Published in final edited form as:

Laryngoscope. 2012 March ; 122(3): 539–542. doi:10.1002/lary.22406.

Screening for Head and Neck Cancer in Liver Transplant Candidates: A Review of 11 Years Experience at the University of Pittsburgh

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Abstract

Objectives/Hypothesis—At our institution, any liver transplant candidate with a recent history of smoking combined with daily use of alcohol prior to a six-month sobriety period warrants formal evaluation by otolaryngology. Given the significant resource consumption and lack of evidence in support of this strategy, we sought to determine the effectiveness of these guidelines in detecting head and neck cancer.

Methods—Under an IRB approved protocol, a search was performed for patients seen at our institution's otolaryngology office from 1999 to 2010. This patient list was cross-matched with the patients evaluated for transplant at University of Pittsburgh Starzl Transplantation Institute during the same timeframe. A search for the diagnosis of HNC among these patients was carried out through both a National Cancer Institute-affiliated clinical research registry and ICD-9 codes from billing records. Otolaryngology attending physicians were also asked to recall detection of HNC upon screening of this patient population.

Results—Of 581 patient evaluations performed by the otolaryngologist for HNC screening prior to liver transplantation from 1999–2009, 1 (0.17% of evaluations) case of head and neck cancer was detected.

Conclusion—Given the consumption of resources required for this screening strategy and the limited yield, it appears that current screening guidelines are ineffective and need to be reconsidered.

Level of Evidence—2c

Keywords

liver transplantation; head & neck cancer; screening; epidemiology

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Financial Interests: None

Conflicts of Interest: None

Introduction

Head and neck cancer encompasses epithelial malignancies that arise from the paranasal sinuses, nasal cavity, oral cavity, pharynx and larynx. The overwhelming majority of these malignancies are head and neck squamous cell carcinoma of the head and neck (HNC). Head and neck cancer is the sixth most common type of cancer, representing about 6% of all cases and accounting for roughly 650,000 new cancer cases and 350,000 cancer deaths worldwide each year. In the United States in 2007, an estimated 45,660 new cases were diagnosed and 11,210 deaths were caused by head and neck cancer.¹ Several known risk factors exist for HNC, most notably tobacco and alcohol exposure. There is a relative risk (RR) of 1.5–10 for tobacco alone for various HNC sites.² Case-control studies have demonstrated the carcinogenic effect of alcohol on the oropharynx with odds ratio (OR) of 8.8 for heavy drinkers (consuming >30 alcoholic drinks/week). There is a markedly multiplicative effect of tobacco and alcohol on the development of HNC in this region with an OR of 37.7 for males who are both heavy drinkers and heavy smokers (smoking > 2 packs per day for 20+ years).³

Alcoholic liver disease (ALD) is the second most common cause of end-stage liver disease (ESLD) leading to orthotopic liver transplant (OLT), after viral hepatitis.⁴ International and domestic studies report between 52–54% of all potential OLT recipients (including non-ALD etiologies) regularly use both alcohol and tobacco prior to the abstinence period.^{5,6} Given the effects of alcohol and smoking on the development of HNC, the patient population requiring OLT theoretically faces a higher likelihood of developing HNC. With greater than one-half of liver transplant candidates exposed to the synergistic effect of alcohol and tobacco on HNC, screening for head and neck cancer may be beneficial at some level in the pre-OLT period. The spectrum of screening for HNC ranges from visual inspection and manual palpation of the oral cavity and oropharynx by a general practitioner to flexible fiberoptic nasopharyngolaryngoscopy by the otolaryngologist. The latter intervention requires significantly greater health care resources yet serves as the gold standard for cancer diagnosis by virtue of its complete visualization of the upper aerodigestive tract.

At present, uniform screening guidelines prior to transplantation do not exist. Individual transplant centers use current evidence in combination with past experience to formulate hospital protocols. At the University of Pittsburgh Medical Center (UPMC) Starzl Transplantation Institute, the governing protocol for at least the last ten years mandates that liver transplantation candidates smoking tobacco of any kind in the past year combined with regular, daily use of alcohol receive an outpatient otolaryngology consult for formal evaluation of head and neck cancer. Given the significant resources consumed by outpatient otolaryngology referrals and subsequent workup, our primary aim was to study the effectiveness of this protocol in detecting head and neck cancer prior to transplantation.

Materials & Methods

The study protocol was approved by the University of Pittsburgh's Institutional Review Board in December 2009. Given the lack of a single database with the information required to answer our objective, a two-part approach was taken to seek liver transplantation patients evaluated for head and neck cancer. First, an electronic search was conducted from the electronic billing records for all outpatient otolaryngology evaluations in the general and head and neck oncology divisions from January 1, 1999 to January 1, 2010. This result list was matched by name, date of birth and medical record number against the Electronic Database Interface for Transplantation (EDIT), a clinical registry maintained by the University of Pittsburgh Starzl Transplantation Institute since 1994. Second, electronic

otolaryngology billing records from all divisions were queried by referring physician being in the liver transplantation department. These results were again matched against the EDIT as mentioned previously.

Patients common to the otolaryngology billing records and EDIT from both search strategies were further investigated based on two methods. These two strategies were related and semi-overlapping in an attempt to capture the intended population. The first strategy filtered patient billing records based upon otolaryngology clinic visits occurring within 180 days after liver transplant evaluation. These records were then examined for associated ICD-9 codes for diagnosis of head and neck cancer. ICD-9 codes considered as head and neck cancer included lips, oral cavity and pharynx (140–149), nose and paranasal sinuses (160), larynx (161) and those associated with unknown primaries (195 and 196).

The second method searched the National Cancer Institute-funded University of Pittsburgh Cancer Institute's Head and Neck Organ-Specific Database (H&N OSD). This clinical database contains patients with tissue-proven head and neck cancer diagnoses or having received the first part or all of their treatment at the University of Pittsburgh Medical Center (UPMC). The matches were then filtered based on patient billing records indicating that the visit to the otolaryngology clinic occurred within 180 days after liver transplant evaluation. In an attempt to validate our research findings, all attending physicians (n=7) currently employed at our institution involved in head and neck cancer screening were asked to recall having discovered suspicious lesions from this patient population.

Results

A total of 70,534 patient encounters were seen in the head and neck surgical oncology & general otolaryngology outpatient clinic over the 11 year period. One-hundred and fourteen patient encounters in all otolaryngology outpatient clinics were identified based on search by referring physician being in the transplantation department over the same 11 year interval (Figure 1). Based on EDIT, 815 (involving 794 unique patients) of the 7743 encounters seen by liver transplantation from 1999–2009 were common to otolaryngology billing records. Of the 794 patients, 580 patients had been seen in otolaryngology clinic within six months of liver transplant evaluation. Eight patients were evaluated twice and only the first evaluations were considered. These 580 patients were considered the population of interest as the chronology of the liver transplantation and otolaryngology evaluations were highly suggestive of head and neck cancer screening referral.

Table 1 demonstrates baseline clinical data including age, gender, race, transplantation received, alcoholic cirrhosis as a primary indication for transplant for the 580 patients in our selection.

The administrative data provided ICD-9 diagnoses and procedure codes for each patient encounter. Table 2 illustrates the number of patients evaluated by flexible fiberoptic laryngoscopy in the otolaryngology clinic and relevant findings per billing records. Additional information in the table includes number of patients with office biopsy by site of lesion.

Eight of the 580 patients had an ICD-9 code of H&N cancer from billing records. The H&N OSD detected 5 patients from the list of 580 patients with a H&N cancer diagnosis. Two of these patients were common to the 8 patients from the first strategy while 3 were new 'hits' (Figure 2). Adding the 8 patients from ICD-9 codes and 3 patients from the OSD, 11 patient charts were further explored.

Subsequent chart reviews for these 11 patients revealed 8 patients with previous diagnosis of H&N cancer, 2 patients with development of H&N cancer post-transplantation (diagnosis made at 3 years and 7 years post-transplant) and 1 patient with thyroid cancer miscoded as head and neck cancer. As a result, 0 patients were found to have head and neck cancer from the administrative and clinical databases at the time of screening.

Otolaryngology faculty in the Head and Neck and General divisions currently employed at our institutions were contacted via e-mail or face-to-face correspondence. Sixty-three percent of the 580 patients were seen primarily by one of the 7 physicians contacted. The physicians were asked to recall any cancers discovered on head and neck cancer screening from liver transplantation referral. Six of the seven attending physicians did not recall ever detecting a cancer on screening. One attending vividly recalled the patient's name, approximate year of diagnosis, site of lesion and subsequent treatment for the cancer. Our database had a record of this patient visit in 2004, but no record of this patient's visit in 1999 was found in EDIT. Further chart exploration, however, revealed that this patient had been seen by otolaryngology in 1999 for head and neck cancer screening referral from liver transplantation. At that time, a suspicious oropharyngeal tongue and ipsilateral neck mass was noted. Biopsy of both sites in the operating room revealed squamous cell carcinoma of the oropharynx. This patient was treated with radiation therapy at that time, re-evaluated in 2004 for liver transplantation (after 5 cancer-free years) and successfully transplanted later in 2004.

Therefore, of 581 (580 from the database and 1 from attending recall) patient evaluations performed by the otolaryngologist for potential HNC screening prior to liver transplantation, 1 (0.17% of evaluations) case of head and neck cancer was detected. Applying the Poisson Exact distribution via STATA Statistical Software Release 10⁷, a 95% confidence interval of 0.0044% to 0.96% of evaluations was obtained.

Discussion

In an era of heightened focus on resource allocation, this paper evaluates the effectiveness of the screening referral pattern of our institution's highly active transplant program. This is the first study to examine the yield from the screening of liver transplantation candidates for head and neck cancer. Our results demonstrate that 1 of the 581 patients seen for head and neck cancer screening yielded a positive result. One method to evaluate the effectiveness of this intervention is through a societal cost-benefit ratio. Costs of screening include indirect costs (patient, caregiver and physician time) and costs of service. Given the difficulty in measuring indirect costs, we will include costs of service using Medicare reimbursement data. The cost of a level IV ENT consult (\$152) added to 27% (percent of patients evaluated by FFL) of the cost of flexible fiberoptic laryngoscopy (\$70) equals an average patient cost of \$171 per visit. Multiplying this value by the 581 patients evaluated equals roughly \$100,000 per positive screen. This cost-benefit ratio represents the amount of health care dollars spent (time costs excluded) to find one head and neck cancer in patients evaluated for liver transplantation.

As a retrospective review, this study suffers from several shortcomings. A prospective study would definitively answer the study question; however, given the rarity of the disease, the required sample size and follow-up render such a study extremely difficult. The clinical databases proved incomplete as evidenced by the physician recall of the lone positive screen. The databases also do not contain complete information regarding measurements of patient alcohol and tobacco usage, which would allow for characterization of relative risks for head and neck cancer. Additionally, the reason for otolaryngology referral was inferred from patient charts but not clearly documented. Other missing information included HNC-

related presenting symptomatology such as hoarseness, otalgia, dysphagia upon visit to the liver transplantation team. Apart from flexible fiberoptic laryngoscopy recorded in the billing records, details of the head and neck cancer screening evaluation such as evaluation by indirect laryngoscopy were not known. Information regarding patients who were lost to follow-up after the liver transplantation or received their post-transplant care at an outside institution is not available.

Despite the abovementioned limitations of this retrospective review, the findings of this study are sufficient to conclude that the current screening protocol needs to be re-examined. In particular, a thorough history and physical examination of patients with a alcohol and tobacco history is warranted. High-risk patients should receive a thorough review of systems including common presenting symptoms of head and neck malignancy. These symptoms include pain, bleeding, ulceration, hoarseness, otalgia, and/or dysphagia.⁸ Orderly visual inspection of the entire oral and oropharyngeal mucosa with particular attention to the tongue, floor of mouth, soft palate, uvula, tonsillar pillars, and the lingual aspects of the retromolar trigones should be performed in this subpopulation. This examination can be performed cheaply and quickly by trained health care professionals with both a high sensitivity and specificity for disease detection.⁹ Patients whom are found to have positive findings on head and neck review of symptoms and/or physical examination should be referred to otolaryngologists for further evaluation.

Conclusion

At present, screening for head and neck cancer among smokers evaluated for liver transplantation has a societal cost (time costs excluded) of \$100,000 per individual detected based on 1 positive screen out of 581 evaluations. The acceptability of this cost-benefit ratio of screening is subject to debate given the scarcity of organs and subsequent investment of resources required for liver transplantation. The overall cost of transplanting a patient with occult HNC is unknown; nevertheless, it appears evident that the use of tobacco and alcohol history alone as per current screening guidelines do not optimally capture high-risk individuals. Future steps toward smarter, resource-effective screening include recording patient symptomatology and performing a complete head and neck physical examination.

Acknowledgments

The authors would like to thank Joseph Donaldson, database manager of Electronic Database Interface for Transplantation (EDIT).

Grant Support:

Dr. Jennifer Grandis - BMS

Dr. Raj Dedhia - National Institutes of Health T32 CA60397 and SPOR P50 CA097190.

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FIGURE 1.
Search Strategy

FIGURE 2.
Potential Positive Screenings from Database Search

TABLE 1

Demographics

	n= 580
Mean age (Years)	53
Female	24%
White	90%
Transplantation Received	47%
Primary Indication for Transplant	
Alcoholic Cirrhosis	45%
Hepatitis C Virus-Induced Cirrhosis	35%

TABLE 2**Diagnostics**

	n= 580
Evaluations with Flexible Fiberoptic Laryngoscopy (FFL) (%)	160 (27%)
<i>Diagnoses (% FFL patients)</i>	
Esophageal Reflux	37 (23%)
Other Vocal Cord Disease *	12 (8%)
Office Biopsy (%)	11 (2%)
<i>By Site</i>	
Nasopharynx	1
Floor of Mouth	1
Mouth	4
Skin	1
Oropharynx	1
Palate/Uvula	3

* includes acute laryngitis, chronic laryngitis, edema of larynx, vocal cord disease NEC, vocal cord paralysis NOS, vocal cord/larynx polyp