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The Role of Primary Surgery in Resectable Stage III/IV Tonsillar Carcinoma

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Abstract

Objective: This study intends to define the role of primary surgery for patients with resectable stage III/IV tonsillar carcinoma.
Materials and Methods: From 1987 to 2004, 82 patients with resectable stage III/IV tonsillar carcinoma were treated curatively with surgery plus radiotherapy (n=22), concurrent chemoradiotherapy (n=25), or radiotherapy alone (n=35). We compared surgery plus radiotherapy with concurrent chemoradiotherapy and radiotherapy alone. The primary endpoint was 5-year overall survival.
Results: The median follow-up time was 39 months (range, 1–216 months). All living patients were followed-up for at least 2 years. The 5-year overall survival for surgery plus radiotherapy was similar to that of concurrent chemoradiotherapy (52.9% *vs.* 58.9%; hazard ratio (HR), 1.46; 95% confidence interval (CI), 0.71–3.01; p=0.31) and radiotherapy alone (52.9% *vs.* 45.7%; HR, 0.87; 95% CI, 0.47–1.62; p=0.66). For 5-year local control, surgery plus radiotherapy was better than radiotherapy alone (68.1% *vs.* 42.8%; HR, 0.39; 95% CI, 0.16–0.98; p=0.045). T4 disease resulted in poorer local control than T1–3 disease (HR, 5.89; 95% CI, 2.36–14.70; p<0.0001). After multivariate analysis, treatment modality had a consistent statistically insignificant impact on all clinical outcomes of interest.
Conclusion: For patients with resectable stage III/IV tonsillar carcinoma, surgery plus radiotherapy is comparable to concurrent chemoradiotherapy and results in better local control than radiotherapy alone. Current evidence is still insufficient to definitively recommend replacing primary surgery with nonsurgical treatment modalities. (*Tzu Chi Med J* 2008;20(1):49–57)

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1. Introduction

For patients with resectable and locoregionally advanced stage III/IV tonsillar carcinoma, two main types of primary therapy are available: primary surgery and nonsurgical treatment modalities. Two randomized trials have compared primary surgery with nonsurgical treatment modalities: the Radiation Therapy Oncology Group (RTOG) 70-03 study compared surgery (S) with radiotherapy (RT), and another trial compared surgery plus radiotherapy (S+RT) with concurrent chemoradiotherapy (CCRT) [1,2]. Although both trials showed comparable outcomes between primary surgery and nonsurgical treatment modalities, inadequate study power, mainly due to practice difficulty, prevented researchers from drawing definitive conclusions for patients in this subgroup. In addition, non-randomized studies have shown diverse results. In a large retrospective study of 384 patients with tonsillar carcinoma, S+RT demonstrated better tumor control than RT alone [3]. A meta-analysis that incorporated 51 reported series, however, did not confirm the benefits of surgery ± RT compared with RT±neck dissection [4].

More evidence is needed to determine whether nonsurgical treatment modalities are as good as primary surgery for patients with resectable stage III/IV tonsillar carcinoma. As a result, in daily practice, although CCRT with deferred surgery is the preferred treatment in many institutions, including ours, primary surgery is still the treatment of choice in others [5]. The best way to answer this issue is with a well-controlled trial with a randomized design. However, randomly comparing patients in a trial has significant practice difficulties; small case numbers and slow allocation often result in inadequate study power. Hence, further randomized trials with adequate power to well define this issue seem unlikely [1,2]. For this reason, we conducted this retrospective study and tried to further extend the evidence line for this issue.

This study intended to define the role of primary surgery for patients with resectable stage III/IV tonsillar carcinoma; S+RT was compared with nonsurgical treatment modalities, either CCRT or RT alone. Analysis of failure patterns, potential prognostic factors, and RT-related toxicities were also explored.

2. Materials and methods

2.1. Study design and endpoints

This case series retrospectively compared S+RT with nonsurgical treatment modalities, either CCRT or RT alone. The null hypothesis stated that no significant differences exist between the S+RT and the other two groups at the primary endpoint, namely 5-year overall survival. The alternative hypothesis, therefore, was that significant survival differences exist between groups on either side. Secondary endpoints were: disease-free survival, locoregional control, local control, distant metastasis-free survival, and disease-specific survival.

2.2. Patient population and data collection

From January 1987 to December 2004, 141 patients with histologically proven tonsillar malignancy were treated at one institution, Tri-Service General Hospital. We excluded 59 patients and included the remaining 82 patients with resectable stage III/IV squamous cell or undifferentiated carcinoma of the tonsil, as shown in Fig. 1. All patients were staged in accordance with the 2002 American Joint Committee on Cancer staging system [6]. According to the staging criteria, T4 disease was subdivided into resectable T4a and unresectable T4b disease. This study excluded patients with unresectable T4b disease. Resectable stage III/IV disease, therefore, was defined as stage III (T_3 N_{0-1}, T_{1-2} N_1), stage IVA (T_{4a} N_{0-2}, T_{1-3} N_2), or non-T4b stage IVB (T_{1-4a} N_3).

For all patients, we reviewed data from the cancer registry database and all original medical charts. Discrepancies were resolved by consensus. Head and neck cross-sectional images, computed tomography, magnetic resonance imaging, or both, were used for staging in all patients. Table 1 shows similar pretreatment characteristics for patients in all groups. No patient was lost to follow-up. All patients were followed-up in the radiation oncology department of Tri-Service General Hospital. Follow-up time intervals were every 1–3 months during the first year after completion of RT, every 3–6 months during the second to fifth year, and every 6–12 months thereafter.

2.3. Treatment modality and policy

All patients were treated curatively with one of the following treatment modalities: S+RT (n=22), CCRT (n=25), or RT alone (n=35). There was no formal treatment policy during the time span of this study. In general, primary surgery was performed less often than the other two organ-preserving treatments with a surgical rate of 26.8% (22/82). Whether primary surgery or a nonsurgical modality was actually conducted depended on the patient's age, associated comorbidities, physician's preference and, more importantly, patient choice. All patients treated surgically received wide excision via a mandibulotomy approach with or without flap reconstruction. No surgery via the intra-oral route was performed. Thirteen patients with neck surgery received an ipsilateral modified

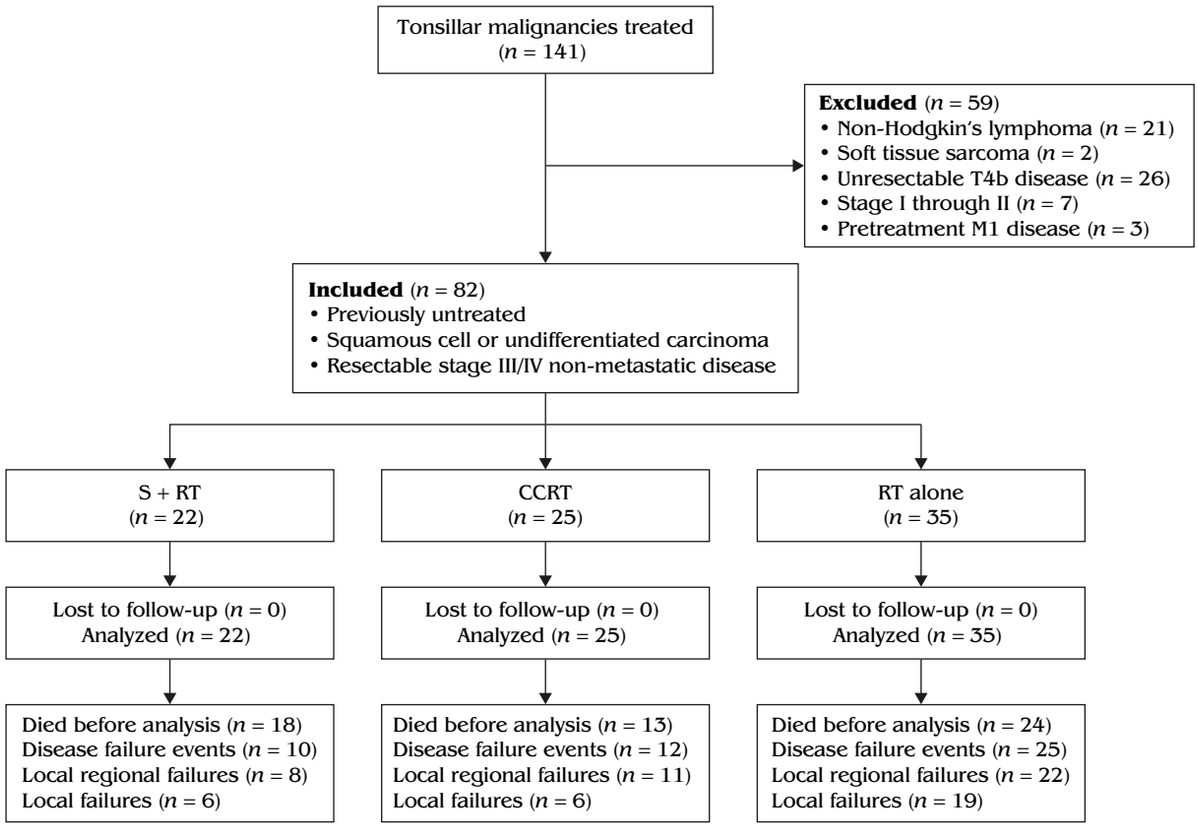

Fig. 1 — Flow diagram of patients.

Table 1 — Pretreatment patient characteristics by treatment modality

	Patient number (%)				*p*	
	S + RT	CCRT	RT alone	Total	S + RT *vs.* CCRT	S + RT *vs.* RT alone
Age					0.25	0.42
>50 yr	13 (59.1)	10 (40.0)	16 (45.7)	39 (47.6)		
≤50 yr	9 (40.9)	15 (60.0)	19 (54.3)	43 (52.4)		
Gender					0.10	1.00
Male	19 (86.4)	25 (100)	29 (82.9)	73 (89.0)		
Female	3 (13.6)	0	6 (17.1)	9 (11.0)		
T classification					1.00	0.58
T1–3	15 (68.2)	17 (68.0)	20 (57.1)	52 (63.4)		
T4	7 (31.8)	8 (32.0)	15 (42.9)	30 (36.6)		
N classification					0.08	0.55
N0–1	8 (36.4)	3 (12.0)	9 (25.7)	20 (24.4)		
N2–3	14 (63.6)	22 (88.0)	26 (74.3)	62 (75.6)		
Stage					0.17	1.00
III	4 (18.2)	1 (4.0)	6 (17.1)	11 (13.4)		
IVA/IVB	18 (81.8)	24 (96.0)	29 (82.9)	71 (86.6)		
Histology					0.29	0.70
Grade 1–2	15 (68.2)	12 (48.0)	22 (62.9)	49 (59.8)		
Grade 3–4	7 (31.8)	12 (48.0)	12 (34.3)	31 (37.8)		
NOS	0	1 (4.0)	1 (2.9)	2 (2.4)		
Total (%)	22 (26.8)	25 (30.5)	35 (42.7)	82 (100)		

S+RT = surgery plus radiotherapy; CCRT = concurrent chemoradiotherapy; RT alone = radiotherapy alone; NOS = not otherwise specified.

radical neck dissection and two had a supraomohyoid neck dissection.

All patients treated with S+RT had postoperative adjuvant RT if any of the following criteria were present: (1) primary disease ≥T3; (2) nodal disease ≥N1. The RT technique used in all patients in the three groups was the same. Conventional RT with bilateral opposed cone-down portals encompassed the primary tumor and bilateral upper neck. The median dose for postoperative RT was 64.8 (range, 54.0–66.8 Gy). In the CCRT and RT alone groups, a median dose of 72 Gy (range, 64.8–78.8 Gy) was given for gross disease. No brachytherapy or intra-oral cone boost was used. A dose of 45–50 s delivered from the lower neck down to the supraclavicular fossae. Cisplatin alone was given concurrently with RT for patients treated with CCRT. We classified normal tissue RT-related side effects according to the RTOG criteria for radiation morbidity [7].

2.4. Definition of endpoints

Overall survival was defined as the time interval from the date of completion of RT to the date of death from any cause. *Disease-free survival* was defined as the time interval from the date of completion of RT to the date of disease failure at any site, or death. *Locoregional failure* was defined as locoregional residual disease 1 month after completion of RT, as shown by clinical or pathological evidence, or locoregional recurrence after an interval in which the patient was free of locoregional disease. *Local failure* was defined the same way as locoregional failure. *Successful salvage* was defined as a disease-free interval of at least 1 year after salvage management for r-M0 recurrence.

2.5. Statistical analysis

Survival and control rates were estimated cumulatively using the Kaplan-Meier method. A curve difference between groups was assessed by the log-rank test. Fisher's exact test was used for assessing differences in binary variables. For estimating effect size, the hazard ratio (HR) was provided with a 95% confidence interval (CI) in addition to the conventional p value.

Multivariate analyses were performed using the Cox proportional hazards regression method. For multivariate analysis, the independent factors of age (≤50 years *vs.* >50 years), gender (male *vs.* female), T classification (T1–2 *vs.* T3–4), N classification (N0–1 *vs.* N2–3), and histology (Grade 1–2 *vs.* 3–4) were put together to analyze all outcomes of interest between groups. All tests were two-tailed and considered to be statistically significant if p was less than 0.05.

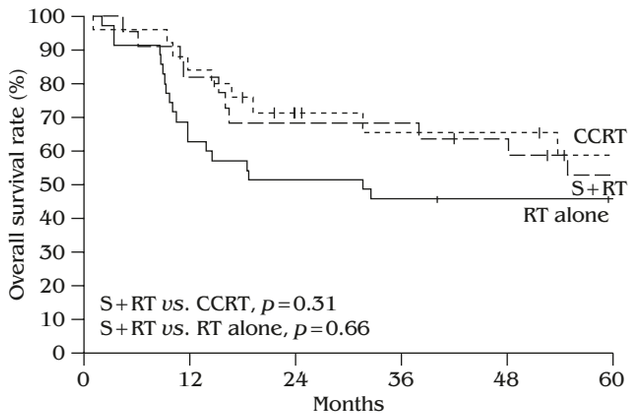

Fig. 2 — Kaplan-Meier estimates of overall survival according to treatment modality.

3. Results

3.1. Patients and tumors

The median follow-up time for all patients was 39 months (range, 1–216 months). At the time of analysis, 27 patients were still alive. All living patients were followed-up for at least 2 years with a median follow-up time of 63 months (range, 25–216 months). This study included 73 men and nine women, with a median age of 50 years (range, 20–81 years). We observed 41 lesions on the right tonsil and 37 lesions on the left. Four patients (4.9%) had bilateral tonsillar primary lesions. At presentation, 73 (89.0%) patients had clinical neck node involvement, and eight of 73 (11.0%) patients had nodal disease in the contralateral side of the neck. By T classification, rates of contralateral side nodal involvement were 2.9% (1/35) for T1–2 and 14.9% (7/47) for T3–4 disease.

3.2. Primary endpoint assessment

There were no statistically significant differences in the primary endpoint of 5-year overall survival between groups as follows: 52.9% in the S+RT group versus 58.9% in the CCRT group (HR, 1.46; 95% CI, 0.71–3.01; p=0.31); 52.9% in the S+RT group versus 45.7% in the RT alone group (HR, 0.87; 95% CI, 0.47–1.62; p=0.66) (Fig. 2, Table 2).

3.3. Secondary endpoints assessment

Table 2 shows bizarre results when comparing S+RT with CCRT but shows better local control for S+RT than for RT alone; there was less impact, in order, from local control through locoregional control to disease-free survival when S+RT was compared with RT alone. For all patients, we observed 47 disease

Table 2 — Five-year clinical outcomes by treatment modality

Outcomes (%)	S + RT *vs.* CCRT				
	S + RT	CCRT	HR	95% CI	*p*
Overall survival	52.9	58.9	1.46	0.71–3.01	0.31
Disease free survival	53.7	48.0	0.82	0.35–1.89	0.63
Locoregional control	59.2	51.0	0.72	0.29–1.78	0.47
Local control	68.1	71.4	1.11	0.36–3.45	0.86
DM-free survival	90.7	82.2	0.67	0.11–3.99	0.66
Disease-specific survival	62.9	65.4	1.10	0.41–2.95	0.84
Outcomes (%)	S + RT *vs.* RT alone				
	S + RT	RT	HR	95% CI	*p*
Overall survival	52.9	45.7	0.87	0.47–1.62	0.66
Disease free survival	53.7	36.7	0.52	0.25–1.09	0.09
Locoregional control	59.2	36.7	0.45	0.20–1.01	0.053
Local control	68.1	42.8	0.39	0.16–0.98	0.045
DM-free survival	90.7	87.3	0.44	0.09–2.15	0.31
Disease-specific survival	62.9	48.6	0.55	0.24–1.25	0.15

S + RT = surgery plus radiotherapy; CCRT = concurrent chemoradiotherapy; RT = radiotherapy; HR = hazard ratio; CI = confidence interval; DM = distant metastasis.

failures, 41 locoregional failures, and 31 local failures (Fig. 1). There were statistically insignificant differences between the S+RT and the other two groups with regard to 5-year disease-free survival (Fig. 3A).

For locoregional control, the median time to locoregional failure was 11 months (range: 1–59 months), and 78.1% (32/41) occurred within the first 2 years after completion of RT. Patients in the S+RT group showed similar locoregional control to those in the CCRT group. Although there was no statistically significant difference between S+RT and RT alone, we found a statistical trend (HR, 0.45; 95% CI, 0.20–1.01; $p=0.053$; Fig. 3B). In addition, we observed no contralateral neck nodal failure in any patient.

For local control, the median time to local failure was 11 months (range: 1–59 months), and 80.6% (25/31) occurred within the first 2 years after completion of RT. Patients in the S+RT group had local control similar to those in the CCRT group but demonstrated a better local control rate than those in the RT alone group, with 68.1% for S+RT and 42.8% for RT alone (HR, 0.39; 95% CI, 0.16–0.98; $p=0.045$; Fig. 3C). The rates for 5-year local control by T classification were as follows: T1, 66.7%; T2, 79.9%; T3, 73.0%; and T4, 27.5%. Because of similar local control results for the T1, T2 and T3 classifications, we grouped patients into T1–3 and T4, showing a highly significant statistical difference ($p<0.0001$; Fig. 4).

3.4. *Failure pattern and salvage management*

For all patients, the main type of disease failure was isolated r-M0 locoregional failure (35/47, 74.5%). Of these, 20 of 35 patients (57.1%) had salvage management for their recurrent disease, but the successful salvage rate was only 35% (7/20). Successful salvage rates by treatment modality were: S+RT, 50.0% (2/4); CCRT, 28.6% (2/7); and RT alone, 33% (3/9). For patients with r-M1 disease failure, the lung (8.5%, 7/82), bone (7.3%, 6/82) and liver (4.9%, 4/82) were the most common sites of distant metastases.

3.5. *Prognostic factors*

In univariate analysis, treatment modality had a statistically non-significant impact on overall survival, disease-free survival, and locoregional control. For local control, S+RT failed to show a statistically significant impact when compared with CCRT, but demonstrated a statistically significant difference compared with RT alone. In addition, T4 disease was the predictive factor affecting local control when compared with T1–3 disease (HR, 5.23; 95% CI, 2.45–11.15; $p<0.0001$).

After multivariate analysis, treatment modality consistently failed to show a statistically significant impact on all clinical outcomes, in terms of overall survival ($p=0.11$), disease-free survival ($p=0.93$), locoregional control ($p=0.59$), local control ($p=0.74$), distant metastasis-free survival ($p=0.83$), and disease-specific survival ($p=0.45$). For all multivariate analyses, only T classification, *T4 versus T1–3*, showed a statistically significant impact on both overall survival (HR, 2.64; 95% CI, 1.37–5.09; $p=0.004$) and local control (HR, 5.89; 95% CI, 2.36–14.70; $p<0.0001$).

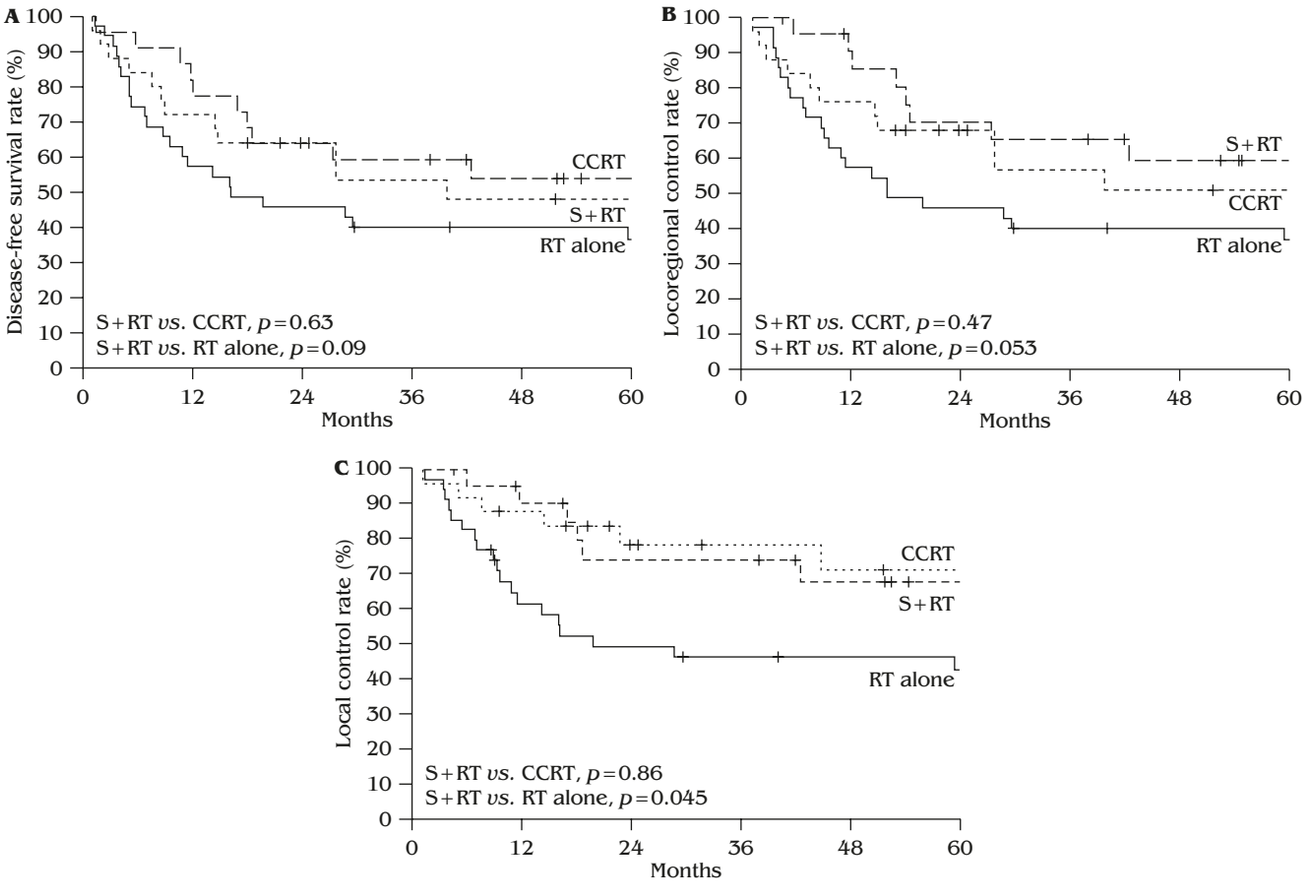

Fig. 3 — Kaplan-Meier estimates, according to treatment modality, of: (A) disease-free survival; (B) locoregional control; (C) local control.

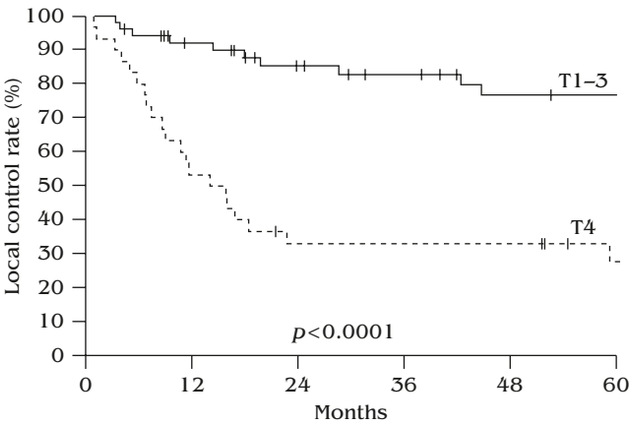

Fig. 4 — Kaplan-Meier estimates of local control according to T classification (T1–3 *vs.* T4).

3.6. Toxicities

No statistically significant differences were found between groups with regard to RT-related toxicities (Table 3). After head and neck irradiation, the most common acute and late toxicity were radiation mucositis and dry mouth, respectively. Four surgical patients had postoperative complications requiring a second surgical intervention, including osteoradionecrosis ($n=1$), poor wound healing ($n=2$), and persistent fistula ($n=1$), for a complication rate of 18.2% (4/22). Four patients had post-RT osteoradionecrosis (4.9%, 4/82), which was successfully treated with surgical intervention.

4. Discussion

This study showed statistically non-significant differences in 5-year overall survival for S+RT compared with CCRT and RT alone; thus, the null hypothesis could not be rejected. For patients with resectable stage III/IV tonsillar carcinoma, nonsurgical treatment modalities, including CCRT, should not yet definitively replace S+RT, despite the current trend for organ preservation. In addition, S+RT showed better local control than RT alone, even though this benefit translated poorly into locoregional control, disease-free survival and, finally, overall survival. For overall survival, T classification (T4 *vs.* T1–3) was the only independent factor.

Table 3 — Radiotherapy-associated toxicities by treatment modality

Toxicity	Treatment modality			*p*	
	S + RT	CCRT	RT alone	S + RT *vs.* CCRT	S + RT *vs.* RT alone
Grade 3–4 mucositis, *n* (%)	12 (54.5)	20 (80.0)	20 (71.4)	0.12	0.26
Late dry mouth					
All grades, *n* (%)	17 (77.3)	20 (80.0)	32 (91.4)	1.00	0.24
Mean grade	3.0	3.4	3.6	0.46	0.23
Neck fibrosis					
All grades, *n* (%)	12 (54.5)	8 (32.0)	16 (45.7)	0.15	0.59
Mean grade	2.4	1.9	1.8	0.54	0.18
Osteoradionecrosis, *n* (%)	1 (4.5)	1 (4.0)	2 (5.7)	1.00	1.00

S+RT = surgery plus radiotherapy; CCRT = concurrent chemoradiotherapy; RT alone = radiotherapy alone.

Table 4 — Studies of S+RT, CCRT, or both, for stage III/IV tonsillar carcinoma

First author (Reference)	Treatment	*n*	Outcomes, % (yr)				Fatal toxicity, *n*
			OS	DFS	LRC	LC	
Soo (2)*	S+RT	60	50% (3)	54% (3)	75% (3)	77% (3)	0
	CCRT	59	40% (3)	43% (3)	68% (3)	80% (3)	0
	p		0.55	0.43	NR	NR	NR
Shirazi (8)	S+RT	38	71% (4)	67% (4)	87%† (4)	94% (4)	0
	CCRT	17	48% (4)	53% (4)	92%† (4)	86% (4)	0
	p		0.27	0.39	0.58	0.29	NR
This study	S+RT	22	52.9% (5)	53.7% (5)	59.2% (5)	68.1% (5)	0
	CCRT	25	58.9% (5)	48.0% (5)	51.0% (5)	71.4% (5)	0
	p		0.31	0.63	0.47	0.86	NR
Perez (3)	S+RT	86	NR	30–62% (5)	NR	68% (5)	2
Laccourreye (9)	S+RT	51	NR	NR	NR	83% (5)	0
Foote (10)	S+RT	16	78–100% (5)	NR	69% (5)	71% (5)	0
Denis (11)*	CCRT	109	22% (5)	27% (5)	48% (5)	59% (5)	1
Fallai (12)*	CCRT	64	40% (5)	36% (5)	48% (5)	NR	3
Jeremic (13)*	CCRT	106	29–32% (5)	NR	72–74%† (5)	48–51% (5)	0
Brizel (14)*	CCRT	56	55% (3)	61% (3)	70% (3)	71% (3)	1
Vokes (15)	CCRT	76	55% (3)	72% (3)	92% (3)	NR	0

*Randomized clinical trial; †regional control rate. OS = overall survival; DFS = disease-free survival; LRC = locoregional control; LC = local control; S+RT = surgery plus radiotherapy; CCRT = concurrent chemoradiotherapy; NR = not reported.

For patients with resectable stage III/IV tonsillar carcinoma, CCRT is preferred to S+RT for organ preservation in many institutions including ours, but S+RT remains the treatment of choice for operable patients in other hospitals (5). This phenomenon shows that there is still no definitive conclusion for comparing primary surgery with nonsurgical treatment modalities (Table 4). Only one randomized trial that compared CCRT with S+RT has been conducted and it showed no significant difference in 3-year disease-free survival (2). In addition, a retrospective study reported comparable overall survival and freedom from disease relapse between primary surgery and RT in conjunction with or without chemotherapy (8). Other evidence from one-treatment-arm studies of either S+RT or CCRT, however, seemed to show that patients treated with S+RT had a better 5-year local control rate than those treated with CCRT, being 68–71% and 48–59%, respectively (Table 4) (9–15). Interpreting data from these studies this way should be done with caution. Nearly all patients treated in S+RT series had resectable disease, but a significant proportion of those treated in CCRT series had unresectable disease, which inevitably presents more disease burden and poorer clinical results than that of resectable disease. Our study, which excluded patients with unresectable disease, showed comparable outcomes between S+RT and CCRT. This observation is similar to that in a prior randomized trial (2). Despite the retrospective nature, our study may further extend the evidence line for this issue.

Uncontrolled local disease is still a significant treatment challenge in T4 tonsillar carcinoma, regardless of treatment modality. In this study, T3 disease

was similar to T1–2 in local control, and T4 tumors showed poorer local control than T1–3 tumors (HR, 5.89; 95% CI, 2.36–14.70; $p<0.0001$). More effective treatment is still needed in addition to primary surgery for patients with T4 disease. Although more severe adverse effects, including lethal toxicities, were reported, S+CCRT demonstrated better locoregional control, disease-free survival and overall survival than S+RT in two well-controlled randomized trials [16,17]. As a result, S+CCRT should be the priority for high-risk and medically suitable patients with primary surgery as their chosen treatment plan, especially for those with T4 disease.

For locoregionally advanced tonsillar carcinoma, CCRT is more effective than RT alone for organ preservation with a cost of more acute but not late toxicity [11,14]. Hence, current treatment guidelines recommend CCRT as the treatment of choice and reserves RT alone for those unsuited to chemotherapy [18]. Conventionally, RT alone with 70 Gy in 35 fractions given to the mid-plane has been considered curative for patients with locoregionally advanced disease, and has been widely adopted in several randomized trials as the active control [11–13]. Our analysis, however, suggests that this conventional 70 Gy fractionation is insufficient for T4 tonsillar carcinoma. For patients with T4 disease, a higher RT dose should be seriously considered. Intensity-modulated radiotherapy (IMRT) has shown a potential role for safely escalating the RT dose without significantly increasing acute or late toxicity [19]. Concurrent chemotherapy-IMRT with an RT dose greater than 70 Gy could be a choice for better organ preservation than conventional CCRT.

A meta-analysis showed that neoadjuvant chemotherapy followed by definitive RT had no additional benefits over RT alone for bulky primary tumors [20]. Recently, a phase II study tested the role of induction chemotherapy followed by CCRT, and reported high complete response and three-year overall survival rates, namely 90% and 70%, respectively [21]. But another phase II trial showed excess acute toxicities for this aggressive combination [22]. Whether this multimodal treatment is useful or harmful may be tested with caution in the context of phase III randomized trials with careful toxicity monitoring. A promising agent of targeted therapy, a monoclonal antibody against the epidermal growth factor receptor, has shown encouraging results when applied concurrently with definitive RT [23]. This combination resulted in better locoregional control and less disease-related mortality without increasing acute toxicity than RT alone, especially for patients with oropharynx cancers. For patients with locoregionally advanced tonsillar carcinoma, further investigation of chemotherapy and IMRT applied concurrently with targeted therapy may be of great value.

A previous study has shown that prior surgery or teeth extraction before RT is a predisposing factor for mandible osteoradionecrosis [24]. In our study, patients treated surgically showed a rate of osteoradionecrosis similar to those seen in nonsurgically treated patients. This study also confirmed that CCRT did not increase RT-related late sequelae [11]. Four out of 22 surgical patients (18.2%) developed severe complications requiring a second surgical intervention. Postoperative swallow and speech morbidities are important for the quality of life of patients treated surgically. This study, however, had incomplete data on these morbidities. These morbidity data should be routinely and prospectively measured in future surgical studies.

This study has several limitations, including the retrospective study nature and small case number. Inevitably, a retrospective study design has some degree of selection bias and, therefore, a lower study power than that of randomized trials [1,2]. On the other hand, the small case number increases the probability of false-negative interpretation. These two main factors decrease the study efficacy. But we would like to emphasize that definitive conclusions for comparing surgery with nonsurgical treatment modalities are still unavailable, and practice difficulty prevents further randomized trials with adequate statistical power from addressing this issue.

S+RT is comparable to CCRT and shows better local control than RT alone for resectable stage III/IV tonsillar carcinoma. In terms of cancer disease control, despite a trend toward organ preservation, current evidence is still insufficient to definitively recommend replacing primary surgery with nonsurgical treatment modalities.

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