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Clinical outcomes and impact of prognostic factors following adjuvant radiotherapy in oral tongue cancer patients

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Abstract

Background: The purpose of the study was to evaluate survival outcomes in post-operative oral tongue cancer patients undergoing adjuvant radiotherapy (RT) at a tertiary cancer care center and to critically review the impact of various clinical-pathological factors on recurrence and survival. Demographic factors, stage of all the histology proven oral tongue cancer, and treatment details were documented. Overall survival (OS) and recurrence-free survival (RFS) were analyzed along with the potential prognostic factors affecting outcome.

Results: One hundred forty-four post-operative oral tongue cancer patients referred to our department for adjuvant treatment were evaluated. Median age at presentation was 45 years. Forty-seven patients had pathological early stage disease (stages I and II) and 95 had locally advanced (stages III and IV) disease while post-op details were not present in 2 patients. At a median follow-up of 87 months (60–124) of alive patients, the median RFS for entire cohort was 62 months while median OS was 74 months respectively. Age, perineural invasion (PNI), and grade of the tumor emerged as independent prognostic factors for OS and RFS. Among patients with early stage disease, depth of invasion (DOI), age, and PNI were found as independent prognostic factors for RFS and OS. In locally advanced disease, higher grade, age, and PNI independently impacted the respective survival end points.

Conclusions: Age (> 45 years), higher grade, and presence of PNI showed inferior survival outcomes across the subgroups (early versus locally advanced disease). This may warrant adjuvant treatment intensification. DOI > 10 mm was particularly found to worsen survival in early node negative SCC oral tongue patients.

Keywords: Oral tongue, Adjuvant radiotherapy, Early and locally advanced

Background

Oral cavity cancer (OCC) constitutes 2% of all the malignancies diagnosed world-wide with an estimated incidence of 3.5 lacs [1], of which 62% arise in the developing countries like India [2]. This high incidence rate is mostly due to the high rate of tobacco chewing habits in this region [3].

Carcinoma oral tongue is the most common oral cavity cancer in the western countries [4, 5], while in India, gingivobuccal is the most common sub-site [6]. There is an increase in incidence of tongue cancers in India as well, especially in the younger population [5, 7]. Localized oral tongue carcinoma (cT1-T2N0) is amenable to surgery and has a good prognosis with 5-year survival rates of 75–89% [8]; in contrast, survival for advanced disease is generally inferior (36–68%) [9, 10]. Partial glossectomy and elective neck dissection is the standard surgical procedure in these cases. Adjuvant therapy is administered to improve local control, when intermediate/high-risk histopathological features are present such

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as involved lymph nodes, advanced T staging (T3/T4), presence of (PNI), and lymphovascular invasion (LVI) [11, 12]. There is level 1 evidence to show that adjuvant chemoradiotherapy (CTRT) in high risk cases, i.e., positive resected margins, extra-capsular extension (ECE), improves disease-free survival (DFS) and overall survival (OS) [13, 14]. For the unresectable group of patients, definitive CTRT is the treatment of choice [15], unless the disease is too advanced/ metastatic and needs palliative care.

We retrospectively evaluated outcomes of postoperative oral tongue cancer patients treated at an academic radiation oncology unit in a tertiary care center, and the impact of various prognostic factors on survival in early and locally advanced stage disease was studied.

Methods

Service evaluation of histologically proven non-metastatic oral tongue cancer patients treated between 2008 and 2013 was done. The study was duly approved by the Institutional Ethics Committee that granted waiver of informed consent owing to retrospective nature of analyses. Analysis was limited to patients receiving post-operative RT with or without chemotherapy. Information regarding patient demographics, clinicopathological features, index staging, interventions, and outcomes were retrieved from case records.

Treatment details

Patients underwent wide local excision or glossectomy (partial, hemi or total) with adequate margins around the tumor for the primary site. Unilateral modified neck dissection (MND) was performed for all patients with a clinically positive neck. Those with clinically/radiologically negative neck underwent at least supraomohyoid neck dissection (SOND). Bilateral neck dissection was considered in cases with midline tumors or involved contralateral L.N.

Patients were referred to the department for decision regarding adjuvant RT. Patients with adverse pathologic features such as advanced tumor stage, positive nodes, positive or close margins (< 5 mm), DOI ≥ 10 mm, and presence of PNI were offered postoperative radiotherapy. At simulation, a radiation planning (RTP) computed tomography scan (3–5 mm slice thickness) of all patients in a supine position, with neck rest and thermoplastic cast, was acquired. Bolus was used whenever there was skin involvement. After patient alignment with external lasers, radio-opaque reference markers were placed on the cast at the level of nasion. One hundred milliliters of Omnipaque or Ultravist (non-ionized) was used as contrast for acquiring CT images which were transferred to treatment planning system (Eclipse version, Varian Medical Systems, USA).

All patients received adjuvant RT using 6MV beams on a linear accelerator (CLINAC 2100C or 600CD, Varian Medical system, USA). Patients were mostly treated with three dimensional conventional RT (3D-CRT). Either anterolateral wedge pair assembly or bilateral parallel opposed fields were placed along with low anterior neck (LAN) field. Field placement was based on tumor and nodal location. Treatment was routinely planned in two phases, with the posterior border moved anteriorly, to spare the spinal cord in the second phase. LAN field was matched with parallel opposed fields using asymmetric collimation. Some patients with early stage disease were treated with Intensity modulated radiotherapy (IMRT). Patients received 60 Gy in 30 fractions (2 Gy per fraction) over 6 weeks as post-op dose. Higher dose up to 64–70 Gy was considered in some patients with positive surgical margins (R1/R2 resection). Patients with high-risk pathological features such as positive margins and ECE positivity received concurrent weekly chemotherapy (Cisplatin (@ 35 mg/m^2) along with post-op RT (CTRT) following intravenous hydration and antiemetic cover, along with mannitol diuresis. On the day of chemotherapy, RT was usually delivered within one hour of administration of chemotherapy.

Statistical analysis

Statistical methods comprised of descriptive analyses of clinicopathological features with special focus on identifying significant prognostic factors, pattern of recurrence, and survival outcome. RFS was calculated from the date of primary surgery till first evidence of clinicopathological recurrence or date of death (from any cause). OS was calculated from date primary surgery till the date of death (from any cause) or last follow-up. Due to the retrospective nature of the study, patients who were lost to follow-up (LFU) with disease were assumed dead due to loco-regional relapse while those without disease were censored. All survival analyses were done using the Kaplan-Meier method and compared using the log-rank test. Prognostic factors included patient characteristics (age) and disease characteristics (tumor grade, DOI, LVI, PNI, ECE, node metastasis (pN+/pN-), pathological stage) as co-variates for univariate analysis (UVA). These factors were selected based on observations in published literature. All significant ($p < .05$) variables were subsequently tested in multivariate analysis (MVA) with the Cox regression using backward conditional method. The cutoff date for all time-to event analyses was 1 January 2020. Any p value ≤ 0.05 was considered as statistically significant. All statistical analyses were done using SPSS version 21.0 (IBM, Armonk, NY)

Results

A retrospective analysis of 230 consecutive histologically proven primary oral tongue cancer patients treated in

the Department of Radiotherapy was done. Of these, 162 patients (70%) underwent curative surgery followed by adjuvant radiotherapy (Fig. 1). Among 162 patients, 18 (11%) had incomplete histopathological/treatment details and were therefore were excluded from the survival analysis. We therefore retrospectively analyzed 144 patients of oral tongue cancer in this audit. The demographic and treatment characteristics of entire cohort are summarized in Table 1. The median age was 45 years and predominantly comprised of male population. Tobacco chewing habit (75%) was documented mainly in younger patients (≤ 45 years) as compared to older sub-group (90% vs. 57%; $p = < 0.0001$). Patients were staged as per the 7th edition of AJCC TMN staging system.

Treatment details

Eight (6%) of 144 patients received neo-adjuvant chemotherapy (NACT) before undergoing curative resection and received a median of three cycles. NACT was planned in these patients owing to clinic-radiological evidence of extensive involvement of floor of mouth ($n = 3$) and borderline resectability due to disease extending to vallecula or base of the tongue ($n = 5$). One hundred forty-one (98%) of 144 patients underwent nodal dissection along with primary disease resection. Of these, 117 (83%) patients had an ipsilateral while in 24 (17%) patients had bilateral nodal dissection (Table 1). All patients received PORT ± chemotherapy (CTRT 57 patients (40%) and RT alone 80 patients (55%)), while in 07 (5%) patients, chemotherapy-related treatment details were not available. The median time to initiation of adjuvant radiotherapy was 7 weeks (range, 3–35 weeks). Radiotherapy treatment details were available for 138 patients (96%). Patients were predominantly treated with 3DCRT technique (78%). The median dose of EBRT was 60 Gy (range 50–70 Gy) with median overall treatment time (OTT) of 45 days (range, 34–63). Twenty-one patients ($n = 15\%$) had OTT of > 50 days. The median total treatment duration (TTD) from date of surgery till the completion of radiotherapy was 13 weeks (range, 5–43).

Tumor characteristics

Histopathological details and staging are summarized in Table 2. Primary tumor size was less than 4 cm in two third of the patients (95/144). Forty-seven patients (33%) had early stage node negative disease (stage I/II) and 95 patients (66%) were locally advanced (stage III/IV) (Table S1). Seventy-two (51%) out of 141 patients who

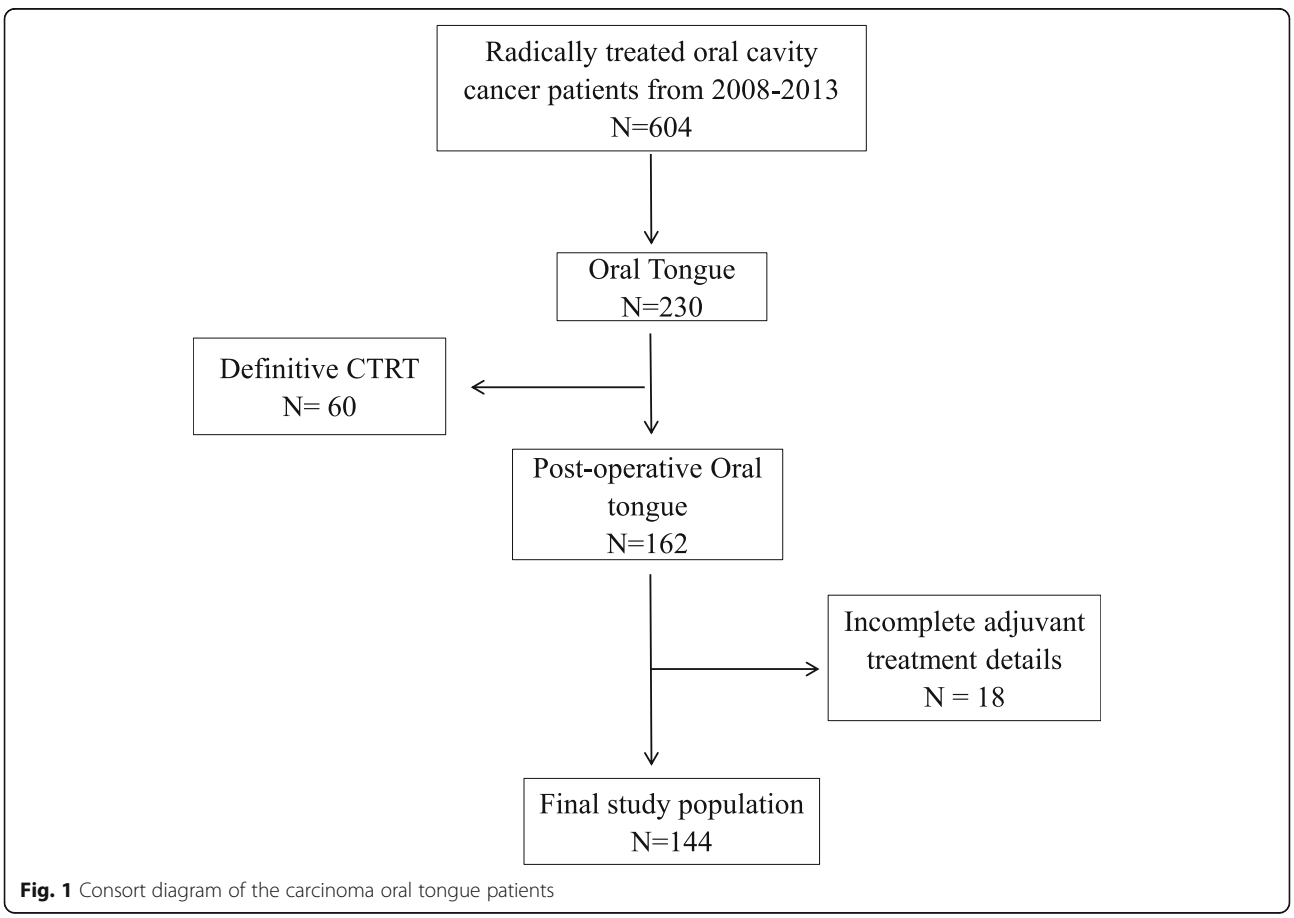

Fig. 1 Consort diagram of the carcinoma oral tongue patients

Table 1 Demographic details and treatment characteristics of the study

Characteristics	Entire cohort (*N* = 144)
Median age (range)	45 years (18–85 years)
Sex (male: female)	123: 21
Addiction	
No addiction	17 (12%)
Tobacco chewer	98 (68%)
Tobacco smoker	34 (24%)
Alcohol and smoking both	08 (06%)
Neo-adjuvant chemotherapy (NACT)	
Yes	08 (06%)
No	136 (94%)
Clinical stage of disease (AJCC 7th)	
Stage I	12 (08%)
Stage II	30 (21%)
Stage III	29 (20%)
Stage IV	23 (16%)
Unknown	50 (35%)
Glossectomy	
With L.N. dissection	141 (98%)
Without L.N dissection	03 (02%)
Extent of L.N. dissection (*N* = 141)	
Ipsilateral	117 (83%)
Bilateral	24 (16%)
Unknown	02 (01)
Pathological stage of disease (AJCC 7th)	
Stage I	26 (18%)
Stage II	21 (15%)
Stage III	29 (20%)
Stage IV	66 (46%)
Unknown	02 (01%)
Pathological stage of disease (AJCC 8th)	
Stage I	07 (05%)
Stage II	17 (12%)
Stage III	33 (23%)
Stage IV	76 (53%)
Unknown	11 (07%)
Dose of RT (median)	60Gy (50-70)
Concurrent chemotherapy	
Yes	57 (40%)
No	80 (55%)
Unknown	07 (05%)

underwent neck dissection were pathologically node positive (pN+ve). Among these, 2/3rd (45/72) had multiple lymph node involvement, i.e., pN2, and 46% (33/72) had ECE. The clinicopathological parameters were similar between early and locally advanced stage groups, except for the higher percentage of patients in locally advanced stage receiving concurrent chemotherapy for reasons of margin positivity and ECE (p = 0.001) (Table S1).

Table 2 Histopathological parameter details

Parameter	Entire cohort (*N* = 144)
Pathological T-classification (pT)	
pT1	48 (33%)
pT2	47 (33%)
pT3	12 (08%)
pT4	35 (24%)
Not known	02 (01%)
Tumor grade	
Low grade (grade I/II)	108 (75%)
High grade (grade III)	20 (14%)
Not known	16 (11%)
Perineural invasion *(PNI)*	
Absent	82 (57%)
Present	41 (29%)
Not known	21 (14%)
Lymphovascular invasion (LVI)	
Absent	107 (74%)
Present	13 (09%)
Not known	24 (17%)
Depth of Invasion (DOI) (mm)	
Median (range)	10 mm (10–30)
≤ 10 mm	69 (48%)
> 10 mm	57 (40%)
Not known	18 (12%)
Pathological nodal staging (pN) (*N* = 141)	
pN0	69 (48%)
pN1	27 (18%)
pN2	45 (32%)
Node metastasis (*N* = 141)	
Negative (pN-ve)	69 (49%)
Positive (pN+ve)	72 (51%)
Extra-capsular extension (ECE) (N = 141)	
Absent	102 (72%)
Present	33 (24%)
Not known	06 (04%)
Margin status	
Negative	114 (79%)
Positive or close	27 (19%)
Unknown	03 (02%)

Restaging as per the current AJCC 8th recommendation was attempted retrospectively based on histopathology findings, to look for stage migration. Fifty-four out of 144 patients (38%) were upstaged when DOI was factored in pT classification. Similarly, thirty-three patients (23%) were upstaged when adding extra-capsular extension to the pN classification. Overall, 14 out of 47 patients (1/3rd) with early stage disease (as per the 7th AJCC staging), in whom both DOI > 10 mm and ECE were present, were restaged as locally advanced (as per the 8th AJCC staging). In terms of impact on outcomes, twenty-three of the pT upstaged 54 patients (43%) had recurrence, and 20 (37%) of these eventually died.

Survival outcomes

The median follow-up of this audit was 87 months (range 59–124). At the time of last follow-up, 57 patients were alive (40%) while 54 (37%) were dead, and 33 patients (23%) were lost to follow-up, with or without disease. The median and 5-year RFS of entire cohort was 62 months (95% CI 31–93) and 52% (Fig. 2a) while OS was 74 months and 57% respectively (Fig. 2b). In the case, worst-case scenario was assumed (i.e., LFU with or without disease considered as an event); median and 5-year RFS was 41 months [(95% CI 22–60); 43%] and OS was 56 months [(95% C.I. 39–73); 49%] respectively.

In the subset analysis, early stage group of patients (7th AJCC staging system) had superior survival outcomes as compared to locally advanced stage group (Tables 3 and 4). Median OS was not reached for early stage patients while it was 68 months for locally advanced group (p = 0.05). At the time of analysis, 1/3rd (14/47) had died in early stage group, while in the locally advanced group, 39 (41%) were dead. LFU was higher in locally advanced group [24% (23/95) versus 20% (09/47) in early disease; p = 0.17].

Our retrospective study showed that addition of chemotherapy to adjuvant RT (CTRT) did not impact on survival outcomes. Five-year OS was 54% for patients receiving CTRT versus 57% for those undergoing adj RT alone (p = 0.20). Similarly, 5-year RFS was 44% versus 53% (p = 0.14) respectively. More patients in the CTRT group had ECE, LVI, and locally advanced stage disease (7th AJCC).

Prognostic factor analysis

The impact of various prognostic factors on OS and RFS is shown in Tables 3 and 4. Age > 45 years [H.R. 1.98; p = 0.01], PNI [H.R. 1.96; p = 0.01], and pN+ve [H.R 1.6; p = 0.07] were found to independently affect OS. For RFS, higher tumor grade [H.R. 2.2; p = 0.01) and PNI [H.R. 1.9; p = 0.01) were found significant on MVA.

The impact of these factors on RFS and OS was further explored in early and locally advanced disease groups separately (Table S2 and S3). In patients with early stage disease (n = 47), DOI > 10 mm and age (> 45 years) predicted for early recurrences on MVA. For OS, PNI and DOI > 10 mm were independent prognostic factors. Among locally advanced stage patients (n = 95),

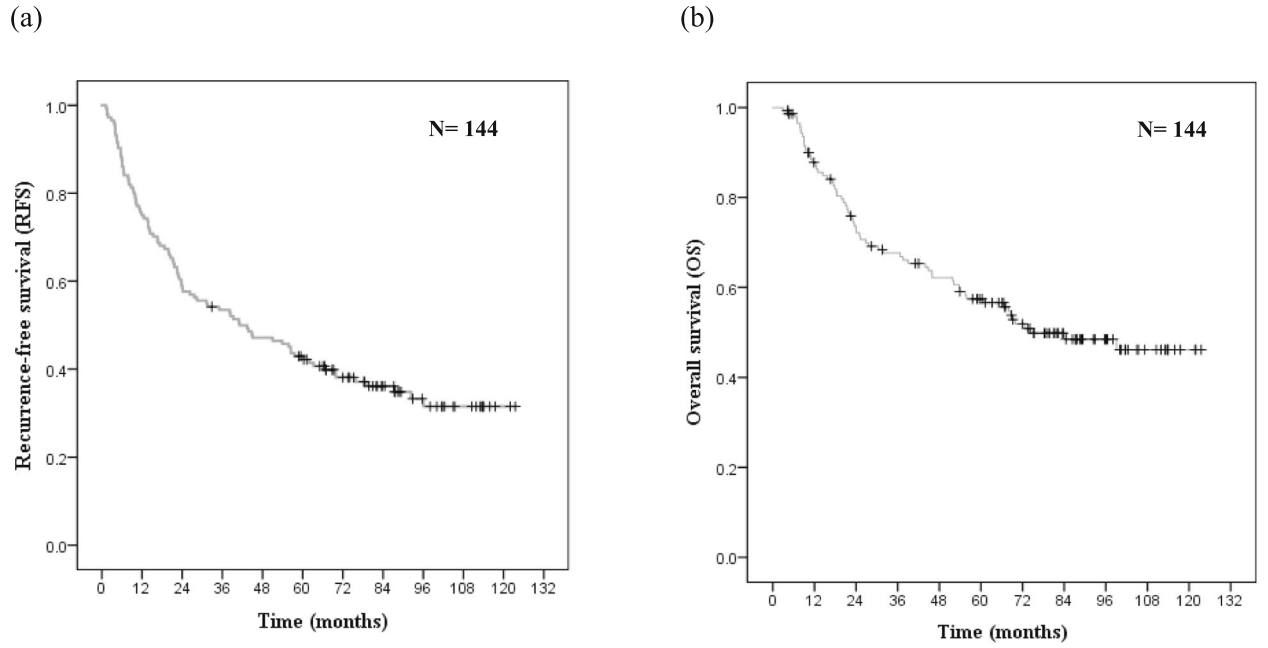

Fig. 2 Kaplan-Meier analysis showing recurrence-free survival (**a**) and overall survival (**b**) of the entire study population

Table 3 Impact of prognostic factors on recurrence-free survival (RFS) (*N* = 144)

Covariates	No. of patients	5-year RFS	Median RFS	Univariate analysis *p* value	Multivariate analysis H.R. (95% C.I.) *p* value
Age					
≤ 45 years	76	58%	87 months	0.17	
> 45 years	68	44%	39 months		
Grade					
Low	108	59%	87 months	**0.04**	2.2 (1.17–4.16)
High	24	32%	20 months		**0.01**
PNI					
Absent	82	58%	76 months	**0.06**	1.90 (1.11–3.4)
Present	41	43%	24 months		**0.01**
ECE					
Absent	102	58%	41 months	**0.06**	
Present	33	37%	17 months		
DOI					
≤ 10 mm	69	57%	70 months	0.32	
> 10 mm	57	47%	35 months		
Node metastasis pN)					
Negative (pN-ve)	69	56%	Not reached	**0.03**	1.53 (0.88–2.67)
Positive (pN+ve)	72	40%	38 months		0.13
Stage (AJCC 7th)					
Early	47	65%	Not reached	0.11	1.3 (0.55–3.06)
Advanced	95	46%	45 months		0.55

higher tumor grade proved as an independent prognostic factor for RFS. For OS, age (> 45 years) and PNI carried a poor prognosis. Treatment-related factors (OTT and TTD) did not impact on survival outcomes in this audit.

On univariate analysis, the significant impact of stage on RFS and OS was seen in patients wherein DOI was ≤ 10 mm (Fig. 3a, b). Beyond 10 mm, the influence of stage diminished considerably and the patients performed poorly (Fig. 4a, b) (Table S4).

Pattern of failure

During follow-up, 60 of 144 patients (42%) developed recurrence, of which 50 (83%) were loco-regional relapse (LRR), 8 had distant relapse (13%), and 2 patients (4%) had loco-regional and distant failure. Sixty-eight of 144 (47%) patients were free of disease at the time of last follow-up. Among patients with LRR (n = 50 + 2), primary site relapse alone was seen in 28/52 (54%) patients, while 17/52 (35%) had only nodal recurrence and 7/52 (13%) had primary and nodal relapse. Patients with pathological nodal metastasis had a high overall failure rate (LRR and distant relapse), (pN+ve 53% vs. 35% pN-ve; p = 0.03, chi-square) and LRR (45% vs. 30%; p = 0.07). Five-year locoregional-RFS was significantly inferior for pN+ve patients (51%) vs. (74%) in pN-ve patients (p = 0.05). Other factors such as age, grade, stage (early and locally advanced), PNI, and DOI were not found to be significant.

Discussion

We report clinic-demographic and survival outcomes of 144 patients with primary oral tongue carcinoma treated with radical surgery and adjuvant radiotherapy. The median age of 45 years was lower than other series of Indian sub-continent [15–18]. Based on the report from 29 population-based cancer registries (PBCR) in India, age-specific incidence rate of oral tongue cancer was highest (58%) in elderly population (60–69 years) [7]. However, trends are changing: a recent study from a tertiary cancer care center in India reported that commonest age of presentation of tongue cancers came down from 6th decade as reported in 1996 to 5th decade in 2012 [18]. Similarly, the western reports also document the median age between 55 and 57 years [8, 19]. The present study is in concordance with other studies showing male preponderance in younger patients as

Table 4 Impact of prognostic factors on overall survival (OS) in study cohort (*N* = 144)

Covariates	No. of patients	5-year OS	Median OS	Univariate analysis *p* value	Multivariate analysis H.R. (95% C.I.) *p* value
Age					
≤ 45 years	76	66%	NR	**0.04**	1.98 (1.15–3.4)
> 45 years	68	48%	52 months		**0.01**
Grade					
Low	108	62%	99 months	0.33	
High	20	47%	52 months		
PNI					
Absent	82	67%	99 months	**0.01**	1.96 (1.14–3.4)
Present	41	43%	25 months		**0.01**
ECE					
Absent	102	62%	99 months	0.19	
Present	33	50%	56 months		
DOI					
≤ 10 mm	69	66%	99 months	0.13	
> 10 mm	57	56%	52 months		
Node metastasis (pN)					
Negative (pN-ve)	69	70%	NR	**0.02**	1.6 (1.0–2.8)
Positive (pN+ve)	72	47%	54 months		**0.07**
Stage (AJCC 7th)					
Early	47	72%	NR	**0.05**	1.24(0.53–2.9)
Locally Advanced	95	51%	68 months		0.62

PNI perineural invasion; *ECE* extra-capsular extension; *DOI* depth of invasion; *NR* not reached
Analysis of histological features was based on available pathology slides and blocks (number of patients provided)

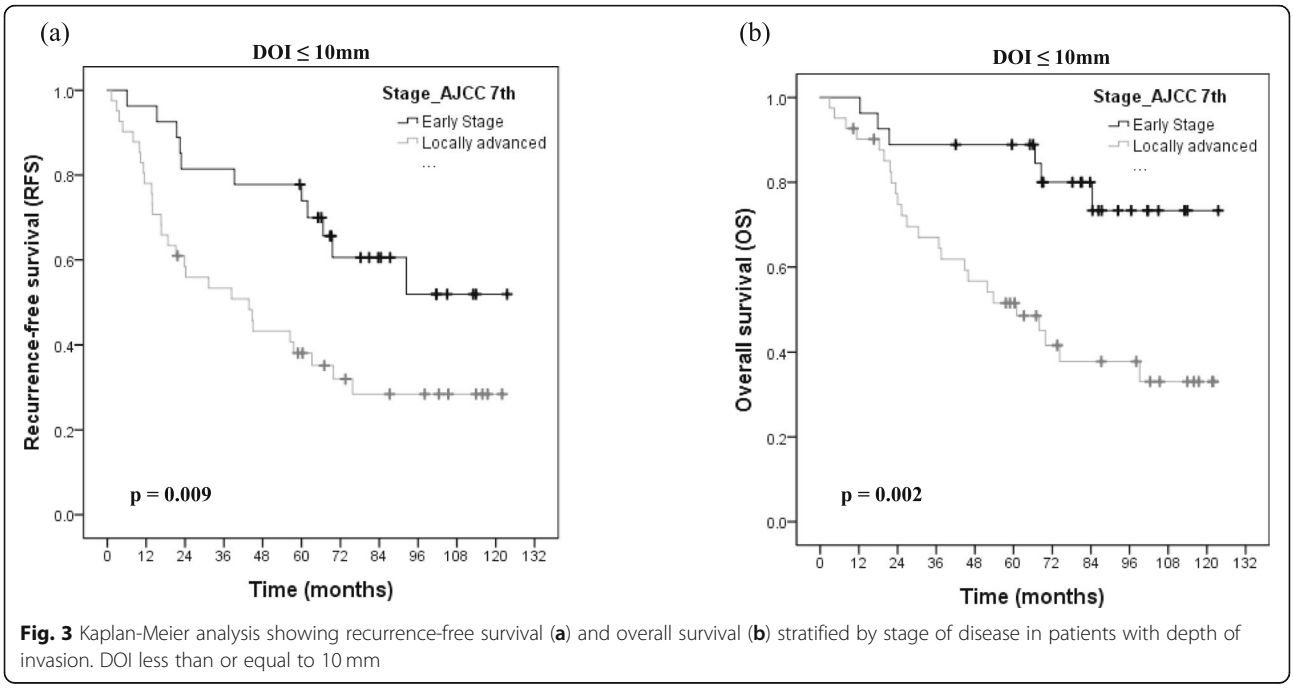

Fig. 3 Kaplan-Meier analysis showing recurrence-free survival (**a**) and overall survival (**b**) stratified by stage of disease in patients with depth of invasion. DOI less than or equal to 10 mm

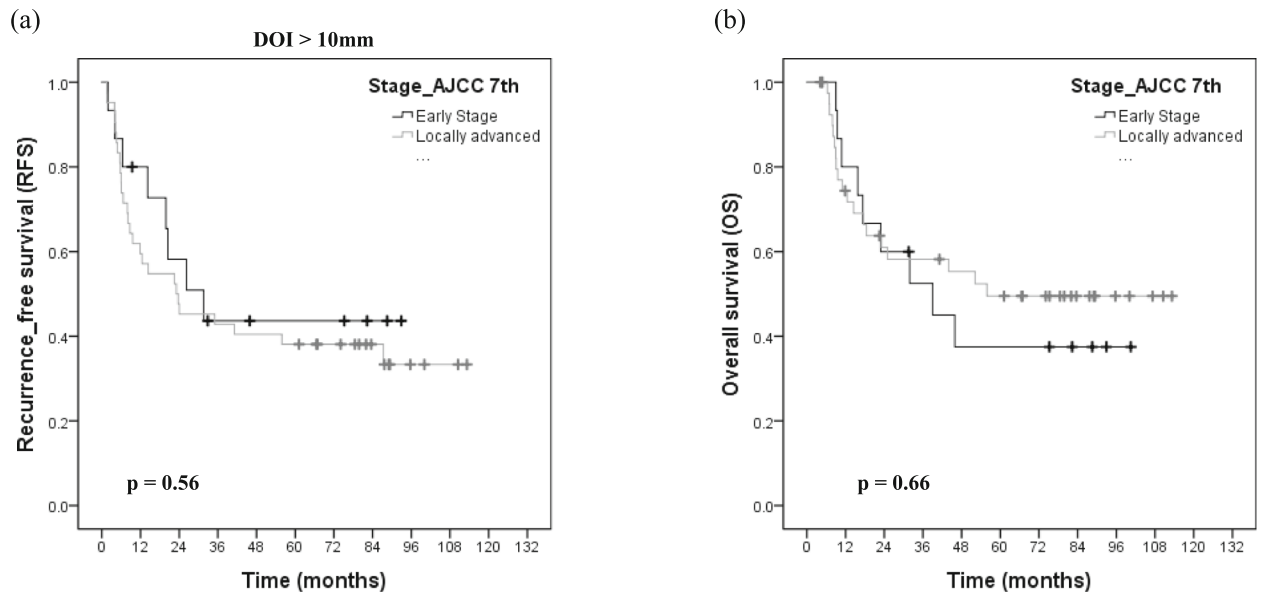

Fig. 4 Kaplan-Meier analysis showing recurrence-free survival (**a**) and overall survival (**b**) stratified by stage of disease in patients with (DOI) greater than 10 mm

compared to the older age group [7, 20]. This could be a cultural practices or skewness of the referral pattern. Nevertheless, in India, an increase in incidence of tongue cancer in younger age group has been observed and attributed to early use of tobacco/smokeless-tobacco [7, 15, 21]. Contrary to other published reports [20], chewing of tobacco was significantly higher ($p < 0.0001$) among younger patients (age < 45 years) as compared to the older ones in this study [75% vs. 44% respectively].

The cases included in this audit were staged as per the then prevalent AJCC 7th edition. However, for the purpose of our understanding of the new staging classification, i.e., 8th edition of AJCC staging system (in practice since 1 January 2018), we restaged these cases based on the information available in the case records. Retrospectively carried out restaging can be challenging due to non-availability of the histopathological details, as was seen in this audit in 12% of cases and therefore could not be re-staged. On restaging, stage migration was observed in 30% of cases; early stage disease was now upstaged due to pT stage in 38% of cases. Similarly, 23% of patients were upstaged with the new nodal classification. A pivotal study by The International Consortium for Outcome Research (ICOR) in Head and Neck Cancer established the role of DOI in OCC staging, and they reported 33% rate of primary tumor pT upstaging [22]. Similarly, Matos et al. externally validated the tumor upstaging in the new staging system in OCC patients and found 23% patients were upstaged in pT and 29% in pN classification [23]. Additionally, they reported that 41% patients upstaged in the pT classification had died and 34% had recurrence. Our experience in this audit was comparable, 37% upstaged in pT stage had died at the time of analysis while 43% had recurrence.

With regard to incidence of known adverse prognostic factors impacting outcome, studies including the present audit has shown that PNI has a higher propensity in oral tongue cancer (28–46%) as compared to other oral subsites [15–17, 24, 25]. The reported incidence of LVI in literature varies widely between 2 and 26% as in the present audit (9%) [25–27]. We report lower incidence of well to moderately differentiated tumors as compared to the literature (75% vs. 90%) [24, 25]. The incidence of close/positive surgical margins in western series is between 17 and 28% [8, 13, 14, 25]. Margin positivity is known to be lesser in experienced hands from high volume centers [16, 26]. However, it also depends upon multiple factors such as the processing technique, definition of positive/close margins, etc., that might influence margin report. In the present audit, 1/5th of the patients had positive/close margins which may have been a reflection of infiltrating nature of disease or prevalent surgical expertise/practice.

As regards the impact of traditional prognostic factors; PNI, ECE, stage, pN+ve, grade, and DOI are known to influence LRR [17, 24, 26, 28–30]. On the other hand, age, ECE, LVI, PNI, stage, and pN+ve proved significant in determining OS [16, 17, 24–26, 28–30]. This is an observation from published series on OCC (including oral

tongue comprising between 30 and 50% cases) [16, 17, 24–26, 28–30]. The present study dealt with tongue cancers alone, with the aim of understanding the biology of disease. In the present audit, high grade and PNI were predictive of early recurrences, while age (> 45 years), PNI, and pN+ve impacted adversely on survival. Many studies including the present analysis suggest favorable survival outcomes in younger patients with age less than 45 years as compared to older patient population [26, 30]. This could be a reflection of more co-morbidity in older individuals, which influence the response to treatment, and the patient's ability to tolerate intense treatment. Therefore, the poorer outcome in the old population may not be entirely due to poor biology of the disease [31].

The impact of stage on survival of patients when stratified based on DOI was noteworthy. In a subset analysis, wherein the patients were staged by AJCC 7th edition, it was seen that DOI (≤ 10 mm) influenced the outcome in early stage disease significantly; however, the influence waned off in locally advanced disease (Figs. 3 and 4). This observation once again emphasizes the need to adopt the new staging system [22]. In fact, it was observed that in advanced disease other factors such as PNI, higher tumor grade, and age influence the outcome (Table S2 and S3).

The reported incidence of loco-regional relapse in carcinoma tongue in literature is around 25–33% [25, 26, 29, 32]. Tumor size (pT), DOI, positive margins, nodal involvement, and ECE are the parameters that affect LRR [13, 14, 25, 32]. The present audit is in concordance with the published reports as 1/3rd cases relapsed loco-regionally in this study. Fifty-six percent of the relapsed cases had LN positive disease at presentation.

The 5-year RFS and OS for entire cohort was 52% and 57%. The outcomes were inferior when compared to western reports of 64–78% [25, 29, 30]. High lost to follow-up rate, aggressive biology, and greater tumor burden are some of the factors that may have contributed to sub-optimal survival. Treatment-related factors could have influenced the final outcome, but the surgical, radiation, and chemotherapy practices were fairly uniform in this homogenous population, and therefore, comparisons were not possible. The only features in this audit that 15% patients had treatment breaks of more than 1 week during radiotherapy and 40% had overall treatment time (OTT) beyond 90 days (that may have included gap between surgery and radiotherapy and/or treatment breaks) may have adversely influenced the outcome in some although comparison was not done due to unequal distribution in the two sub-groups.

This was a retrospective audit and therefore pitfalls of an audit remain. Missing data in case records was the primary limitation. Review of the slides by a dedicated pathologist for confirming the findings, and inclusion of the missing data for complete and uniform reporting, was not possible in all the cases. Treatment-related acute and late toxicity documentation was limited in case records. As mentioned above, the treatment practices were similar, and therefore, hypothesis generation was not possible from this audit. The impact of radiotherapy technique could not be ascertained since most patients were treated with 3DCRT using same department protocol. Lastly, despite several telephonic/postal attempts, high LFU rate (23%) was a big confounding factor, and therefore, the actual fate of these patients remained unknown.

The strength of this audit was exclusively unselected population of oral tongue patients who underwent radical surgery and PORT thereby removing any element of selection bias with regard to the treatment offered. We analyzed the data using the post-op stage; therefore, the exact pathological stage was known in the patients for prognostication. An attempt was made to study the impact of DOI using 8th edition AJCC staging system before actually adopting it prospectively in clinical practice. A subset analysis in early and locally advanced stage patients provided greater insight on potential prognostic factors affecting survival in these groups.

This study has been analyzed at a time when oncologists have recently migrated to using AJCC 8th edition. The exact impact of introduction of new prognostic factors was studied and therefore ensures wider applicability of the new staging system in routine practice and with greater conviction.

Conclusions

Survival outcomes of oral tongue cancer patients in northern India remain sub-optimal, as shown in this single-institution study. Tobacco chewing remains the most significant risk factor especially in younger population. Advanced presentation and presence of adverse prognostic factors such as higher grade, L.N. involvement (aggressive tumor biology), and PNI were the main reasons for inferior outcomes. Incorporation of DOI in pT staging allows better stratification of carcinoma of the oral tongue patients.

Abbreviations

AJCC: American Joint Committee for Cancer; CTRT: Chemo-radiotherapy; DFS: Disease-free survival; ECE: Extra-capsular extension; ICOR: International Consortium for Outcome Research; IMRT: Intensity modulated radiotherapy; LAN: Low anterior neck; LFU: Lost to follow-up; LRR: Loco-regional relapse; LVI: Lymphovascular invasion; MVA: Multivariate analysis; MND: Modified neck dissection; OCC: Oral cavity cancer; OS: Overall survival; OTT: Overall treatment time; PBCR: Population-based Cancer Registry; PNI: Perineural invasion; PORT: Post-op radiotherapy; SOND: Supraomohyoid neck dissection; TTD: Total treatment duration; UVA: Univariate analysis; 3DCRT: Three-dimensional radiotherapy

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s43163-021-00168-9.

Additional file 1: Table S1. Clinico-pathologic details of Early and Locally advanced stage cohort.

Additional file 2: Table S2. Analysis of potential prognostic factors for RFS in "Early" and "Locally advanced" stage.

Additional file 3: Table S3. Analysis of potential prognostic factors for OS in "Early" and "Locally advanced" stage.

Additional file 4: Table S4. Impact of stage on survival outcomes when stratified based on depth of invasion.

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Authors' contributions

SP contributed in the study concept and was involved in the data collection, analysis, literature research, and manuscript preparation and editing. PL was instrumental in designing the study, data interpretation, manuscript editing, and literature research. She was also involved in maintaining the integrity of the entire study and its accuracy. SM was involved in the study design, data interpretation, and statistical analysis and did the literature research for manuscript preparation. PG contributed in the data collection, literature research, and manuscript preparation. KJMD contributed in the study design and data interpretation and also took responsibility for maintaining the accuracy and integrity of the entire study. SK contributed in the data interpretation, analysis, and manuscript preparation. VN was involved in the data collection, analysis, and literature research. KB contributed in the study design, data interpretation, and manuscript editing. SK was instrumental in designing the study, data interpretation, and manuscript editing and took up the role as guarantor of integrity of the entire study. All authors have read and approved the manuscript.

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Availability of data and materials

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

Declarations

Ethics approval and consent to participate

The study was duly approved by the Institutional Ethics Committee, Sanjay Gandhi Post- Graduate Institute of Medical Sciences (SGPGIMS), Lucknow-226014, the reference number of the study is SGPGI- IEC-2017-102-CP-Exp dated 01.05.2017. That also granted waiver of consent due to the retrospective nature of analyses.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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