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The outcome of early-stage glottic carcinoma patients treated with radiotherapy: Egyptian National Cancer Institute (NCI-Egypt) experience

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The outcome of early-stage glottic carcinoma patients treated with radiotherapy: Egyptian National Cancer Institute (NCI-Egypt) experience

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Abstract

Background: Radiotherapy (RT) is an appropriate treatment option for early-stage glottic cancer (ESGC) that achieves high local control and preserves voice quality. However, the optimal radiation treatment schedule remains unknown.

We present our institution's 14-year experience in treating ESGC with definitive radiotherapy between 2005 and 2019 inclusively.

Materials and methods: We reviewed the medical records of 104 patients; 63 (60.5%) were treated with conventional fractionation (CF), and 41 (39.5%) were treated with hypofractionated radiotherapy (HF). The clinical T-stage was T1a in 50 patients (48%), T1b in 27 (26%), and T2 in 27 (26%). Age, gender, anterior commissure involvement, stage, radiotherapy technique, radiation fraction size, and overall treatment time (OTT) were analyzed as prognostic factors. The survival outcomes, local regional control (LRC), and laryngeal preservation rate were evaluated.

Results: The 5-year overall survival (OS) and LCR were 83.3% and 78%, respectively. On univariate analysis, treatment with CF ($p = 0.02$), prolonged OTT > 49 days in CF and > 40 days in HF ($p = 0.04$), and RT total dose < 66 Gy ($p = 0.03$) were associated with poor LRC. Multivariate analysis showed a non-significant association with LRC (all $p > 0.05$). The 5-year OS rate in the CF and HF-treated patients was 84.9% and 72.1%, respectively ($p = 0.99$), and in patients who had T1a, T1b, and T2 disease, were 78.2%, 96.0%, and 82.1%, respectively ($p = 0.43$). All patients and tumor variables showed no statistically significant

association with OS. Only low-grade acute toxicity was observed.

Conclusion: Non-inferiority results supported the HF schedule to ESGC, including high local disease control and decreased overall treatment time. Our study supports its efficacy in the primary care of ESGC with manageable side effects.

Key words: glottic cancer; radiotherapy; hypofractionation

Introduction

Laryngeal cancer (LC) is the 22nd most common cancer (0.89% of all cancers) and the 18th most deadly (1.39% of cancer deaths) worldwide. Its incidence and prevalence have grown by 12.0 and 23.8 during the previous three decades [1].

According to Globocan 2020, LC incidence in Northern Africa accounts for 4480 new cases with a male-to-female ratio of 9 to 1. In Egypt, LC was the 17th most common cancer (1.2% of all cancers) and the 15th most deadly (1.2% of cancer deaths) in 2020 [2].

In the Egyptian National Cancer Institute (NCI, Egypt), LC represented 6.2% of respiratory system tumors and 0.2% of total malignant tumors with a male-to-female ratio of 1.5:1 in the period from 2000 to 2011 [3].

The goals in treating patients with early-stage glottic larynx cancer (ESGC) are to cure the disease and preserve laryngeal function to boost the quality of life [4].

Materials and methods

This retrospective study reviewed all patients with early-stage glottic carcinoma (T1–2 N0) treated with definitive radiotherapy (RT) at the Radiation Oncology Department of the National Cancer Institute, Cairo University, between 2005 and 2019. The inclusion criteria were age 18 years or more and early-stage (I–II) pathologically confirmed squamous cell carcinoma of the glottis. Patients with stages III–IV LC, synchronous primary cancer, history of prior neck surgery or chemotherapy, and without survival data were excluded.

All patients were treated supine and had a thermoplastic head and neck mask. Most patients were treated using a 2D technique from 2005 to 2012, while others were treated with 3D conformal RT from 2013 to 2019. In the 2D technique, the treated volume was irradiated by two parallel opposing fields. The field borders were the inferior aspect of the hyoid bone superiorly, the lower edge of the cricoid cartilage inferiorly, and the anterior border of the vertebral bodies posteriorly. Anteriorly, the fields would extend 1 cm beyond the skin, overlying the anterior aspect of the thyroid cartilage. In the 3D technique, The gross tumor volume (GTV) was defined as the bilateral true vocal cords to include any gross disease that

can be delineated. The clinical target volume (CTV) was the larynx extending from the level of the thyroid notch superiorly to the bottom of the cricoid cartilage inferiorly. PTV was created by adding 5 mm (mediolateral and anteroposterior) and 10 mm craniocaudal margin. Radical RT dose in conventional fractionation (CF) was 66–70 Gy, and in hypofractionation (HF), 63 Gy (stage I) to 65.25 Gy (stage II) with 2.25 Gy per fraction, five days a week.

The overall treatment time (OTT) was calculated from the day starting RT to the day of completion. Any break during radiation was regarded as an unplanned treatment break. The treatment response and side effects were assessed at least once a week during RT. Local response was evaluated 2-4 months after treatment by local imaging [computed tomography (CT) or magnetic resonance imaging (MRI)], laryngoscopy, or both. Early and late side effects were assessed according to Radiation Therapy Oncology Group (RTOG)/ European Organisation for. Research and Treatment of Cancer (EORTC) criteria. Complete response was defined as the absence of clinical, radiological, or endoscopic evidence of any residual primary or nodal disease. Any abnormal finding was well documented, and relapse was confirmed histo-pathologically (e.g., local or loco-regional relapse). Overall survival (OS) was calculated from the date of starting RT to the date of death or last follow-up. Loco-regional control (LRC) was calculated from the date of the end of RT to the date of occurrence of local or loco-regional failure. Gender, age (≥ 60 *vs.* < 60 years), smoker (yes, No), stage, pathological grading, anterior commissure involvement (yes vs. no), fraction size, total RT dose, and overall treatment time were evaluated as prognostic factors.

Statistical methods

Statistical analysis was conducted using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY, United States). Quantitative variables were presented as mean and standard deviation, or median and range, and compared using student t-test or Mann-Whitney U test according to their distribution. Survival analysis was done using the Kaplan-Meier method, and a comparison between two survival curves was done using the log-rank test. Multivariate analysis was done using the Cox-regression method for the significant factors affecting survival on univariate analysis. A p-value of 0.05 or less was considered to be statistically significant.

Results

The study included 104; four of them (3.8%) were females, with a male-to-female ratio of 25:1. The median age at diagnosis was 59.5 (range: 27–85 years), with only ten patients

(9.6%) 40 years or younger. According to Eastern Cooperative Oncology Group performance status, most patients (87.5%) presented with PS I. A history of tobacco consumption was reported in 84.6% of patients. Before starting RT, the mean hemoglobin level was 12.8 ± 2.03 gm/dl. The primary tumor stage was T1a in 50 patients (48%), T1b in 27 (26%), and T2 in 27 (26%). The local staging was performed by contrast-enhanced CT scan (82.8%) and MRI (3.9%). A CT chest was performed for all patients to complete staging procedures. Sixty-three patients (60.6%) were treated with CF, and 41 (39.4%) were treated with HF. Patients and tumor characteristics are summarized in Table 1.

Table 1. Demographics and clinical characteristics according to radiation fractionation schedules

	All Cases (n = 104)	**CF (n = 63)**	**HF (n = 41)**	**p-value**
Age (years)				
< 60	52 (50%)	32 (50.8%)	20 (48.8%)	0.841
≥ 60	52 (50%)	31 (49.2%)	21 (51.2%)	
Sex				
Male	100 (96.2%)	61 (96.8%)	39 (95.1%)	
Female	4 (3.8%)	2 (3.2%)	2 (4.9%)	0.659
PS				
I	91 (87.5%)	53 (84.1%)	38 (92.7%)	0.197
II	13 (12.5%)	10 (15.9%)	3 (7.3%)	
Smoking				
Non-smoker	11 (10.6%)	7 (11%)	4 (9.7%)	
Smoker	88 (84.6%)	53 (84%)	35 (85.4%)	0.976
Missing data	5 (4.8%)	3 (5%)	2 (4.9%)	
Grade				
I	14 (13.5%)	8 (12.7%)	6 (14.6%)	
II	79 (76%)	47 (74.6%)	32 (78%)	0.674
III	11 (10.5%)	8 (12.7%)	3 (7.4%)	
T stage				
T1a	50 (48%)	34 (54%)	16 (39%)	
T1b	27 (26%)	14 (22.2%)	13 (31.7%)	0.317
T2	27 (26%)	15 (23.8%)	12 (29.3%)	
Commissure				
Not involved	65 (62.5%)	43 (68.3%)	22 (53.6%)	
Anterior	36 (34.6%)	19 (30.2%)	17 (41.5%)	0.260
Posterior	3 (2.9%)	1 (1.5%)	2 (4.9%)	
Image				
CT	86 (82.8%)	55 (87.3%)	31 (75.7%)	
MRI	4 (3.9%)	1 (1.5%)	3 (7.3%)	
Both	3 (2.8%)	1 (1.5%)	2 (4.9%)	0.177
Missing data	11 (10.5%)	6 (9.7%)	5 (12.1%)	

Data are expressed as number (%). CF — conventional fractionation; HF — hypofractionation; PS — Performance Status; CT — computed tomography; MRI — magnetic resonance

Treatment characteristics

From 2005 to 2012, 49/104 (47.1%) patients were treated with CF using the 2D-RT technique. The median RT dose in patients who received CF was 66 Gy (59–70.2 Gy). However, 6 (6.1%) patients received less than the prescribed dose. The daily dose was 1.8-2 Gy per fraction, and the mean field size was 6.8 × 7 cm. Between 2013 and 2019, CF significantly declined compared to the HF radiation schedule (22.2% *vs.* 100%; p = 0.001). The RT dose in patients who received the HF schedule was 63 Gy for T1 and 65.25 Gy for the T2 stage. The daily dose was 2.25 Gy per fraction, and 28/41 (68.3%) patients were treated with the 3D-RT technique compared to 9.5% in the CF group (p = 0.0001). The mean field size used was 6 × 6.5 cm. The tumor biological effective dose (BED 10) estimated for the schedule was 77.175 Gy for T1 and 79.93 Gy for T2.

Fifty-nine patients (56.7%) experienced treatment interruption during the RT course. A higher percentage of patients treated with the CF schedule had treatment interruption than those treated with the HF schedule (38.5% *vs.* 18.3% respectively; p = 0.085) with no statistically significant difference.

The mean OTT was 53.0 ± 9.9 days (range: 44-79 days) in the CF group and 43.0 ± 9.6 days (range: 35-70 days) in the HF group (p = 0.001). Thirty-two of 59 patients (54.2%) in CF experienced treatment delays of more than 49 days. Meanwhile, 18/41 patients (46.2%) in the HF group were delayed more than 40 days (p = 0.001). The causes of unplanned treatment interruption among the 59 patients were treatment toxicity in 4 patients (6.7%), machine down status and/or maintenance in 12 (20.3%), non-medical reasons in 20 (33.8%), public holidays in 6 (10.1%), and unspecified causes in 17 (28.8%). All patients in the HF group completed the planned RT schedule, compared to 90.5% in CF, with a statistically significant difference observed between the two treatment groups (p = 0.042). Treatment characteristics are summarized in Table 2.

Table 2. Radiation therapy details

	Total (n = 104)	**CF (n = 63)**	**HF (n = 41)**	**p–value**
Treatment period				

2005–2012	49 (47.1%)	49 (77.8%)	0 (0%)	0.001
2013–2019	55 (52.9%)	14 (22.2%)	41 (100%)	
Radiation technique				
2D	70 (67.3%)	57 (90.5%)	13 (31.7%)	0.0001
3D	34 (32.7%)	6 (9.5%)	28 (68.3%)	
Radiation dose [Gy]				
T1	65 (59–70)	66 (60–70.2)	63 (60–65)	0.001
T2		66 (59–70)	65.25 (63–65)	
Fraction number	31.5 (25–39)	33 (30–39)	T1: 28 (25–29)	0.001
			T2: 29 (28–29)	
Fraction size [Gy]	1.8–2.25	1.8–2.0	2.25	
Field width [cm]	6.6 (5–9)	6.8 (5–9)	6 (5–7)	0.04
Field length [cm]	6.7 (5–10)	7 (5–10)	6.5 (5–8)	0.50
Radiation gap [days]	8 ± 9.8 (3–44)	8.3 ± 10 (3–36)	7.6 ± 9.5 (4–44)	0.72
OTT [days]	50 (35–79)	53 (44–79)	43 (35–70)	0.001
No. of RT interruption cases	59 (56.7%)	40 (38.5%)	19 (18.3%)	0.085

Data are expressed as number (%), or median (range); OTT — overall treatment time; RT — radiation therapy

Toxicity profiles

Radiation treatment was well-tolerated, and no severe complications were observed. All patients reported grade 1-2 of skin and mucous membrane toxicity during treatment. Low-grade acute dysphagia was observed in 61 patients (62.2%), more observed in the CF group than in the HF group (81.4% *vs.* 72.2% respectively; p = 0.33).

Loco-regional control (LRC)

The follow-up duration ranged between 1.2–10.8 years. Among the 104 patients, 6 (5.7%) were lost to follow-up after the radiation course was completed and were excluded from the analysis. Of the 98 patients assessed, complete clinical response (CR) was reported in 95 patients (97.1%), while three (2.9%) experienced primary progressive disease during RT and underwent salvage total laryngectomy.

After a complete initial response, 18/95 patients (18.9%) experienced disease recurrence. The median time to disease failure after the end of radiation treatment was 10.8 months (range 1.6–36 months). Local recurrences were observed in 15/18 (83.3%), while 3/18 patients (16.7%) experienced loco-regional disease recurrence. The 5-year LRC rates were 78% in the whole group, 79% in stage I (T1a 77% and T1b 81%), and 80% in stage II (p = 0.87). After seven years, the LRC rate declined from 78% to 62.6% due to late loco-regional relapse (Fig.

1, 2). Salvage total laryngectomy was done for 15 patients (83.3%), and 3 (16.7%) were assigned to best supportive care due to poor performance status. The 5-year larynx-preservation rate was 82% in the whole group, 76% in the CF, and 91% in the HF group (p = 0.145). It was 82% in stage I and 81% in stage II (p = 0.80). After a successful salvage laryngectomy, the ultimate local control rates were 92.5%, T1a 90.3%, T1b 100%, and T2 100% (p = 0.21). No distant metastasis was observed among our patients.

By univariate analysis, the local recurrence was significantly higher in the CF group compared to the HF group (21% vs. 7.3%, respectively; p = 0.026).

The 5-year LRC rate was significantly higher in the HF group than in the CF group (90.7% *vs.* 69.2%, respectively, p = 0.02). In subgroup analyses, the 5-year LRC for stage T1 was 70% and 88.5% in the CF and HF groups, and for stage T2, 73% vs. 100%, respectively (p = 0.05), trending to be a statistically significant difference.

Also, the 5-year LRC rate was significantly inferior in patients who experienced prolonged OTT > 49 days in the CH group and > 40 days in the HF group (60% vs. 80%, respectively; p = 0.04). In contrast, patients who had OTT < 40 days in the HF group showed a significantly superior 5-year LRC rate than patients with OTT < 49 days in the CF group (100% vs. 77% respectively, p = 0.04) (Fig. 3).

The 5-year LRC rate was 33.3% in patients treated with less than 66 Gy compared to 85.7% in patients treated with 66-70 Gy and 91% in the HF group (p = 0.030) (Fig. 4). Despite the 5-year LRC rate in patients with the high-grade tumor being worse than those with grade I and II, this was not statistically significant (63.6% *vs.* 100% and 84.6%, respectively; p = 0.051). Other clinical covariates showed no significant association with LRC (Tab. 4).

By multivariable analysis, type of radiation fraction size [hazard ratio (HR): 0.774, 95% confidence interval (CI): 0.427–1.405, p = 0.400], total radiation dose (HR: 2.469, 95% CI: 0.548–11.127; p = 0.239) and OTT (HR: 0.897, 95% CI: 0.355–2.267; p = 0.817) had no impact on, LRC (Tab. 3).

Table 3. Multivariate analysis for loco-regional control

Risk factors	**Hazard ratio (95%CI)**	**p-value**
Radiotherapy fraction size	0.774 (0.427–1.405)	0.4
Total radiation dose	2.469 (0.548–11.127)	0.239
Overall treatment time	0.897 (0.355–2.267)	0.817

CI — confidence interval

Overall survival

Among the 98 patients, 11 (11.2%) died of recurrent laryngeal cancer during follow-up. For the whole patient cohort, the 5-year OS rate was 83.3%. Univariate analysis showed no significant difference in the 5-year OS rate between the CF and HF groups (84.9% and 72.1%, respectively, p = 0.99). The 5-year survival rates of patients with T1a, T1b, and T2 disease were 78.2%, 96%, and 82.1%, respectively (p = 0.43). Other patients and tumor variables showed no significant association with OS rate, as shown in Table 4.

Table 4. Univariate analysis: prognostic factors for 5-year loco-regional control and overall survival

Prognostic factors	**Loco-regional-free survival (%)**	**p-value**	**Overall survival (%)**	**p-value**
Age [years]				
< 60	79.6	0.274	89.8	0.973
> 60	87.7		89.5	
Sex				
Male	85.1	0.063	89.2	0.489
Female	50		100	
Performance status				
I	84.8	0.386	89.4	0.81
II	75		91.7	
Smoking				
Yes	80.7	0.907	83	0.972
No	81.8		90	
Pathological grade				
I	100	0.051	92.9	0.144
II	83.6		91.6	
III	63.6		72.7	
Commissure involvement				
Yes	75.2	0.72	88.5	0.21
No	83.3		91.5	

Regarding OTT, the 5-year OS rate was 95.2% for treatments < 49 days in the CF and 76 % for treatment duration greater than 49 days. Meanwhile, it was 100% for treatment < 40 days in the HF compared to 80% for OTT > 40 days with no statistically significant difference (p = 0.17). The total radiation dose was not a significant factor in univariate analysis for OS. The 5-year OS for patients who received the prescribed RT dose in the HF and CF were 72.1% and 85%, respectively, and 75% received less than the prescribed RT dose in the CF group

with no statistically significant difference (p = 0.962).

Discussion

In our study, the 5-year LCR and larynx-preservation rates were 79%, 82% for T1 and 80%, and 81% for T2, respectively (p = 0.87), which are consistent with several studies that reported LRC ranges of 73-85% and 62-83%, for T1 and T2 respectively [5, 6]. In several studies, stage T2 was independently associated with a lower cure rate, with a 20% higher risk of local recurrence than the T1 stage [7]. Our study showed no significant difference between T1 and T2 tumors in the 5-year LCR and larynx-preservation rates.

The median age in this study was 59.5 years (27–85 years). This age was younger than the average age of patients reported in a recently published retrospective analysis of ESGC [8, 9]. Additionally, the incidence of ESGC in patients below 40 years (9.6%) is comparable to several studies that reported less than 10% in those younger than 40 [10].

Accelerated tumor clonogenic repopulation during prolonged radiation therapy leads to tumor resistance and treatment failure [11]. HF and hyper-fractionation decreased the OTT and improved the LCR. The RTOG 9512 shows no significant difference in the hyper-fractionation arm for 5-year LCR and survival outcomes compared to CF. However, the authors reported higher rates of acute toxicity in the hyper-fractionation arm. These findings increased the interest in HF schedules. At our institution, the adoption of HF schedules for ESGC has increased over the past few years, which explains the small patient percentage (39.4%) treated with the HF schedule in our study. This strategy is consistent with the guidelines recommending HF as the standard of care for ESGC [12].

We demonstrated a significantly superior 5-year LRC in the HF group compared to the CF group (91% vs. 69.2%, respectively; p = 0.04) in univariate analysis. There was an increase in the 5-year laryngeal preservation rate in the HF group compared to the CF group (91% vs. 76% respectively) with no significant difference (p = 0.145), which may be due to the small patient number reviewed in the study. Our finding is consistent with the results of several trials that identified increased fraction size (HF) as an important prognostic factor for high LRC [11, 12].

A Japanese study by Yamazaki et al. used a fraction size of 2.25 Gy in stage T1 glottic carcinoma, similar to the fraction size used in our institute. The authors reported that the 5-year LCR of HF was significantly superior to CF (92% *vs.* 77%, respectively; p = 0.004) [13]. Another series of 585 patients with ESGC treated with CF and altered fractionations (ART) were reviewed by Chera et al. [14]. The 5-year LCR was more than 90% for stage 1

and between 70% to 80% for T2 tumors. The T2 stage, fraction size, and OTT > 41 days were associated with inferior LCR outcomes on multivariate analysis. Additionally, Kodaira et al. included 370 patients with T1-2 glottic carcinoma. They showed a significant benefit in LCR at three years with HF compared to CF (81.7% vs. 79.9% respectively, p = 0.047), and no significant difference was observed in 3-year OS between both groups [15].

In contrast, two trials reported no significant benefit in LCR rates at five years with HF. A prospective randomized trial published by the Korean Radiation Oncology Group enrolled 156 patients with ESGC. They reported a better 5-year local progression-free survival rate in the HF group compared to CF (88.5% *vs.* 77.8%, HR 1.55, p = 0.213), but with no significant difference [16]. Another prospective trial by Salas-Salas et al. reported similar results at five years of both HF and CF schedules, either for LCR (86.2% vs.83.7%, p = 0.86), larynx preservation (93% vs. 91%, p = 0.97) and OS (78.3% vs.78.2%, p = 0.68) respectively [17]. Recently, a large meta-analysis included 11 trials concluded that HF and hyper-fractionation improve LCR for the T1 stage and in the setting of anterior commissure involvement. Still, this benefit did not extend to the T2 stage. Similarly, we demonstrated no significant benefit of HF schedule on T2 tumor (p = 0.05) [18]. Therefore, treatment approaches like upfront surgery or concomitant chemo-radiotherapy may be used for T2 bulky tumors [18].

The importance of total radiation dose as a prognostic factor for LCR has also been reported in several studies. In the univariate analysis, we observed that the 5-year LCR in patients who received a total radiation dose below 66 Gy in CF was worse than in patients in the HF group and in the CF who received their prescribed dose (33% *vs.* 90.7% and 73% respectively; p = 0.03). However, in multivariate analysis, radiation dose below 66 Gy was not identified as an independent factor for LCR. Song et al. reported a significantly lower 5-year LCR in patients treated with < 66 Gy compared to patients treated with ≥ 66 Gy (54.5% vs. 85.7% respectively; p = 0.014) [19]. Meanwhile, Hendriksma et al. reported no impact of total dose below or above 68 Gy on the oncological outcomes of patients with T2N0 glottic carcinoma [20]. Tong et al. observed total BED 15 less than 65 Gy was related to poorer tumor control [21].

Although it is well established that AC involvement had worse outcomes than ESGC, conflicting results have been published in the literature about its impact. Some studies demonstrate a significant correlation between AC and a higher recurrence rate; others do not. These inconsistent results may be attributed to the anatomical complexity of AC, variations in the clinical definition of the AC area, its close contact with the larynx's visceral spaces, the difficulty of exposing the vertical extension of the tumor involving the AC due to a narrow-

angle and possible under dosage of tumors with AC close to the skin [22]. A systematic review included 57 studies for both RT and transoral laser microsurgery (TLM) that assessed AC involvement as a prognostic factor in patients with ESGC. The authors reported no significant impact of AC involvement on LCR, OS, and laryngeal preservation in 67.6% and 75.0% of studies in the RT and TLM groups, respectively [20,22]. These findings support our observation that there was no impact of the AC infiltration on LCR and OS in our study. However, improved planning techniques and the use of IGRT in practices can reduce the negative effect of anterior commissure infiltration on LCR.

A Dutch group studied the impact of OTT on LCR in ESGC treated with definitive RT for T1N0 disease. The OTT was the most crucial predictor of LCR, with a 5-year LCR of 95% for treatments between 22-29 days and 79% for treatment duration ≥ 40 days [23]. In the current study, the 5-year LCR was significantly inferior in patients who experienced prolonged OTT of more than 49 days in the CH group and more than 40 days in the HF group (60% vs. 80%, respectively; p = 0.04) in univariate analysis. However, it was not an independent factor for LCR in multivariate analysis, which is consistent with the finding of Okubo et al. [24].

In the current study, the 5-year OS was 86.3% for the whole patient cohort, and we found that alternating radiation fractions were not associated with improvement of OS. The 5-year OS in the CF and HF groups were 84.9% and 72.1%, respectively (p = 0.99). Our finding is consistent with those reported in many studies of no impact of HF schedule on survival outcome [13, 15, 17, 25].

Several studies addressed the long-term side effects after radiotherapy treatment and attempted to reduce toxicity [26]. In our cohort, the radiation treatment was well-tolerated, with only acute low-grade dysphagia as prevalent toxicity among our patients (81.4% *vs.* 72.2% respectively; p = 0.33) in the CF and HF group, respectively.

There were some limitations to our study; the number of patients was small, and due to its retrospective nature, missing data for late toxicity scoring, which partly limited the reliability of our comparison of toxicity between the CF and HF treatment. For the same reason, we could not assess the patient's voice quality after treatment. Therefore, a longer follow-up is required to evaluate the HF schedule's effectiveness as a treatment and as late toxicities.

Conclusion

Non-inferiority results supported the HF schedule to ESGC, including high local disease

control and decreased overall treatment time. Our study supports its efficacy in the primary care of ESGC with manageable side effects.

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Conflict of interest

None declared.

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Figure 1. Loco-regional control rate for all patients

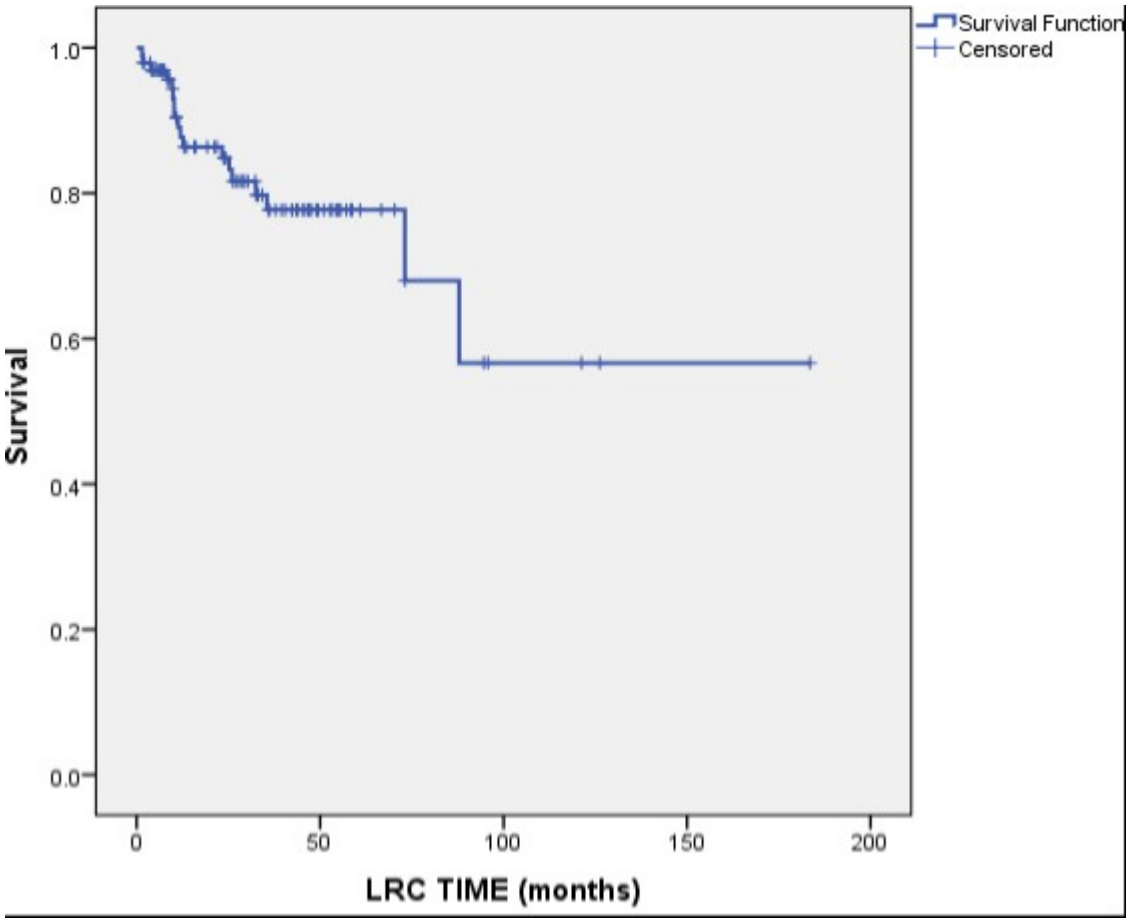


Figure 2. Loco-regional control rate according to T stage

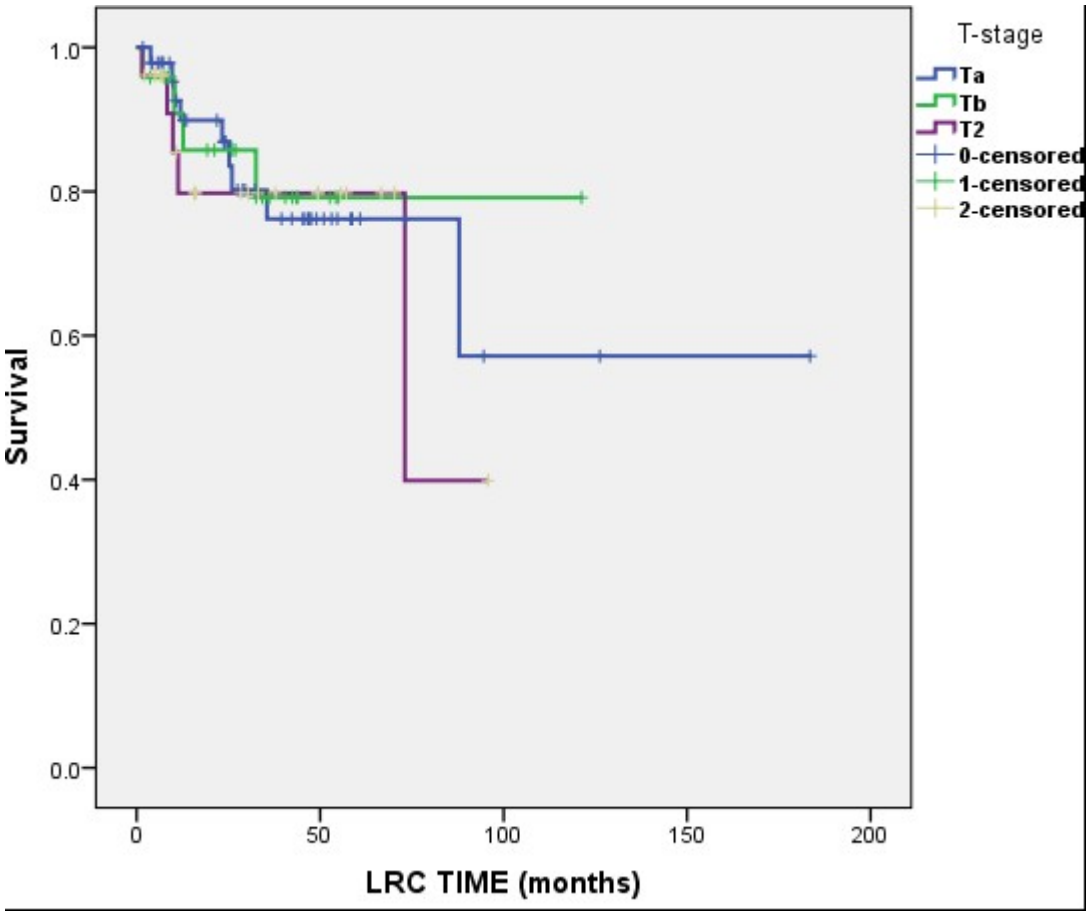


Figure 3. Loco-regional control rate according to overall treatment time (0TT)

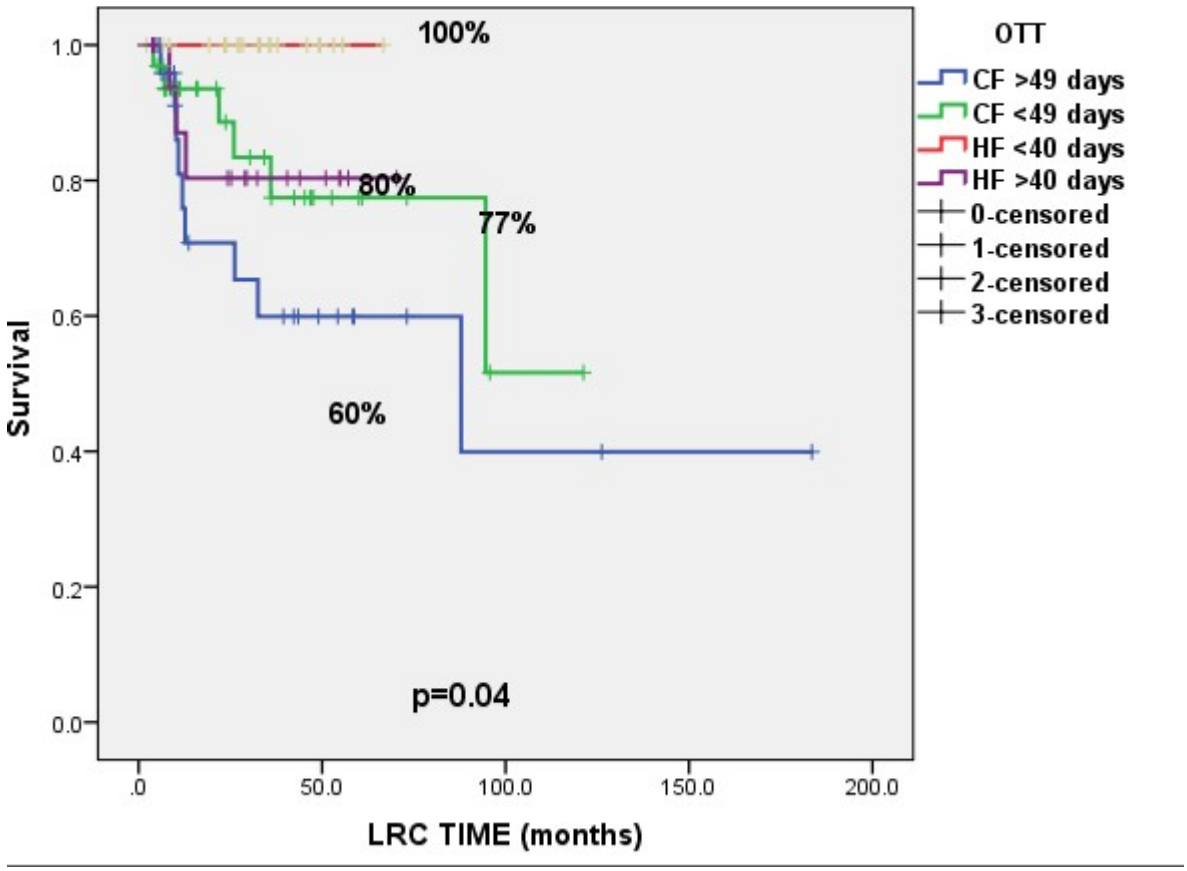
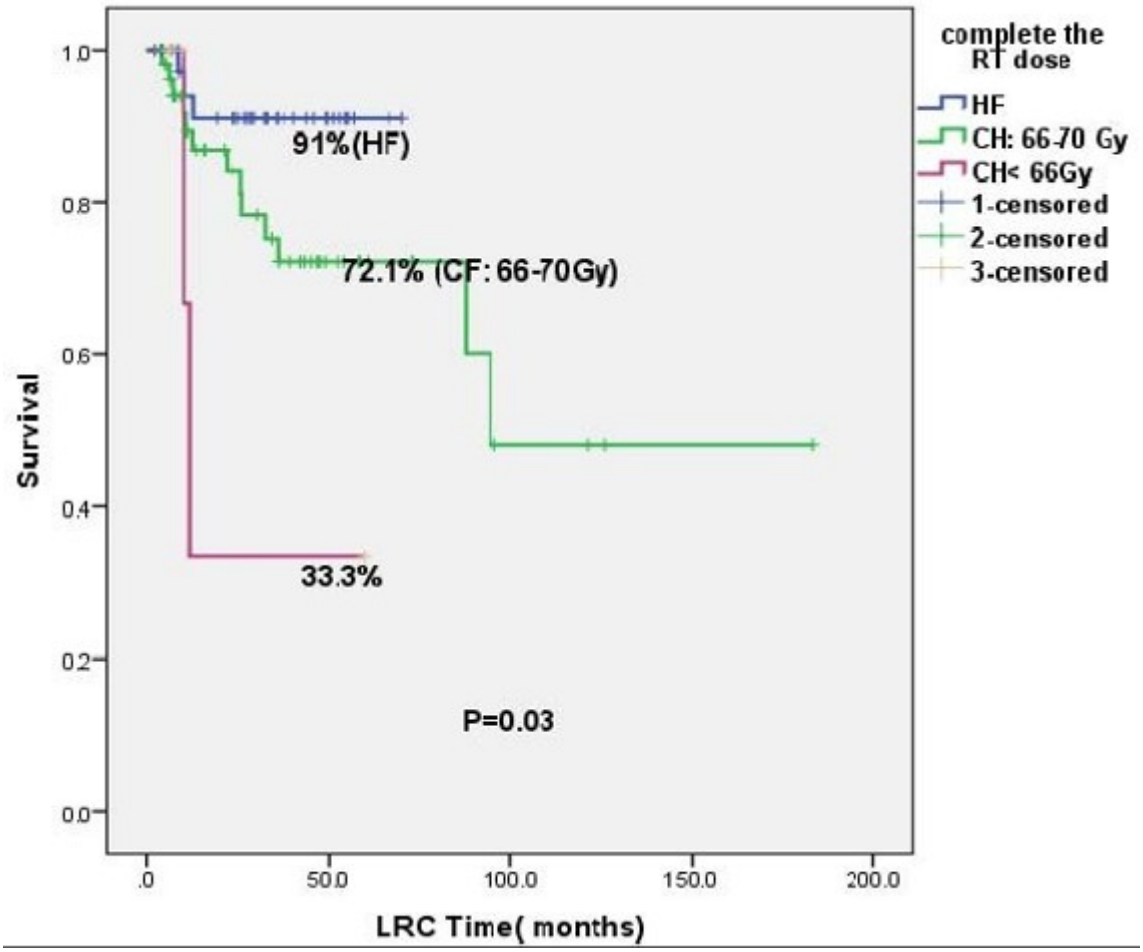


Figure 4. Loco-regional control rate according to radiation doses


complete the RT dose
HF
CH: 66-70 Gy
CH< 66Gy
1-censored
2-censored
3-censored
91%(HF)
72.1% (CF: 66-70Gy)
33.3%
P=0.03
Survival
LRC Time(months)
1.0
0.8
0.6
0.4
0.2
0.0
.0
50.0
100.0
150.0
200.0