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Timing of Surgery and Adjuvant Radiation Therapy for Sinonasal Malignancies: Effect of Surgical Approach

Roy Xiao, MD, MS¹, Rohan R. Joshi, MD², Qasim Husain, MD¹, Jennifer R. Cracchiolo, MD³, Nancy Lee, MD⁴, Jillian Tsai, MD⁴, Yao Yu, MD⁴, Linda Chen, MD⁴, Jung J. Kang, MD⁴, Sean McBride, MD⁴, Nadeem Riaz, MD, MSc⁴, Benjamin R. Roman, MD, MSHP³, Ian Ganly, MD, PhD³, Viviane Tabar, MD⁵, Stacey T. Gray, MD¹, Marc A. Cohen, MD, MPH³

¹Department of Otolaryngology- Head and Neck Surgery, Massachusetts Eye and Ear Infirmary, Harvard University, Boston, MA, USA

²Department of Otolaryngology- Head and Neck Surgery, Case Western Reserve University, Cleveland, OH, USA

³Department of Head and Neck Surgery, Memorial Sloan Kettering Cancer Center, New York, New York, U.S.A.

⁴Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, New York, U.S.A.

⁵Department of Neurosurgery, Memorial Sloan Kettering Cancer Center, New York, New York, U.S.A.

Abstract

Background.—Timely postoperative radiation therapy (RT) within 50 days of surgery for head and neck cancers provides a survival advantage.

Methods.—Using the NCDB, we performed a propensity score-matched analysis comparing patients undergoing open or endoscopic surgery for squamous cell carcinoma (SCC) of the nasal cavity and paranasal sinuses from 2010–2015.

Results.—Among 168 pairs, patients undergoing endoscopic surgery had shorter time to surgery (24.2 vs. 36.7 days, $p < 0.001$) and shorter postoperative time to RT (PTTR, 51.2 vs. 58.4 days, $p = 0.020$). On multivariable linear regression, endoscopic surgery predicted shorter PTTR ($\beta = -7.6$, $p = 0.013$). Using the Kaplan-Meier method, patients in the longest PTTR quartile had decreased overall survival (Q1 vs. Q4, 3-year OS 76.5% vs. 53.3%, $p = 0.007$), a durable finding when adjusted for covariates (Q1 vs. Q4, HR 0.50, $p = 0.008$).

Corresponding Author: Marc A. Cohen, MD, MPH, Department of Head and Neck Surgery, Memorial Sloan Kettering Cancer Center, 1250 First Avenue, 10th Floor, C-1075, New York, NY 10065, Phone: (212) 639- 3769, cohenm2@mskcc.org.

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Conclusions.—Patients undergoing endoscopic surgery for sinonasal SCC experience shorter PTTR. Shorter PTTR is associated with extended OS.

Keywords

National Cancer Database; overall survival; postoperative time to radiation therapy; sinonasal squamous cell carcinoma; time to surgery

Introduction

Malignant sinonasal tumors constitute 3% of head and neck malignancies.¹ These lesions most commonly arise from the nasal cavity, followed by the maxillary and ethmoid sinuses.² Squamous cell carcinoma (SCC) is the most common histology and carries a poor prognosis with a 5-year overall survival ranging from 30.2% to 59.5%.^{3–6} The traditional surgical management of advanced sinonasal tumors with skull base invasion involves open surgical resection via a craniofacial approach, as it offers excellent access and visualization for optimal complete resection.^{7–10} Open surgery requires a facial incision and for those undergoing craniofacial resection, a craniotomy. Although these techniques are effective and in many cases the only appropriate approach, they are associated with significant rates of wound infections and central nervous system complications.^{9–11} As a result, for the properly selected candidate, an endoscopic approach to sinonasal tumor resection has become an increasingly attractive alternative to open surgery, with the literature demonstrating reduced complications and comparable rates of complete resection.^{12–19}

Recent studies have reported that delays in treatment for head and neck cancers²⁰ are associated with clinical-to-pathologic upstaging and inferior survival.^{21,22} One recent study demonstrated that postoperative time to radiation therapy (RT) of at least 50 days was associated with inferior overall survival.²³ However, within the context of sinonasal cancers, no studies have been performed specifically investigating the timing of postoperative treatment. Furthermore, the relationship between surgical approach and postoperative time to RT (PTTR) has not been studied. In the present study, we sought to assess differences in radiation treatment timing between patients undergoing open surgery and those undergoing endoscopic surgery, as well as associations with treatment timing with long-term survival. We hypothesized that given the decreased time required for postoperative healing and the decreased risk of adverse events following endoscopic surgery, patients undergoing endoscopic approaches experience shorter PTTR. In addition, we hypothesize that shorter PTTR is associated with extended overall survival.

Methods

Data Source

The National Cancer Database (NCDB) is a nationwide clinical oncology database jointly sponsored by the American College of Surgeons and the American Cancer Society. The NCDB contains hospital registry data on malignancies, treatments, and outcomes from more than 1,500 Commission on Cancer-accredited facilities, representing more than 70% of newly diagnosed cancer cases in the United States and including more than 34 million

historical records since 1985.²⁴ The data used in the study are derived from a de-identified NCDB file. The ACS and CoC have not verified and are not responsible for the statistical methodology employed, or the conclusions drawn from these data. Additionally, this study was exempt from institutional approval, as all data analyzed were from the NCDB with no identifying information; accordingly, no written informed consent was required.

Patient Population

For the present study, we searched the NCDB for all patients recorded from 2010 to 2015 with head and neck cancers, and selected tumors originating from the nasal cavity and paranasal sinuses. The following International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) histology codes were used to confirm patients with sinonasal SCC: 8070, 8071, 8072, 8074, 8075, 8083. The following ICD-O-3 topological codes were used to confirm patients with SCC of the nasal cavity and paranasal sinuses: C300, C310, C311. Patients treated without a primary surgical approach or postoperative RT were excluded. Patients treated by non-open, non-endoscopic surgical approaches or unknown surgical approaches were excluded. Patients with unknown clinical staging or distant metastatic disease at diagnosis were excluded. Patients were not excluded on the basis of missing pathologic staging. Patients with missing outcomes, such as length of hospital stay following surgery, unplanned 30-day readmissions, and overall survival (OS) status, were also excluded. Patients were grouped into two cohorts, one treated with open surgery and one treated with endoscopic surgery; a propensity score match was then performed to arrive at two balanced cohorts for analysis.

Study Outcomes and Variable Definitions

The primary outcome of the study was PTTR, measured as days elapsed between surgery and RT. Patients were also grouped based upon PTTR quartile to examine the general effect of PTTR duration rather than smaller day-by-day changes. Sociodemographic, disease, treatment, and follow-up data were extracted for each patient from the NCDB. Patient comorbidity was assessed using the Charlson comorbidity index, reported in the NCDB as the Charlson-Deyo score, with three possible truncated values of 0, 1, or more than 1.^{25,26} Additional time points recorded included time from diagnosis to surgery (TTS), time from diagnosis to RT (TTR), and time from surgery to discharge (LOS). Additional outcomes of interest included unanticipated 30-day readmission and OS using the time from diagnosis to death or last follow-up.

Statistical Analysis

A propensity score match was performed to arrive at two balanced cohorts of patients treated with open or endoscopic surgery. To perform the propensity score match, we created a logistic regression model where the response variable was surgical approach. All variables listed in Table 1 were included in the model. The match was made using the predicted values on the logit scale from the final model using the MatchIt 3.0.2 package.²⁷ Propensity scores within one unit of each other on the logit scale were considered a match, and the ratio of open to endoscopic patients was fixed at 1:1. To measure covariate balance between the two groups, we computed the standardized difference for each variable before and after matching.²⁸ The following formulas were used to calculate standardized differences: $100(X_2$

$-X_1)/[(S_2^2 + S_1^2)/2]^{1/2}$, X_2 and X_1 are sample means in the endoscopic and open groups, respectively, and $S_2^2 + S_1^2$ are the corresponding sample variances for continuous variables; $100(P_2 - P_1)/[(P_2(1 - P_2) + P_1(1 - P_1))/2]^{1/2}$, P_1 and P_2 are the sample proportion in the endoscopic and open groups, respectively, for categorical variables. Standardized differences less than 10.0 in absolute value were considered balanced.²⁸

After establishing the matched cohorts, quantitative outcomes were compared using the Wilcoxon rank-sum test for non-parametric comparisons and qualitative outcomes were compared using Pearson's chi-squared tests. Kaplan-Meier analysis was performed to estimate TTS, LOS, TTR, and PTTR, and log-rank tests were used to compare distributions between patients receiving open surgery and those undergoing endoscopic surgery. Kaplan-Meier analysis was also performed to estimate OS with log-rank tests comparing survival distributions. Multivariable linear regression was used to identify independent predictors of PTTR, and Cox proportional hazards regression was used to identify independent predictors of OS. Backward stepwise regression was used to arrive at the final model, with $p < 0.20$ as the stopping criterion. All values of $p < 0.05$ were considered statistically significant. All data were analyzed using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria)²⁹ and graphs were produced using GraphPad Prism 7.³⁰

Results

Patient Characteristics

A total of 831 patients met inclusion criteria. A Consolidated Standards of Reporting Trials diagram detailing the complete process for establishing our final cohort is shown in Figure 1. Among these patients, 663 underwent open surgery and 168 underwent endoscopic surgery. Prior to the propensity score match, several patient characteristics were unbalanced, with endoscopic patients more often having nasal cavity tumors (59.5% vs. 48.1%, standardized difference 23.02), T1 tumors (20.2% vs. 15.5%, standardized difference 12.30), and N0 disease (89.3% vs. 82.1%, standardized difference 20.68) compared to patients undergoing open surgery (Table 1). Following the propensity score match, we arrived at our final cohorts with 168 patients in each. Nearly all variables were found to be balanced, with only rare characteristics being unbalanced due to small sample size: unknown race, other government insurance, no insurance, treatment at community facilities, and treatment at unknown facilities.

Timing of Patient Treatments and Outcomes

The two matched cohorts were compared to assess for differences in treatment timing associated with surgical approach (Table 2). Patients who underwent endoscopic surgery were found to have significantly shorter median TTS (16.5 [IQR 0.0–38.5] vs. 29.0 [13.3–51.0] days, $p < 0.001$). Following surgery, patients who underwent endoscopic surgery had significantly shorter median LOS (1.0 [0.0–3.0] vs. 3.0 [0.0–7.0] days, $p < 0.001$). Patients who underwent endoscopic surgery had significantly shorter TTR (69.5 [46.3–92.8] vs. 85.0 [62.0–116.0] days, $p < 0.001$), as well as PTTR (46.0 [35.0–61.8] vs. 51.5 [40.0–63.8], $p = 0.010$). No significant difference in 30-day unplanned readmission rate was observed between endoscopic and open surgery (2.4% vs. 3.6%, $p = 0.748$). The Kaplan-Meier method

was also employed to visually compare the distributions of TTS, LOS, TTR, and PTTR as shown in Figure 2.

The results of our multivariable linear regression to model PTTR are reported in Table 3. The lowest median ZIP-code level income was associated with significantly longer PTTR on multivariable regression ($> \$63,000$ vs. $< \$38,000$, $\beta = -12.7$, 95% Confidence Interval [CI] -20.7 to -4.8 , $p=0.002$). Patients treated at comprehensive community centers had significantly shorter PTTR compared to those treated at academic facilities on multivariable regression ($\beta = -10.3$, 95% CI -17.6 to -2.9 , $p=0.006$). Patients with decreased comorbidity load had shorter PTTR (CDCC 1 vs. 0, $\beta = -8.3$, 95% CI -16.5 to -0.2 , $p=0.046$) while more severe comorbidity load had no statistically significant difference in PTTR (CDCC 3 vs. 0, $\beta = 15.1$, 95% CI -0.7 to 30.8 , $p=0.061$) on multivariable regression. Nodal classification had an inconsistent association with PTTR, as cN1 patients had shorter PTTR ($\beta = -10.4$, 95% CI -20.7 to -0.1 , $p=0.021$) but cN2 patients had longer PTTR ($\beta = 10.8$, 95% CI 1.6 to 19.9 , $p=0.016$). Patients who underwent endoscopic surgery had significantly shorter PTTR compared to those who underwent open surgery ($\beta = -3.6$, 95% CI -6.5 to -0.7 , $p=0.016$).

Kaplan-Meier curves estimate OS for all patients and comparing OS distributions between subsets of patients defined by PTTR are reported in Figure 3. 3-year OS for the entire cohort was 68.2%. When patients were subset by PTTR relative to the median PTTR of 49 days, patients with PTTR less than 49 days had significantly extended OS compared to those with PTTR of at least 49 days (74.2% vs. 61.4%, $p=0.043$). When patients were further subset by PTTR quartile, there was no statistically significant difference observed at 3-year OS between the lowest three quartiles (76.5% vs. 72.0% vs. 70.5%). In contrast, the quartile of patients with the longest PTTR of at least 63 days had significantly shorter 3-year OS (53.3%, $p=0.007$).

Cox proportional hazards regression modeling OS adjusting for covariates is reported in Table 4. Increasing T classification was found to be prognostic of inferior OS (HR 2.02, 95% CI 1.20–3.63, $p=0.008$). Finally, shorter PTTR was associated with significantly extended OS; compared to the longest PTTR quartile (Q4, ≥ 63 days), Q3 (49–62 days, HR 0.57, 95% CI 0.33–0.95, $p=0.032$), Q2 (37–48 days, HR 0.51, 95% CI 0.31–0.84, $p=0.007$), and Q1 (< 37 days, HR 0.50, 95% CI 0.29–0.83, $p=0.008$) all predicted extended OS.

Discussion

Given the established link between treatment delays and inferior outcomes for patients with head and neck cancer,^{20–22} it is critical to understand the relationship between surgical approach and timing of treatments. Sometimes open surgical resection is the only approach suitable for a sinonasal tumor; however, when there are options available between an open and endoscopic approach, it is imperative to understand the nuances between approaches with respect to treatment outcomes. In the present study, after performing a propensity-score match to arrive at comparable cohorts of patients with sinonasal tumors, patients who underwent endoscopic surgery were found to have significantly decreased wait times with shorter TTS, total TTR, and PTTR. When modeling PTTR, patients who underwent

endoscopic surgery had postoperative waiting times more than one week shorter than those who underwent open surgery. Additionally, patients who had extended PTTR were found to have the worst OS outcomes with the longest PTTR quartile of at least 63 days achieving only 53.3% 3-year OS. Taken together, these data reveal a possible advantage of endoscopic surgery in the appropriately selected patient, in addition to the potential for reduced complications.^{12–19}

Murphy et al. recently used the NCDB to report increases in time to treatment initiation in recent years across patients with cancer of the oral cavity, oropharynx, larynx, and hypopharynx.²⁰ Additionally, follow-up studies have revealed such delays in treatment to be associated with increased mortality,²¹ with clinical-to-pathologic upstaging likely functioning as the underlying mechanism with increasing delays.²² When examining PTTR using the NCDB, one recent study showed that patients with head and neck cancers waiting at least 50 days for postoperative RT experienced significantly inferior OS.²³ Another recent study by Tumati et al. assessed relationships between treatment delays and adverse cancer outcomes like locoregional recurrence and distant metastases.³¹ Time from biopsy to surgery greater than 50 days was associated with increased distant metastases, while time to radiation therapy greater than 43 days was associated with locoregional recurrence. While no prior studies have specifically investigated patterns of delay in treating sinonasal cancers, it follows that treatment delays are suboptimal and best avoided if possible.^{32–34}

The use of propensity-score matching in this study ensured comparable cohorts of patients treated with either open or endoscopic surgery. After establishing these cohorts, endoscopic patients experienced significantly shorter wait times for treatments, both following diagnosis awaiting surgery and following surgery awaiting adjuvant RT. While not the focus of the present study, the greatest difference in wait time was observed for time to surgery. Patients undergoing open surgery had wait times more than 50% longer than those undergoing endoscopic surgery (36.7 vs. 24.2 days), perhaps suggesting faster preoperative preparation for endoscopic cases. More notably, and as hypothesized, endoscopic patients waited approximately one week less than open patients following surgery for adjuvant RT. Of note, delays in both TTS and PTTR for patients undergoing open surgery resulted in a nearly 20-day delay in total TTR compared to those undergoing endoscopic surgery.

Using multivariable linear regression the endoscopic approach continued to significantly predict shorter PTTR by more than three days. Overall patient complexity, approximated by the CDCC measure of comorbidity status, had an inconsistent relationship with PTTR, as CDCC score of 1 had decreased PTTR, while CDCC greater than 1 had no statistically significant association with PTRR; however, given the likely increased risk of adverse events following surgery as well as delayed healing among patients with greater comorbidity load, it follows that the most ill patients are also the most challenging to optimally manage and can result in delayed adjuvant treatment. Furthermore, patients from the lowest median household income level (<\$38,000) consistently had significantly longer PTTR than all other income levels by nearly two weeks. Additionally, certain treatment settings had an association with PTTR with comprehensive community centers having the shortest PTTR compared to academic centers. These findings identifying access to care, income, comorbidity and treatment facilities as potential predictors of PTTR are consistent with

findings by prior studies and warrant further investigation.^{35,36} Of note, sex, race, ethnicity, and insurance status were not associated with PTTR. While there is no method to confirm our hypothesized causative path with endoscopic surgery requiring shorter postoperative healing permitting shorter PTTR, this model demonstrates that endoscopic surgery is a significant factor contributing to shorter PTTR as the only significant variable after adjusting for covariates.

Finally, the relationship between PTTR and OS was assessed using both the Kaplan-Meier method and Cox proportional hazards regression. When the entire cohort of patients was subset by PTTR, longer PTTR was significantly associated with inferior OS. Patients were first subset relative to median PTTR, revealing significantly longer OS for patients with PTTR less than 49 days. When further subset analysis is performed by PTTR quartile, the benefit of earlier treatment becomes less clear. The fourth quartile, with PTTR of at least 63 days, had a significantly lower 3-year OS of 53.3% compared to those with PTTR less than 63 days. Taken together, this relationship between extended PTTR and inferior OS along with the association between endoscopic surgery and decreased PTTR further demonstrate the advantages of endoscopic surgery for sinonasal cancers in the appropriately selected patient.

There are several limitations within the present study that must be considered when interpreting the data. Like all registries, the NCBDB inherently carries the potential for selection, information, and recall bias, as well as unmeasured confounding factors. While we used strict inclusion criteria to produce the final cohort for our analyses in order to minimize bias, the generalizability of our findings is uncertain; further analyses using additional population-based data sets or prospective studies could be instrumental in validating our results. In addition, while matched pairs were used for our cohorts, care should be taken in comparisons between groups. For example, advanced T4 tumors are more likely to be represented in the open cohort, as these lesions are less amenable to an endoscopic approach. Similarly, endoscopic surgery is more likely to be performed at specialized tertiary centers which could contribute to differences in treatment timing. Despite the size of the NCBDB, power was limited in this analysis due to the small sample of patients undergoing surgery and postoperative RT with complete data. Additionally, the NCBDB is limited to only 30-day readmission as a short-term outcome and OS as an endpoint, which precludes further understanding of cancer-specific outcomes. Furthermore, while we found a longer time to both surgery and radiation for the open group, there may be a subtle difference in comorbidities not adequately accounted for using the evenly matched CDCC in our matched groups. This is an inherent flaw in database analysis and should be kept in mind with interpretation of the data. Finally, although a single research hypothesis was tested in the present investigation, multiple comparisons were made to examine this hypothesis and perform additional secondary testing, significantly increasing the potential for false discovery.

Conclusion

Patients undergoing surgical resection for sinonasal squamous cell carcinoma experience significantly decreased delays in treatment when undergoing endoscopic surgery compared

to those who undergo open surgery. Both time from diagnosis to surgery and time from surgery to adjuvant radiation therapy are significantly shorter for patients undergoing endoscopic surgery. While the exact time point needed to start radiation therapy after surgery is unclear, postoperative time to radiation therapy is a potentially modifiable risk factor associated with overall survival. In addition to shorter healing times and reduced adverse events, endoscopic surgery for sinonasal tumors, in the appropriately selected patient, offers the additional benefit of significantly reduced wait times that may ultimately extend overall survival.

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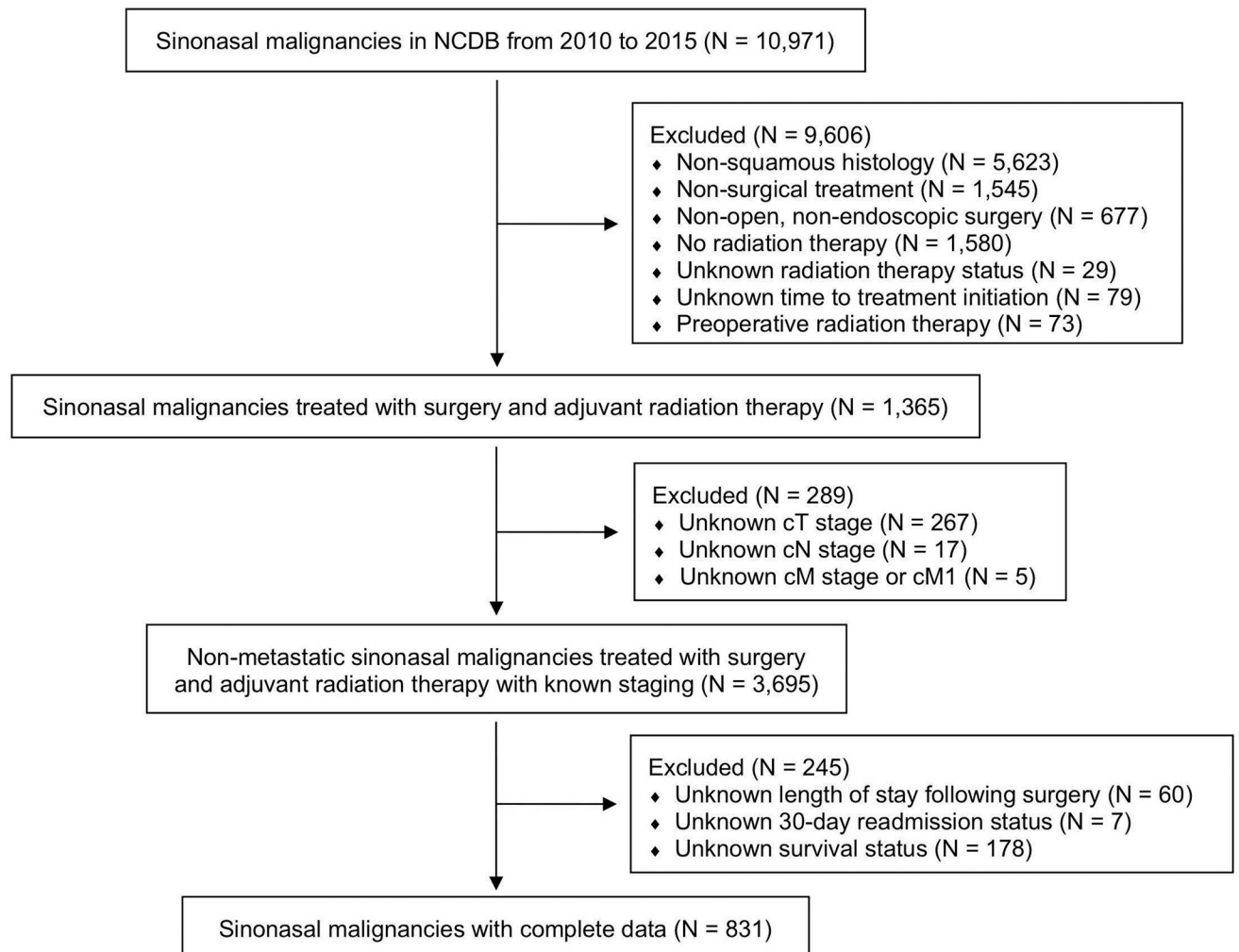


Figure 1. Consolidated Standards of Reporting Trials Diagram Detailing the Study Inclusion Criteria

NCDB, National Cancer Database; N, number; cT, tumor classification; cN, node classification; cM, metastasis classification; cM1, positive metastasis classification

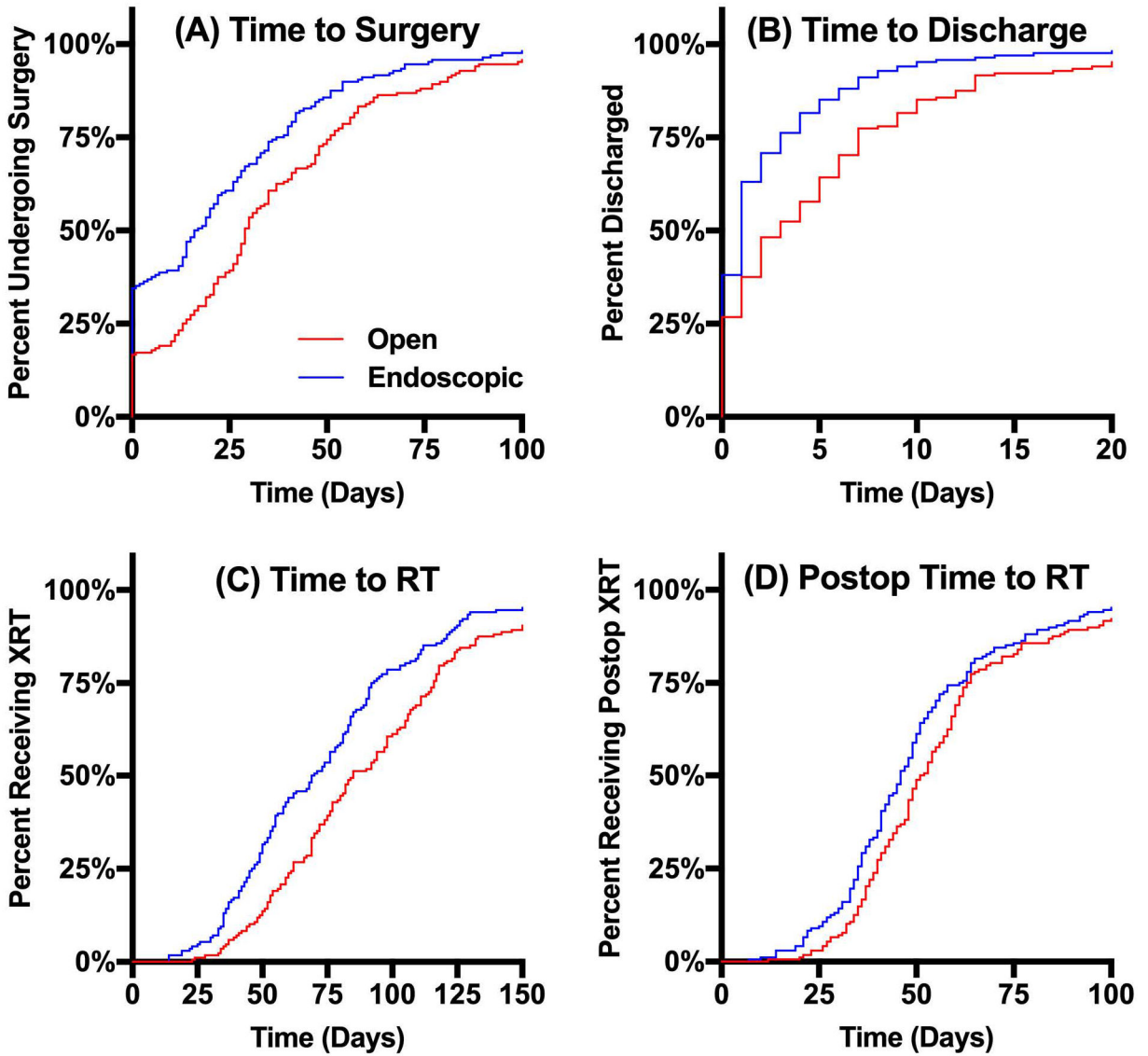


Figure 2. Kaplan-Meier Curves Estimating Times to Events

Kaplan-Meier estimates of time to events subset by surgical approach. (A) Median time to surgery did not have a statistically significant association between endoscopic surgery and open surgery (16.5 vs. 29.0 days, $p < 0.001$). (B-D) Median time to discharge (1.0 vs. 3.0 days, $p < 0.001$), median time to RT (69.5 vs. 85.0 days, $p < 0.001$), and median postoperative time to RT (46.0 vs. 51.5 days, $p = 0.010$) were all significantly shorter for patients undergoing endoscopic surgery compared to those undergoing open surgery.

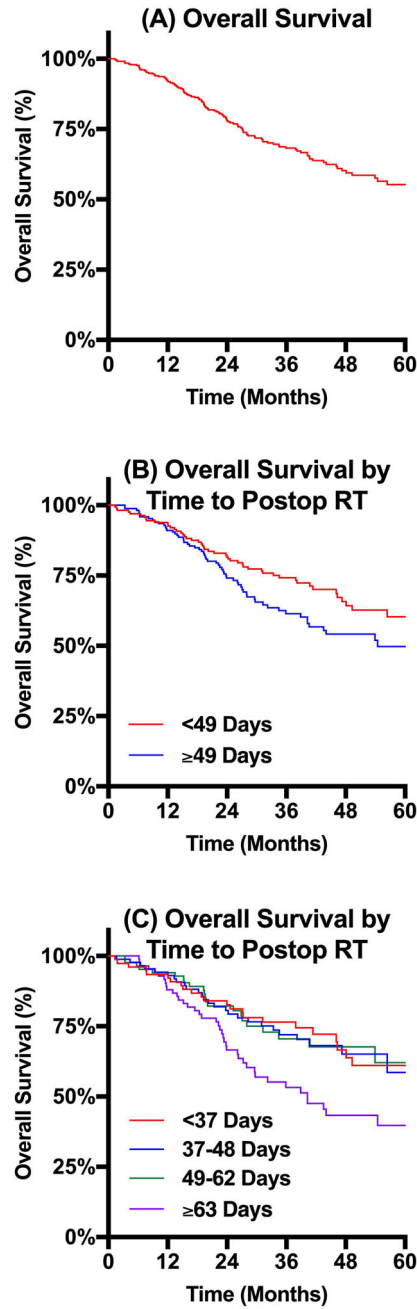


Figure 3. Kaplan-Meier Curves Estimating Overall Survival
 Kaplan-Meier estimates of overall survival. (A) Overall survival for the complete cohort had a 68.2% 3-year OS. (B) Overall survival subset by postoperative time to RT relative to the median (49 days) revealed significantly longer survival for patients waiting less than the median compared to those waiting at least the median (3-year OS 74.2% vs. 61.4%, $p=0.043$). Overall survival subset by quartile of postoperative time to RT revealed no significant differences in OS between the first three quartiles (3-year OS 76.5% vs. 72.0%

vs. 70.5%), but significantly shortened OS for the quartile with the longest wait (3-year OS 53.3%, $p=0.007$).

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Table 1.

Summary Patient Characteristics

Characteristic	All Patients			Matched Patients		
	Open	Endoscopic	Std Diff [†]	Open	Endoscopic	Std Diff [†]
N	663	168		168	168	
Age (Years)	62.7±12.4	62.7±12.8	0.00	63.3±11.5	62.7±12.8	-4.93
Sex						
Male	434 (65.5%)	105 (62.5%)	-6.25	111 (66.1%)	105 (62.5%)	-7.52
Female	229 (34.5%)	63 (37.5%)	6.25	57 (33.9%)	63 (37.5%)	7.52
Race						
White	557 (84.0%)	142 (84.5%)	1.37	144 (85.7%)	142 (84.5%)	-3.37
Black	73 (11.0%)	22 (13.1%)	6.45	21 (12.5%)	22 (13.1%)	1.80
Other	31 (4.7%)	3 (1.8%)	-16.41	3 (1.8%)	3 (1.8%)	0.00
Unknown	2 (0.3%)	1 (0.6%)	4.48	0 (0.0%)	1 (0.6%)	10.99
Hispanic Ethnicity						
Non-Hispanic	608 (91.7%)	157 (93.5%)	6.88	159 (94.6%)	157 (93.5%)	-4.65
Hispanic	40 (6.0%)	8 (4.8%)	-5.31	6 (3.6%)	8 (4.8%)	5.99
Unknown	15 (2.3%)	3 (1.8%)	-3.53	3 (1.8%)	3 (1.8%)	0.00
Insurance Status						
Private Insurance	260 (39.2%)	67 (39.9%)	1.43	70 (41.7%)	67 (39.9%)	-3.66
Medicare	288 (43.4%)	78 (46.4%)	6.03	79 (47.0%)	78 (46.4%)	-1.20
Medicaid	67 (10.1%)	16 (9.5%)	-2.02	18 (10.7%)	16 (9.5%)	-3.98
Other Government	13 (2.0%)	3 (1.8%)	-1.46	1 (0.6%)	3 (1.8%)	11.04
Uninsured	29 (4.4%)	4 (2.4%)	-11.05	0 (0.0%)	4 (2.4%)	22.18
Unknown	6 (0.9%)	0 (0.0%)	-13.48	0 (0.0%)	0 (0.0%)	0.00
ZIP-Code Level Income (\$)						
< 38,000	149 (22.5%)	29 (17.3%)	-13.05	24 (14.3%)	29 (17.3%)	8.23
38,000–47,999	149 (22.5%)	43 (25.6%)	7.26	47 (28.0%)	43 (25.6%)	-5.42
48,000–62,999	180 (27.1%)	50 (29.8%)	5.99	46 (27.4%)	50 (29.8%)	5.31
63,000	183 (27.6%)	45 (26.8%)	-1.80	49 (29.2%)	45 (26.8%)	-5.35
Unknown	2 (0.3%)	1 (0.6%)	4.48	2 (1.2%)	1 (0.6%)	-6.36
CDCC						
0	480 (72.4%)	127 (75.6%)	7.30	128 (76.2%)	127 (75.6%)	-1.40
1	148 (22.3%)	28 (16.7%)	-14.17	25 (14.9%)	28 (16.7%)	4.94
2	27 (4.1%)	9 (5.4%)	6.11	12 (7.1%)	9 (5.4%)	-7.03
3	8 (1.2%)	4 (2.4%)	9.04	3 (1.8%)	4 (2.4%)	4.19
Facility Type						
Academic/Research	442 (66.7%)	99 (58.9%)	-16.19	100 (59.5%)	99 (58.9%)	-1.22
Comprehensive Community	109 (16.4%)	44 (26.2%)	24.11	48 (28.6%)	44 (26.2%)	-5.38
Community	19 (2.9%)	9 (5.4%)	12.56	4 (2.4%)	9 (5.4%)	15.54
Integrated Network	71 (10.7%)	11 (6.5%)	-15.02	14 (8.3%)	11 (6.5%)	-6.88
Unknown	22 (3.3%)	5 (3.0%)	-1.72	2 (1.2%)	5 (3.0%)	12.58

Characteristic	All Patients			Matched Patients		
	Open	Endoscopic	Std Diff [†]	Open	Endoscopic	Std Diff [†]
Transition Between Facilities for Treatment						
No	231 (34.8%)	71 (42.3%)	15.46	77 (45.8%)	71 (42.3%)	-7.05
Yes	432 (65.2%)	97 (57.7%)	-15.46	91 (54.2%)	97 (57.7%)	7.05
Cancer Primary Site						
Sinuses	344 (51.9%)	68 (40.5%)	-23.02	70 (41.7%)	68 (40.5%)	-2.44
Nasal Cavity	319 (48.1%)	100 (59.5%)	23.02	98 (58.3%)	100 (59.5%)	2.44
Clinical T Classification						
1	103 (15.5%)	34 (20.2%)	12.30	33 (19.6%)	34 (20.2%)	1.50
2	115 (17.3%)	28 (16.7%)	-1.60	23 (13.7%)	28 (16.7%)	8.36
3	144 (21.7%)	35 (20.8%)	-2.20	34 (20.2%)	35 (20.8%)	1.49
4	301 (45.4%)	71 (42.3%)	-6.25	78 (46.4%)	71 (42.3%)	-8.26
Clinical N Classification						
0	544 (82.1%)	150 (89.3%)	20.68	149 (88.7%)	150 (89.3%)	1.92
1	52 (7.8%)	6 (3.6%)	-18.19	9 (5.4%)	6 (3.6%)	-8.69
2	67 (10.1%)	12 (7.1%)	-10.72	10 (6.0%)	12 (7.1%)	4.45

Values are presented as mean ± standard deviation or number (%).

Abbreviations: N, Number; ZIP, Zone Improvement Plan; CDCC, Charlson/Deyo Comorbidity Condition; T, Tumor; N, Node.

[†]Standardized difference = $100(X_2 - X_1) / [(S_2^2 + S_1^2) / 2]^{1/2}$, X_2 and X_1 are sample means in the endoscopic and open groups, respectively, and $S_2^2 + S_1^2$ are the corresponding sample variances for continuous variables. Standardized difference = $100(P_2 - P_1) / [(P_2(1 - P_2) + P_1(1 - P_1)) / 2]^{1/2}$, P_2 and P_1 are the sample proportion in the endoscopic and open groups, respectively, for categorical variables. Standardized differences less than 10 in absolute value are considered to be balanced.

Table 2.

Treatment Timing and Outcomes

Characteristic	Open	Endoscopic	<i>p</i> -value
Time from Diagnosis to Surgery (days)	29.0 [13.3–51.0]	16.5 [0.0–38.5]	<0.001*
Time from Surgery to Discharge (days)	3.0 [0.0–7.0]	1.0 [0.0–3.0]	<0.001*
Time from Diagnosis to RT (days)	85.0 [62.0–116.0]	69.5 [46.3–92.8]	<0.001*
Time from Surgery to RT (days)	51.5 [40.0–63.8]	46.0 [35.0–61.8]	0.010*
30-Day Unplanned Readmission	6 (3.6%)	4 (2.4%)	0.748

Values are presented as median [interquartile range] or number (%). *P*-values calculated using the Wilcoxon rank-sum test or Pearson's chi-squared test comparing characteristics between groups.

Abbreviations: RT, Radiation Therapy.

* Statistically significant: *p* 0.05

Table 3.

Multivariable Linear Regression Model Predicting Postoperative Time to RT:

Characteristic	Univariable		Multivariable	
	β (95% CI)	<i>p</i> -value	β (95% CI)	<i>p</i> -value
Age	0.2 (−0.1 to 0.4)	0.151	0.2 (−0.1 to 0.5)	0.101
Sex				
Male	[ref]		-	-
Female	1.0 (−2.1 to 4.2)	0.529	-	-
Race				
White	[ref]		-	-
Black	8.1 (−8.2 to 24.3)	0.330	-	-
Other	−4.2 (−26.2 to 17.8)	0.708	-	-
Unknown	−3.9 (−45.9 to 38.1)	0.857	-	-
Hispanic Ethnicity				
Non-Hispanic	[ref]		-	-
Hispanic	0.7 (−11.8 to 13.2)	0.911	-	-
Unknown	6.2 (−9.7 to 22.1)	0.445	-	-
Insurance Status				
Private Insurance	[ref]		-	-
Medicare	5.2 (−3.6 to 14.1)	0.246	-	-
Medicaid	4.8 (−5.2 to 15.8)	0.395	-	-
Other Government	2.2 (−20.9 to 25.2)	0.854	-	-
Uninsured	−16.3 (−39.4 to 6.7)	0.164	-	-
ZIP-Code Level Income (\$)				
< 38,000	[ref]		[ref]	
38,000–47,999	−12.6 (−20.7 to −4.6)	0.002*	−12.4 (−20.4 to −4.3)	0.003*
48,000–62,999	−13.4 (−21.4 to −5.5)	0.001*	−13.4 (−21.4 to −5.4)	0.001*
63,000	−13.8 (−21.8 to −5.8)	<0.001*	−12.7 (−20.7 to −4.8)	0.002*
Unknown	54.0 (28.8 to 79.2)	<0.001*	52.9 (27.6 to 78.1)	<0.001*
CDCC				
0	[ref]		[ref]	
1	−6.9 (−15.2 to 1.5)	0.107	−8.3 (−16.5 to −0.2)	0.046*
2	−0.6 (−11.3 to 10.1)	0.910	−1.4 (−12.0 to 9.1)	0.788
3	11.5 (−4.6 to 27.7)	0.161	15.1 (−0.7 to 30.8)	0.061
Facility Type				
Academic/Research	[ref]		[ref]	
Comprehensive Community	−7.8 (−15.1 to −0.5)	0.037*	−10.3 (−17.6 to −2.9)	0.006*
Community	9.7 (−3.5 to 22.9)	0.149	7.4 (−5.8 to 20.6)	0.270
Integrated Network	6.0 (−4.3 to 16.3)	0.253	4.9 (−5.4 to 15.2)	0.351
Unknown	−5.7 (−22.8 to 11.4)	0.514	−0.1 (−18.1 to 17.8)	0.987
Transition Between Facilities for Treatment				

Characteristic	Univariable		Multivariable	
	β (95% CI)	<i>p</i> -value	β (95% CI)	<i>p</i> -value
No	[ref]		-	-
Yes	0.8 (-2.3 to 3.8)	0.623	-	-
Cancer Primary Site				
Sinuses	[ref]		-	-
Nasal Cavity	-2.2 (-5.3 to 0.8)	0.153	-	-
Clinical T Classification				
1	[ref]		-	-
2	-2.1 (-8.5 to 4.3)	0.523	-	-
3	1.3 (-4.5 to 7.0)	0.668	-	-
4	3.0 (-1.6 to 7.6)	0.196	-	-
Clinical N Classification				
0	[ref]		[ref]	
1	-8.1 (-18.5 to 2.2)	0.124	-10.4 (-20.7 to -0.1)	0.021*
2	8.5 (-0.8 to 17.7)	0.072	10.8 (1.6 to 19.9)	0.016*
Surgical Approach				
Open	[ref]		[ref]	
Endoscopic	-3.6 (-6.6 to -0.6)	0.020*	-3.6 (-6.5 to -0.7)	0.016*

β , Beta Coefficient; ZIP, Zone Improvement Plan; CDCC, Charlson/Deyo Comorbidity Condition

* Statistically significant: *p* 0.05.

Table 4.

Cox Proportional Hazards Regression Model Predicting Overall Survival:

Characteristic	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.01 (0.99–1.03)	0.204	-	-
Sex				
Male	[ref]		-	-
Female	0.81 (0.54–1.18)	0.277	-	-
Race				
White	[ref]		-	-
Black	1.13 (0.64–1.86)	0.656	-	-
Other	1.25 (0.21–3.97)	0.759	-	-
Hispanic Ethnicity				
Non-Hispanic	[ref]		-	-
Hispanic	1.31 (0.51–2.74)	0.538	-	-
Unknown	1.04 (0.17–3.29)	0.953	-	-
Insurance Status				
Private Insurance	[ref]		-	-
Medicare	1.22 (0.82–1.82)	0.325	-	-
Medicaid	0.89 (0.43–1.84)	0.754	-	-
Other Government	0.83 (0.11–6.06)	0.852	-	-
Uninsured	0.59 (0.08–4.27)	0.566	-	-
ZIP-Code Level Income (\$)				
< 38,000	[ref]		-	-
38,000–47,999	0.88 (0.48–1.62)	0.690	-	-
48,000–62,999	1.05 (0.59–1.88)	0.867	-	-
63,000	1.10 (0.61–1.99)	0.745	-	-
Unknown	2.12 (0.49–9.17)	0.363	-	-
CDCC				
0	[ref]		-	-
1	1.01 (0.58–1.65)	0.984	-	-
2	1.40 (0.65–2.64)	0.360	-	-
3	2.33 (0.71–5.60)	0.144	-	-
Facility Type				
Academic/Research	[ref]		-	-
Comprehensive Community	0.75 (0.48–1.17)	0.197	-	-
Community	1.55 (0.62–3.83)	0.377	-	-
Integrated Network	0.61 (0.27–1.41)	0.220	-	-
Unknown	0.27 (0.04–1.93)	0.098	-	-
Transition Between Facilities for Treatment				
No	[ref]		-	-
Yes	0.88 (0.61–1.28)	0.509	-	-

Characteristic	Univariable		Multivariable	
	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
Cancer Primary Site				
Sinuses	[ref]		-	-
Nasal Cavity	0.82 (0.56–1.19)	0.283	-	-
Clinical T Classification				
1	[ref]		[ref]	
2	1.02 (0.48–2.13)	0.948	1.04 (0.49–2.16)	0.926
3	1.39 (0.72–2.72)	0.323	1.33 (0.69–2.61)	0.394
4	2.09 (1.24–3.75)	0.005*	2.02 (1.20–3.63)	0.008*
Clinical N Classification				
0	[ref]		-	-
1	1.26 (0.44–2.79)	0.626	-	-
2	1.39 (0.65–2.60)	0.369	-	-
Surgical Approach				
Open	[ref]		[ref]	
Endoscopic	1.33 (0.92–1.94)	0.133	1.41 (0.96–2.08)	0.079
Time from Diagnosis to Surgery (days)	1.00 (0.99–1.00)	0.575	-	-
Time from Surgery to Discharge (days)	1.00 (0.98–1.01)	0.907	-	-
Time from Surgery to RT (days)	1.01 (1.00–1.02)	<0.001*	-	-
Q4 (> 63 days)				
Q4 (> 63 days)	[ref]		[ref]	
Q3 (49–62 days)	0.51 (0.30–0.85)	0.010*	0.57 (0.33–0.95)	0.032*
Q2 (37–48 days)	0.53 (0.32–0.86)	0.010*	0.51 (0.31–0.84)	0.007*
Q1 (<37 days)	0.49 (0.29–0.81)	0.006*	0.50 (0.29–0.83)	0.008*
Margins				
Negative	[ref]		-	-
Positive	1.50 (0.98–2.28)	0.059	-	-
Unknown	1.15 (0.69–1.86)	0.579	-	-
30-Day Unplanned Readmission				
No	[ref]		-	-
Yes	0.69 (0.17–1.84)	0.504	-	-

β, Beta Coefficient; ZIP, Zone Improvement Plan; CDCC, Charlson/Deyo Comorbidity Condition

* Statistically significant: *p* 0.05.