The outcomes of patients with advanced laryngeal carcinoma: a multicentric retrospective study

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Aim To evaluate long-term oncological and functional outcomes of patients who underwent total laryngectomy (TL) or primary (chemo)radiotherapy ([C]RT) for laryngeal carcinoma.

Methods We retrospectively reviewed the outcomes of 202 patients treated in three medical centers between January 1999 and October 2020: 146 patients underwent TL and 56 (C)RT. The groups were adjusted according to sex, age, and TNM stage. The matched sample enrolled 112 patients: 54 (48.2%) in the (C)RT and 58 (51.8%) in the surgery group. Overall survival (OS) and disease-free survival (DFS) were assessed.

Results All laryngectomy patients belonged to a single category according to the Vienna classification system (IA), which precluded its use for survival subgroup analysis. Out of 112 patients, 43.8% (n=49) achieved speech rehabilitation with voice prosthesis, 1.8% (n=2) with esophageal speech, 3.6% (n=4) with an electrolarynx, and 2.7% (n=3) with none of these options. Primary (C)RT patients did not require any voice rehabilitation. Oral nutrition was achieved completely in 79.2% of patients (n=80), partially in 9.9% (n=10), and not at all in 10.9% (n=11) of patients. The swallowing function was better in the surgery group ($p<0.001$) with less G-tube ($p<0.001$) dependence. At the end of follow-up (mean 59.2 months), DFS and OS were significantly better in the primary surgery than in the primary (C)RT group ($p<0.001$ for both).

Conclusion Surgical treatment of advanced laryngeal tumors without pharyngeal involvement yields significantly better oncological and functional outcomes than primary (C)RT. Sufficient voice rehabilitation could be achieved in the vast majority of cases.

INTRODUCTION

Laryngeal carcinoma is a significant public health challenge, with approximately 187,000 cases and 111,000 deaths each year (1). Although laryngeal carcinomas account for merely 1-2% of malignant tumors, they represent up to 25% of malignant head and neck tumors (2). While patients with an early-stage laryngeal carcinoma have a good oncological outcome with a 5-year survival rate of 90%, those with advanced-stage cancer (stage III-IV) present with a 5-year survival rate of 50-60% and a poor functional outcome (3-5). Certainly, the primary goals of any oncological treatment modality are disease control and overall survival. Nonetheless, it is also important to preserve organ function and achieve a satisfactory quality of life.

For more than a century, total laryngectomy was the "gold standard" in the treatment of advanced-stage laryngeal cancer. This has partially changed since the 1990s, when the Veterans' Affairs trial showed that the same outcome was achieved with induction chemotherapy followed by radiotherapy (6). Numerous oncology centers have embraced the new concept of treatment. Certainly, patients were more tempted by the option of having a natural voice, without loss of the larynx and without permanent tracheostomy. Today, however, despite early knowledge, more and more centers are choosing surgery as their first-line treatment.

This study's primary aim was to evaluate the functional and oncological outcomes of patients who underwent primary TL without partial pharyngectomy in three centers and compare the findings to patients who underwent primary (chemo)radiotherapy. In addition, we evaluated the recently developed Vienna classification system (Table 1) (7) in a homogeneous group of patients who underwent TL or primary radiation, which corresponds to groupings IA of the classification.

PATIENTS AND METHODS

Study cohort

We retrospectively reviewed the medical records of 202 patients with primary advanced-stage (III and IVa) laryngeal squamous cell carcinoma (LSCC) who were treated between January 1999 and October 2020. All patients were discussed at multidisciplinary tumor boards before undergoing treatment. Among them, 119 patients (58.9%) were treated at the Department of Otorhinolaryngology and Head and Neck Surgery of the Clinical Hospital Center Rijeka, Croatia, and 83 patients (41.1%) were treated at the Department of Otorhinolaryngology and Head and Neck Surgery of the Medical University of Vienna, Austria, and the Institute of Head and Neck Diseases, Evangelical Hospital Vienna, Austria. Surgical treatment included total laryngectomy with/without neck dissection and postoperative radiotherapy (PORT) according to NCCN guidelines (8,9). The choice of neck dissection was primarily guided by the presence, location, and extent of regional nodal metastases, evolving from selective approaches to comprehensive (modified) radical dissections (8,9). Patients who underwent additional partial or total pharyngectomies and those with tumor recurrences were excluded from the study. Neither regional nor free flap reconstructions were performed. Primary (C)RT was carried out in 56 patients (27.7%). The median total radiation dose was up to 70 Gy (range: 35-72 Gy) delivered in 35 fractions with concurrent cisplatin at 100 mg/m^2 every 21 days or 40 mg/m^2 every week for seven weeks, which is the current standard of care. The multidisciplinary team for head and neck tumors followed the criteria for a more aggressive treatment approach (concurrent [chemo] radiotherapy), and candidates were usually younger than 75 years of age with an Eastern Cooperative Oncology Group score of 0-1 or Karnofsky score of ≥ 70-80% (8,9).

Data collection

We collected data on basic patients' characteristics (sex, age); tumor characteristics (TNM classification, stage, grading, recurrence); treatment (type of surgery, PORT, and primary [C]RT); follow-up (time to recurrence and time to death); and functional outcome (voice rehabilitation, swallowing outcome, and G-tube dependence). All patients were informed about all possible complications and side effects after surgery and radiotherapy treatment.

The Vienna Laryngopharyngectomy Classification System and functional points of interest

The study group was classified regarding functional outcomes and complications according to the Vienna Laryngopharyngectomy Classification System (7) (Table 1) into group IA. Additional groups of IR and IIR were introduced to label patients treated with radiation. Furthermore, functional points of interest such as speech rehabilitation and swallowing outcomes were evaluated at the last follow-up. Speech rehabilitation was

TABLE 1. Vienna Functional Classification System

Type of surgery		Salvage surgery		Type of radiotherapy	
I	laryngectomy	A	non-salvage	I	primary (chemo)radiotherapy -R*
II	laryngectomy with partial pharyngectomy	B	salvage	II	salvage (chemo)radiotherapy -R
III	laryngectomy with total pharyngectomy				

* group R was added to the initial Vienna Functional Classification System to label patients treated with primary and salvage radiotherapy.

performed through the insertion of a voice prosthesis, acquisition of esophageal speech, or if these options failed, with an electrolarynx. Patients were grouped into those who swallowed properly (total oral nutrition); were partially taking food orally and through a feeding tube (partial oral nutrition); and those who were tube-dependent and were not able to feed themselves through a reconstructed neopharynx (no intake per mouth). Our cohort was followed up from the diagnosis of LSCC to the last clinical examination or death. In case of recurrence or second cancer, the exact date of the event was listed. Mortality data were grouped by cause of death due to primary disease, secondary primary tumor, or some other cause.

Oncological outcome

Overall survival (OS) was defined as the period from the start of therapy to the end of follow-up or death of any cause. Death of any cause represented an event, while unknown outcomes or loss to follow-up were counted as censored events. The freedom-from-recurrence was defined as the time from the date of surgery to the date of recurrence and was calculated only in patients after complete surgical resection (R0) and with full information on recurrence status. Disease-free survival (DFS) was defined as the time from the start of therapy to the date of recurrence or death.

Statistical analysis

Unless otherwise specified, data are reported as means ± standard deviations (SD). The associations between nominal variables were assessed with a chi-square test, while the associations between continuous variables were assessed with an unpaired t-test. Kaplan-Meier analyses and log-rank tests were used for survival analysis. Univariate and multivariate binary logistic regression analyses were performed to evaluate the prognostic impact of clinical variables, staging, tumor and lymph node classification, age, sex, and treatment on total oral nutrition and G-tube dependence. Odds ratios (ORs) and 95% confidence intervals (CIs) are presented. All tests were two-sided, and p-values below 0.05 were considered statistically significant. Statistical analysis was performed using SPSS, version 27.0 (IBM SPSS Inc., Armonk, NY, USA).

RESULTS

Study cohort

Out of 202 patients, 178 (88.1%) were male. The mean age was 63.1 ± 9.5 years. Patients treated with primary (C)RT were slightly older (mean age 66.6 ± 9.6 years) than surgically treated patients (61.8 ± 9.1 years). Regarding tumor size (T-classification), 7 (3.5%) T2, 126 (62.4%) T3, and 69 (34.2%) T4a tumors had positive neck nodes in 76 (37.6%) patients. A total of 104 (51.5%) patients had clinical stage-III and 98 (48.5%) patients had stage-IVa disease. PORT was applied in 112 (55.4%) patients (Table 2).

Oncological outcome

At the end of the follow-up, 91 (45%) patients were alive and 111 (55%) died. Significantly fewer patients died in the surgically treated group (70/146, 47.9%) than in the primary (C)RT group (41/66, 62.1%, p = 0.001). Recurrent disease was observed in 44 (21.8%) patients. Of these, 17 (8.4%) patients had local, 12 (5.9%) regional, and 15 (7.4%) distant recurrence, with significant differences between the examined groups (p=0.015). Kaplan-Meier plots showed that surgically treated patients had better OS than patients treated with primary (C)RT (p<0.001; Figure 2). Furthermore, similar results were obtained in the analysis of DFS (p<0.001; Figure 3). In addition, curves were created for more homogeneous groups of patients concerning T classification (T3 and T4a groups of patients treated with surgery versus [C]RT). In both groups, surgically treated patients had better five- and ten-year OS (Figure 4A). The curves for DFS (Figure 4B) showed a similar pattern.

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TABLE 2. Clinical characteristics of patients who underwent primary total laryngectomy, which corresponds to the Vienna Functional Classification Class IA, and patients who underwent primary (chemo)radiotherapy ([C]RT)

		Total n (%)	(C)RT n (%)	Surgery n (%)	p-value
Characteristics		202 (100)	56 (27.7)	146 (72.3)	
Age (mean ± standard deviation)		63.1 ± 9.5	66.6 ± 9.6	61.8 ± 9.1	0.001
Sex	female	24 (11.9)	13 (54.2)	11 (45.8)	
	male	178 (88.1)	43 (24.2)	135 (75.8)	0.004
T-classification	T1	0 (0)	0 (0)	0 (0)	
	T2	7 (3.5)	4 (57.1)	3 (42.9)	
	T3	126 (62.4)	28 (22.2)	98 (77.8)	
	T4	69 (34.2)	24 (34.8)	45 (62.5)	0.036
N-classification	N0	126 (62.4)	21 (16.7)	105 (83.5)	
	N1	30 (14.9)	8 (26.7)	22 (73.3)	
	N2	41 (20.3)	23 (56.1)	18 (43.9)	
	N3	5 (2.5)	4 (80.0)	1 (20.0)	< 0.001
Tumor stage	III	104 (51.5)	21 (20.2)	83 (79.8)	
	IV	98 (48.5)	35 (35.7)	63 (64.3)	0.018
Recurrence	no	104 (51.5)	21 (20.2)	83 (79.8)	
	yes	98 (48.5)	35 (35.7)	63 (64.3)	0.018
	local	17 (8.4)	10 (58.8)	7 (41.2)	
	regional	12 (5.9)	4 (33.3)	8 (66.7)	
	distant	15 (7.4)	2 (27.7)	13 (86.7)	0.015
Outcome	alive	91 (45.1)	15 (16.5)	76 (83.5)	
	dead	111 (54.9)	41 (36.9)	70 (63.1)	0.001

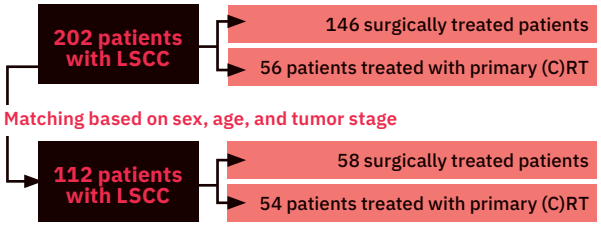

FIGURE 1. The number of patients in the surgery and (chemo) radiotherapy ([C]RT) groups before and after matching according to sex, age, and tumor stage.

However, since patients in the primary (C)RT group had a worse N-stage and tumor stage (p<0.001 and p=0.018, respectively) and were significantly older (p=0.001), we adjusted the differences between groups according to sex, age, and TNM stage. The matched cohort consisted of 112 patients: 54 (48.2%) treated with primary (C)RT and 58 (51.8%) treated with surgery (Figure 1). Clinical characteristics of the matched cohort are shown in Table 3.

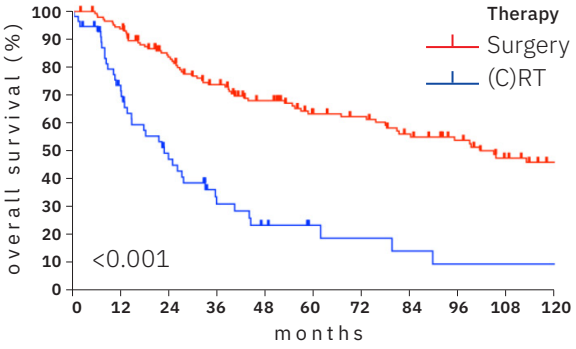

FIGURE 2. Overall survival in the surgery and (chemo) radiotherapy ([C]RT) groups .

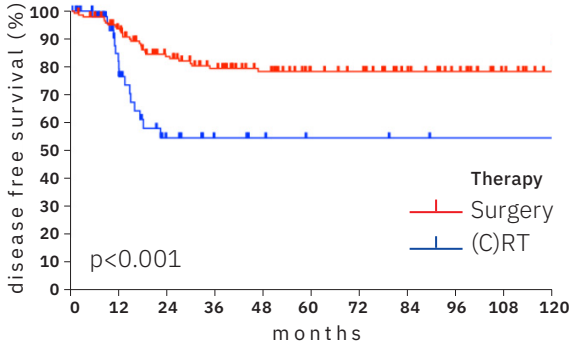

FIGURE 3. Disease-free survival in the surgery and (chemo) radiotherapy ([C]RT) groups .

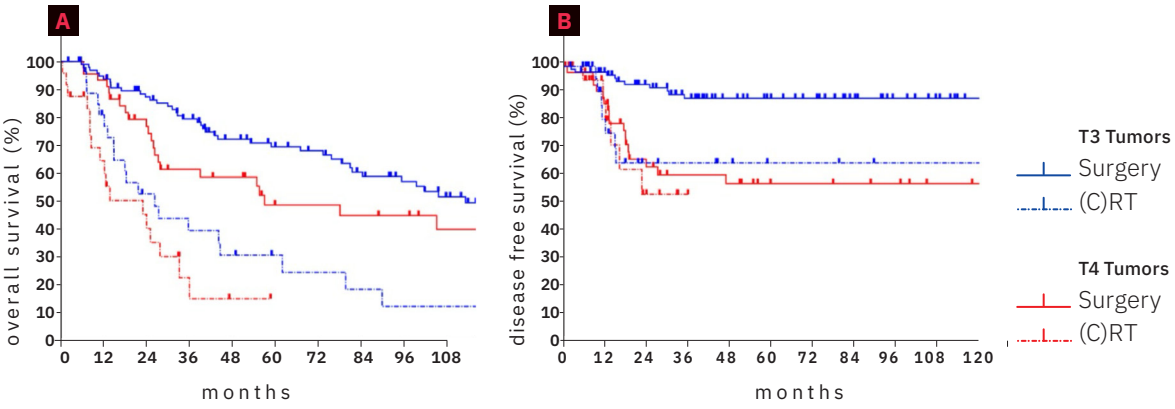

FIGURE 4. Overall survival (A) and disease-free survival (B) for T3 and T4a tumors in the surgery and (chemo)radiotherapy ([C]RT) groups

TABLE 3. Clinical characteristics of 112 patients after matching of the groups based on sex, age, and tumor stage*

		Total n (%)	(C)RT n (%)	Surgery n (%)	p-value
Characteristics		112 (100.0)	54 (48.2)	58 (51.8)	
Sex	female	24 (21.4)	13 (54.2)	11 (45.8)	
	male	88 (78.6)	41 (46.4)	47 (53.4)	0.646
Age (mean ± SD)		66.2 ± 9.1	66.4 ± 9.7	66.0 ± 8.6	0.821
T-classification	T1	0 (0)	0 (0)	0 (0)	
	T2	4 (3.6)	4 (100.0)	0 (0)	
	T3	62 (55.4)	28 (45.2)	34 (54.8)	
	T4	46 (41.1)	22 (47.8)	24 (52.2)	0.104
N-classification	N0	54 (48.2)	21 (38.9)	33 (61.1)	
	N1	21 (18.8)	8 (38.1)	13 (61.9)	
	N2	33 (29.5)	21 (63.6)	12 (36.4)	
	N3	4 (3.6)	4 (100.0)	0 (0.0)	0.017
Tumor stage	III	44 (39.3)	21 (47.7)	23 (52.3)	
	IV	68 (60.7)	33 (48.5)	35 (51.5)	1.000
Recurrence	no	81 (72.3)	39 (48.1)	42 (51.9)	
	yes	31 (27.7)	15 (48.4)	16 (51.6)	1.000
	local	14 (12.5)	10 (71.4)	4 (28.6)	
	regional	9 (8.0)	4 (44.4)	5 (55.6)	
	distant	8 (7.1)	1 (12.5)	7 (87.5)	0.067
Outcome	alive	81 (72.3)	39 (48.1)	42 (51.9)	
	dead	31 (27.7)	15 (48.4)	16 (51.6)	1.000
	cancer	14 (12.5)	10 (71.4)	4 (28.6)	
	2nd cancer	9 (8.0)	4 (44.4)	5 (55.6)	
	other reason	8 (7.1)	1 (12.5)	7 (87.5)	0.067
2nd cancer	no	93 (83.0)	43 (46.2)	50 (53.8)	
	yes	19 (17.0)	11 (57.9)	8 (42.1)	
	HNSCC	2 (1.8)	2 (100.0)	0 (0.0)	0.230

* Abbreviations: **SD** – standard deviation, **(C)RT** – (chemo)radiotherapy, **HNSCC** – head and neck squamous cell carcinoma, **2nd cancer** – second primary cancer.

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At the end of the follow-up (mean 59.2 months), 43 patients (38.4%) were alive and 69 (61.6%) patients died. Patients treated with primary (C)RT had a significantly higher rate of mortality than surgically treated patients (p=0.012). The causes of mortality were associated with recurrence or progression of the disease in 36 (32.1%) patients and with second primary tumors in 9 (8.0%) patients. Other causes (cardiovascular and long-term diseases) were observed in 24 (21.4%) patients. Mortality causes did not significantly differ between the study groups (p=0.076).

After matching, surgically treated patients had significantly better OS than patients treated with primary (C)RT (p = 0.012; Table 3), with consistent findings observed at 1, 3, and 5 years (Table 6). Furthermore, recurrent disease was observed in 31 (27.7%) patients. Of these, 14 (12.5%) patients had local, 9 (8%) regional, and 8 (7.1%) distant recurrence, with no significant difference between the examined groups (p=0.067). However, local disease control was worse in patients treated with primary (C)RT compared with surgically treated patients (71.4% vs. 28.6%, respectively), but with a lower rate of distant failures (12.5% vs. 87.5%, respectively). The rates of regional recurrences were approximately equal in both groups (44.4% vs. 55.6%, respectively). Furthermore, disease control in primary (C)RT patients was not significantly different than in surgically treated patients (p=0.067).

Functional outcomes

The functional outcomes were the achievement of adequate oral nutrition, G-tube dependence, and voice rehabilitation. Oral nutrition was fully achieved in 79.2% (n=80) of patients, partially in 9.9% (n=10), and not at all in 10.9% (n=11). Feeding was better in the surgery group (p<0.001) with less G-tube (p<0.001) dependence. Functional outcome data of both groups are shown in Table 4. Multivariate analysis showed that total oral nutrition and G-dependence were strongly related to the type of therapy (p<0.001 and p=0.005, respectively). Furthermore, disease recurrence was significantly associated with insufficient attainment of complete oral nutrition in both univariate and multivariate analyses (p=0.013 for both), whereas the association of disease recurrence with G-tube dependence was demonstrated only in univariate analysis (p=0.037). In particular, patients who received primary (C)RT (Table 5) and had a relapse had a 0.04-9.8-fold higher risk of remaining G-tube dependent without adequate nutrition compared with surgically treated patients without a relapse. Additionally, there was no significant difference between treatment modalities in the incidence of post-therapeutic pharyngeal stenosis, which was 5.9% overall (n=6).

Out of 58 patients in matched cohorts, 43.8% (n=49) achieved speech rehabilitation with voice prosthesis, 1.8% (n=2) by esophageal speech, 3.6% (n=4) using an electrolarynx, and 2.7% (n=3) did not achieve speech rehabilitation. All patients treated with primary (C)RT (n=54; 48.2%) did not need any voice rehabilitation. There was no significant difference regarding voice rehabilitation between Rijeka and Vienna centers (p=0.499).

TABLE 4. Functional outcomes in advanced-stage laryngeal cancer*

		Total n (%)	(Chemo)radiotherapy n (%)	Surgery n (%)	p-value
Characteristics		112 (100.0)	54 (48.2)	58 (51.8)	
Oral nutrition†	no	11 (10.9)	11 (20.4)	0 (0.0)	
	partial	10 (9.9)	8 (14.8)	2 (3.4)	
	total	80 (79.2)	24 (44.4)	56 (96.6)	< 0.001
G-tube dependence	no	96 (85.7)	40 (41.7)	56 (58.3)	
	yes	16 (14.3)	14 (87.5)	2 (12.5)	< 0.001
Pharyngeal stenosis	no	96 (94.1)	39 (41.1)	56 (58.9)	
	yes	6 (5.9)	4 (66.7)	2 (33.3)	0.397

* Functional outcomes were assessed in a subgroup of 112 patients who had been matched according to sex (p=0.646), age (p=0.821), and tumor stage (p=1.000).

† Unknown in 11 cases.

TABLE 5. Binary logistic regression analysis assessing the predictors of G-tube dependence and oral nutrition*

		Univariable analysis			Multivariable analysis		
		OR	p-value	95% CI	OR	p-value	95% CI
G-tube dependence	Age (< 66†)	1.04	0.938	0.36-3.01			
	Sex (female)	2.60	0.099	0.84-8.09	2.26	0.218	0.62-8.25
	T-classification (T4)	1.53	0.435	0.53-4.41			
	N-classification (N0)	0.44	0.150	0.14-1.35	0.53	0.325	0.15-1.87
	Tumor stage (stage III)	0.92	0.875	0.31-2.73			
	Primary (C)RT (yes)	9.80	0.004	2.11-45.54	9.71	0.005	1.99-47. 31
	Recurrence (yes)	3.17	0.037	1.07-9.43	3.33	0.052	0.99-11.24
Total oral nutrition	Age (< 66†)	1.10	0.846	0.42-2.88			
	Sex (female)	1.08	0.899	0.35-3.34			
	T-classification (T4)	1.48	0.448	0.54-4.07			
	N-classification (N0)	1.80	0.243	0.67-4.81			
	Tumor stage (stage III)	0.70	0.463	0.27-1.83			
	Primary (C)RT (yes)	0.05	< 0.001	0.01-0.21	0.04	< 0.001	0.01-0.19
	Recurrence (yes)	0.28	0.013	0.10-0.77	0.21	0.013	0.06-0.72

* Abbreviations: **OR** – odds ratio, **CI** – confidence interval, **(C)RT** – (chemo)radiotherapy.
† Median age was used for dichotomizing patients into a younger and an older group.

TABLE 6. Overall survival and freedom from recurrence in outcome matched sample

CHARACTERISTICS		Overall survival				Freedom from recurrence			
		1-year	3-year	5-year	p-value	1-year	3-year	5-year	p-value
Sex	female	81.7	62.5	51.9		90.5	56.6	56.6	
	male	82.3	50.1	31.8	0.053	91.9	64.1	64.1	0.506
Age	< 66*	83.5	56.4	41.0		94.2	62.2	62.2	
	≥ 66*	80.8	46.5	34.2	0.118	88.2	63.0	63.0	0.945
Group	surgery	91.1	67.6	51.1		94.6	67.8	67.8	
	(chemo)radiotherapy	72.4	33.8	23.4	< 0.001	87.0	55.8	55.8	0.138
Tumor stage	III	85.0	55.6	49.3		88.4	72.1	72.1	
	IV	80.5	49.4	31.0	0.237	93.5	56.7	56.7	0.167
T-classification	T2	75.0	50.0	0.0		66.7	0.0	0.0	
	T3	87.9	60.9	46.5		92.3	74.7	74.7	
	T4	75.3	39.0	28.0	0.284	89.8	50.4	50.4	0.003
N-classification	N -	84.0	55.2	46.9		90.7	69.4	69.4	
	N +	80.5	48.5	29.7	0.051	92.2	56.0	56.0	0.154

* Median age was used for dichotomizing patients into a younger and an older group.

DISCUSSION

To date, the treatment of patients with advanced laryngeal carcinoma represents a huge challenge. In particular, disease-specific survival of patients with advanced laryngeal cancer has not improved for half a century (4,10), and the five-year survival ranges between 50 and 60% (4). In the post-Second World War era, laryngectomy was the standard of treatment until the late 1980s and early 1990s, when laryngeal preservation protocols significantly changed the disease management (6,11). Interestingly, in the meantime, we are again witnessing increasing numbers of patients undergoing laryngectomy with or without adjuvant radiotherapy.

Although a huge number of studies testify to almost the same oncological outcome and locoregional disease control (6,11-13), still 33-66% of patients end up having salvage surgery (14-16). Unfortunately, salvage total laryngectomy with flap reconstruction has a significantly high rate of early and late postoperative complications (16-18). According to the proposed Vienna classification, salvage operations are linked to worse functional outcomes compared with non-salvage surgeries (7).

In our study, patients who underwent surgery had significantly higher survival than those who underwent primary (C)RT. The survival rate of patients after primary (C)RT was approximately 25% compared with 60-70% after surgery. Similar differences are shown in numerous studies (2,19-24). Furthermore, our study showed that patients treated with primary (C)RT had poorer locoregional disease control and a lower distant failure rate, which aligns with the results by Forastiere et al (25). This study, in particular, suggests that local recurrences were significantly more common in the primary (C)RT arm, whereas the rates of distant metastases and second primary carcinomas were higher after primary surgery in the overall analyzed group, while after matching, these differences did not reach statistical significance.

Advanced-stage laryngeal tumors pose a threat not only to patient survival but also to laryngeal functions such as swallowing and speech. In our study, oral intake was established in 89.1% of patients, which aligns with previous publications (7,26). According to a recent meta-analysis (27), an early establishment of oral food intake leads to a risk of developing pharyngocutaneous fistula (PCF). However, these results should be interpreted with caution due to the heterogeneity of the included studies (27). PCF, G-tube dependence, and inability to eat adequately not only prolong the hospital stay and increase the treatment cost but also reduce the quality of life.

In general, dysphagia is linked to surgical or post-radiation changes in the tissue surrounding the pharyngeal segment. Subsequently, these sequelae lead to a reduced contraction of the pharyngeal muscles with a difficult and prolonged bolus passage (28). Chemoradiation trials reported that swallowing dysfunction was noticed in 15-30% of all patients (6,25). Our results showed a slightly better outcome for surgically treated patients compared with those treated by (C)RT. Surgically treated patients failed less, achieving adequate swallowing, developed less stenosis, and were less G-tube dependent.

The biggest challenge after a total laryngectomy is achieving adequate communication and a good quality of life (26). We observed management differences between surgical centers regarding the choice of voice restoration techniques. In particular, two rehabilitation methods were preferred: esophageal speech or implantation of a voice prosthesis, as mostly performed in Rijeka. The overall rate of patients who achieved speech (90%) in our cohort is satisfactory and consistent with other studies (26).

However, there are certain limitations to our study, primarily related to the retrospective analysis of data and inadequate group homogenization when taking into account the use of chemotherapy and the extent and type of neck dissection in specific treatment modalities, which carry an inherent risk of information bias. Furthermore, the group of patients treated with primary (C)RT had a higher baseline N stage of the disease, which might have affected the survival rate in this group. Further prospective trials should stratify patients with advanced tumor stages into the surgical and primary (C)RT groups.

In conclusion, our study showed that surgically treated patients with advanced laryngeal tumors without pharyngeal involvement had lower mortality and a better oncological response than those treated with primary (C)RT. Furthermore, the functional outcomes in terms of oral nutrition and voice achievement were satisfactory, which contributes to the quality of life.

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Declaration of authorship
BM, SJ, FT, BME conceived and designed the study; BM, SJ, SG, BME acquired the data; all authors analyzed and interpreted the data; BM, SJ, FT, BME drafted the manuscript; BM, SJ, SG, MCG, BME critically reviewed the manuscript for important intellectual content; all authors gave approval of the version to be submitted; all authors agree to be accountable for all aspects of the work.

Competing interests
All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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