Sex-based differences in sinonasal cancer outcomes

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Introduction

Sinonasal cancers (SNC) are rare, histologically heterogeneous malignancies of the nasal cavity and paranasal sinuses. Prior studies evaluating sex as a prognostic factor have mixed findings and are often limited by single-institution cohorts or older registry eras, reducing generalizability (1–3); international and subtype-specific analyses likewise show mixed results and suggest that histology, grade, and stage may drive observed differences (4–6). Although contemporary population datasets expand coverage and capture care-delivery metrics, sex is not consistently analyzed as an independent covariate, and access-to-care mediators remain underexplored (7). To our knowledge, the largest study to date includes 10,518 NCDB cases from 2004–2013 (8). Accordingly, a modern, comprehensive assessment is needed to determine whether sex-specific differences in SNC exist in current U.S. practice and to what extent they reflect stage, histology, treatment selection, and treatment timelines rather than intrinsic effects of sex.

Methods

A retrospective analysis of deidentified National Cancer Database (NCDB) data included 36,777 patients with sinonasal cancer diagnosed from 2004–2022. The NCDB, drawn from Commission on Cancer (CoC)-accredited hospitals, captures 73.7% of incident United States cancers annually. All statistical analyses were performed in R. Overall survival was estimated with Kaplan–Meier analysis. Univariable and multivariable Cox proportional hazards models were used to assess independent predictors of survival, focusing on sex-specific variations. Between-sex differences in covariates were tested with chi-square and Mann–Whitney U tests; treatment comparisons used Fisher's exact or chi-square tests as appropriate.

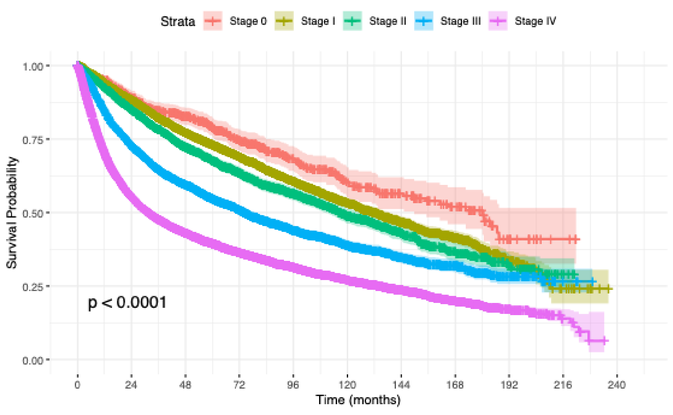

Figure 3. Nasal cancer survival, stratified by stage at diagnosis.

Results

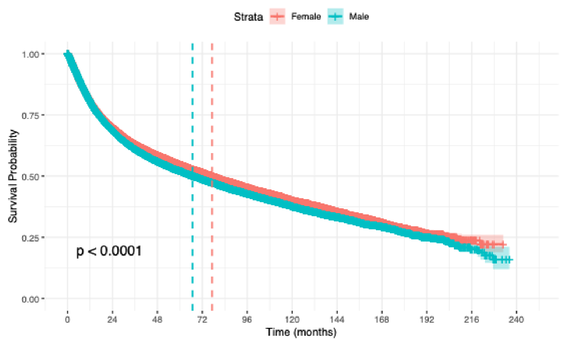

Figure 1. Nasal cancer survival, stratified by sex. Median survival length (months) is marked by vertical dotted lines.

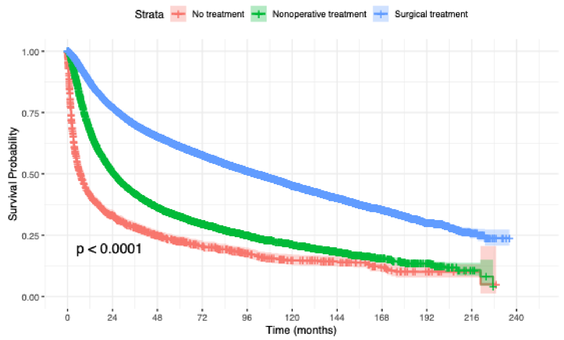

Figure 2. Nasal cancer survival, stratified by treatment modality.

Table 1. Biomedical and socioeconomic differences in survival predictors, stratified by sex.

Confounder	No. - Male	No. - Female	p
Sex	21,989 (59.8%)	14,794 (40.2%)	
Median age ± sd, years	63 ± 14.3	65 ± 15.5	< 0.001
Race			< 0.001
White	18472 (84%)	12082 (81.7%)	
Black	2142 (9.7%)	1691 (11.4%)	
Asian/Pacific Islander	758 (3.4%)	580 (3.9%)	
Other	330 (1.5%)	239 (1.6%)	
Insurance status			< 0.001
Medicare	9456 (43%)	7167 (48.4%)	
Private	8624 (39.2%)	5514 (37.3%)	
Medicaid	1888 (8.6%)	1178 (8%)	
Not insured	866 (3.9%)	432 (2.4%)	
Income quartile			0.008
First	3460 (15.7%)	2184 (14.8%)	
Second	4503 (20.5%)	3039 (20.5%)	
Third	5166 (23.5%)	3493 23.6%)	
Fourth	6105 (27.8%)	4257 (28.8%)	
Facility type			< 0.001
Academic/Research Program	11820 (53.8%)	7685 (51.9%)	
Community Cancer Program	851 (3.9%)	528 (3.6%)	
Comprehensive Community Cancer Program	4759 (21.6%)	3417 (23.1%)	
Integrated Network Cancer Program	3087 (14%)	2097 (14.2%)	
Median year of diagnosis ± sd	2014 ± 5.4	2014 ± 5.4	0.038
Primary Site			< 0.001
C30.0 Nasal cavity	11418 (51.9%)	7728 (52.2%)	
C30.1 Middle ear	357 (1.6%)	353 (2.4%)	
C31.0 Maxillary sinus	6141 (27.9%)	3895 (26.3%)	
C31.1 Ethmoid sinus	1871 (8.5%)	1273 (8.6%)	
C31.2 Frontal sinus	246 (1.1%)	134 (0.9%)	
C31.3 Sphenoid sinus	569 (2.6%)	482 (3.3%)	
C31.8 Overlapping accessory sinuses	345 (1.6%)	255 (1.7%)	
C31.9 Accessory sinus, NOS	1042 (4.7%)	674 (4.6%)	
Median time to treatment ± sd, days	25 ± 36.3	24 ± 38.7	< 0.001
Stage			0.063
0	456 (2.1%)	257 (1.7%)	
I	3058 (13.9%)	1936 (13.1%)	
II	1649 (7.5%)	1046 (7.1%)	
III	2431 (11.1%)	1652 (11.2%)	
IV	7438 (33.8%)	4440 (30%)	
Grade			< 0.001
Well differentiated	1953 (8.9%)	1450 (9.8%)	
Moderately differentiated	5233 (23.8%)	3043 (20.6%)	
Poorly differentiated	5356 (24.4%)	3169 (21.4%)	
Undifferentiated	1414 (6.4%)	837 (5.7%)	
Charlson - Deyo Score			< 0.001
0	17223 (78.3%)	11792 (79.7%)	
1	3209 (14.6%)	2086 (14.1%)	
2	929 (4.2%)	593 (4%)	
3	628 (2.9%)	323 (2.2%)	
Surgical Treatment, % received	15827 (72%)	10688 (72.2%)	0.308
Radiation Treatment, % received	13195 (60%)	8435 (57%)	< 0.001
Chemotherapy Treatment, % received	7655 (34.8%)	4265 (28.8%)	< 0.001

Cohort and broad survival trends

Sinonasal cancer was identified in 36,777 patients; 40.2% (n = 14,794) were female. In a univariate cox proportional hazards model, men had worse overall survival than women (Hazard Ratio (HR) = 1.07, p = 1.1e-05). Notably, the estimated median overall survival time was 10.4 months longer in women than in men (77.2 vs. 66.8 months).

This gendered survival difference was robust to adjustment in a multivariable cox proportional hazards model which adjusted for confounders such as facility type, facility location, age, race, insurance status, income, Charlson-Deyo score, year of diagnosis, primary site, histology, T/N/M scores, stage, grade, delay from diagnosis to treatment, and receipt of surgical, radiotherapy, or chemotherapy treatment (HR = 1.14, p = 7.21e-09). Stage at diagnosis was the strongest predictor of outcomes in the multivariable setting (HR = 2.63, p = 7.65e-11). Surgery was associated with better survival vs. nonsurgical care (HR = 0.54, p < 2e-16), as was receipt of radiotherapy vs. none (HR = 0.70, p < 2e-16); chemotherapy was not associated with a change in survival (HR = 0.94, p = 0.052).

Sex-based differences in the most impactful predictors of survival

After controlling for clinical and sociodemographic confounders as above, women were less likely than men to receive surgery (adjusted OR = 0.89, p = 0.033) and less likely to receive chemotherapy (adjusted OR = 0.88, p = 0.013). The likelihood of radiotherapy was similar by sex (adjusted OR = 0.93, p = 0.14). Men were more likely to be diagnosed at stage IV than women (33.8% vs. 30%); however, the overall stage at diagnosis was not different between the two sexes (p = 0.063).

Discussion

Prior studies exploring sinonasal cancer outcomes by sex have had mixed findings. Some did not find a statistically significant difference; others found that men with sinonasal cancer or one of its histological subtypes have higher all-cause mortality. This study, encompassing more than 36,000 patients, represents the largest case-level analysis of sinonasal cancer survival to date and uses the most current data available at the time of this analysis. We found that men with sinonasal cancer survive a median of 10.4 months less than women. Overall hazard ratio for men with sinonasal cancer was statistically significantly greater than 1, a finding robust to adjustment for possible social and biomedical confounders. Although the size of this study gave statistical power to uncover small distributive differences in confounders, these statistically significant differences were not practically significant in their effect on survival difference by sex.

Given its robustness to adjustment for confounders, the survival disparity may represent an underlying biological or yet-unmeasured social cause. Our study is limited by its coverage of 73.7% of the US population, as patients who receive care not at Commission on Cancer (CoC)-accredited hospitals were not included. Additionally, the observational nature of this study limits our analysis to correlation without proof of causation of these differences. Future research directions include exploration of genetic and more granular social drivers of disease to further explore these findings.

Conclusion

Male sex is associated with poorer survival from sinonasal cancer, a finding not easily explained by potential confounders in the initial presentation, like the stage of disease, delay to treatment, or treatment modality. More research is needed to identify possible biological and social causes for this difference.

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