

Survival Outcomes in Oral Cavity Cancer Patients with Positive Margins: Is Adjuvant Treatment Comparable to Re-resection? A Multi-institutional Study

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ABSTRACT

Objectives: To study differences in disease-free survival (DFS) and overall survival (OS) in patients with oral cavity squamous cell carcinoma (OCSCC) and positive margins based on subsequent treatment status.

Study Design: Retrospective, cohort

Methods: Using the institutional cancer registries from Mass Eye and Ear, Nebraska Methodist Hospital and University of Kansas, we identified treatment naïve patients with pathologic stage T1/T2 OCSCC surgically treated between 2005 and 2017. Patients with positive margins, i.e., invasive carcinoma or carcinoma in situ involving or <1 mm from the resection margin, on final histopathological examination were identified and stratified in to three groups: 1) no further treatment after initial resection, 2) re-resection in a subsequent procedure and 3) adjuvant radiation (XRT) +/- chemotherapy. Primary outcomes were 2- and 5-year DFS and OS.

Results: Sixty-one patients with positive margins were identified. Mean age at diagnosis was 63.7 (SD 15.5). Thirty-three (54%) patients were males and 42 (69%) had pT1 disease. Sixteen (26%) patients had no further treatment, 33 (54%) had re-resection and 12 (20%) received XRT +/- chemotherapy. Five-year DFS and OS were 29% and 49% for Group 1, 70% and 88% for Group 2 and 83% and 91% for Group 3, respectively (Log-rank test: p=0.02 and p=0.008, respectively). On pairwise comparison, Groups 2 and 3 showed better DFS and OS compared to Group 1.

Conclusions: Patients with early-stage OCSCC with positive margins treated with re-resection or XRT +/- chemotherapy had better DFS and OS compared to patients with no further treatment. There was no statistically significant difference between patients treated with re-resection vs XRT +/- chemotherapy. Given the small sample size, more institutions are needed to improve statistical power and better understand the optimal management of early stage surgically treated OCSCC patients with positive margins.

INTRODUCTION & METHODS

- Oral cavity squamous cell carcinoma (OCSCC) is treated surgically with the aim of achieving complete resection with negative margins (>5 mm)
- Positive margin is a well-known adverse prognostic feature in OCSCC often prompting treatment with adjuvant therapy (XRT) or re-resection. In fact, it is one of the indications for treatment with chemotherapy.
- Many studies have shown the adverse effects of positive margins on survival and recurrence but few have investigated the best approach to treatment (re-resection vs XRT +/- Chemotherapy vs both)
- Patients with initial OCSCC treated surgically for pT1/T2 disease (with or without neck dissection) between 2005-2017 were identified using the institutional cancer registries of Mass Eye and Ear, Nebraska Methodist Hospital and University of Kansas.
- Only patients with positive margins were included in this study. Positive margin was defined as invasive carcinoma or carcinoma in situ involving or <1 mm from the resection margin on final histopathological examination. These patients were stratified into 1 of 3 groups based on further treatment status: 1) no further treatment after initial resection, 2) re-resection in a subsequent procedure and 3) adjuvant radiation (XRT) +/- chemotherapy
- Patients without neck dissection were considered node negative. Patients with N+ on pathology were excluded as were patients with DOI>10.
- Overall survival (OS) was measured from the time of surgery to the last documented communication with the patient. Disease free survival (DFS) was measured from the time of surgery to last documented note from oncologic provider
- Kaplan-Meier survival curves were generated for survival analyses. All patients were assumed to be censored unless documented as deceased. Microsoft Excel and Stata were used for statistical analyses

FIGURE 1. 2-YEAR OVERALL SURVIVAL BY TREATMENT GROUP

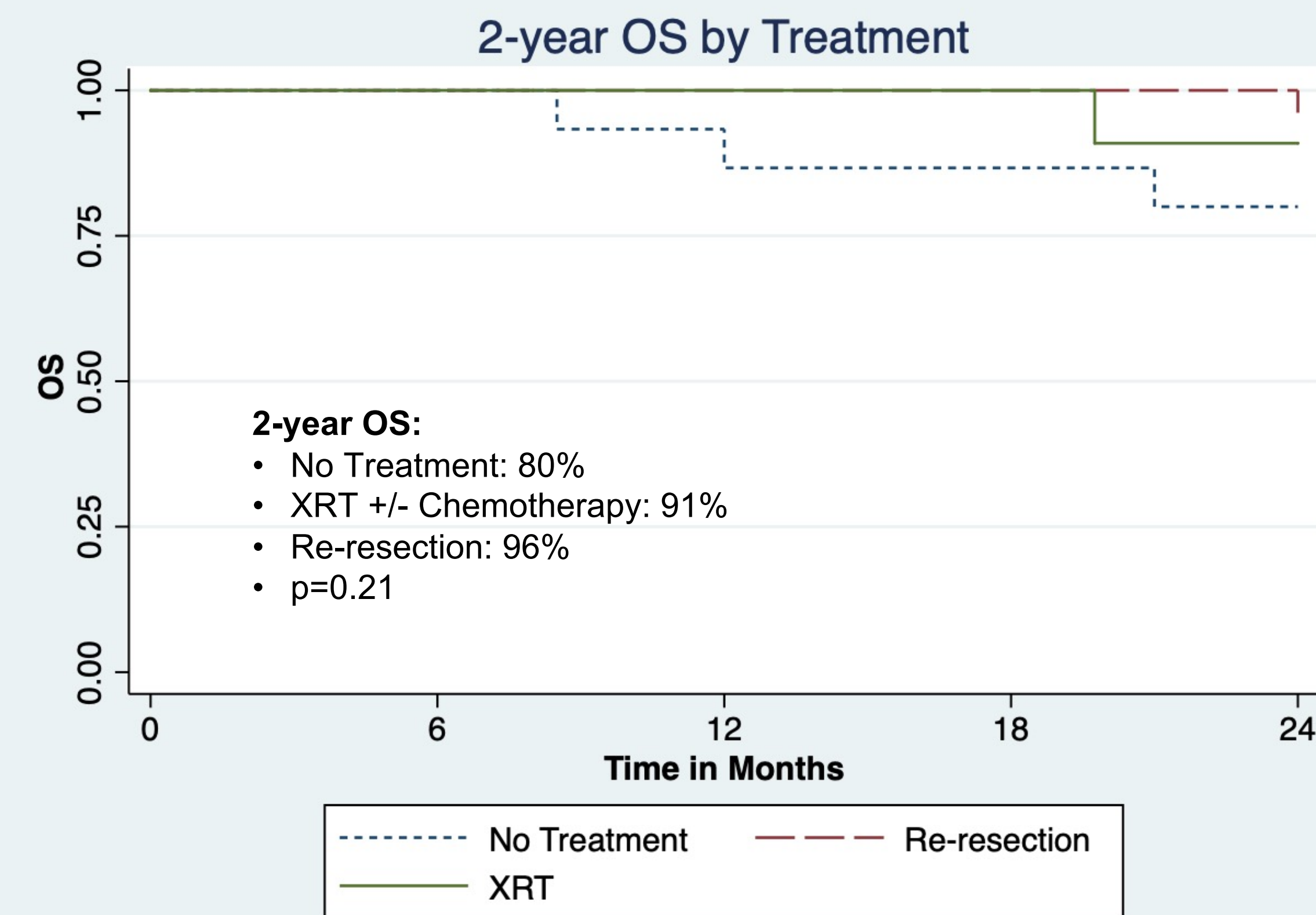


FIGURE 2. 5-YEAR OVERALL SURVIVAL BY TREATMENT GROUP

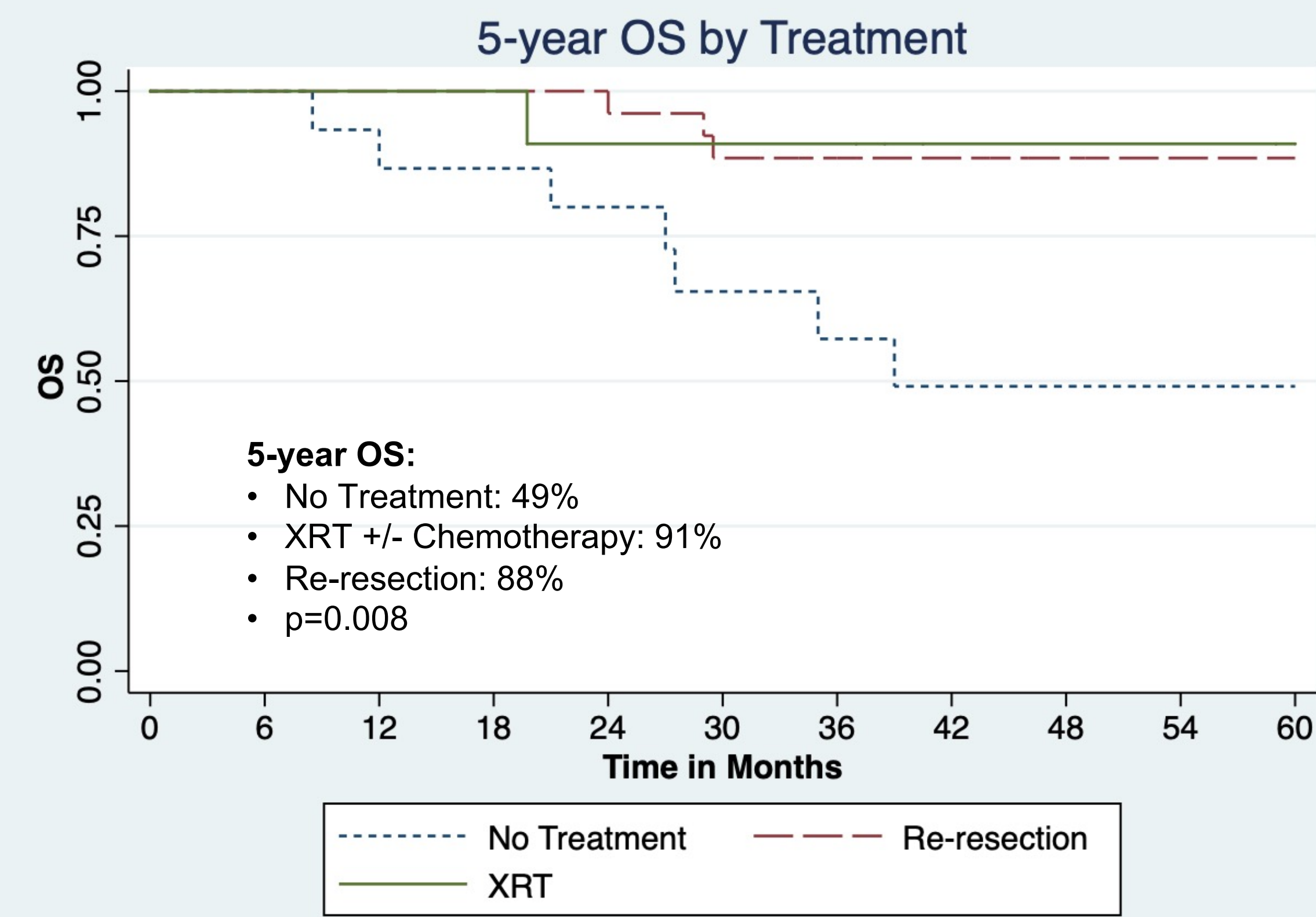


FIGURE 3. 2-YEAR DISEASE FREE SURVIVAL BY TREATMENT GROUP

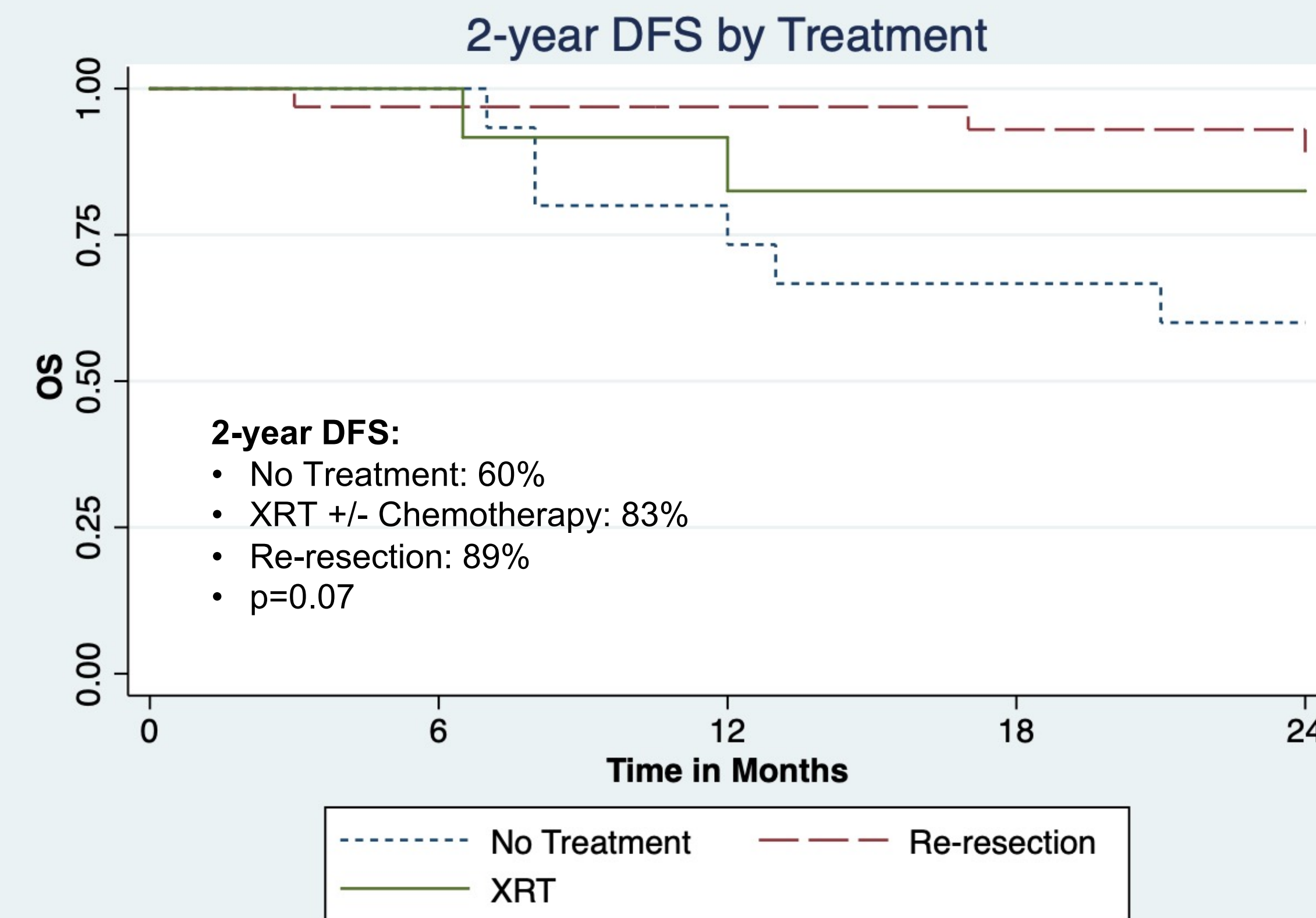
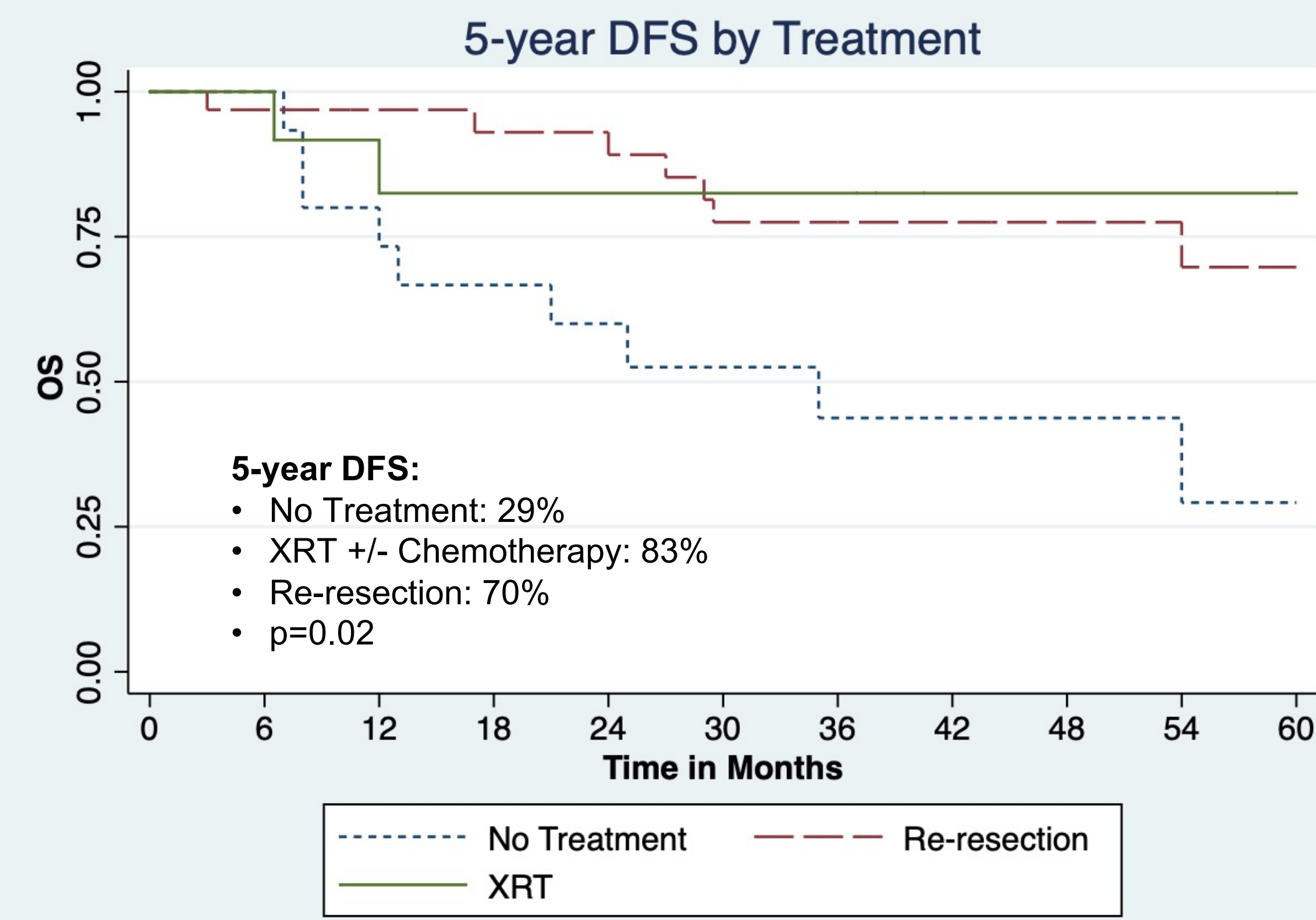


FIGURE 4. 5-YEAR DISEASE FREE SURVIVAL BY TREATMENT GROUP



RESULTS AND DISCUSSION

- 61 patients (males = 33; 54%) were identified, with mean age 63.7 years (SD 15.5)
- 42 (69%) patients had pathologic T1 disease
- 16 (26%) patients had no further treatment, 33 (54%) underwent re-resection and 12 (20%) received XRT +/- chemotherapy
- 13 (21%) patients had PNI and 8 (13%) had LVI
- Median follow up time was 39 months (IQR 27-75). 2- and 5-year OS and DFS are shown in Figures 1 – 4.
- For OS, at 2 years, there was no significant difference between the 3 groups. However, at 5 years, at least one of the groups had worse survival than the rest. Pairwise comparison between the groups showed a significant difference between those underwent re-resection vs no treatment (p = 0.007) and between those receiving XRT +/- chemotherapy vs no treatment (p=0.04). Pairwise comparison between re-resection and XRT +/- chemotherapy showed no significant difference.
- For DFS, at 2 years, there was a trend when comparing the 3 groups. Pairwise comparison showed significant difference between those undergoing re-resection vs no treatment only. At 5 years, at least one of the groups had worse survival than the rest. Pairwise comparison between the groups showed a significant difference between those undergoing re-resection vs no treatment (p = 0.01) and between those receiving XRT +/- chemotherapy vs no treatment (p=0.04). Pairwise comparison between re-resection and XRT +/- chemotherapy showed no significant difference.
- There was a 3% difference in OS at 5 years between the XRT +/- chemotherapy group and the re-resection group. This is unlikely to be of clinical significance and was not statistically significant. On the contrary, there was a 13% difference in DFS at 5 years between the same groups and while this was not statistically significant, it is might be of clinical significance.
- However, whether XRT +/- chemotherapy is better than re-resection in terms of DFS remains an open question given the small sample size.

Table 1. Baseline Characteristics					
		No Treatment 16	Re-resection 33	XRT +/- Chemotherapy 12	p-value
Age (mean ± SD)		68.9 ± 17.7	62.6 ± 15.2	60.0 ± 12.2	0.26
	Sex	Male 6 (38%)	20 (61%)	7 (58%)	0.30
PNI	Female	10 (62%)	13 (39%)	5 (42%)	
	Present	4 (25%)	3 (9%)	6 (50%)	0.011
LVI	Absent	12 (75%)	30 (91%)	6 (50%)	
	Present	3 (19%)	1 (3%)	4 (33%)	0.021
Pathologic T stage	Absent	13 (81%)	32 (97%)	8 (67%)	
	1	11 (69%)	25 (76%)	6 (50%)	0.26
DOI (mean ± SD)	2	5 (31%)	8 (24%)	6 (50%)	
		4.2 ± 2.3	4.0 ± 2.1	5.0 ± 2.5	0.59

Table 2. Pairwise Comparisons (p-values)				
	2-year OS	5-year OS	2-year DFS	5-year DFS
Re-resection vs XRT	0.51	0.86	0.54	0.64
XRT vs No Treatment	0.45	0.04*	0.26	0.04*
Re-resection vs No Treatment	0.08	0.007*	0.02*	0.01*

CONCLUSIONS

- Further treatment in the form of re-resection or XRT +/- chemotherapy is important to improve overall and disease-free survival of early-stage oral cavity cancer patients with positive margins
- Our study is limited by sample size. Thus, whether XRT +/- chemotherapy is better than re-resection remains an open question. More institutions are needed to improve power and discern results with certainty

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