

Hypopharyngeal Squamous Cell Carcinoma: Outcomes from a Tertiary Care Center

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Introduction

Hypopharyngeal squamous cell carcinoma (SCC) has a poor prognosis approximating 30-35% 5-year overall survival and poor disease specific survival with as many as 50% of patients demonstrating failure at the primary site within one year of treatment. The historic standard of treatment for hypopharyngeal SCC has been surgery, which in the case of locally advanced disease usually entails laryngopharyngectomy.

Despite advancements in surgical techniques and delivery of radiotherapy there has not been a large improvement in the overall survival of patients treated for hypopharyngeal SCC over the last 2-3 decades.

Review of landmark studies such as the VA trial have renewed interest in organ preservation therapies, and specifically in comparing survival outcomes among patients treated with either definitive surgery or definitive chemoradiotherapy. Therefore, we sought to compare outcomes among patients utilizing surgery or organ preservation therapy in the management of hypopharyngeal SCC.

Methods and Materials

After obtaining approval from the IRB, a retrospective review was conducted of all patients who presented to Memorial Sloan Kettering Cancer Center for the management of hypopharyngeal squamous cell carcinoma from 1998 to 2018. Cases were collected from within the patient database using diagnostic codes to identify those patients with neoplasms of the hypopharynx. Patients were included if they had a histologically confirmed diagnosis of squamous cell carcinoma of the hypopharynx who received partial or complete treatment at MSKCC. For those who completed part of their treatment outside the institution, data was only included for patients who had complete outside records that were able to be retrieved.

Patient data, including patient demographics, tumor characteristics utilizing AJCC 7th TNM stage, treatment characteristics, and disease and survival outcomes were collected for each patient. Patients were classified as being treated with primary surgery or radiation therapy based on whichever treatment was administered first.

Data were analyzed using chi-square statistics, Cox regression analyses, and Kaplan Meier curves. Survival duration was calculated starting from date of diagnosis. A p-value <0.05 was considered significant. Analyses were conducted using IBM SPSS v26 software.

Results

Characteristic	RT/CCRT*	RT/CCRT + Salvage Surgery	Primary Surgery
Patients	161	24	53
Age Mean (SD)	65.6 (9.9)	63.8 (9.4)	65.6 (11.9)
T Classification (%)			
T1	20 (12.4%)	1 (4.2%)	4 (7.5%)
T2	58 (36%)	8 (33.3%)	13 (24.5%)
T3	54 (33.5%)	10 (41.7%)	17 (32.1%)
T4	29 (18%)	5 (20.8%)	19 (35.8%)
N Classification (%)			
N0	43 (26.7%)	11 (45.8%)	29 (54.7%)
N1	24 (15%)	4 (16.7%)	3 (5.7%)
N2	85 (52.7%)	8 (33.3%)	20 (37.7%)
N3	9 (5.6%)	1 (4.2%)	1 (1.9%)
M Classification (%)			
M0	161 (100%)	24 (100%)	53 (100%)
M1	0	0	0
Induction chemotherapy	25 (15.5%)	8 (33.3%)	2 (3.8%)
Adjuvant chemotherapy	N/A	2 (8.3%)	9 (17%)
Radiation dose			
Mean (range)	6904 (4500-7400)	6676 (4500-7200)	6040 (4500-7000)
Adjuvant XRT**	N/A	2 (8.3%)	28 (52.8%)
Adjuvant XRT among T3/T4	N/A	2 (8.3%)	22 (41.5%)
Duration follow up	35 months	42 months	30 months
Median (range)	(1-211)	(11-253)	(4-195)

*Radiation therapy without chemotherapy/concurrent chemoradiotherapy

**XRT: radiation therapy

Table 1. Baseline characteristics of the study population.

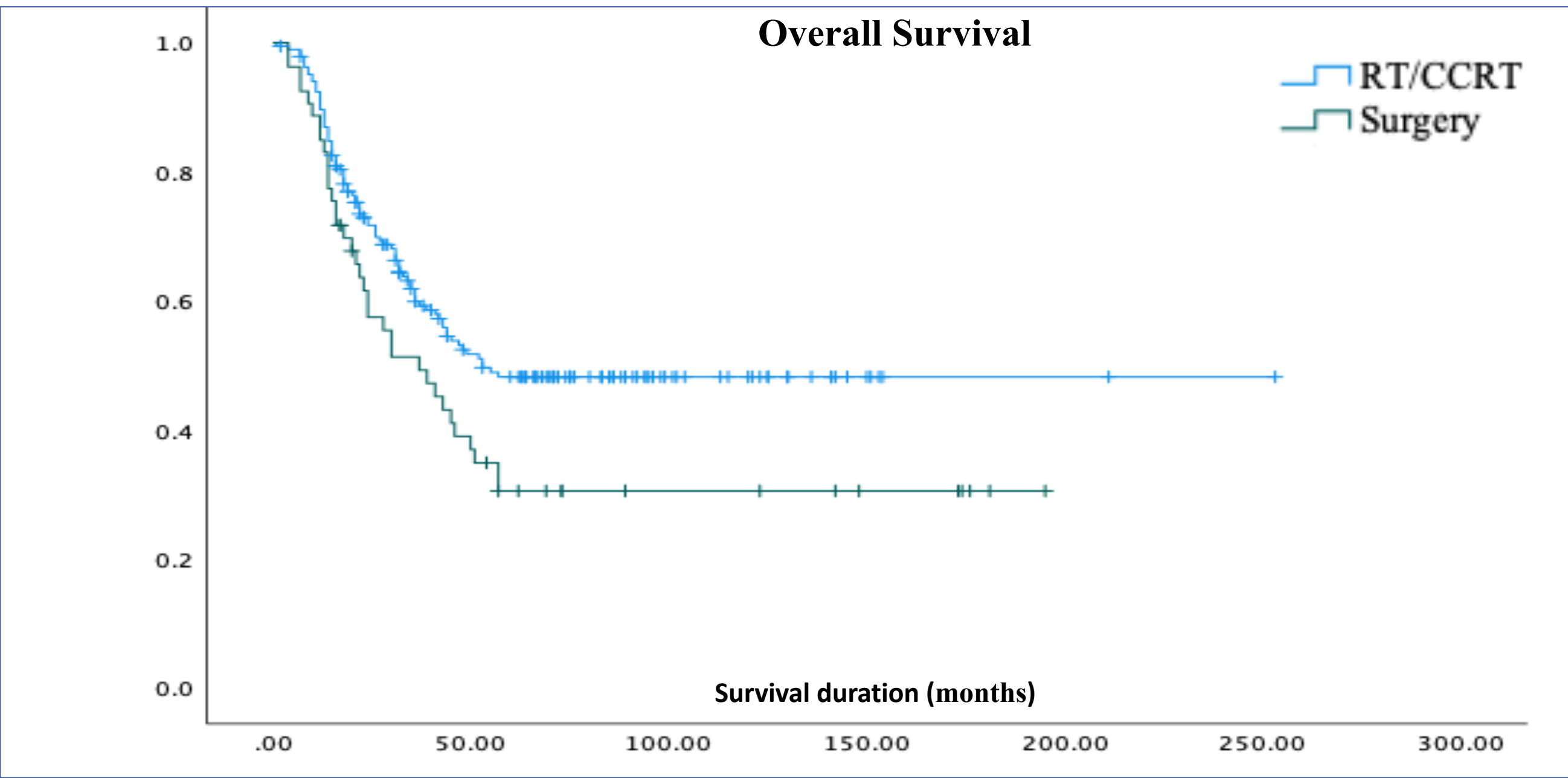


Figure 2. The median overall survival (OS) was 47 months for the total cohort. There was a statistically significant difference in the median OS between those patients who underwent definitive CCRT and those patients who underwent surgical resection (53 months versus 37 months respectively, p=0.026). The median disease specific survival (DSS) was not reached for the total cohort or the definitive chemoradiation group; the median DSS for the surgical therapy group was 51 months (p=0.142) (following figure). The OS and DSS for the definitive chemoradiation therapy group was 53% and 66.5% respectively at 5 years. The 5-year OS and DSS of the primary surgical therapy group was 34% and 56.6%% respectively.

There were no significant differences in local (LR) or regional nodal recurrence (NR) rates between patients in the CCRT and primary surgery groups, (p=0.177, p=0.427, respectively). Among patients with T4 stage disease, there were no differences in survival when undergoing surgery compared to definitive CCRT (OS, p=0.280; DSS, p=0.129). Increasing age, use of adjuvant chemotherapy, and increasing T-stage were all predictors of worse overall survival. Age, use of adjuvant chemotherapy, and increasing T stage were also predictive of worse disease specific survival. Increasing nodal stage was also associated with worse DSS, but not OS. Induction chemotherapy was not significantly predictive of OS or DSS. Lastly, among patients who underwent definitive RT or CCRT, age, T stage, and N3 stage were significant predictors of risk of salvage laryngectomy. Use of induction was not significantly predictive of risk of laryngectomy.

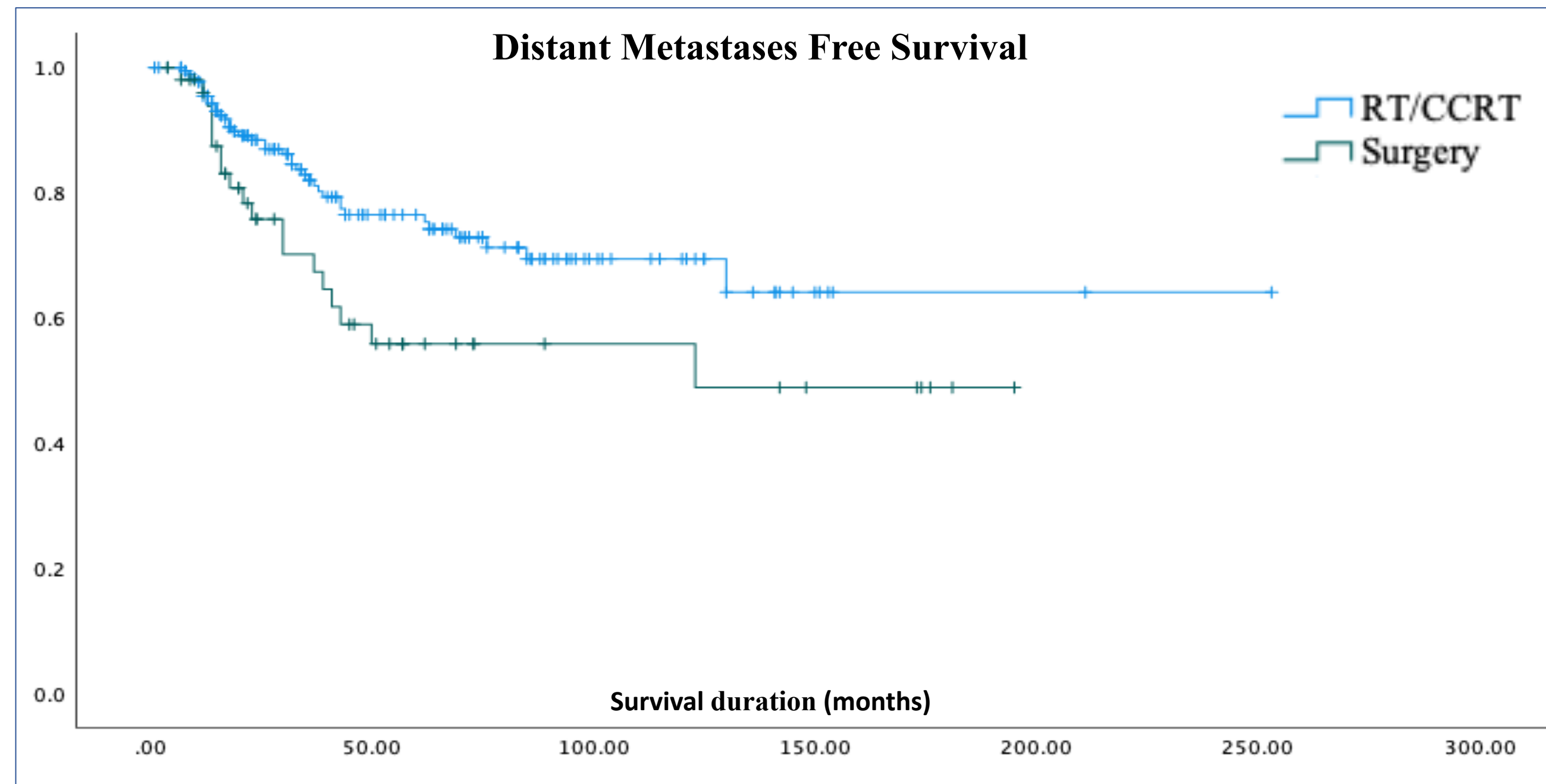
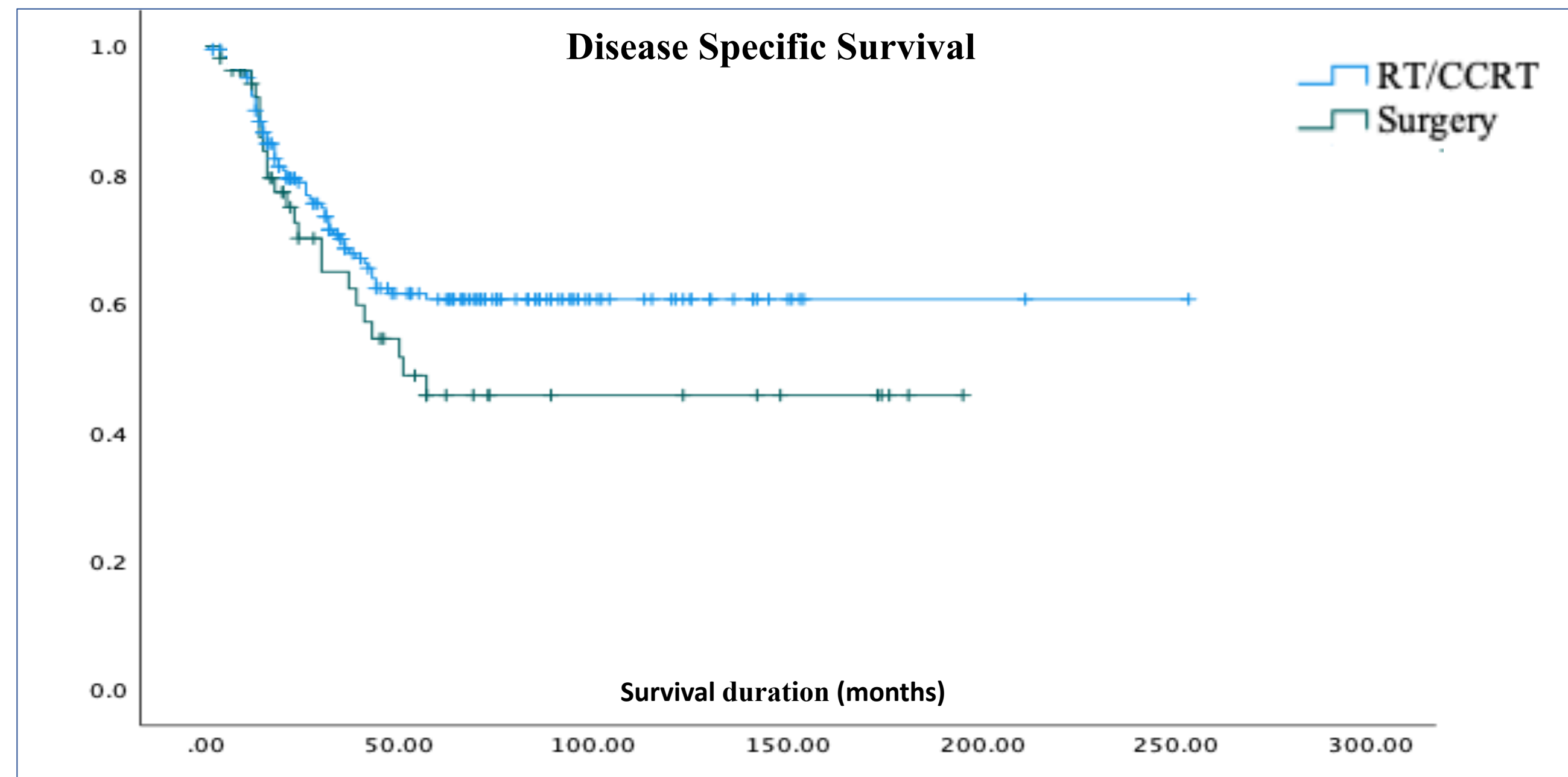


Figure 1. Median distant metastasis free survival (DMFS) was significantly greater in the RT/CCRT group (48 months) compared to the primary surgery group (24 months) (p=0.02)



Discussion

Definitive radiation therapy with or without chemotherapy had significantly improved OS compared to primary surgery; no significant difference in DSS was noted between the two modalities. This may suggest that RT and/or CCRT were better tolerated compared to surgery. Alternatively, this may be secondary to underpowering of the study. There were no significant differences in OS or DSS between treatment modalities based on T stage alone. This was surprising given prior studies reporting better outcomes with surgery in T4 disease and is likely due to the small sample size of our surgical cohort in each T-stage classification.

Treatment with CCRT had improved rates of distant metastases (DM) regardless of T stage or need for salvage surgery. It is likely that the addition of systemic therapy decreased the overall risk of developing DM and that those at highest risk received the greatest benefit. However, we did not find similar improvements in outcomes for patients receiving induction chemotherapy.

Lastly, age and increasing T stage were associated with worse OS and DSS, and N3 stage was associated with worse DSS. This was not surprising as older patients are expected to have lower tolerance of any treatment and increasing T-stage is associated with higher risk of metastases. The use of adjuvant chemotherapy among patients receiving primary or salvage surgery was also associated with significantly worse survival. This is likely related to the fact that only patients with high-risk findings following surgical extirpation were recommended for adjuvant chemotherapy and radiation, thus making it an indicator of high-risk disease.

Limitations of the study include the retrospective design which is subject to biases and missing data. There was also a shift from primary surgery to primary CCRT over the study period, as well as minor changes to the AJCC staging systems used during the study. Finally, we cannot account for confounding factors that may have influenced treatment decisions and recommendations (such as patient comorbidities and concerns regarding side effects).

Conclusion

Use of definitive radiation with or without chemotherapy improved overall survival, but not disease specific survival. The use of chemotherapy appeared to have a protective effect against development of distant metastases, however, use of induction chemotherapy was not associated with an improvement in outcomes. Age and increasing stage at presentation negatively impact survival regardless of treatment modality. Further research with a large patient cohort is needed to elucidate the protective effects of organ preservation therapies on patient outcomes compared to primary surgical resection.