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Early stage laryngeal cancers treated by external beam radiotherapy and their relapse: Free survival

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Abstract
Background: Laryngeal cancer accounts for approximately one fourth of all head and neck cancer & about 2% of all body tumors& it is the tenth commonest cancer in Iraq. Possible treatment options for early stage laryngeal cancer with curative intent are either surgery or radiotherapy.
Objectives: The aim of this case series study is to identify the relationship between the parameters of the study with laryngeal cancer, and also to evaluate the local control rate of early stage laryngeal cancer after treatment with external beam radiotherapy.
Methods: a case series study of 41 patients (3 patients- Tis, 23 patients- T_1, 15 patients- T_2) treated with 3DCRT in Baghdad Radiotherapy and Nuclear medicine Center, Baghdad Medical City Complex, Baghdad, Iraq, during period between January 2017 & Dec 2020.
Results: The results of the study showed that the common age group were (56-65) yrs, most of them were males in 70.7%, cigarette smoking also were recorded in 70.7%, all cases were SCC (100%), majority were glottic cancer in 85.4%, most of cases were T_1 in 56.1%, most of cases were (grade 2) in 63.4%.
Regarding results of disease relapse; mean period of follow up was 25.95± 13.559 months, the relapse incidence was 12.2%, the site of relapse was local, mean time of relapse was 10.6±3.578, and relapse free survival for the patients in this study was 45.45±3.07 months. Local control according to T staging were Tis up to 100%, T_1 up to 79%, T_2 up to 75%.
Conclusion: Relapse free survival in this study was 45.45± 3.07 months, parameters had significant impact on relapse free survival were site, grade, stage, radiotherapy dose. Local control rates by radiotherapy were reaching up to 100% in Tis & up to 79% in T_1&up to 75% in T_2.

Keywords: Laryngeal cancer, Radiotherapy, Relapse free survival, Local control, laryngectomy

Introduction
Laryngeal cancer accounts for approximately 1/4th of all head and neck cancer [1]; it forms 2% of total body tumors. It's the 10th commonest cancer in Iraq in 2008 [2] Risk factors for developing laryngeal cancer are smoking, alcohol consumption, voice abuse [2]. More common in men than women by incidence of 5.2 vs. 1.1 respectively [2]. In blacks than whites. Some studies reported HPV association with laryngeal cancer [4] but the prevalence vary widely, so the obvious association still unclear. The most common histology is SCC which accounts more than 95% [1]. Glottis is the most common site about 69%, mostly present with early stage (Tis- T_1-T_2) disease and have the lowest incidence of metastasis as compared with supraglottic (about 30%) and subglottic (1%-5%)as they have rich lymphatic supply [5-7]. Treatment options early stage disease are endoscopic Laser resection, radiotherapy or partial hemilaryngectomy [8].
Early stage disease is treated by surgery or definitive RT depending on the health status, operability and consideration of laryngeal preservation [9]. The ASCO recommend that patients with early stage disease should be managed with laryngeal preserving modalities [8].
Either definitive RT or as adjuvant treatment. For early stage glottic cancer treated by RT, 5 year local control rate for T_1 up to 95% [10-14], for T_2 up to 75% [13, 14, 15]. The largest series of patients treated with conventional RT for T_1-T_2 glottic cancer was published by Al-Mamgani in 2013 [13].1050 patients was treated using either conventional or accelerated fractionation (66 Gy using 2.0 Gy fractions delivered either 5 or 6 times per week) was evaluated. Local control was 85% at 5 years, w higher local control in the accelerated

fractionation group compared with the conventional group (87 vs 81%; p = 0.006). Primary RT is an effective treatment for (carcinoma in situ) of the larynx. However, conservative surgical approaches such as micro excision, laser ablation, or vocal cord stripping are considered sufficient for initial treatment [5, 16]. Repeated biopsies, strippings, or laser excisions may be counterproductive and lead to worsening of voice quality. RT is usually reserved for recurrences or for diffuse lesions that are not suitable for limited surgery as the first therapy. The local control rates reported in modern series of patients with Tis treated with RT range from 70% to 100% and are similar to rates described for invasive T_1 disease [17, 18]. Most patients developing recurrent laryngeal Tis undergo salvage surgery; total laryngectomy. Control rates after irradiation are similar to those reported for early invasive disease, recurrences in patients with Tis take longer to manifest. Most series report median times to failure of greater than 2 yrs, but the majority recur within 5 yrs of treatment [5]. For supraglottic cancer, studies done [19-21], local control for T_1 ranging from 73% -100%, for T_2 between 60%-89%. For subglottic cancer; management of subglottic cancer is controversial, some authors reporting favorable outcomes after RT alone, while others have reported favorable outcomes after surgery [22], RT is preferred for early stage, for advance stage laryngectomy & post-operative RT is indicated [23].

Conventional fractionation range 60Gy-70Gy with 2 Gy per fraction 5 Fx per week. Hypofractionation for T_1 disease 2.25 Gyis better control rate than 2 Gy per Fx [24]. Definitive doses for glottic cancer T_1- 63 Gy/28 Fx, Single cord irradiation T_1a, smaller field with shorter hypofractionation 58Gy/16Fx by IMRT [25].

T_2-65.25Gy/29Fx. For supraglottic cancer; Conventional 70Gy/35 fx.; Hyperfraction 76.8Gy/1.2Gy per Fx twice daily [26]. For subglottic cancer which carry worse prognosis than other sub sites [7]. RT dose 70Gy/35 Fx. Or accelerated hyper fractionation 76Gy/56Fx (10Fx per week) [27]. Post-operative doses: 60 -66 Gy in 2 Gy/Fx for high risk area and 44 -50 Gy for low to intermediate risk area.

The Aim of the Study: assess early stage laryngeal cancer according to age, sex, smoking status, site, treatment modality, grade and histology. Evaluation of local control for early stage laryngeal cancer after treatment with 3DCRT.

Methods

Study Design

After approval from collage of Medicine \ university of Baghdad, a case series study of 41 patients with early stage laryngeal cancer (Tis- 3 patients, T_1N0- 23 patients, T_2N0- 15 patients), treated with 3DCRT were included and identified. The patients demographic data and pathologic features, details of the primary tumor were recorded. The accuracy of the data was further validated for each patient using medical records and or surgical histopathological reports.

Setting

The study done for patients who treated in Baghdad Radiotherapy &Nuclear Medicine Center, Baghdad Medical City Complex, Baghdad, Iraq, during period between January 2017 & Dec 2020.

- **Inclusion criteria:** TisN0M0, T_1N0M0, T_2N0M0 laryngeal cancer.
- **Exclusion criteria:** Advanced disease (T_3, T_4, nodal disease) &metastatic disease.

Data Collection

Data were collected retrospectively with review of medical records. The following variables were studied: age, sex, TNM staging, histopathology, grades, treatment modality, & dose of RT & No. of fractions, any relapse of disease (time and site of relapse).

(CT) simulator: A commercially available CT simulator (Philips Company) was used in all patient simulation scans as well as phantom studies**.**

Target Volume Delineation was done by the radiation oncologist using Monaco System Version 5.11.03. Treatment planning system wasXIO 5.10.03 from Elekta [28]. MOSAIQ system 2.60 from Elekta [29]. LINAC**;**In this study th was Elekta infinity (Elekta Oncology Systems, Crawley, UK).

Ethical considerations

The medical Ethical committee of college of medicine/Baghdad University approved this study (code; 1582 in 24/11/2021). All patients were verbally informed about the study and they were asked the permission to be part of the study. All personal information was kept anonymous. Data were exclusively used for the sake of this study**.**

Statistical Analysis

performed using SPSS v24 (IBM Inc., Chicago, IL, USA). Descriptive statistics consist of numbers, and percentages were measured. Mean, median, range, min, max, and SD for categorical data calculated. Uni- and multivariate analyses calculated by using Log-rank with a 95% confidence interval for each survival analysis separately. The Kaplan Meier method was applied to study disease-free survival rates. A two-sided P value of le**ss** than 0.05 was considered statistically significant**.**

Results

The mostly distributed age group was (56-65 years) in 15 patients (36.59%), followed by group (>65 years) in 13 patients, (31.7%). The mean age was 59.98±9.358 yrs. Males were (29, 70.7%), females were (12, 29.3%). Smoking, we recorded 29 (70.7%), non-smoker (12, 29.3%), (90.2%) of without family history of laryngeal cancer whereas (9.8%) had family history. Out of 41 cases, 39 patients (95.2%) had hoarseness. All cases were SCC (100%). Glottic tumor in (35 patients, 85.4%). 5-patients (12.2%) were supraglottic disease, and one-patient (2.4%) was subglottic. Tumor stage, T_1 (23 patients, 56.1%), while T_2(15 patients, 36.6%). Tis reported in 3patients (Figure 1). Most of cases were grade II (26 patients, 63.4%), grade I (15 patients, 36.6%). About surgery, they didn't undergo surgery (35 patients, 85.4%), while those underwent surgery (6 patients, 14.6%). 2cases received CCRT, while 39 patients, (95.1%)didn't received CTX.

About RT dose, 70Gy/35F in 18(43.9%) patients. Other doses were 66Gy, 65.25Gy, 63Gy, 44Gy and 60Gy (Fig.1).

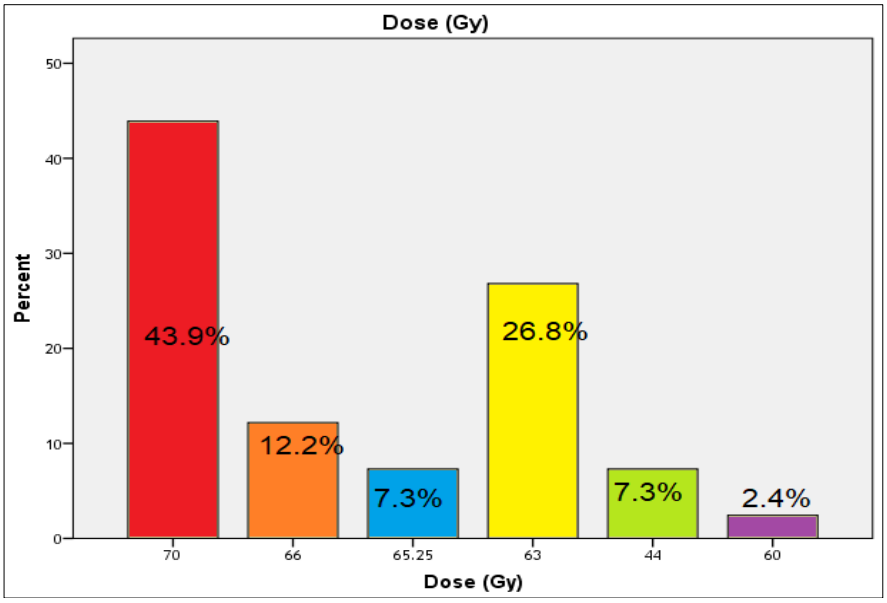

Fig 1: Patientsdistribution in relation to RT doses. (No.=41)

Regarding RT treatment delay (weeks), the periods listed in Table 1. The mean time of delayed was 12.98±6.247 weeks (median=12 weeks), ranged from 4 weeks to 36 weeks.

Table 1: Distribution according to RT treatment delay (No.=41).

Delay (week)	No.	%
4-12	25	61.2
13-36	16	38.8
Total	41	100

Organ at risk (OAR): The mean, median and maximum with minimum doses received by OAR. In this study, the dose of spinal cord of 9-patients received above 45Gy (22%), while the rest were within the tolerance. Among parotids, 12(29.3%) of right parotid and 11(26.8%) of left parotid received more than 26Gy. In relation to brain stem and both cochlea, no one received RT doses exceed the tolerances.

Results of disease relapse: The mean period of follow-up was 25.95±13.559 months (median =23, range = 6-56). 36 patients, (87.8%) cases were without relapse, only 5 patients developed relapsed. (Figure 2). Site of relapse was local recurrence in larynx in 5-patients, the mean time of relapsing was 10.6±3.578 (median =12, range = 6-15) (Figure 3).

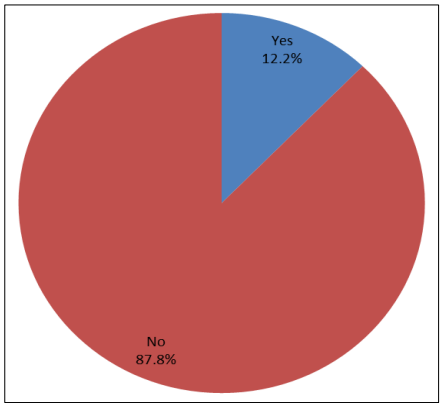

Fig 2: Patients distribution in relation to relapse (No.=41).

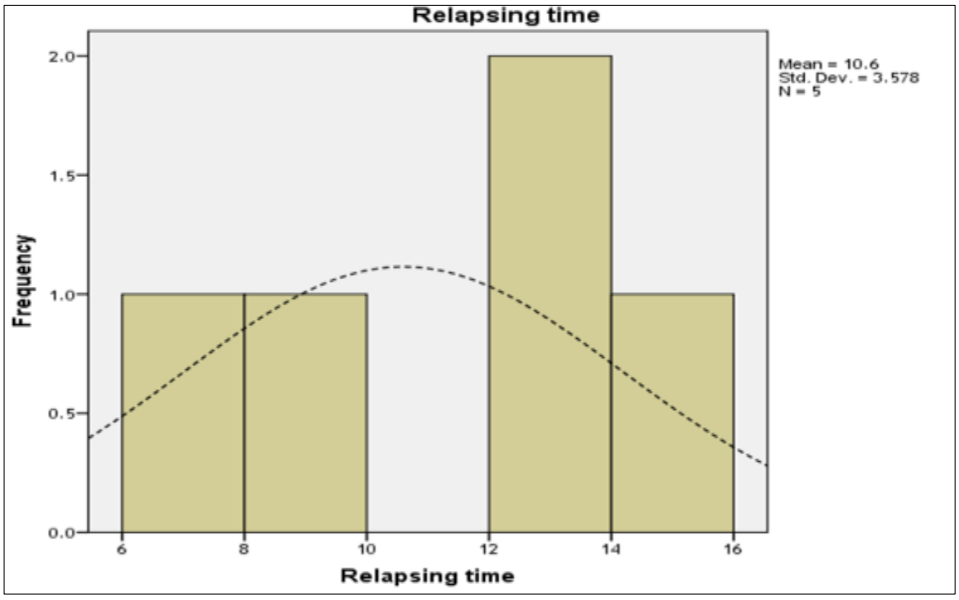

Fig 3: The time of relapsing of this study (No.=41).

Relapse free survival (RFS) or Disease free survival (DFS); The RFS for patients in this study was 45.45±3.07 months (95%CI; 39.434-51.473) (Figure 4).

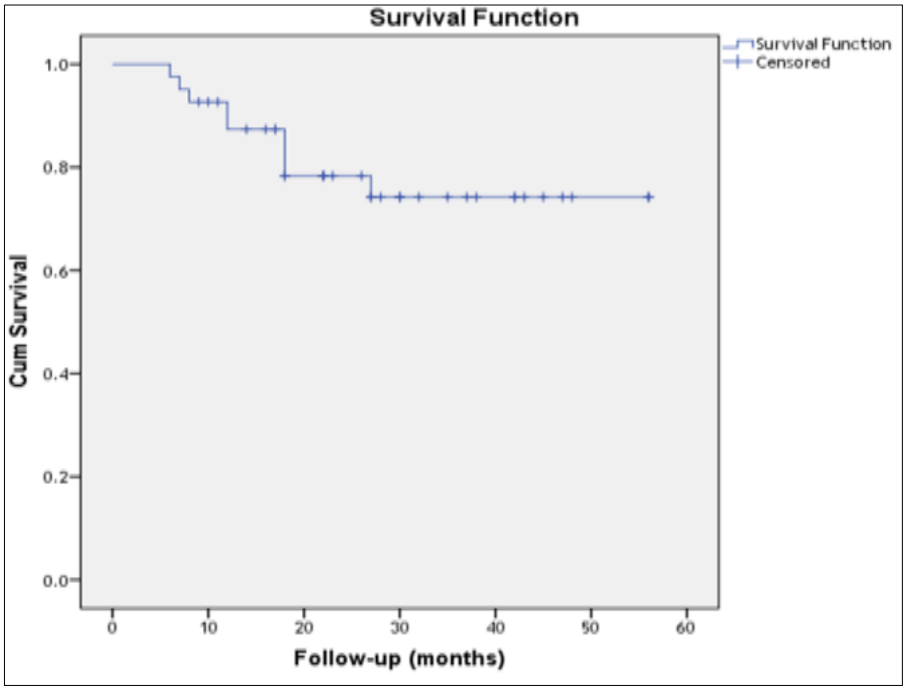

Fig 4: RFS curve of this study.

In the univariate analyses of RFS for gender, age groups, smoking, family history, chief complain, tumor site, T stage, grade, surgery, RT dose, and CCRT, were listed in Table (2).

Table 2: Univariate analyses of RFS.

	Mean	Log Rank (Mantel-Cox)	95%CI	P value
Gender [M vs. F]	47.644 vs. 36.55	0.663	40.989-54.3	0.415
Age [>56 vs. ≤56]	31.12 vs. 20	2.84	25.8-34.6	0.242
Smoking [No vs. Yes]	52.38 vs. 42.59	2.148	45.73-59.02	0.143
Family history [No vs. Yes]	45.5 vs. 29.5	0.003	39.117-51.88	0.96
Complain [HOV vs. other]	NA	2.235	NA	0.327
Site of tumor [Glottic vs. other]	30.68 vs. 27	5.646	25.94-35.42	0.05
T [Tis vs. T1/2]	30.33 vs. 28.589	5.917	5.174-55.49	0.049
Grade [G1 vs. G2]	43.533 vs. 39.3	6.435	33.05-54.02	0.031
Surgery [No vs. Yes]	30.6 vs. 28.33	0.344	25.6-35.6	0.557
RT [70G vs. others]	37.445 vs. 30.2	13.9	30.133-44.758	0.016
CCRT [No vs. Yes]	30.775 vs. 20.5	1.193	26.26-35.287	0.275

Discussion

In this study, age group was (56-65 years) in 15(36.59%), with a mean age was 59.98±9.358 years. This agrees with studies conducted in Babylon [29], Mosul [30], and Baghdad [31]. Whereas Cetinayak *et al*., [32], and Shen *et al*., [33] reported median age slightly higher than reported by this study. Brandstorp-Boesen *et al*., [34] studied 1, 616 patients their mean age was 67.6 years, a range of 14±93yrs. About gender male to female ratio in the current study is (2.4:1), which is different from that reported by AL-Timimi and Naji (3.6:1) [29], Atiyah (1.9:1) [31], Cetinayak *et al*., (23.9:1) [32], Shen *et al*., (12:1) [33], Brandstorp-Boesen *et al*., (6.6:1) [34], and Anschuetz *et al*., (8.7:1) [35]. These discrepancies revealed a very wide M: F ratio. In men older than 45 years, the risk is around 5 times higher than in women [36]. Laryngeal cancer is the neoplasm with the largest M toFratio in most populations [37, 38]. Smokers were recorded 29 (70.7%) cases, which is lower than reported by Atiyah (98.6%) [31], Brandstorp-Boesen *et al*., (88.8%) [34]), and Shen *et al*., (100%) [33]. 39(95.2%) complained of hoarseness, in addition, one case presented with dysphagia and another with a sore throat. This agrees with ALTimimi and Naji [29], who reported that hoarseness was the main presenting symptom in most of the patients (73%), 11% respiratory obstruction, 7% cervical mass, and dysphagia in 12%. 9.8% of patients in this study had a positive family history, this is suggested that family history is a weak independent risk factor. All cases were SCC (100%), Glottic tumors in (85.4%) of patients. AL-Timimi and Naji [29], they identified supraglottic cancer in (25%), glottis 60%), infraglottic (0.7%), and piriform sinus tumor (14%), besides, they found SCC in (95%). Also, BrandstorpBoesen *et al*., [34] reported 69.7% were glottic, 27.1% supreglottic, and 3.2% subglottic. Cetinayak *et al*., [32] and Shen *et al*., [33], studied only glottic laryngeal carcinoma. Anschuetz *et al*., [35], reported that the prevalence of glottic, supraglottic,

subglottic, and transglottic of cancer was 58.9%, 26%, 2.7%, and 12.4%, respectively. About tumor stage, T_1 (56.1%), T_2(36.6%, Tis (7.3%). Tumor grade, grade II (63.4%), grade I (36.6%). Similarly, AL-Timimi and Naji, (2%) with Tis. (13%) in stage I, (35%) in stage II, (35%) in stage III, and (15%) in stage IV [29]. Brandstorp-Boesen *et al*., they found T_1 in 41.3% and T_2 in 23.9%, while advanced and metastasis 34.8% [34]. A disagreement was seen with Cetinayak *et al*. study, Tis in (12.7%), T_1 in (69.9%), and T_2 in (17.4%) [32]. Whereas Shen *et al*., reported a high rate of T_1 (85.7%) than T_2 (14.3%) [33]. Anschuetz *et al*., found T_1 in 47.8%, T_2 in 24.7%, T_3 in 16.6%, and T_4 in 10.1% [35]. Regarding management, (85.4%) didn't undergo surgery while (14.6%) underwent surgery were found in There are only 2 cases that received CCRT, however, 39(95.1%) of patients didn't receive chemotherapy. These disagree with AL-Timimi and Naji (29) since they treated all cases of laryngeal cancer surgically followed by RT, but the results are close to that reported by Anschuetz *et al*., [35] primary treatment modality was RT (75.3% - n = 359/477), whereas 24.7% (n = 118/477) underwent primary surgery. Brandstorp-Boesen *et al*., reported that RT used in 62.4%, laser microsurgery in 20.5%, total laryngectomy in 11.1%, CCRT in 3.4%, and follow-up in 2.6% [34]. Anschuetz *et al*., reported that laser microsurgery used in 52.5%, subtotal laryngectomy in 14.4%, total laryngectomy in 33.1%, RT in 58.5%, and CCRT in 27.5% [35]. These could be explained by the difference in T stages and grading between this study and other studies. According to the RT dose, 70Gy/35F (43.9%) patients. Other doses were 66Gy, 65.25Gy, 63Gy, 44Gy, and 60Gy. The RT was delayed with a median equal to 12 weeks (4 weeks to 36 weeks). RTdoses range from 60 Gy to 70 Gy given in 2-Gy fractions [17]. In general, a dose of 60 Gy is given to patients with no obvious clinical disease after striping, 66 Gy to those with bulky T_1, and 68 Gy to 70 Gy to patients with T_2 lesions. Most centers deliver 2 Gy per day, five fractions per week. Several studies evaluating the importance of dose per fraction principally for T_1 disease show that 2 Gy per fraction yields better control rates [16, 17]. An agreement of current study protocols with investigators from Osaka randomized patients to either 2Gy or 2.25 Gy per fraction and demonstrated an improvement in control in patients receiving the higher dose per fraction. Patients with T_1 glottic diseasetreated with more hypofractionated regimens, and 63 Gy in 28 fractions is a common regimen [18]. (DAHANCA 6) trial (14) randomized 690 patients with glottic carcinoma to either 5 or 6 fractions of radiation per week. Each fraction was 2 Gy, and the total dose ranged from 62 to 68 Gy, depending on tumor size. While all stages were allowed, 86% of the accrued patients had T_1-2 disease (50% and 36%, respectively). Similar to the RTOG hyper-fractionation trial, the study found 8%improvement in local control in tumors treated with the 6-fraction/week schedule [15]. Based on the similar results of hyperfractionation and the DAHANCA trials [14], if altered fractionation is desired, the DAHANCA approach may be more facile for both the treating facility and the patient. Nearly 1/3rd of patients with early to intermediate-stage supraglottic neoplasms present with palpable cervical lymphadenopathy [39] and another third have subclinical nodal involvement detected by elective neck dissections [16]. Voice-preserving treatment options for early and intermediate-stage tumors are supraglottic laryngectomy or primary RT. Local control rates in the most surgical series range from 80- 90% [16, 17]. Although, the results showed that the dose of the spinal cord of 9-patients received was above 45Gy (22%), while the rest were within the tolerance. Among parotids, 12(29.3%) of right parotid and 11(26.8%) of left parotid received more than 26Gy. The brain stem and both cochelea, not received RT doses exceed the tolerances. In this study we observed doses of RT exceeding tolerance doses of OAR which might cause adverse effects or early and late RT toxicities or complications. Otherwise, Anschuetz *et al*., [35] recorded early and late complications of RT as followed: pharyngeal stenosis (4.6%), laryngeal stenosis (24.7%), chondroradionecrosis (2.5%), and soft tissue necrosis (4.4%). Shen *et al*., [33] documented side effects for the EBRT group as 39.6% of patients had grade 1 acute skin side effects, 59.3% had grade 2 acute skin side effects, and 1.1%) had grade 3acute skin side effects. Patients with grade 1 laryngitis were 24.2%, and those with grade 2 accounted for 75.8%. In terms of late side effects, grade 1 skin reactions occurred in 26/91 (28.57%) patients, and grade 1 edema occurred in 16/91 (17.58%) patients. Cetinayak *et al*., [31] reported RTOG grade 3 late side-effects was recorded only in 1(0.3%) patient after 12 months from RT. Although, the results showed that the dose of the spinal cord of 9 patients received was above 45Gy (22%), while the rest were within the tolerance. Among parotids, 12(29.3%) of right parotid and 11(26.8%) of left parotid received more than 26Gy. The brain stem and both cochlea, not received RT doses exceed the tolerances. In this study we observed doses of RT exceeding tolerance doses of OAR which might cause adverse effects or early and late RT toxicities or complications. Otherwise, Anschuetz *et al*., [35] recorded early and late complications of RT as followed: pharyngeal stenosis (4.6%), laryngeal stenosis (24.7%), chondroradionecrosis (2.5%), and soft tissue necrosis (4.4%). Also, Shen *et al*., [33] documented side effects for the EBRT group as 39.6% of patients had grade 1 acute skin side effects, 59.3% had grade 2 acute skin sideeffects, and 1.1%) had grade 3acute skin side effects. Patients with grade 1 laryngitis were 24.2%, and those with grade 2accounted for 75.8%. Interms of late side effects, grade 1 skin reactionsoccurred in 26/91 (28.57%) patients, and grade 1edema occurred in 16/91 (17.58%) patients. Cetinayak *et al*., [32] reported RTOG grade 3 late side-effects wasrecorded only in 1(0.3%) patient after 12 months from RT. In this study, the overall mean and median period of follow-up was 25.95 and 23 months respectively. Nearly, similar to the mean of follow-up of Chedid *et al*., (28.9 months) (40), but it is much lower than the median follow-up of Cetinayak *et al*., (72 months) [32]. The median follow-up time was 42 months (12-92) for Shen *et al*., [33], whereas Anschuetz *et al*., [35] recorded a median follow-up of surviving patients of 51 months. Brandstorp-Boesen *et al*., study [34] have a long period of follow-up reaching 15 years (180 months). The relapse incidence was 12.2%, and All local recurrence in this study, which is lower than the recurrence rate of Anschuetz *et al*., (28.7%) [35]. In a study by Shen *et al*., [33] the local recurrence occurred in 23 patients: 7patients in stage T_1aN0, 12 patients in stage T_1bN0, and 4 patients in stage T_2N0. The average time from treatment to recurrence was 17 months (3-45 months), and 18 out of 23 (78.26%) patients experienced recurrence within two years after treatment. Chedid *et al*., [40] reported 21 cases of local and regional recurrences; 10 were exclusively local (47.62%),

five were exclusively regional (23.8%), five were local and regional (23.85), and one was local with a distance metastasis (4.76%). In agreement with Cetinayak *et al*., [32] data, local failure was detected in 31(10.36%) patients, and the median time to local failure was 22 (1-84) months. In the current study, the crude mortality rate was 22%. 9 patients were dead while 32(78%) patients were still alive. About 3(33.33%) of dead cases were related to cancer, while 6(66.66%) weren't. Similarly, in a study by Shen *et al*., [33] 5 out of 23 patients died (21.74%) as 3(60%) patients had pulmonary metastasis and bonemetastasis, and 2(40%) patients died of other diseases, which dislike the results of the current study. Cetinayak *et al*., [32] reported that patients most frequentlydied due to non-malignant (42 (14%)) reasons. Only 16(5.4%) patients died due to laryngeal carcinoma, another 31(10.7%) patients had died of other cancers. In the comparison with Chedid *et al*., [40] by the end of the study period 29 patients had died because of the disease, and 5 had died due to other causes, the current study results showed a better outcome. The RFS for patients in this study was 45.45±3.07 months (95%CI; 39.434-51.473). Disagreement with other studies like Shen *et al*., [33], found that for stage T_1, the 3-year PFS and OS rates of the EBRT group were 94.8% and 95.6% and for stage T_2, the 3-year PFS and OS rates were 83.3%, 75% respectively. Also, the global survival was 47.5%; the 5-year DFS rate was 42.5% and the 5-year DFS was 38% in patients undergoing RT only and 49% for CCRT [40]. Cetinayak *et al*., [32] reported that DFS for 5 and 10 years according to stages were 95.8% and 95.8% for Tis; 95.5% and94.5% for T_1;& 88.6% & 81.2% for T_2 diseases, respectively. Brandstorp-Boesen *et al*., [34] found that 5-years DFS ranged from 32.0% to 54.5%, and 23.0% (T_3) to69.1% (T_1a). However, this negativity can be ruled out by smaller treatment volumes and better planning and using image-guided radiotherapy techniques [32]. It has been known that factors like RT technique, RT energy, fractional dose, total dose, and treatment duration influence the success of radiotherapy in disease-free control and survival [32, 41, 39]. The univariate analyses of RFS for gender, age groups, smoking, family history, chief complaint, surgery, and CCRT have non-significant alteration on RFS of patients with early laryngeal cancer after EBRT, while tumor site (P=0.05), T stage (P=0.049), grade (P=0.031), and RT dose (P=0.016) are negatively associated with survival as predictors factor influence DFS of those patients beyond EBRT. Brand storp-Boesen *et al*., study [34] disliked these findings, their multivariate analysis revealed that age >60 years, use of alcohol, T_3±T_4 tumors, and ≥N2-status were prognostic factors for OS among glottic patients, and among supraglottic are age >60 years, use of alcohol, ≥N2-status, and CCRT. Cetinayak *et al*., [32] reported that stage, gender, anterior commissure involvement, RT technique, and RT energy (doses) were evaluated. In DFS, stage and anterior commissure involvement were found statistically significant. The RT technique was not found to be significant.

Conclusions

Laryngeal cancers are more common in men than women, Smoking is well established risk factor, Parameters have significant impact on RFS are site (glottis), grade (G1), stage (Tis) and RT dose (70 Gy) which are statistically significant, Local control rates by RT are reaching up to 79% in T_1 and 75% in T_2 and 100% in Tis, The doses of RT exceeding tolerance some of OAR which might cause early and late RT toxicities, RFS of this studywas 45.45±3.07 months.

Authors' contributions

1. Conceptualization; Data Curation; Investigation; Methodology; Resources; Software; Writing - original draft and Writing - review & editing
2. Conceptualization; Data Curation; Methodology; Project administration; Writing - original draft and Writing - review & editing
3. Conceptualization; Data Curation; Investigation; Project administration; Resources; Writing - original draft and Writing - review & editing
4. Conceptualization; Data Curation; Methodology; Writing - original draft and Writing - review & editing

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None.

Conflicts of interest

The authors declare no conflict of interest regarding this article.

Ethical approval

The Medical Ethical Committee of the Department of Medical Oncology, Baghdad Oncology Teaching Hospital, Baghdad Medical City Complex approved this study.

Availability of data

On request.

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