis; P.S.—Primary Guidance and conceptualization; A.B.—wrote the main manuscript text; D.T.—refined the data and collected the information; A. R. and A.S. P. S.—prepared the tables; M.A. and N.K.B.—prepared the figures; S. N., K. S. and A. K. S.—reviewed the manuscript and edited finally; R.Y.—did the biostatistics.
- Acknowledgements: not applicable.

Conflicts of Interest

There are no financial or non-financial competing interests among the authors.

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Abbreviations

SCC	Squamous cell carcinoma
PPV	Positive predictive value
CECT	Contrast enhanced computerised tomography
AJCC	American joint committee on cancers
SPECT	Single photon emission computed tomography
NPV	Negative predictive value
SD	Standard deviation
SPSS	Statistical package for social sciences
HPE	Histopathological examination
MRI	Magnetic resonance imaging
CBCT	Cone beam CT