Factors That Affect ACC Recurrence and Survival

Patterns of Recurrence and Survival of Head and Neck Adenoid Cystic Carcinoma After Definitive Resection.

Oplatek A, Ozer E, et al:

Laryngoscope 2010; 120 (January): 65-70

Many clinical factors can predict poor outcome in head and neck ACC, but we are poorly equipped to treat these patients.

**Objective:** To determine factors that predict for recurrence and long-term survival in patients with head and neck adenoid cystic carcinoma (ACC).

**Design:** Retrospective review.

**Participants:** 113 patients treated at a single academic medical center between 1990 and 2007 with head and neck ACC.

**Methods:** Clinicopathologic data were acquired as well as overall survival and time to recurrence. The main outcome was to look for factors that affected recurrence and survival among patients who underwent definitive oncologic surgery.

**Results:** 113 patients with head and neck ACC were treated between 1990 and 2007, and 99 patients were chosen who had adequate clinical data. The mean age at diagnosis was 54 years (range, 20 to 83 years), and there were 55 women and 44 men. The parotid was involved in 25 patients, submandibular in 16, sinonasal in 35, oral cavity in 15, larynx in 5, and external auditory canal in 3. T1 disease existed in 32 patients, T2 in 27 patients, T3 in 19 patients, and T4 in 21 patients. Only 7 patients (7.1%) had cervical nodal metastasis. The overall 5- and 10-year survival was 78% and 55%, respectively. The 7 patients with lymph node positive disease had a mean survival of 46 months versus lymph node negative patients with a mean survival of 98 months ($P = 0.001$). On univariate analysis, patients with advanced T-stage cancers had significantly shorter survival rates ($P = 0.002$), as did those with advanced histological grade ($P = 0.023$). Patients with minor salivary gland tumors also had shorter survival time than those with major salivary gland involvement ($P = 0.027$). The recurrence rate was 53%, with a mean time to recurrence of 63 months. The presence of perineural invasion and lymphovascular invasion was significantly associated with recurrence ($P = 0.033$ and 0.001, respectively), and lymphovascular invasion was an independent predictor of recurrence on multivariate analysis ($P = 0.002$). Advanced stage and positive margins were predictive of early recurrence.

**Conclusions:** Significant prognostic factors in ACC survival and recurrence include T-stage, site, nodal positivity, and perineural and lymphovascular invasion.

**Reviewer's Comments:** This was a nice descriptive study looking at retrospective factors that might impact ACC recurrence and survival. Nothing new here in terms of findings, but it does support other studies that have looked at similar patient cohorts. It does highlight that we are doing well at locoregional control, but continue to be plagued by distant metastases in this indolent, yet progressive disease. (Reviewer-Patrick K. Ha, MD).

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Keywords: Adenoid Cystic Carcinoma, Resection, Recurrence, Survival

Print Tag: Refer to original journal article
The majority of patients are able to successfully acquire TE speech, and the indicator most linked with failure is a high level of comorbidity.

**Objective:** To evaluate voice prosthesis success and predictors for success and failure.

**Design:** Retrospective analysis of 103 subjects over an 8-year period.

**Participants:** 103 individuals undergoing total laryngectomy (TL) or total pharyngolaryngectomy (TPL) were included. Closure for TL patients was achieved with mucosal suture or pec flap, while tubed radial forearm free flap was used for TPL patients. Approximately 29% underwent preoperative radiotherapy and 38% underwent postoperative radiotherapy; 47% underwent chemotherapy at some point of treatment. Of the 103 patients, 87 underwent tracheoesophageal puncture (TEP) with prosthetic valve insertion, 91% at the time of the laryngectomy.

**Methods:** A standardized physical examination form was developed to rate oral diet and speech intelligibility. Outcomes were recorded at the 6-month postoperative visit or at the last visit prior to death for those who did not survive to 6 months. Data regarding the longevity of each prosthesis, the number of prosthesis replacements, complications, and demographics were recorded.

**Results:** Oral diet was normal or minimally impaired 6 months after surgery in 70% of patients. Of those unable to resume an oral diet, 6 had tumor recurrence, 4 had pharyngeal stenosis, and 2 had radionecrosis. Univariate analysis showed predictors for poor oral outcomes included circular TPL, hypopharyngeal primary, and pec flap reconstruction. The success rate for TE speech was 82%. A high level of comorbidity (ASA ≥3) was the only factor in univariate analysis predictive of success with TE speech. Shorter prosthesis lifetime was linked to female gender, circular TPL, hypopharyngeal tumor, and pec flap in univariate analysis. Twenty-six percent of patients experienced leakage around the prosthesis that was successfully managed with prosthesis downsizing or collagen injections. The late complication rate was 16%.

**Conclusions:** Surgical voice restoration can provide a high rate of success for voice restoration after laryngectomy; however, the surgeon must be aware of factors that may impact short- and long-term success.

**Reviewer’s Comments:** Recent publications have explored factors that influence the success of voice rehabilitation after total laryngectomy. Factors such as tumor size/location, reconstruction, and exposure to radiation/chemotherapies have been postulated to impact voice prosthesis success. In this series, 82% of patients successfully accomplished TE speech, a figure consistent with prior reports. Although a number of factors are postulated to contribute to failure (such as neuro/psychological factors, motivation, recurrence, and granulation tissue), the only factor univariate analysis identified as a significant contributor to TE speech failure was a high comorbidity level. It is probable that those with high comorbidities experience many of the aforementioned factors, and it is reasonable to consider each of them when considering candidacy for TE puncture. (Reviewer-Heather Starmer, MACCC-SLP).

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Keywords: Laryngectomy, Voice Prosthesis, Voice Rehabilitation

Print Tag: Refer to original journal article
**Health Literacy -- Important Consideration in Laryngectomy Population**

*Health Literacy and Health Care in an Inner-City, Total Laryngectomy Population.*

Beitler JJ, Chen AY, et al:

Am J Otolaryngol 2010; 31 (January-February): 29-31

Inner-city laryngectomy patients are at high risk for poorer outcomes secondary to poor HL.

**Background:** Health literacy (HL) refers to the individual's ability to obtain, process, and understand basic health information in order to make appropriate health-related decisions. When HL is low, patients are at risk for inadequate access to and use of health care.

**Objective:** Assessment of HL in the laryngectomy population has been understudied, therefore, the authors sought to assess literacy in an inner-city population.

**Design:** Cross-sectional design.

**Participants:** A single institution's tumor registry was used to identify patients undergoing total laryngectomy (TL) over a 14-year period; 30 patients were eligible for the study, but only 8 were able to participate.

**Methods:** Validated, structured questionnaires were administered during face-to-face interviews. This included the Medical Outcomes Study SF-12, the Short Test of Functional Health Literacy in Adults, the Voice Handicap Index, and the American Speech-Language-Hearing Association Intelligibility Scale.

**Results:** Of the 30 patients eligible for the study, 14 could not be located, 4 refused to participate, and 4 were either deceased or too ill to participate. Demographic analysis revealed that 75% were African American, 88% were male, 50% had less than a high school education, and the median annual income was <$10,000. More than one-third of the patients had severely inadequate HL scores. Specifically, 63% were unable to interpret an appointment card, 50% were unable to interpret when a medication should be taken, and 33% could not determine how to take a medication on an empty stomach.

**Conclusions:** Because of the significant difficulties observed in the inner-city population regarding HL, this population may warrant greater consideration of larynx-sparing interventions.

**Reviewer's Comments:** This paper brings to light some of the challenges that may significantly impact patient outcomes after laryngectomy. Of particular concern is whether the patients included in this survey were more likely to have higher literacy rates than those who were not located or refused to participate. It is sobering to consider that these figures may be on the low end of reality in an inner-city population. Additionally, as this test was administered face-to-face, there is potential that subjects may have inflated their responses. Even if the data in this series are reflective of the reality of an inner-city population, it reflects a substantial factor that warrants consideration when determining the best course of treatment for patients. The authors suggest that with socioeconomically disadvantaged patients, larynx-sparing procedures may be of paramount importance. Unfortunately, these patients are most at risk for presenting for treatment once their cancer has advanced to stages not amenable to organ preservation. As a community, we must then adjust our treatment paradigms to provide additional support to ensure our patients comprehend treatment recommendations. This can only be accomplished using a multidisciplinary model of support. (Reviewer-Heather Starmer, MACCC-SLP).

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Keywords: Health Literacy, Laryngectomy

Print Tag: Refer to original journal article
A high JB or JBD can be a cause of pulsatile tinnitus, vertigo, and conductive or sensorineural hearing loss.

**Background:** Venous circulation is especially prone to vascular abnormalities, and the jugular bulb (JB) is no exception. Usually, these anomalies are of no consequence, but they have been reported to cause dehiscence of the posterior canal, hearing loss, vertigo, and pulsatile tinnitus.

**Objective:** To report on a series of high JBs and JB diverticula (JBD) that eroded into inner ear structures.

**Design:** Retrospective case review.

**Participants:** 11 patients who presented at the authors’ institution over a 12-month period were included. Patient age at presentation was between 5 and 82 years; 6 patients were male and 5 were female.

**Methods:** Work-up included audiologic evaluation, cervical vestibular evoked myogenic potentials (VEMP), and high-resolution CT.

**Results:** Distribution between the left and right sides was uniform, with 6 presenting with left-sided erosion. A JBD was the cause of erosion in 6 of the 11 cases. Tinnitus was present in 9 of these 11 patients, and in 3 individuals, pulsatile tinnitus was the primary complaint. Eight patients had hearing loss that was equally likely to be conductive or sensorineural in origin. Only 2 patients had dizziness or vertigo complaints. VEMP thresholds were measured in 6 patients and were found to be significantly reduced in 3. The JB eroded into the vestibular aqueduct in 9 cases, the posterior semicircular canal in 4 cases, and the inner ear in 6 cases. Erosion into inner ear structures was not mentioned in the radiology report in 10 of 11 cases. None of the patients in this series received surgical treatment.

**Conclusions:** The most common presenting symptoms in this series were conductive hearing loss and pulsatile tinnitus. Although other series have reported vertigo as a common symptom, it was uncommon in this series.

**Reviewer’s Comments:** This paper points out an interesting potential cause of hearing loss, tinnitus, and vertigo that we should include in our differential diagnosis of these patients. However, I would urge caution in interpreting the finding of JB erosion based on the finding CT scan alone. Based on the superior canal dehiscence literature, we know that the finding of a bony dehiscence on CT does not necessarily mean that a dehiscence actually exists. Even the best quality CT scanner has a limited resolution, so it is possible that a thin layer of bone will be missed. In the superior canal dehiscence literature, the dehiscences on CT scan are about 10x more common than dehiscences in actual temporal bones. Before I would consider invasive treatment in this patient population, I would make sure that the dehiscence is confirmed by another objective finding such as decreased VEMP thresholds or sound-induced nystagmus in the posterior canal plane. (Reviewer-Benjamin T. Crane, MD).

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Keywords: Hearing Loss, Tinnitus, Vertigo, Posterior Canal Dehiscence, CT, VEMP

Print Tag: Refer to original journal article
Active Middle Ear Implant vs Open-Fit Hearing Aid -- Which Is Better?

Active Middle Ear Implant Compared With Open-Fit Hearing Aid in Sloping High-Frequency Sensorineural Hearing Loss.

Boeheim K, Pok S-M, et al:

Otol Neurol 2009; epub ahead of print (December 29):

Active middle ear implant offers an improvement over a hearing aid in several conditions.

**Background:** Severe high-frequency sensorineural hearing loss (SNHL) can be difficult to rehabilitate with a traditional hearing aid (HA). Acoustic feedback can be a problem as can the “occlusion effect.” Open-fit HAs have recently become more successful at solving this problem. A second competing solution is the active middle ear implant (AMEI). This system avoids the feedback problem by delivering vibration directly to the ossicular chain. The occlusion effect is also eliminated using the AMEI system because no ear mold is required.

**Objective:** To determine if AMEI or open-fit HA provides better rehabilitation of high-frequency SNHL.

**Design:** Prospective study

**Participants:** 10 adults with stable, symmetrical, sloping SNHL were included. These patients were implanted with a Vibrant Soundbridge Model 404. Patients then used this device on a daily basis for 5 to 56 months, with the mean usage being just over 2 years.

**Methods:** Testing was conducted using pure tones, the Freiburger Monosyllabic Word Tests in quiet, and the Oldenburg Sentence testing in background noise. Patients were fitted with the Oticon Delta 8000 HA, which they wore for 30 minutes prior to testing.

**Interventions:** AMEI versus HA.

**Results:** Both systems offered significant improvements over the unaided condition, and the 2 devices produced similar results at all frequencies except at 1,000 Hz where the AMEI had a significantly better threshold. Both the HA and AMEI also had significantly better speech reception scores relative to the unaided condition in quiet, although the AMEI and HA did not yield significantly different results. However, in noise conditions, the AMEI had significantly better performance than the HA.

**Conclusions:** AMEI demonstrated better performance than the HA in several test conditions.

**Reviewer's Comments:** One issue with this study is acclimatization or improvements in auditory perception that occur with prolonged use. The importance of these effects is controversial, but the patients in this study had little experience with the HA as they only began using this model 30 minutes prior to being tested. However, all the patients were long-term AMEI users, so if acclimatization did have an effect, it would favor the AMEI. Almost all of these patients used conventional HAs prior to the AMEI. Thus, all the patients in this study are patients who were presumably not satisfied with their HA to begin with. Thus it is unclear if these results can be applied to the wider population of patients with high-frequency hearing loss who have not yet used a HA. Based on these results, it is clear that good results can be obtained with either an open-fit HA or an AMEI. The results suggest that the AMEI may be better under some conditions, but this difference is small.

(Reviewer-Benjamin T. Crane, MD).

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Keywords: Hearing Loss, Audiology, Middle Ear Implant, Hearing Aid

Print Tag: Refer to original journal article
Exostoses in San Diego surfers occur primarily in the right ear.

Background: Exostoses are benign bony growths of the external auditory canal that are usually attributed to cold water swimming.

Objective: To review a series of canalplasty cases to see if the laterality of disease can be explained by prevailing winds. The rates of complications and hearing loss are also discussed.

Design: Retrospective chart review.

Participants: 61 patients who had exostoses removed at the University of California, San Diego Medical Center during a 17-year period.

Methods: The severity of exostoses was determined from retrospective review of the preoperative report in each patient's medical records. Wind direction was taken from a National Oceanic and Atmospheric Administration database. Average temperatures were taken from data measured at Scripps Pier.

Interventions: Canalplasty.

Results: Patients had a mean age of 43 years, with all but 2 of the patients in the series being male and all but 2 being surfers. Right ear canalplasty was performed in 42 cases and left ear canalplasty was performed in 41 cases. It was found that twice as many patients had more severe exostoses in their right ear as compared with the left ear. This difference was significant at the 0.03 level. The authors hypothesize that the laterality of exostoses may be due to evaporative cooling within the external auditory canal caused by wind. It was thought that most San Diego surfers spend their time sitting on surfboards facing West as they wait for waves. The wind generally came from the North, and thus was predominantly at the surfer's right ear. Complications of the surgery were reviewed and there was 1 occurrence of tympanic membrane perforation. There were no instances of temporomandibular joint or facial nerve damage. Minor complications included exposed bone in the external auditory canal in almost 18%, which resolved in time in every case. Scarring causing stenosis occurred in 4 cases, and aural polyps developed in 3 cases. Hearing outcomes were also reviewed and generally did not change significantly.

Conclusions: Exostoses occur more commonly in surfers in the ear exposed to the wind.

Reviewer's Comments: One weakness of this study is that it is a retrospective review. Thus we do not have any information on surfing habits of these patients, such as when they surfed, during what season, and if they wore ear plugs. Much is made of the direction of the prevailing wind and the direction these surfers likely faced; however, it is worthy of mention that every other study of exostoses that studied the laterality of disease also found it worse on the right side, so there might just be a right-sided predominance. It is mentioned that the indications for surgery in this series included conductive hearing loss, although we do not know how many patients had conductive hearing loss. It is interesting that the average hearing did not improve after surgery. (Reviewer-Benjamin T. Crane, MD).

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Keywords: Exostoses, Cold Water Swimming, Wind, Conductive Hearing Loss

Print Tag: Refer to original journal article
Does Size of Conductive Hearing Loss Equal Size of SSCD?

The Relationship Between the Air-Bone Gap and the Size of Superior Semicircular Canal Dehiscence.

Yuen H-W, Boeddinghaus R, et al:

Otolaryngol Head Neck Surg 2009; 141 (December): 689-694

These authors found a significant correlation between superior canal dehiscence size and conductive hearing loss.

**Background:** Superior semicircular canal dehiscence (SSCD) is caused by loss of bone over the superior canal, which can cause a variety of symptoms including disequilibrium, vertigo, sound-induced oscillopsia, conductive hearing loss, and authophony. Exactly which symptoms arise and the severity of these symptoms can vary from one individual to the next. It is usually difficult to predict the symptoms based on the anatomy of the dehiscence alone.

**Objective:** To correlate the size of SSCD with the size of the air-bone gap (ABG)

**Design:** Retrospective review.

**Participants:** 23 patients diagnosed with SSCD.

**Methods:** Patients had SSCD diagnosed based on history, clinical findings, audiometry, and CT. All patients had an acoustic reflex and 3 had vestibular-evoked myogenic potential (VEMP) testing. Dehiscence size was measured on CT reconstructed in the superior canal plane.

**Interventions:** Surgical repair was performed in 10 ears.

**Results:** In 6 ears, there was no air-bone gap (ABG). In all 6 ears with no gap, the dehiscence was <3 mm. In the remaining 22 patients, the ABG averaged between 500 and 2,000 Hz ranging from 3 to 27 dB, with a mean of 10 dB. Approximately one-third of patients had bone conduction thresholds that were negative, and these patients had dehiscences >3 mm. In the ears that had surgery, 7 patients had at least some closure of their ABG, and 3 had an increase in ABG. A regression analysis demonstrated that the size of the dehiscence was correlated with ABG with an $R^2$ of 0.78. This correlation was significant.

**Conclusions:** In this series, dehiscence >3 mm demonstrated an ABG, and the magnitude of this ABG is correlated with dehiscence size.

**Reviewer's Comments:** In some sense, it is logical that a larger dehiscence should cause a larger ABG since a larger opening should theoretically allow more acoustic energy to be dissipated through the dehiscence. However, in the author's own companion study as well as other studies, the size of the dehiscence does not correlate with auditory symptoms. Furthermore, repair of the dehiscence in this study sometimes led to a greater ABG. Finally, several other groups have previously looked for a correlation between SSCD size and ABG without finding a significant correlation. Many of these previous series had more patients than this series. Why was it that this group found a correlation between ABG and dehiscence size? The authors never comment on this, and it is hard to say. The size of the dehiscence was never directly measured even in the 10 ears taken to surgery. CT scan is notorious for over estimating dehiscence size because thin bone around the opening falls below the resolution of the scanner. (Reviewer-Benjamin T. Crane, MD).

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Keywords: Conductive Hearing Loss, Superior Semicircular Canal Dehiscence, VEMP, Vertigo

Print Tag: Refer to original journal article
Those with occupational noise exposure have worse hearing, but are also more likely to smoke, be poorly educated, and be involved with firearms.

**Background:** Noise-related hearing loss is recognized as a significant public health issue. Several reports have correlated hearing loss with noise exposure. However, in many previous studies, groups were not carefully screened for other factors that might have contributed to hearing loss, since those exposed to occupational noise tend to also have other risk factors.

**Objective:** To review the National Health and Nutrition Examination Survey (NHANES) to correlate hearing loss with other potential associated factors.

**Design:** Cross sectional study.

**Participants:** Individuals randomly selected to be representative of the U.S. population were included. A total of 3853 subjects had audiometry; <10% of those tested were excluded, usually due to poor test-retest reliability.

**Methods:** Data collected in these subjects also included race, smoking history, blood pressure, and medical and medication history. Exposure to recreational noise, occupational noise, and firearm use was also determined. Occupational noise was defined as noise that required a raised voice for at least 3 months. Two methods were used to quantify the effect of occupational noise. First, the “Annex C” method was used; this method was used for the population represented in the American National Standards Institute (ANSI S3.44) standard. In this analysis, only the effects of age, gender, race, and occupational noise exposure were considered. In the second analysis, the multivariate analyses also included socioeconomic status, other noise exposure, and cardiovascular risk factors.

**Interventions:** Observational study only.

**Results:** One-third of the participants reported occupational noise exposure. Those with noise exposure were significantly more likely to be white, poorly educated, male, smokers, and engaged in leisure activities that involved firearms. The authors compared the current database analysis with the previously described Annex C analysis. Both databases revealed a significant correlation between occupational noise exposure and hearing loss, but in the current analysis, the effect was attenuated, which lowered the odds ratio to 1.6 from the 1.9 in the Annex C model. The variance also increased slightly when these new factors were included.

**Conclusions:** This study demonstrates that the risk factors for acquired hearing loss may be more complicated than previously thought. Although occupational noise exposure is clearly associated with hearing loss, there are also many associated factors that tend to be present in the population of patients who are exposed to occupational noise.

**Reviewer's Comments:** This data set does not provide a lot of detail on the duration or severity of the noise exposure. However, the study does point out some interesting contributing factors to hearing loss that we should be aware of in our patients and consider in interpreting future studies of this type. (Reviewer-Benjamin T. Crane, MD).

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Keywords: Hearing Loss, Noise Exposure, Hearing Aids

Print Tag: Refer to original journal article
How Much of the Abstract Can We Believe in the Otolaryngology Literature?

Do Abstracts in Otolaryngology Journals Report Study Findings Accurately?

McCoul ED, Vengerovich G, et al:

Otolaryngol Head Neck Surg 2010; 142 (February): 225-230

The authors find some important information is often omitted from abstracts.

**Background:** With the declining popularity of printed journals and the availability of abstracts free from on-line sources, the abstracts themselves are increasingly becoming a source of medical information both for physicians and patients. However, there have been few studies of the reliability of these abstracts themselves.

**Objective:** To determine how accurately findings are described in the abstracts of otolaryngology journals.

**Design:** Literature review.

**Participants:** 4 high-circulation otolaryngology journals between January and June of 2008 were reviewed. The journals chosen were *Otolaryngology - Head and Neck Surgery*, *Laryngoscope*, *Archives of Otolaryngology - Head and Neck Surgery*, and *Annals Of Otology, Rhinology, and Laryngology*.

**Methods:** Articles were limited to original research reports. The authors developed an instrument with 20 items that could be used to evaluate articles. After an initial review, the authors shorted this instrument to 17 items by removing 3 items that were not reliable. Using these 17 items, 25 articles were reviewed by 3 of the authors. These items were then scored based on inter-rater reliability; they were then abbreviated to 12 items. The items included reporting of the research design, patient-care setting, geographic region, number of patients included and lost to follow-up, source of data, if quantitative results are given, measures of statistical significance, any adverse events, and limitations of the study.

**Results:** A total of 418 articles were included. Research design was almost always present in the abstract, 97% reported sample size, 94% reported quantitative results, and 45% reported statistical measures; 67% of abstracts reported quantitative information. Only 12% indicated the number of drop outs, 17% reported harms, and 4% reported limitations of the study. There was no significant relationship between omission rate and type of article as classified by level of evidence or journal of publication.

**Conclusions:** The authors conclude that using the abstract as the sole source of information may lead to biased or inappropriate conclusions.

**Reviewer's Comments:** Simply putting more information into the abstract is unlikely to make the literature more clear. Those of us who review manuscripts should be careful to make sure the claims made in the abstract are well supported. Most journals give strict limits on abstract length, which limits the amount of detail that can be presented. I do not think it is necessary to present information such as 95% confidence intervals or limitations in study design in the abstract. What I find a more pressing problem is when the abstract misrepresents the findings of the study by either presenting data that is not discussed elsewhere in the paper or that contradict findings presented later. I was hoping the authors would address this issue for the otolaryngology field as it has been addressed in other fields. (Reviewer-Benjamin T. Crane, MD).

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Keywords: Literature Review, Otolaryngology

Print Tag: Refer to original journal article
Predicting Complications in Microvascular Reconstruction for Head and Neck Defects

Prospective Analysis of Outcomes and Complications of 300 Consecutive Microvascular Reconstructions.

Nuara MJ, Sauder CL, Alam DS:

Arch Facial Plast Surg 2009; 11 (July-August): 235-239

Previous radiation therapy, surgery, and DM contribute to higher complications in head and neck microvascular reconstruction.

**Background/Objective:** Microvascular reconstructions of the head and neck continue to evolve and gain popularity. This study examines a prospective database of patients requiring microvascular reconstruction of head and neck defects to determine factors that may be important in predicting surgical outcomes.

**Methods:** A database comprised of 300 consecutive free flap reconstruction cases of head and neck defects performed in a tertiary care setting over a 6-year period was reviewed. The data were collected prospectively. Perioperative medical conditions including coronary artery disease (CAD), hypertension (HTN), and diabetes mellitus (DM), as well as previous cancer treatments, including surgery and/or radiation, were documented. Surgical and medical postoperative complications were documented as well. Predictors of complications were identified based on a multivariate regression analysis model.

**Results:** Flap survival was >98%. At least 1 complication was seen in 52 patients (17.3%). The most common complication was wound infection, seen in 32 patients (10.7%). Patients with a history of radiation treatment and surgery had a statistically significant increase in complications than did patients with no previous treatment. The presence of DM was also significant in predicting complications. Age, CAD, and HTN were not found to be statistically significant predictive factors. Donor site complications were seen in 45 patients (15.0%), with partial loss of skin graft being the most common complication.

**Conclusions:** Microvascular reconstruction continues to remain the mainstay for treatment of large head and neck cancer defects. Previous radiation therapy, surgery, and the presence of diabetes are predictive of postoperative complications.

**Reviewer's Comments:** This study showed an impressive microvascular success rate and provides useful clinical indicators in treating a patient who is a candidate for microvascular reconstruction. Limitations of this study include the fact that given that the database was created prospectively, it excludes the possibility of analyzing other clinical perimeters that were not included in the original database, such as patient's smoking status. Furthermore, no long-term follow-up is available; therefore, late complications, such as hardware exposures, are not analyzed in this study. While DM was found to be a significant predictor of adverse clinical outcome, the number of patients with DM in this study is relatively small. (Reviewer-Tang Ho, MD).

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Keywords: Microvascular Reconstructions, Head and Neck Cancer Defect, Complications

Print Tag: Refer to original journal article
Improving Skin Paddle Viability of Pectoralis Major Myocutaneous Flap

Improving Skin Paddle Survival in Pectoralis Major Myocutaneous Flap Reconstruction of Head and Neck Defects.

Ramakrishnan VR, Yao W, Campana JP:

Arch Facial Plast Surg 2009; 11 (September/October): 306-310

The viability of the skin paddle of a pectoralis major myocutaneous flap may be improved by positioning the skin paddle entirely over the pectoralis major muscle.

Background/Objective: The reliability of the skin paddle of a pectoralis major myocutaneous flap has been questionable based on literature data, with skin paddle loss in the range of 1% to 29% reported. The authors report their favorable experience with the flap and their modification on the standard flap harvest technique that may help to increase the viability of the pectoralis major myocutaneous flap skin paddle.

Methods: A retrospective review was done of 81 cases of pectoralis flap performed for head and neck reconstruction by the senior author over a 14-year period. Among these, 76 flaps were harvested with skin paddle. Data were collected on patients' comorbidities and complications. The lateral thoracic artery contribution to the flap was divided in all cases to increase mobility. The skin paddle of the pectoralis major myocutaneous flap was harvested so that it overlaid the pectoralis muscle entirely, and care was taken so the skin paddle did not extend over the rectus sheath.

Results: The majority of the flaps were used for reconstruction of oral cavity and oropharyngeal defects (34 and 17, respectively). A total of 22 complications were recorded among the 81 flaps performed. No total flap loss was reported. Major skin paddle loss (>25% surface area) was seen in 3 patients (4%). Partial skin paddle dehiscence was seen in 6 patients, and fistulas were reported in 3 patients, with all of the latter, treated conservatively. Donor site wound complications were seen in 5 patients (6%).

Conclusions: Despite the increasing popularity of microvascular free tissue transfer in head and neck reconstruction, pectoralis major myocutaneous flap remains a valuable and versatile reconstructive option for the surgeon.

Reviewer's Comments: With the increasing popularity of microvascular free tissue transfer, it would appear that radial forearm free flap may have taken over pectoralis major flap as the workhorse in head and neck reconstruction. In addition to its bulkiness, one of the issues with pectoralis major flap is the unreliability of its skin paddle. These authors believe that the cause for the majority of the distal skin flap necrosis is secondary to extension of the skin paddle over the rectus sheath during the harvest. As they pointed out in the study, multiple anatomic vascular studies have suggested that the distal skin paddle of the pectoralis major myocutaneous flap is based off of a random blood supply. The authors have achieved impressive success with this modification of the flap harvest technique. (Reviewer-Tang Ho, MD).

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Keywords: Pectoralis Major Myocutaneous Flap, Head & Neck Reconstruction, Skin Paddle Survival

Print Tag: Refer to original journal article
Selective elevation of the lateral brow may achieve a more effective rejuvenation of the upper face.

Background: The ideal eyebrow has been described as an arch with the brow apex terminating above the lateral limbus, with the medial and lateral ends of the brow at the same horizontal level. Aesthetically, it has been shown that a medial eyebrow below or at the level of the supraorbital rim with an apex lateral slant is preferred. The traditional brow-lift procedures often produce brow shape and positions that create a surprised look, likely due to over-elevating the medial brow.

Objective: To objectively compare the brow positions of young versus mature women.

Methods: Randomly selected cohorts of women aged 20 to 30 years (n=36) and 50 to 60 years (n=34) were photographed. Eyebrow position was determined by measuring from a reference horizontal plane drawn between the medial canthi to vertical points on the upper brow margin at the medial canthus, pupil, and lateral canthus. Patients who had prior brow surgery, plucked eyebrows, and botulinum toxin treatment of the upper one-third of the face were excluded from the study.

Results: Eyebrow positions of the 20- to 30-year-old group were found to be 15.7, 19.8, and 21.3 mm above the medial canthal reference line above the medial canthus, pupil, and lateral canthus, respectively. The lateral brow was significantly higher than the mid brow. The brow positions for the 50- to 60-year-old group were at 19.1, 22.4, and 22.4 mm, respectively. The brow positions of the older group were higher at all 3 measured points. The difference was statistically significant for the medial and mid brow (P <0.05).

Conclusions: With aging, there appears to be paradoxical elevation of the medial and mid brow positions. Hence, brow-lift procedures that primarily elevate the medial and mid brow are unlikely to provide aesthetic improvement. Selective elevation of the lateral brow may achieve a more desirable effect.

Reviewer's Comments: This study is intriguing and challenges the traditional notion of brow descent with aging. The findings of this study suggest that, on average, the medial and mid brow ascends, or at least remains level with aging in many patients. Although, the authors also acknowledge that this does not apply to all individuals and is subject to individual variations. Nevertheless, the study offers a potential explanation for why many brow-lift procedures even though having accomplished elevation result in suboptimal aesthetic improvement of the upper face and may appear unnatural. (Reviewer-Tang Ho, MD).

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Keywords: Browlift, Brow Position, Facial Rejuvenation

Print Tag: Refer to original journal article
Direct muscle neurotization may be a useful adjunctive facial reanimation procedure in the pediatric population.

**Background/Objective:** The surgical treatment of facial paralysis often requires multi-stage reconstructive procedures for functional and aesthetic restoration. Options range from dynamic facial sling to free tissue transfer. In this study, the senior author's experience with the technique of direct muscle neurotization to augment the function of the eye sphincter, to improve the smile, and to strengthen the depressor muscle as part of the multi-staged facial reanimation surgery in the pediatric population is presented.

**Design:** Retrospective analysis of the records of 37 patients who underwent direct muscle neurotization with interposition nerve graft.

**Methods:** The study population was divided into 3 groups based on the targeted area of facial reanimation. Twenty-eight patients were included in the group for improvement of eye closure and blink, 15 patients were in the group for improvement of smile, and 19 patients were in the group for depressor augmentation. Analyzed factors including age, denervation time, etiology of the lesion, previous reconstructive procedures, and types of muscles responsible for animation.

**Results:** The age of patients ranged from 1 to 16 years, with a mean of 9 years. The time of denervation ranged from 3 months to 15 years, with a mean of 6.72 years. All patients experienced improvement based on evaluations of independent investigators. Age was negatively correlated with the functional result after direct muscle neurotization, and better results were achieved in patients aged <13 years. EMG studies showed 36% improvement in score in eye closure, a 37% improvement for smile, and a 30% improvement in depressor function after the procedure.

**Conclusions:** The use of direct muscle neurotization may be a useful adjunctive procedure in facial reanimation in selected candidates.

**Reviewer's Comments:** Surgical rehabilitation of the paralyzed face is a challenging task partly because of all the different options available. An individualized treatment plan based on the patient's condition and his or her wish is key. The process usually involves multi-stage procedures. As this study has shown, direct muscle neurotization may be a useful adjunctive procedure in the treatment plan. However, as the procedure is usually done in conjunction with other surgeries, it is difficult to assess how much improvement is due to the neurotization procedure. The procedure's effectiveness may also depend on the types of muscle that are being neurotized (native facial muscles, local pedicled muscles, and free transplanted muscles). (Reviewer-Tang Ho, MD).

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Keywords: Facial Paralysis, Facial Reanimation, Muscle Neurotization

Print Tag: Refer to original journal article
The endoscope has its place in sinonasal tumor management, but clinical judgment to select the appropriate patients should supersede any specific approaches.

**Objective:** To review the authors’ series in the management of sinonasal cancer treated with endoscopic resections.

**Design/Methods:** This was a retrospective review of the records of patients at M.D. Anderson with biopsy-proven malignancy in the sinonasal tract from 1992 to 2007. The charts were analyzed for final histology, staging, type of surgery, survival outcomes, recurrence, and complications particular to endoscopic resections.

**Results:** 120 patients were treated with endoscopic resections of sinonasal cancer in this series. Of these, 22.5% also had an open craniotomy for a combined cranio-endoscopic approach. The histology consisted of esthesioneuroblastoma, adenocarcinoma, squamous cell carcinoma, sarcoma, and others. There was no preponderance of one specific histology. In general, however, the advanced-stage tumors were treated with combined open craniotomy and endoscopic approaches. Positive margins were noted in 15% of cases. Fifty percent of cases were treated with surgery alone, reflective of the fact that approximately 50% were early stage tumors. The other half of cases were treated with adjuvant modalities (postoperative radiation therapy or chemoradiation therapy). The rate of cerebrospinal fluid leakage was 3%. A notable finding was that overall survival for those with persistent disease after incomplete resection was significantly worse. The authors found no differences in overall survival between those treated with endoscopic resection only versus combined cranio-endoscopic surgery. The 5- and 10-year disease-specific survival rates were 87% and 80%, respectively.

**Conclusions:** Endoscopic resection of sinonasal cancer in well-selected patients has acceptable oncologic outcomes.

**Reviewer’s Comments:** Despite the recent trends in endoscopic resections of sinonasal cancer, most reports have been small case series and have concentrated on esthesioneuroblastoma. This is a comprehensive retrospective review from M.D. Anderson of 120 patients who had been treated with endoscopic resections of all types of sinonasal cancers. Given that all types of tumor at all stages were combined for this analysis, it is difficult to assess whether the survival rate from this series can be compared to other modalities of treatment. Although the authors quote their survival rates as >80%, this number is pooled from all histologies, so it is difficult to make sense of this number. However, the authors acknowledge that the advanced-stage tumors were typically treated with combined endoscopic and open craniotomy approaches. They explicitly state that they have a low threshold for combining approaches for advanced tumors. With greater skull base defects, the open approaches allowed the authors to perform duraplasty with vascularized pericranial flaps. This may have contributed to the low complication rates for cerebrospinal fluid leaks (3%). The take-home message is that the endoscope has its place in sinonasal tumor management, but clinical judgment to select the appropriate patients should supersede any specific approaches. (Reviewer-Young J. Kim, MD).

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Keywords: Sinonasal Cancer, Endoscopic Resection

Print Tag: Refer to original journal article
**Objective:** The authors examined the relationship between the use of intraoperative vasopressor use and free flap complications, given the recent documentation of high free flap survival rates in our literature.

**Design/Methods:** This is a retrospective case series comparing 2 cohorts of patients who underwent free flap tissue transfer surgery. The authors compared one cohort who received intraoperative vasopressors with another who did not receive any intraoperative vasopressors. The amount and type of vasopressor used and free flap complications documented within 7 days postoperatively or at discharge were noted.

**Results:** 241 cases were screened, and 169 cases had sufficient documentations for inclusion. Overall, the free flap survival rate was 96.5%; 82% of cases had received vasopressors. Of these, 2.9% had free flap failures, and 29% had free flap complications. Among the non-vasopressor group, 6.7% had free flap failures, and 30% had free flap complications.

**Conclusions:** From this series, the authors noted that the use of vasopressors was more frequent than expected, but this did not result in overall free flap failure or free flap complications.

**Reviewer's Comments:** Since the concept that vasopressors should be avoided during free flap surgery was predominantly based on animal studies, this retrospective case series study was quite a welcome. The findings were also intriguing since the use of vasopressors intraoperatively was not associated with higher rates of free flap failure. Some points need to be mentioned, however. Of the patients in this study, 82% received some form of vasopressors, and it is unclear when they received the vasopressors. Vasopressor given early in the ablative portion of the surgery may not affect the reconstructive phase of the surgery, which is performed at the tail end of the operation. Also, given that only 30 of 241 patients did not receive a vasopressor, it is unclear if the statistical analysis is valid. Regardless, the authors report that 8 patients received phenylephrine drips throughout the surgery, and none had free flap complications. (Reviewer-Young J. Kim, MD).
This article presents the most recent 2009 NIH guidelines for surgical management of patients with asymptomatic hyperparathyroidism

**Objective/Background:** This is a review of the most recent guidelines for the surgical management of asymptomatic hyperparathyroidism. Previously, the National Institutes of Health (NIH) published a guideline in 1990. This guideline was revised twice since then, and another revision was presented in 2009. The authors of this report summarize the most revised guidelines.

**Methods:** The authors reviewed the NIH guidelines and reported the most recent revisions.

**Results:** In terms of the guidelines, several key indications for surgery remained unchanged. Surgery should be recommended for those >50 years old. Also unchanged is the actual value of serum calcium. The threshold value for calcium is 1.0 mg/mL above the upper limit of normal. What changed in 2009 is the recommendation that the glomerular filtration rate (GFR) should be obtained, and those with GFR <60 mL/min are surgical candidates. Previously, the primary measurement of renal function was creatinine clearance, but the NIH now recommends GFR measurements. The 2009 NIH guidelines also do not use 24-hour urine calcium measurements. In terms of bone density, patients with a T score less than -2.5 at any site are candidates for surgery. For those not having surgery, annual serum calcium and creatinine levels are recommended. A bone density test is recommended every 1 to 2 years.

**Reviewer's Comments:** The NIH guidelines and the subsequent revisions should be noted by all otolaryngologists managing patients with hyperparathyroidism. Not included in these guidelines are the non-quantifiable symptoms of fatigue or other neurocognitive symptoms. Level 1 evidence is needed for following these symptoms. Also not included in the guidelines are considerations of co-morbid cardiovascular diseases that can be exacerbated with hyperparathyroidism. It should be noted that these NIH guidelines are simply that – “guidelines” – and that these recommendations should not be used proscriptively to the letter. (Reviewer-Young J. Kim, MD).

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Keywords: Primary Hyperparathyroidism, Parathyroidectomy, NIH Guidelines

Print Tag: Refer to original journal article
**Mucosal Eosinophilia Negatively Affects QOL After Endoscopic Sinus Surgery in CRS**


Soler ZM, Sauer D, et al:

Otolaryngol Head Neck Surg 2010; 142 (January): 64-71

Patients with non-eosinophilic chronic rhinosinusitis without nasal polyps have the lowest improvement in quality of life measures after endoscopic sinus surgery.

**Background:** Many investigators have argued for the inclusion of eosinophilic inflammation as a feature to define a specific subset of patients with chronic rhinosinusitis (CRS). Previous studies have, in fact, shown that mucosal eosinophilia correlates with baseline objective disease severity, as defined by CT, endoscopy, and olfactory testing.

**Objective:** To determine whether eosinophilic status can predict long-term outcomes in patients with CRS after endoscopic sinus surgery.

**Design:** This is a prospective cohort study performed at a single academic tertiary care center.

**Participants:** 102 patients were included, with a mean follow-up of 16.5 months.

**Methods:** For each patient, preoperative and postoperative quality of life (QOL) was assessed using the Chronic Sinusitis Survey, Rhinosinusitis Disability Index, and the 36-Item Short Form Health Survey. Sinus mucosal specimens were obtained from each patient at the time of surgery, and the degree of eosinophilia was assessed.

**Results:** No differences in disease-specific and general health QOL scores were observed between patients with and without eosinophilia (defined by >10 or <10 eosinophils/HPF). A statistically significant improvement after surgery was seen across most QOL indices for patients regardless of eosinophilia. However, patients with eosinophilia showed significantly less improvement in most QOL indices compared to patients without eosinophilia.

**Conclusions:** The greatest improvement in QOL scores was seen in patients with non-eosinophilic CRS without nasal polyposis. The least improvement in QOL scores was seen in patients with eosinophilic CRS without nasal polyposis.

**Reviewer's Comments:** Many authors have argued the importance of a clinical classification scheme that categorizes CRS patients into groups with or without mucosal eosinophilia and/or nasal polyposis, arguing in many cases that these data may provide important prognostic information. This proposal is supported by the current study by Soler et al. The authors note that, in CRS patients without nasal polyps, the presence of mucosal eosinophilia predicted the least improvement in QOL after surgery compared to CRS patients without eosinophilia, 2 groups of patients who might otherwise be indistinguishable clinically. This ability to predict postoperative QOL outcomes did not apply to patients with nasal polyposis, considered by many investigators to be a different disease process entirely. This study is strengthened by its large sample size, adequate follow-up, and multitude of clinically validated QOL measures. These findings are useful, both to clinicians and patients, in predicting long-term prognostic information and in surgical planning. (Reviewer-Justin H. Turner, MD, PhD).

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Keywords: Eosinophilia, Endoscopic Sinus Surgery, Quality of Life, Chronic Rhinosinusitis

Print Tag: Refer to original journal article
Does Endoscopic Resection of Pituitary Tumors Affect Olfactory Function?

Olfactory Changes After Endoscopic Pituitary Tumor Resection.
Hart CK, Theodosopoulos PV, Zimmer LA:

Otolaryngol Head Neck Surg 2010; 142 (January): 95-97

The transnasal endoscopic approach to pituitary tumors has no clinically significant effect on olfaction.

**Background:** Endoscopic pituitary tumor resection is a minimally invasive approach that results in reduced morbidity compared to earlier approaches. In the past, the sublabial transseptal transsphenoidal approach was associated with olfactory deficits in up to 12% of patients. The impact of the endoscopic approach to pituitary lesions is unknown.

**Objective:** To evaluate the effect of endoscopic pituitary surgery on olfactory function.

**Design:** This case series was gathered from a single tertiary care academic institution.

**Participants/Methods:** A total of 57 consecutive patients were enrolled in the study, all of whom underwent transnasal endoscopic resection of a pituitary lesion. Patients underwent preoperative and postoperative olfactory evaluation using the University of Pennsylvania Smell Identification Test (UPSIT). Preoperative and postoperative scores were then compared.

**Results/Conclusions:** The average preoperative UPSIT score was 31.7. The average postoperative scores were 30.0 at 1 month and 32.9 at 3 months after surgery. Mean changes in the number of incorrect answers were statistically significant at 1 month postoperatively, but did not reach statistical significance at 3 months.

**Reviewer's Comments:** Cells of the olfactory neuroepithelium are found primarily along the cribriform plate, superior turbinate, and superior nasal septum. Since the transnasal transsphenoidal endoscopic approach to the sella requires resection of the posterior septum, one might expect some effect on olfactory function in these patients. In the current study, Hart et al. report a minimal impact of this procedure on objective measures of olfactory function. Although there was a marginally significant difference in UPSIT scores 1 month after surgery, the authors correctly note that this is at a time when mucosal surfaces are generally edematous, with likely resulting changes in air flow patterns to the olfactory cleft. As expected, 3 months postoperatively when this local inflammation has typically resolved, olfactory function is unchanged. The authors do, however, fail to recognize the possible role of olfactory neuroepithelial damage with subsequent olfactory neuronal regeneration in the recovery of function postoperatively. Furthermore, although the study has an adequate patient population, there are several shortcomings, including a lack of demographic and/or rigorous statistical analyses. It is nonetheless likely that the findings are accurate and suggest that olfactory changes after endoscopic pituitary approaches are equal to or less than those of earlier approaches. (Reviewer-Justin H. Turner, MD, PhD).

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Keywords: Endoscopic Sinus Surgery, Pituitary, Olfaction

Print Tag: Refer to original journal article
Reciprocal papillomatosis in the pediatric population is associated with a lower rate of dysplasia than adult-onset disease.

**Background:** Cidofovir use was recently reported to be associated with progressive dysplasia in isolated case series. However, it is unclear if cidofovir can cause dysplasia in patients with papillomatosis. Moreover, although there is evidence that adult-onset laryngeal papillomatosis is associated with malignancy in 2% to 4% of cases, it is unclear whether laryngeal papillomas in the pediatric population behave in a similar fashion.

**Objective:** To document the rate of transformation in juvenile-onset recurrent respiratory papillomatosis (RRP), and to determine whether cidofovir use in this population increases the risk of dysplastic transformation.

**Design/Methods:** This is a retrospective analysis during a 10-year period at a pediatric tertiary academic center. Included were all patients with RRP who underwent surgical treatments with pathologic specimens. Clinical data, demographics, number of surgeries, exposure to tobacco, and symptoms of reflux were noted. Specimens were analyzed by pathologists for mitotic activity, basal cell hyperplasia, disordered maturation, nuclear abnormalities, cytoatypia, metaplasia, or any features of HPV infection. Dysplasia was defined as the absence of maturation above the basal cell layer or having mitotic features.

**Results:** 21 patients were evaluated in this series, with a total of 123 specimens. Among these specimens, only one had dysplasia. Seven of these patients received cidofovir, and none developed dysplasia.

**Conclusions:** The association between dysplasia and recurrent respiratory papillomatosis is rare, and the authors found no association between cidofovir use and dysplasia in this series.

**Reviewer's Comments:** Given the low number of patients in this series, the authors used the total number of specimens as their denominator to conclude that the rate of dysplasia is low (<1%). However, the error lies in the fact that these biopsies are not excisional biopsies, so the true rate of dysplasia is not clear. Regardless, the rate of dysplasia in this series suggests that juvenile-onset RRP may be a different disease from adult-onset RRP. In adult-onset RRP, Dr. Jonas Johnson and others have reported dysplasia rates as high as 55%. One reassuring result in this series was that cidofovir use was not associated with dysplasia in the pediatric population. (Reviewer-Young J. Kim, MD).

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**Keywords:** Recurrent Respiratory Papillomatosis, Cidofovir, Dysplasia

**Print Tag:** Refer to original journal article
PET-CT scan may offer the best way to localize the primary tumor site in patients with cervical carcinoma with an unknown primary site.

**Background/Objective:** Patients with an unknown primary site with neck metastasis are a constant diagnostic dilemma for otolaryngologists. Currently, there are no clear winners on which imaging modalities offer the best chance for detecting the primary site. The authors, therefore, reviewed their series in the management of unknown primary tumors.

**Design/Methods:** This is a retrospective review of the medical records of 183 patients with an unknown primary tumor at a single academic institution over a 10-year period. Excluded were those with previous head and neck cancer or those with primary tumors of the neck (lymphoma or sarcoma). Patients with an unknown primary on initial consultation underwent imaging studies, including CT, MRI, PET, or PET-CT. They also underwent operative endoscopies, directed biopsies, and tonsillectomies. The main outcome measure was the rate of identification of the primary tumor site with the various imaging and operative methods.

**Results:** Of 2245 patients, 183 patients were included in the study; 78.2% presented with level II lesions. CT was the modality of choice during the first half of the time period, with almost 80% of patients undergoing the procedure. A PET-CT scan was initiated during the second half of the study and constituted 28% of the imaging work-up. Only 7% of patients underwent MRI, while 22% had PET. The rate of successful localization of the primary site was 9.5% for CT, 14.6% for PET, and 44.2% for PET-CT. MRI was unable to detect any primary site. Overall, the combination of PET-CT and panendoscopy with directed biopsies with or without tonsillectomy had the best yield in determining the primary site.

**Conclusions:** PET-CT combined with panendoscopy and directed biopsies (including tonsillectomy) had the best likelihood of localizing the primary tumor site.

**Reviewer's Comments:** Although these authors recommend the superiority of PET-CT in the work-up of unknown primary tumors, their data are flawed at several levels. First, one obvious flaw is sampling bias. CT scans were used exclusively early in the series, while PET-CT scans were used exclusively in the second half. It is unclear if the patient population (or the disease pattern) may have accounted for the improved sensitivity of PET-CT over other imaging modalities. Second, it is unclear how the various methods were analyzed to render them either positive or negative. Third, it is unclear how the use of panendoscopy and directed biopsies affected the imaging modalities. Given that detection with PET-CT scans are typically still limited to lesions <1 cm, there is a lack of biological feasibility that PET-CT scans are superior to other imaging techniques. Overall, this paper lacks the ability to generalize the results to other otolaryngologists. (Reviewer-Young J. Kim, MD).