

ORIGINAL RESEARCH

Second primary squamous cell carcinomas treated with trans oral robotic surgery: Oncological and functional results

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Abstract

Background: Recovery of swallowing in patients treated with trans-oral robotic surgery (TORS) is in general considered as favorable. However, patients afflicted with a secondary primary carcinoma of the head and neck may be more vulnerable to swallowing dysfunctions after trans-oral surgery as a consequence of previous treatments.

Methods: This is a retrospective monocentric study on patients undergoing TORS for second primary squamous cell carcinoma between 2013 and 2017 (follow-up until June 2021). Swallowing performance was assessed via the functional outcome swallowing scale (FOSS). Also, overall survival (OS), disease-free survival (DS) and disease-specific survival (DSS) were evaluated.

Results: Eighteen patients (median 62 years) underwent TORS with curative intent for T1-2 oropharyngeal and supraglottic secondary primaries. The average follow-up was of 52 months. All cases were resected R0 using TORS. 84% of patients had a post-treatment FOSS score equal or better upon last follow-up compared with pre-treatment. Only one patient required a percutaneous gastrostomy long term. DSS/DFS/OS at 5 years was 94%, 60%, and 67%, respectively. The main cause of death was metachronous pulmonary neoplasia.

Conclusions: Our study demonstrates encouraging results in terms of swallowing recovery in patients undergoing TORS for selected secondary primaries of the oropharynx and supraglottic larynx. Further studies into trans-oral surgery for this condition seem therefore warranted.

Level of Evidence: Case series; Level 4.

KEYWORDS

second primary, squamous cell carcinoma, survival, swallow function, TORS, transoral robotic surgery

1 | INTRODUCTION

Second primary (SP) malignancies represent a major cause of morbidity and mortality in patients with head and neck squamous cell carcinoma (HNSCC).¹ The incidence of SPs ranges between 2% and 8%

and SPs constitute the cause of one-quarter of deaths in head and neck cancer patients.^{2–4} The first definition of SP was given by Warren and Gates and has been since modified by the National Cancer Institute⁵ as follows: each of the tumors must be histo-pathologically confirmed; each tumor must be locally distinct and separated by

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normal mucosa; the probability of the SP being the metastasis of the primary disease must be excluded, and finally the same localization of the primary is possible if the second primary occurs more than 5 years after the index tumor. SPs can be separated into two groups: synchronous (diagnosed <6 months of the index tumor) and metachronous (>6 months). SPs are relatively common in HNSCC and likely due to field cancerization,^{5,6} which is a consequence of tobacco and alcohol consumption.⁷⁻⁹ The particularity of SPs compared with a recurrence of a primary squamous cell carcinoma is the intrinsic long-term risk for developing it.²

Transoral robotic surgery (TORS) is a well-established single modality treatment of primary early-stage (T1-T2) of oropharyngeal and supraglottic cancer and an alternative to transoral laser microsurgery (TLM) or radiotherapy (RT).¹⁰⁻¹³ The oncological efficacy of this procedure in cases of primary tumor treatment has been proven in several multicentric studies and systematic reviews.¹⁴ Studies on the application of TORS for SPs are however missing.

Several validated observer rated outcome scores exist for the functional assessment of oropharyngeal dysphagia in post-operative oropharyngeal cancer patients.¹⁵ The Functional Outcome Swallowing Scale (FOSS) is one of the most widely used and can therefore be employed to assess long-term swallowing function of patients with SPs.¹⁶

Curative treatment of second primary malignancy is a challenging and increasingly frequent problem in head and neck oncologic centers. Patients are typically polymorbid, and radiation treatments are often no more possible. The purpose of this retrospective second primary case series was to explore whether TORS can preserve swallowing function whilst providing reasonable oncological control of the disease.

2 | MATERIALS AND METHODS

2.1 | Patients

A review was conducted on all patients treated with TORS for an HNSCC in a Swiss tertiary center (Lausanne, Centre Hospitalier Universitaire Vaudois - CHUV) between January 1, 2013 and December 31, 2017. Inclusion criteria for the retrospective study on SPs were the following: indication for TORS for a SP, having a FOSS score prior TORS and another at minimum 3 months after TORS. The FOSS score was determined by an ENT specialist or speech pathologist. Briefly, the FOSS score stages are the following: stage 0 = normal function and asymptomatic; stage I = normal function but with episodic or daily symptoms of dysphagia; stage II = compensated abnormal function manifested by significant dietary modifications or prolonged mealtime (without weight loss or aspiration); stage III = decompensated abnormal function with weight loss of 10% or less of body weight over 6 months due to dysphagia, or daily cough, gagging, or aspiration during meals; stage IV = severely decompensated abnormal function with weight loss of more than 10% of body weight over 6 months due to dysphagia, or severe

aspiration with bronchopulmonary complications, nonoral feeding recommended for most of nutrition, and stage V = nonoral feeding for all nutrition.¹⁶ Prior surgery all patients were staged and screened for regional/distant metastasis. The pre-surgical evaluation consisted of an ENT clinical status, a triple endoscopy, and MRI/CT and PET-CT. The cases were discussed during a multidisciplinary tumor board meeting. Patients with a follow-up of <6 months were excluded from the analysis.

N = 18 patients underwent TORS for SPSCC between January 1, 2013 to December 31, 2017. A large majority of patients were male (89%) and younger than 65-year-old (72%). Average time between last past primary and second primary operated by TORS was 58 months. Half of the group (n = 9) had only one HNSCC past primary, one third (n = 5) had four or more primary HNSCCs. The average time between first primary and SP was 94 months. Of all (N = 18) SPs, seven were in the tonsil, six in the base of the tongue, two in the soft palate, two in the supraglottic larynx and one in the lateral pharyngeal wall (Table 1).

Data collection started in April 2021 after previous approval by the Swiss local ethical commission (CER-VD; Project 2021-00353). Participants gave informed consent prior to participation. The data collection was ended at the end of June 2021.

2.2 | Statistical analysis

For this study we used usual descriptive statistics including percentage, mean and absolute numbers for the analysis of patient's characteristic, second primary characteristics and oncological and functional outcome. To evaluate the primary functional outcome, we used a Shapiro-Wilk test of normality with a *p* value of <0.05 being considered significant. We then used a nonparametric statistical hypothesis test (Wilcoxon signed rank test) with a *p* value of <0.05 being considered significant. The secondary outcomes (OS, DFS, DSS) were analyzed using a Kaplan-Meier survival analysis. All analyses were performed with statistics package SPSS Version 27.

3 | RESULTS

3.1 | Margins and swallowing outcomes

All patients had a R0 resection. In six cases, the closest margin was >5 mm and in seven cases ≥3 mm, and in five cases >1 mm. In only one case, the closest margin was 0.1 mm and after multidisciplinary discussion no adjuvant treatment was given without any recurrence. Margins were revised in three patients by TORS and one patient using trans oral laser surgery. Only one patient was treated with adjuvant radiation therapy.

None of the patients was depending on a nasogastric tube (NG) or percutaneous endoscopic gastrostomy (PEG) before TORS. A nasogastric feeding tube (NG) was placed in the peri-operative setting in 14 cases, in the other four cases no NG tube or PEG

TABLE 1 Patient characteristics

Variables		Number of patients (%)
Age, years	<65	13 (72)
	median 62 years, range 46–78 years	>65
Sex	Male	16 (89)
	Female	2 (11)
Number of primary squamous cell carcinomas	1	9 (50)
	2	2 (11)
	3	2 (11)
	4+	5 (28)
Site	Tonsil	7 (39)
	Base-of-tongue	6 (33)
	Soft palate	2 (11)
	Posterior pharynx	1 (6)
	Supraglottic larynx	2 (11)
cT staging	T1	14 (78)
	T2	4 (22)
	T3–T4	0 (0)
cN staging	N0	17 (94)
	N1	1 (8)
	N2	0 (0)
	N3	0 (0)
pT staging	Tis	3 (17)
	T1	9 (50)
	T2	6 (33)
	T3–T4	0 (0)
pN staging	No neck dissection	14 (78)
	N0	3 (17)
	N1	1 (5)
	N2	0 (0)
	N3	0 (0)
M staging	M0	18 (100)
	M1	0 (0)
HPV-status	p16 positive	4 (22)
	p16 negative	12 (67)
	p16 unknown	2 (11)
Margin status	R0, >5 mm	6 (33)
	R0, ≥3 mm	7 (39)
	R0, >1 mm	4 (22)
	R0, 1 mm	1(6)
Adjuvant treatment	Radiation	1 (6)
	Chemo-radiation	0 (0)
	No treatment	17 (94)

TABLE 1 (Continued)

Variables		Number of patients (%)
NG, days	No NG	4 (22)
	<8	7 (39)
	7–14	5 (28)
	>14	2 (11)
PEG feeding	Long-term	1 (5)
	Short-term	3 (17)

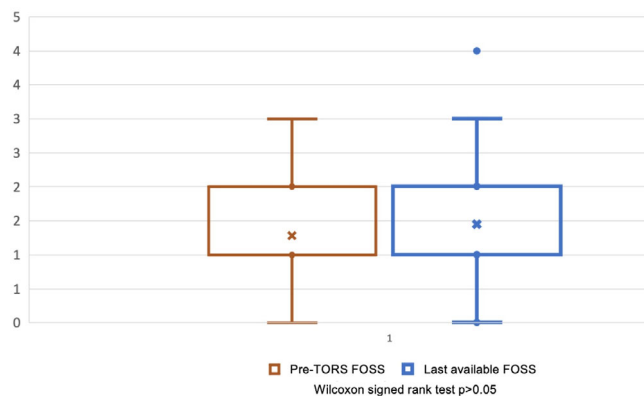


FIGURE 1 Swallowing outcome comparing pre- and post-TORS FOSS scores. Wilcoxon signed rank test did not show a significant difference ($p < 0.05$)

was necessary. Most NG-tubes (86%) were taken out in <14 days after TORS procedure. Three patients needed PEG placement; one patient remained dependent until the end of follow-up.

Fifteen patients have been monitored in an intensive care unit (ICU) for the first 24 h post TORS, no patient stayed more than 48 h in the ICU nor needed tracheostomy placement.

The mean time span between pre-TORS FOSS and last documented FOSS was 47 months (Figure 1). The majority ($n = 12$) of patients presented a pre-TORS FOSS grade I, only one patient was grade 0. Four patients had a FOSS score of 2, and one a score of 3.

The last available FOSS score was equal or better in comparison to pre-TORS FOSS for 15 (84%) patients. Three patients had a worse FOSS score after treatment. The mean follow-up after TORS was 52 months.

3.2 | Survival

DSS at 5 years was 94% as a consequence of one patient dying from loco-regional recurrence during 5 years of follow-up after TORS (Figure 2A).

One third ($n = 6$) of the cases presented with at least one new SP after the resection of the index lesion. DFS at 5 years was 60% and OS at 5 years 67% (Figure 2B,C). The most prevalent cause of death was pulmonary neoplasia ($n = 4$), followed by progression of another

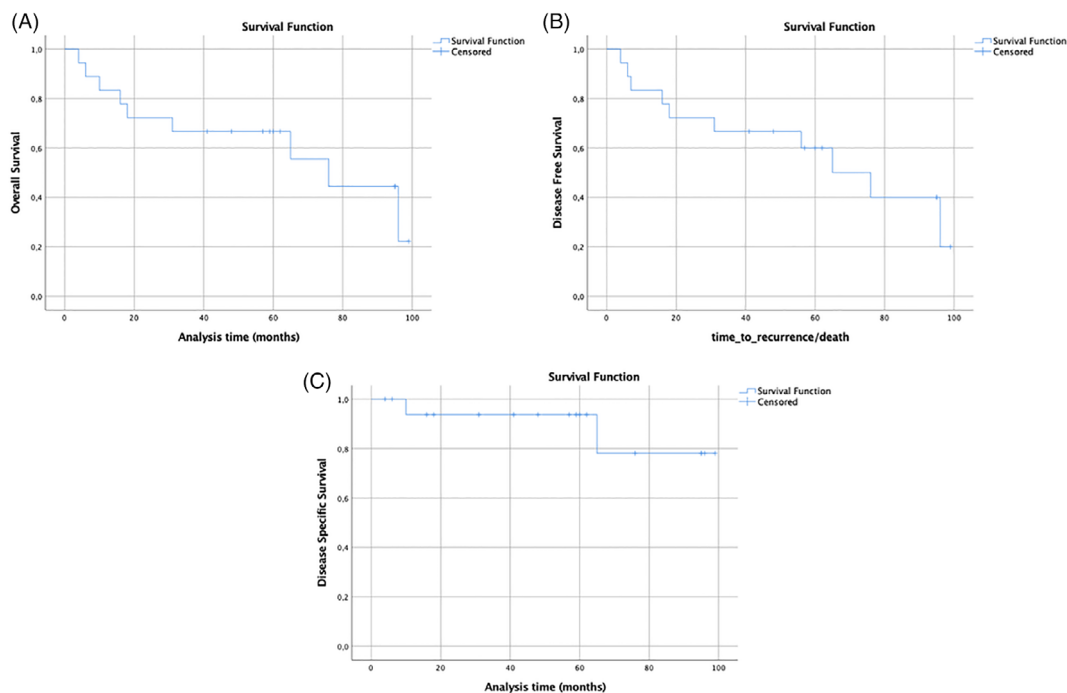


FIGURE 2 Survival of patients: (A) Overall survival (OS); (B) Disease Free Survival (DFS); and (C) Disease Specific Survival (DSS)

SP ($n = 2$). Other causes were hepatic cholangiocarcinoma ($n = 1$), cerebral stroke ($n = 1$), and recurrence/progression of a previous primary HNSCC ($n = 1$).

4 | DISCUSSION

Our retrospective analysis of patients operated with TORS for a second HNSCC localization allows us to discuss several aspects. As shown by several recent studies SP incidence of HNSCC is larger in male smokers with a p16 negative status.^{1,17} Especially SP of the oropharynx occurs significantly more often in patients with non-irradiated squamous cell carcinomas.¹⁸ We report 18 cases of SP of the oropharynx and supra-glottis of which a p16 status was available in $n = 16$; 89% of patients. Data show a predominance of p16 negative status ($n = 12$; 67%). Our cohort consists mostly of young males, which seems due to the intrinsic predisposition of this subgroup to develop a long history of cancer. An interesting fact is the time interval between the first tumor and the TORS intervention to treat the second localization; this interval lasts on average about 8 years. However, in more than one case it exceeded even 15 years. In this long oncological course before the TORS operation, patients had an average of 2.44 different localizations of HNSCC. This could support specific follow-up schedules for this at-risk population.^{19,20} At the functional level, these long cancer histories are reflected in an altered quality of life. In fact, the pre-treatment FOSS score with a mean value equivalent of 2 (compensated abnormal function manifested by significant dietary modifications or prolonged

mealtime, stable weight) confirms the functional fragility of patients presenting with SPs of the head and neck.

Globally, with an average follow-up of 47 months, FOSS scores post-TORS remained stable. We conclude therefore that TORS in this frail population may preserve swallowing function at the pre-treatment level and can be chosen for this selected patient population as a treatment option. DSS rates are favorable suggesting good loco-regional control after TORS of the index lesion. However, patients will gradually succumb to their field cancerization along the course of their disease and most frequently die from pulmonary primaries as demonstrated by the OS rates of 67% at 5 years.

It is however remarkable that over 50% of the patients examined in this study suffering from field cancerization resulting in often several SPs lived nearly 13 years with their disease.

Patients with second primary squamous cell carcinomas of the head and neck typically tend to have a long history of cancer with multiple treatments and consecutive functional impairment.²¹ Our study demonstrates that TORS can obtain good preservation of swallowing function in this fragile population and reasonable oncological control. Larger and prospective studies are needed to confirm these results.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENT

Swiss ethical commission (CER-VD) approved this retrospective study (Project-ID 2021-00353).

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