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National Trends in Surgery for Sinonasal Malignancy and the Effect of Hospital Volume on Short-Term Outcomes

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Abstract

Objective: To characterize trends in the management of sinonasal malignancy with a focus on the impact of hospital volume on surgical care and outcomes.

Study Design: Retrospective cohort study.

Methods: Time trends were analyzed among patients admitted for surgical resection of sinonasal malignancy in the National Inpatient Sample (NIS) between 1988 and 2009. Subset analysis was performed on cohorts with skull base or orbital involvement or who underwent neck dissection. Patient characteristics and hospital attributes were correlated with morbidity and mortality.

Results: Over 22 years, we identified 3850 cases from 879 hospitals. 24.3% of patients had complications and 0.8% of hospitalizations resulted in mortality. Cases with skull base or orbital involvement, or including neck dissection had more complications and a longer length of stay. Prevalence of neck dissection increased over time.

Thirty-two hospitals averaged more than 5 cases per year, accounting for 28% of all surgeries. These centers were predominantly large (73.3%), urban (96.7%), teaching (90%) institutions and performed more high-risk cases – 32.4% of neck dissections, 44.6% of orbital cases, and 43.1% of skull base cases. Compared to lower-volume centers, these centers had more cardiopulmonary complications and electrolyte abnormalities but there was no difference in the length of stay. A greater proportion of cases were recently performed at high-volume centers.

Conclusion: Complicated surgeries are more likely to be performed at higher-volume hospitals, which also entail a higher complication rate. High-risk cases resulted in higher rates of complications but were not associated with a higher mortality rate.

Key Words: paranasal sinus cancer, sinonasal surgery trends, National Inpatient Sample

Level of Evidence: 2c

Introduction

Sinonasal cancers are uncommon – accounting for only between 1-3% of head and neck cancers.[1,2] A wide range of tumors can originate in the sinonasal cavities including squamous cell carcinoma, adenocarcinomas, and neuroendocrine carcinomas. These carcinomas are typically asymptomatic until they progress to an advanced stage with local invasion and a potential constellation of symptoms including chronic nasal discharge, epistaxis, nasal obstruction, anosmia, neuropathies, proptosis, edema, and visual disturbances. Depending on the tumor type, regional lymph node or distant metastases occur with varying frequency. Due to the proximity to vital structures such as the orbit, carotid artery, and brain, primary tumors frequently present as locally advanced disease.

Given the low incidence and heterogenous histology of sinonasal cancers, there are no randomized trials indicating the optimal management. Management of sinonasal cancers varies with histology, but the current standard approach has traditionally been combined-modality treatment with surgery and radiotherapy for advanced-stage disease with or without chemotherapy. Several retrospective studies suggest that improved local control is achieved when surgery is included in the treatment plan, but a selection bias militating against unresectable tumors may explain the poorer results reported with primary radiation-based approaches.[2]

A few institutions have published their experiences with sinonasal cancers.[1,3-9] but these institutional case series each contain fewer than 75 patients and represent differing perspectives related to treatment and overall approach to sinonasal cancers over prolonged time periods. The University of Florida experience using a radiotherapy-only approach and a combined radiotherapy-surgical approach found the control rate with radiotherapy alone was 43%, while combined-modality therapy achieved a control rate of 84% with primary surgery followed by radiation.[4] Similarly, the M.D. Anderson Cancer Center experience, with greater inclusion of surgery and post-operative radiotherapy, achieved a 82% 5-year survival rate.[1] Case studies employing a variety of treatment regimens have suggested a rate of local recurrence of 28-41% and 5-year actuarial survival rates of 40-82%.[1,3-9]

While surgery in combination with radiation plays a definitive role in the management of many sinonasal cancers, limited data exists regarding the patterns of surgical care as it is delivered across the United States. Sinonasal and skull base surgery is a specialized enterprise that benefits from the deployment of a multidisciplinary team, with high potential for immediate and severe life-threatening complications which may require urgent surgical intervention. There is little data documenting the context in which surgery for sinonasal cancer is performed, where high risk surgeries are performed, or

whether there is any variation in outcomes among high- and low-volume surgical centers. We sought to examine contemporary patterns of sinonasal cancer surgery in the United States over a period spanning 1988 to 2009. In this study, through analysis of a national inpatient database, we investigated the short-term surgical outcomes of sinonasal cancer surgery patients and evaluated the impact of hospital volume on these outcomes.

Materials and Methods

Data Source

A retrospective cross-sectional analysis of patients who underwent surgical resection of primary cancer of the nasal cavities and paranasal sinuses was performed using data from the National Inpatient Sample (NIS) from the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality. The NIS is the largest database of all-payer inpatient discharge information, sampling approximately 20% of all non-federal US hospitals and including approximately 9 million hospital admissions each year. Each NIS entry includes all diagnosis and procedure codes of activity during the patient's hospitalization at the time of discharge, as well as patient demographics, hospital characteristics, and short-term complications of the hospitalization.

Data Extraction

All available data from 1988 through 2009 were queried. Patients admitted for primary head and neck cancer with a primary procedure of surgical resection in the maxillary, frontal, ethmoid, or sphenoid sinuses were identified. Higher-risk surgeries were identified by associated orbital or skull base surgical codes as well as surgeries requiring neck dissection. Hospital mortality and perioperative morbidity such as post-operative infections, cardiopulmonary complications, hemorrhagic complications, nerve palsies, and deep vein thrombosis were identified.

Statistical Analysis

The total number of hospitalizations was plotted annually from 1988 to 2009 and hospital volume was assessed for each hospital in the database. Hospital-level data was stratified by hospital caseload to compare complication rates between higher- and lower-volume hospitals. The Pearson chi-square test was used to analyze differences between low- and high-volume hospitals as well as

differences in complication rates. All analyses were performed using Python 2.7 (Python Software Foundation, www.python.org) and R 2.13 (R Foundation, www.r-project.org).

Results

We identified 3850 cases of sinonasal surgery between 1988 and 2009 (Figure 1). Patients had a mean age of 61 years and stayed on average 6.8 days in the hospital. Consistent with previous accounts, we found a male predominance in the studied population, comprising 57.2% of all patients. Aggregate patient race, sex, age, and insurance status did not vary between high- and low-volume centers (Table 1), and the overall distribution of demographic characteristics has not changed over time (Supplemental Figures 2-4). The volume of sinonasal cancer surgery has not changed appreciably over the last twenty years, but a greater proportion of these surgeries are now being performed at higher-volume centers (Figure 1, $R^2 = 0.268$, $p > 0.001$).

In order to investigate the impact of surgical volume on short-term outcomes, we separated hospitals into centers that perform relatively higher numbers of sinonasal cancer surgery cases (greater than 5 cases per year) and centers that perform fewer sinonasal cancer surgery cases (less than 5 cases per year). Thirty-two hospitals that averaged more than 5 cases per year were identified and these hospitals accounted for 28% of all sinonasal surgery cases. These hospitals were more frequently represented in high-risk cases, accounting for 32.4% of all cases requiring neck dissection, 44.9% of cases with orbital involvement, and 45.7% of cases with skull base involvement, despite comprising only 3.6% of all hospitals that performed a sinonasal cancer surgery (Table 2). At high-volume centers, 26.1% of cases were high-risk cases, compared to 15.0% of cases at low-volume centers. High-volume centers tended to be teaching hospitals ($P > 0.001$), and large, urban hospitals were also more represented (Table 3).

Less than 1% of hospitalizations resulted in short-term mortality and 36.9% of patients had complications ranging from neuropathies and visual impairment to infections and cardiopulmonary arrest (Table 4). Cardiopulmonary complications were the most common class of complications, representing about half of all complications, while visual defects and neuropathies directly resulting from the surgery were present in a minority of cases. There was a statistically significant difference in overall complication rate between high- and low-volume centers (Chi-squared test, $p = 0.018$), with higher rates of cardiopulmonary complications ($p = 0.024$) and peri-operative electrolyte abnormalities

(p = 0.002) seen at high-volume centers. There was no difference in mortality between high-volume and low-volume centers (p = 0.122). High-volume centers had longer lengths of stay compared to low-volume centers (7.79 days vs. 6.31 days, p < 0.001) and this difference was sustained even upon direct comparision of high-risk cases between high- and low-volume centers (10.58 days vs. 8.59 days, p = 0.003) and non-high risk cases between high- and low-volume centers (6.84 days vs. 5.89 days, p = 0.004).

There were 715 cases that included neck dissection, had orbital involvement, or had skull base involvement, of which 277 were performed at high-volume centers and 418 were performed at low-volume centers. Two cases had surgeries that met all three criteria and 59 patients had surgeries that met two of the three criteria. Patients with high-risk surgery had longer lengths of stay (9.34 days vs. 6.13 days, p < 0.001) and had higher rates of morbidity and mortality. Among these high-risk surgeries, 29.4% resulted in the listed complications, compared to 23.2% of cases without such extensive surgical intervention (p < 0.0001). For complicated cases, there was no observed difference in mortality between high-volume and low-volume centers. Over the period between 1988 and 2009, the number of cases per year has remained relatively constant over time, but a greater proportion of surgeries were performed at high-volume centers (p < 0.001). There was a decrease in mortality over time, but there was an increase in the rate of complications.

Discussion

Sinonasal cancers are a highly heterogeneous collection of morbid neoplasms often initially treated with surgery and adjuvant radiotherapy. Initially, these cancers can be clinically silent or mimic benign disease such as sinusitis or upper respiratory infections, resulting in late detection when cancers are advanced, as evidenced by a relatively high proportion of locally advanced disease extension at presentation.[10] Demographic analysis reveals that our findings are consistent with population-based data from other major national database analyses, showing a male-predominant patient population mostly between 50-70 years of age that has not significantly changed in incidence over the last twenty years.[10] Our data did not show significant changes over time in patient race or insurance status.

Tumor staging is not possible with the NIS, but paranasal sinus tumors are defined as advanced in stage by spreading beyond the paranasal sinuses to the cranial vault, orbit, or other adjacent structures, or via lymphatic spread. Thus the prevalence of advanced disease at initial presentation is

demonstrated by the fact that 26.1% of patients treated at higher volume centers underwent surgery with neck dissection, had orbital involvement, or had skull base involvement. The data reveals an increase in the number of complex cases over time, with an especially marked increase in the number of cases with neck dissection. Causes for this evolution are not immediately clear and could be due to better detection of advanced disease, improved recognition of disease pathology, or more aggressive management philosophies. Previous case series show between 39-95% of cases present initially with advanced disease (Stage III or IV).[1,9] In the NIS data, there was no trend over time towards less advanced disease, which is consistent with case series estimates, suggesting the proportion of patients with advanced disease at first presentation has remained constant.[5]

In the National Inpatient Sample, high-volume centers are more likely to perform more extensive surgeries involving the skull base or orbit, and these centers also performed more neck dissections. Greater awareness and the ability to deploy advances in the surgical management of sinonasal cancer could explain the higher rates of referral over time to high-volume, more experienced centers. Previous studies have shown decreased morbidity, decreased mortality, and decreased lengths of stay at higher-volume centers for surgical management of a variety of head and neck.[11-13] High-volume surgeons, more commonly found at high-volume centers, have also been found to have decreased perioperative complications, improved long term survival in cancer, and reduced hospital costs.[14-17] These effects have been especially seen in complicated cases.[15] In our sample, despite performing more extensive surgeries, high-volume centers had equal or lower rates of infection, neuropathy or visual impairment (despite more skull base and orbit surgery), and mortality. Particularly in cases with skull base involvement, it could be advantageous to have surgery at a high-volume center with an integrated approach including neurosurgical and advanced postoperative support. Alternatively, since this study lacks tumor staging data, it is also possible that equivalently advanced-stage tumors are being treated with less aggressive surgeries at low-volume centers.

Although there has been an increase in the number of complex sinonasal surgeries performed, there has been a decrease in perioperative mortality. Prior studies of skull base surgery have demonstrated an improved mortality over the past 40 years primarily due to decreased infection rates and improved reconstructive techniques. These techniques have allowed more extensive extirpative surgeries without an increase in mortality. The incidence of infectious complications has gone down over time, while there in has been an increase in the number of electrolyte abnormalities and cardiopulmonary complications. These trends are in keeping with the findings of our study, in which

high-risk surgeries are performed with greater complexity of postoperative management but without concomitant increases in mortality.

Even though high-volume institutions provide more care for high-risk cases, there was no difference in the mortality rate between high- and low-volume centers. There was no difference in the incidence of infectious complications, surgical complications (neuropathies, visual disturbances, or hemorrhage), or length of stay. High-volume institutions had a higher rate of cardiopulmonary complications and electrolyte complications, suggesting that larger surgeries were attempted which might have required greater levels of volume resuscitation. Higher rates of these two categories of complications are the primary contribution to an increased overall complication rate at high-volume hospitals.

A limitation of this study is that the National Inpatient Sample does not keep track of long-term outcomes from these hospitalizations. While we were able to show there is little perioperative mortality (0.8%), we were unable to examine long-term survival or complications. Further investigation would be necessary to compare the efficacy of various treatment options.

Conclusion

This study characterizes current trends in the initial management of sinonasal cancer. Complicated surgeries are more likely to be performed at high-volume hospitals, which also entail a higher complication rate primarily due to the complexity of postoperative management. High-risk cases resulted in a higher rate of complications but were not associated with a higher mortality rate.

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References

1. Allen MW, Schwartz DL, Rana V, et al. Long-term radiotherapy outcomes for nasal cavity and septal cancers. *Int J Radiat Oncol Biol Phys*. 2008;71(2):401–406. doi:10.1016/j.ijrobp.2007.10.031.
2. Barnes L, Tse LLY, Hunt JL, et al. Tumours of the nasal cavity and paranasal sinuses: Introduction. In: Pathology and Genetics of Head and Neck Tumours, Barnes L, Eveson JW, Reichart P, Sidransky D. (Eds), IARC, Lyon 2005. p.9.
3. Robbins KT, Ferlito A, Silver CE, et al. Contemporary management of sinonasal cancer. *Head Neck*. 2011;33(9):1352–1365. doi:10.1002/hed.21515.
4. Mendenhall WM, Amdur RJ, Morris CG, et al. Carcinoma of the nasal cavity and paranasal sinuses. *Laryngoscope*. 2009;119(5):899–906. doi:10.1002/lary.20196.
5. Thorup C, Sebbesen L, Danø H, et al. Carcinoma of the nasal cavity and paranasal sinuses in Denmark 1995-2004. *Acta Oncol*. 2010;49(3):389–394. doi:10.3109/02841860903428176.
6. Dulguerov P, Jacobsen MS, Allal AS, Lehmann W, Calcaterra T. Nasal and paranasal sinus carcinoma: are we making progress? A series of 220 patients and a systematic review. *Cancer*. 2001;92(12):3012–3029.
7. Hawkins RB, Wynstra JH, Pilepich MV, Fields JN. Carcinoma of the nasal cavity--results of primary and adjuvant radiotherapy. *Int J Radiat Oncol Biol Phys*. 1988;15(5):1129–1133.
8. Grau C, Jakobsen MH, Harbo G, et al. Sino-nasal cancer in Denmark 1982-1991--a nationwide survey. *Acta Oncol*. 2001;40(1):19–23.
9. Fasunla AJ, Lasisi AO. Sinonasal malignancies: a 10-year review in a tertiary health institution. *J Natl Med Assoc*. 2007;99(12):1407–1410.
10. Turner JH, Reh DD. Incidence and survival in patients with sinonasal cancer: a historical analysis of population-based data. *Head Neck*. 2012;34(6):877–885. doi:10.1002/hed.21830.
11. Gourin CG, Forastiere AA, Sanguineti G, Marur S, Koch WM, Bristow RE. Impact of surgeon and hospital volume on short-term outcomes and cost of oropharyngeal cancer surgical care. *Laryngoscope*. 2011;121(4):746–752. doi:10.1002/lary.21456.
12. Gourin CG, Frick KD. National trends in laryngeal cancer surgery and the effect of surgeon and hospital volume on short-term outcomes and cost of care. *Laryngoscope*. 2012;122(1):88–94. doi:10.1002/lary.22409.
13. Gourin CG, Frick KD. National trends in oropharyngeal cancer surgery and the effect of surgeon and hospital volume on short-term outcomes and cost of care. *Laryngoscope*. 2012;122(3):543–551. doi:10.1002/lary.22447.
14. Finlayson EVA, Goodney PP, Birkmeyer JD. Hospital volume and operative mortality in cancer surgery: a national study. *Arch Surg*. 2003;138(7):721–725; discussion 726. doi:10.1001/archsurg.138.7.721.
15. Cheung MC, Hamilton K, Sherman R, et al. Impact of teaching facility status and high-volume centers on outcomes for lung cancer resection: an examination of 13,469 surgical patients. *Ann Surg Oncol*. 2009;16(1):3–13. doi:10.1245/s10434-008-0025-9.
16. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. *N Engl J Med*. 2003;349(22):2117–2127. doi:10.1056/NEJMsa035205.
17. Birkmeyer JD, Sun Y, Wong SL, Stukel TA. Hospital Volume and Late Survival After Cancer Surgery. *Ann Surg*. 2007;245(5):777–783. doi:10.1097/01.sla.0000252402.33814.dd.

Table 1. Patient Demographics for Sinonasal Cancer Surgery

		High-Volume Centers (≥ 5 Cases/Year)	Low-Volume Centers (< 5 Cases/Year)
Age, mean (SD)		59.8 ± 14.3	62.0 ± 17.2
Sex, n (%)	Female	424 (40.0)	1214 (43.5)
	Male	633 (60.0)	1568 (56.2)
Race, n (%)	White	632 (59.6)	1424 (51.1)
	Black	53 (5.0)	214 (7.7)
	Hispanic	54 (5.1)	163 (5.8)
	Asian/Pacific Islander	30 (2.8)	65 (2.3)
	Native American	1 (0.1)	9 (0.0)
	Other or unknown	271 (26.0)	879 (31.5)
Primary payer, n (%)	Private	440 (41.5)	1288 (46.2)
	Medicaid	69 (6.5)	214 (7.7)
	Medicare	480 (45.2)	1066 (38.2)
	Self-pay	40 (3.8)	75 (2.7)
	Other or unknown	27 (2.5)	110 (3.9)
Total, n (%)		**1061 (28.5)**	**2789 (71.5)**

Table 2. Number of Hospitals, Sinonasal Cancer Surgeries Stratified by Hospital Caseload

	1988 to 2009					
	Hospitals, n (%)	**Cases (%)**	**Cases with Neck Dissection (%)**	**Cases with Orbital Involvement (%)**	**Cases with Skull Base Involvement (%)**	**Complicated Cases, Total (%)**
High-Volume Hospitals (≥5 Cases/Year)	32 (3.6)	1061 (28.5)	79 (32.4)	106 (44.6)	128 (43.1)	277 (38.7)
Low-Volume Hospitals (<5 Cases/Year)	847 (96.4)	2789 (71.5)	165 (67.6)	130 (53.4)	169 (56.9)	418 (61.3)
Total	**879 (100)**	**3,850 (100)**	**244 (100)**	**236 (100)**	**297 (100)**	**715 (100)**

Table 3. Hospital Characteristics of Admissions for Sinonasal Cancer Surgery

		High-Volume Centers (≥ 5 Cases/Year)[a]	Low-Volume Centers (< 5 Cases/Year)[a]
Hospital size, n (%)[b]	Small	3 (10.0)	113 (13.6)
	Medium	5 (16.7)	254 (30.7)
	Large	22 (73.3)	461 (55.7)
Hospital type, n (%)	Teaching	27 (90.0)	346 (41.8)
	Non-teaching	3 (10.0)	482 (58.2)
Hospital location, n (%)	Urban	29 (96.7)	707 (85.4)
	Non-urban	1 (3.3)	121 (14.6)
Complex Cases, n (%)[c]	Neck Dissection	79 (7.4)	165 (5.9)
	Orbital Involvement	106 (10.0)	130 (4.7)
	Skull Base Involvement	128 (12.0)	169 (6.1)
Total, n (%)		**32 (100.0)**	**847 (100.0)**

Data are cumulative, 1988-2009. [a]Hospital characteristics were not found for 2 high-volume and 19 low-volume hospitals.
[b]Hospital size classification is dependent on number of beds and hospital type. For example, for urban, teaching hospitals, "small" signifies < 300 beds and "large" signifies > 500 beds. [c]Percentage obtained from total number of cases by each subset.

Table 4. Complications of Sinonasal Cancer Surgery

	Total	High-Volume Centers	Low-Volume Centers	P[a]
Deaths, n (%)	30 (0.8)	4 (0.4)	26 (0.9)	0.122
Infectious, n (%)				0.119
Surgical Site Infection	70 (1.8)	14 (1.3)	56 (2.0)	
Urinary Tract Infections (UTIs)	71 (1.8)	16 (1.5)	55 (2.0)	
Pneumonia	30 (0.8)	9 (0.8)	21 (0.8)	
Unspecified Postop Infection	17 (0.4)	3 (0.2)	14 (0.5)	
Cardiopulmonary, n (%)				0.024[b]
Stroke	16 ((0.4)	8 (0.8)	8 (0.3)	
Cardiac Arrest	8 (0.2)	1 (0.1)	7 (0.3)	
Other Cardiac Complications	456 (11.8)	127 (12.0)	329 (11.8)	
Pulmonary Complications	239 (6.2)	87 (8.2)	152 (5.4)	
Other, n (%)				
Neuropathies	51 (1.3)	13 (1.2)	38 (1.4)	0.861
Visual Impairment	76 (2.0)	20 (1.9)	56 (2.0)	0.908
Hemorrhage	46 (1.2)	12 (1.1)	34 (1.2)	0.953
Electrolyte Abnormalities	312 (8.1)	110 (10.4)	202 (7.2)	0.002[b]
Total Complications	**1392 (36.9)**	424 (40.0)	998 (35.8)	0.018[b]

[a]Chi-square test comparing high-volume and low-volume centers. [b]P < 0.05.

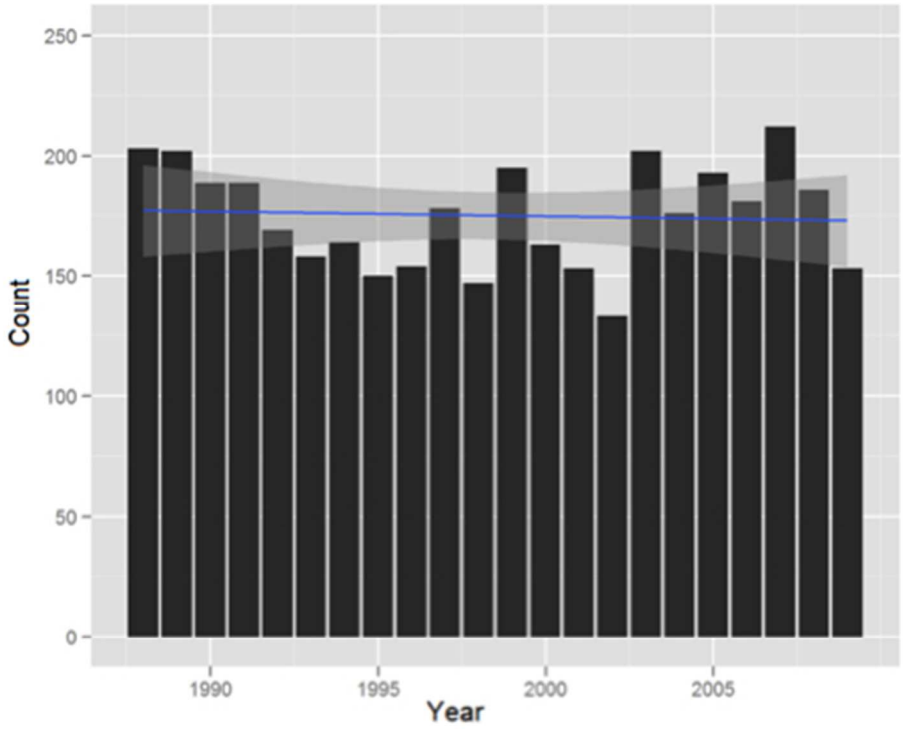

Figure 1A: The total number of sinonasal cancer surgeries per year has not changed significantly over the last twenty years.

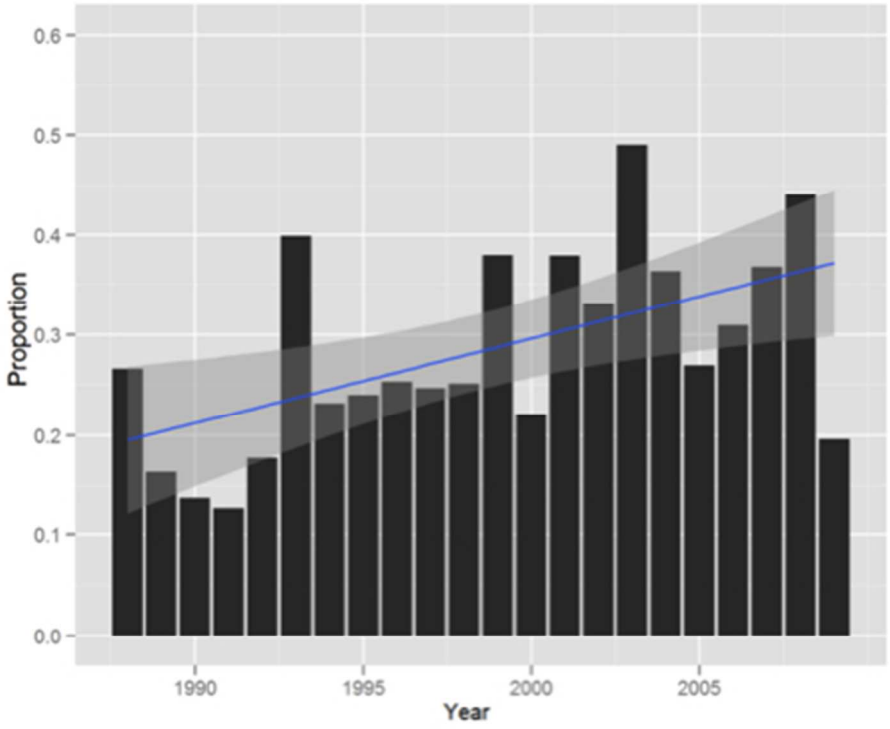

Figure 1B: An increasing proportion of sinonasal cancer surgeries per year are performed at high-volume centers.

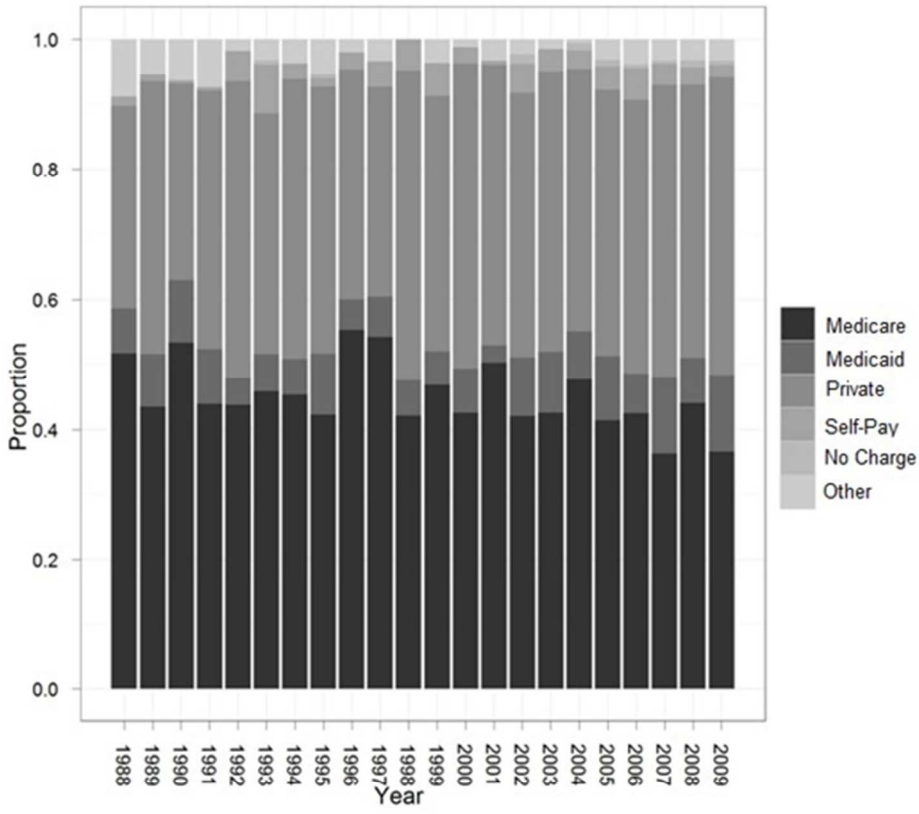

Figure 2: Sinonasal surgery patients' insurance status has not significantly changed over time.
166x151mm (96 x 96 DPI)

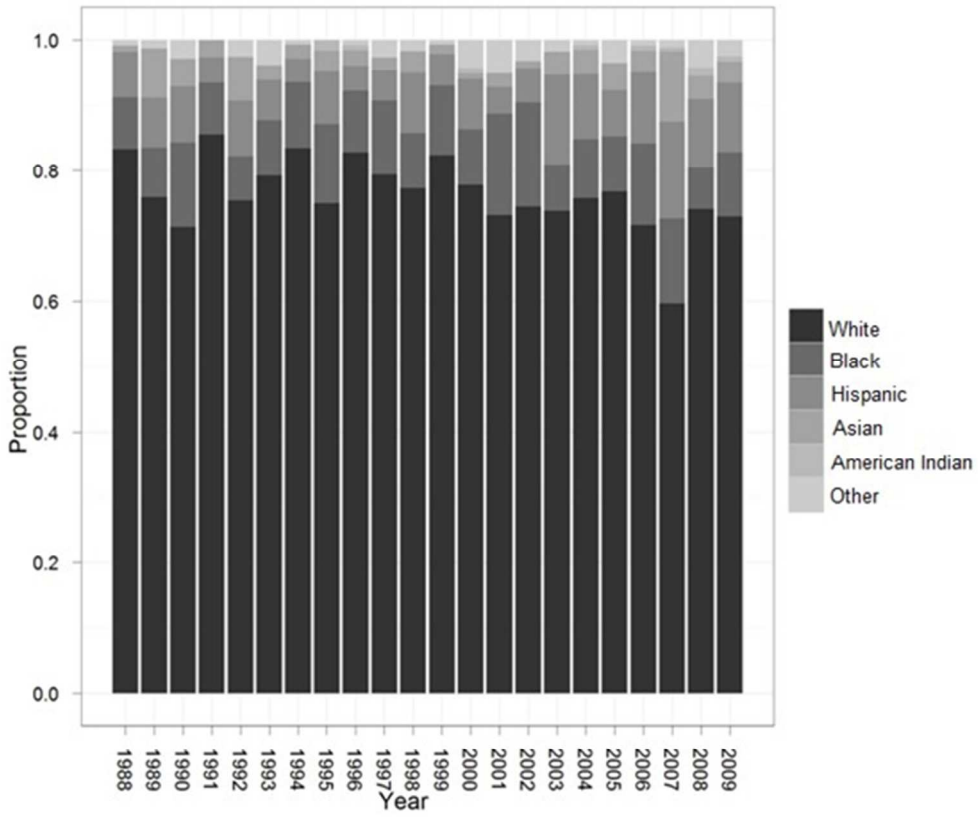

Figure 3: Sinonasal surgery patients' race has not significantly changed over time.
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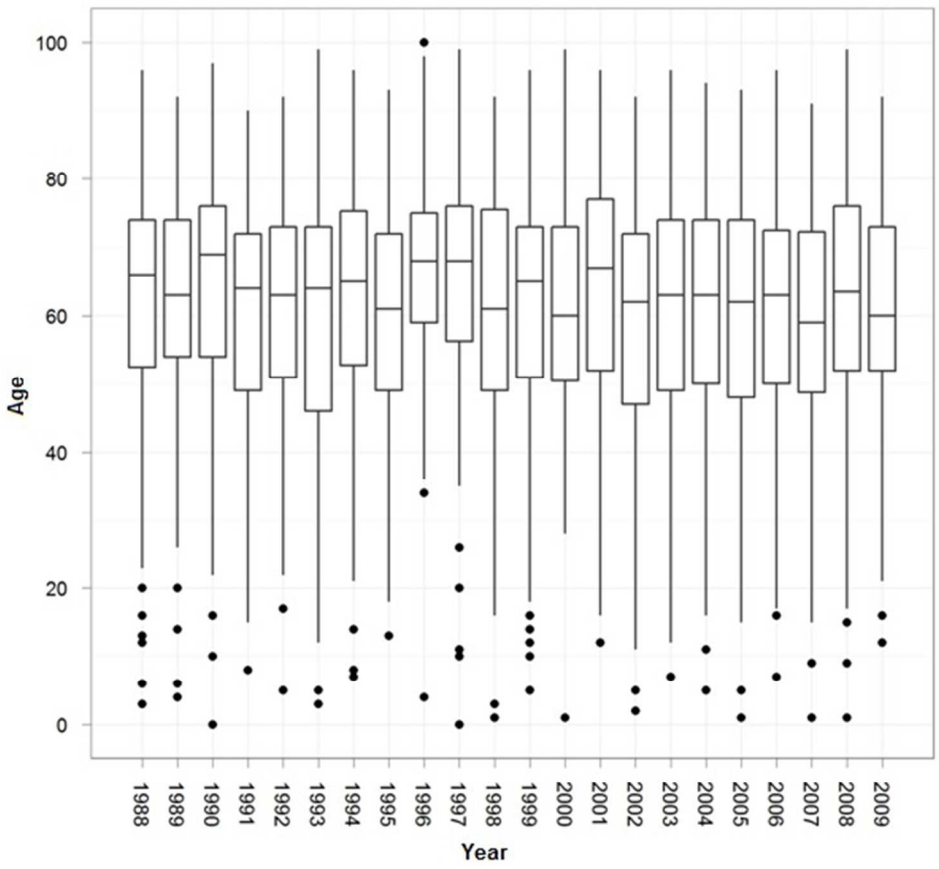

Figure 4: Sinonasal surgery patients' age distribution has not significantly changed over time.
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