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Head and Neck Carcinoma in the Young Patient

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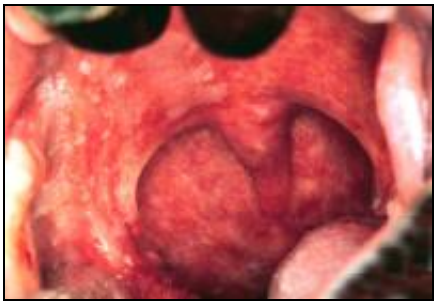
Introduction

Problem

Head and neck squamous cell carcinoma (HNSCC) typically develops in the sixth to seventh decade of life. Since Byers identified this subset of patients in 1975, clinicians have become increasingly aware of patients who develop HNSCC at a young age, variably defined as age 30 years and younger, 40 years and younger, or 50 years and younger.[1] These patients may represent a distinct cohort with different risk factors and disease behavior.

This article addresses this cohort, defined here as young adults, age 20-45, with HNSCC. As discussed below, these cancers tend to occur in the oral cavity and oropharynx, rather than other head and neck subsites. This article primarily addresses squamous cell carcinoma (SCC), but other histology is noted when appropriate. This article does not address pediatric head and neck tumors, and the reader is referred to other chapters for this topic.



Reddening of the soft palate, perhaps with scattered areas of white and velvet red patches, tobacco-induced squamous cell carcinoma involving the tongue base and/or supraglottis, and a firm, mobile mass that is palpable at the left carotid bifurcation.

Frequency

The incidence of HNSCC in young patients is approximately 1-8% of all head and neck cancers, based on modern reports from the United States, Canada, Great Britain, Spain, Scandinavia, India, and Japan.[2,3,4,5,6,7,8,9,10,11] Current evidence suggests that this incidence may be increasing.

From 1973-2001, Shiboski et al demonstrated an increase of approximately 1-4% in the incidence of oral cavity and pharynx cancer among young whites based on subsite.[4] Similarly, Schantz and Yu noted a 60% increase in the incidence of tongue cancer in young patients from 1973-1997, with no increase in incidence for other age groups.[12] Both studies used National Cancer Institute Surveillance, Epidemiology, and

End Results (SEER) data for their analyses. The etiology of this increasing trend is unclear, although marijuana use and human papillomavirus (HPV) infection are possible explanations.[4,7,3]

Gender

Although HNSCC generally remains more common in males, even among young patients, some studies have reported a higher relative incidence in females.[8,13,11,14]Furthermore, one report demonstrated a reversal of the typical male-to-female ratio in favor of women within the 35-year-old or younger age group.[10]

Additionally, these cohorts of young women lack the typical associated risk factors of alcohol, tobacco, and betel nut exposure and may represent a unique subset even within young HNSCC patients.[10,14,15,1]

Funk proposed the following 3 groupings of young patients with head and neck cancer:[14]

- Group I is composed of young women (<35 years) with few to no risk factors and aggressive squamous cell carcinoma (SCC)
- Group II are typically young males (<40 years) with heavy risk factors and disease typical of older patients
- Group III has a slight male predominance but fewer risk factors and relatively well-differentiated disease.

In Funk's review of oral cancer in the National Cancer Data Base (NCDB) between 1985 and 1996, the predominant group was Group III.[14]If this categorization is valid, the group of patients predominating any given study may change the significance of gender and other factors.

Race

Among the few studies that address race, conflicting data are found in young patients with HNSCC. Shiboski et al found an overall higher percentage of oral cavity and pharynx cancer among young whites compared with young African Americans from a 1973-2001 SEER database analysis and found the incidence of these cancers increased in that time period only among young whites.[4]

However, Kolker et al, looking at statistics from metropolitan Detroit, a predominantly African American area of Michigan, found a higher incidence of oral and pharyngeal cancer among African Americans compared with whites in the 50 and under age group.[16]Similarly, Slotman et al found a higher incidence of HNSCC in African Americans younger than 45 years in 2 disparate locations.[17]The first was in East Orange, Virginia, where 21% of the 847 patients studied from 1968-1980 were African American. The second was the New Jersey Medical School, where 74% of the 219 patients studied from 1970-1980 were African American.

Both sites found a trend toward younger age at presentation for African Americans. In the first site, 13% of African Americans presented before age 45, compared with 3% of whites; in the second site, 15.3% of African Americans presented before age 45, compared with 2% of whites. Slotman and colleagues also noted a lower 5-year survival rate for African Americans in all age groups.

No data exist in the above studies to explain the racial differences in age at presentation. Slotman and colleagues suggested that their African American patients may have started using tobacco and alcohol at a younger age, but the authors did not provide comprehensive data to support this theory.[17]Clearly, except for the SEER data, the above studies are small and subject to the populations they survey, which may bias their findings.

Site

HNSCC in the young patient tends to occur in the oral cavity and oropharynx.[3]In the oral cavity, the oral tongue is the most common subsite in the young in most series;[8,12,18,14,11]the floor of the mouth has been reported as a less common subsite in the young patient compared

with older patients.[14]

The incidence of oral tongue and tonsil cancer seems to be increasing among younger patients.[19,12,4,20]The association of oropharyngeal cancer with HPV infection (see Etiology and Risk Factors) lends circumstantial evidence to that virus's role in the etiology of HNSCC in the young adult. Because HPV's role in the etiology of oral cancer is controversial, HPV carcinogenesis is not yet a convincing explanation for the increase in both oral cavity and oropharyngeal tumors.

Within the oral cavity, certain non–SCC histologies also account for a substantial proportion of cancers in the young patient. In particular, adenocarcinoma and Kaposi sarcoma tend to occur on the palate, making the palate another oral cavity subsite that is more common in young patients compared with older patients.[14]

Larynx cancer accounts for a lower percentage of HNSCC in young patients compared with older patients,[3]and nasopharyngeal carcinoma is more common in older adults than in the younger adult.[21]

Stage

Many of the studies comparing young patients who have HNSCC with old patients with HNSCC use tumor stage as a matching criteria for creating the older, "control" cohort, thus limiting the data comparing stage at presentation. Only those studies looking at whole populations can reliably comment on differences in stage at presentation. Schantz and Yu reviewed the 1973-1997 SEER database and found younger patients to be more likely to present with localized disease than older patients.[12]Similarly, Funk's review of the 1985-1996 NCDB demonstrated younger patients to present at an earlier stage across all types of histology, and a statistically significant higher proportion of stage I disease among young patients when analyzed only for squamous cell carcinoma (SCC).[14]

Contrary to these findings, in small single-institution studies, Verschuur and colleagues and Veness and colleagues both found a higher rate of nodal metastases at presentation in younger patients.[3,22]However, Veness and colleagues also found older patients to be more likely to present with a higher T stage compared with younger patients; this latter finding was echoed by Sasaki and colleagues in their single-institution series.[8]In summary, although a propensity for increased nodal metastases among some young patients may exist, this has yet to be clearly defined, and evidence from the largest databases suggests young patients present at similar or earlier stages than older patients.

Histology

In Byers's report from 1975, his young patients (<30 years old) with oral tongue squamous cell carcinoma (SCC) had a high percentage (almost 50%) of high-grade histology.[1]Four of those patients were female and 7 were male. Since that publication, histology has been addressed specifically by a handful of studies that contradict the assertion that younger patients tend to have more aggressive histology. Atula and colleagues reviewed 34 Finnish patients younger than 40 years with squamous cell carcinoma (SCC) of the tongue and found the vast majority (70%) to have well-differentiated tumors.[23]No older population was reported for comparison. Similarly, Sasaki and colleagues found 66% of young tumors (patients <40 years) to be well-differentiated, compared with only 33% in their older cohort.[8]

However, in a publication focused specifically on margin assessment in oral cavity tumors, Spiro and colleagues incidentally found young patients, defined as younger than age 50 years, to make up a higher percentage of high-grade lesions (38%) than low-grade lesions (17%).[24]This paper scored tumors based on infiltration at the margins, with higher-grade lesions demonstrating infiltrative cords or nests rather than the "pushing" border of lower-grade lesions. In Spiro and colleagues' series, those patients with higher-grade lesions tended to present with nodal metastases and distant disease but did not have a higher rate of locoregional recurrence compared with lower-grade lesions. Unfortunately, a subset analysis for young patients was not performed for these parameters, so one cannot comment definitively on stage at presentation or recurrence from this paper.

Using Funk's grouping, Byers's findings may be explained by involving primarily the unique subset of young patients with aggressive disease (Group I). Spiro's findings would not fall into that category, and indeed Spiro's definition of young was considerably older than Byers' definition.

Spiro also had many older patients as well as younger patients with aggressive histology. A bimodal distribution of aggressive histology (the youngest patients and older patients having more aggressive histology) is possible, but this cannot be proven from the available data.

Finally, note again that not all oral cavity or head and neck tumors in the young are squamous cell carcinoma (SCC). Funk found a higher percentage of non–SCC histology, particularly adenocarcinoma and Kaposi sarcoma, in patients younger than 35 years compared with their older counterparts. In that series, approximately 48% of oral cavity cancers in patients younger than 35 years were SCC, versus 88% in patients 36-65 years and 91% of patients older than 65 years.[14]

Etiology and Risk Factors

Tobacco and alcohol

In young patients, studies have found a variable and sometimes absent relationship with these traditional risk factors. Several small studies have fallen on both sides of this debate, with some finding a lower rate of tobacco and alcohol use among young head and neck squamous cell carcinoma (HNSCC) patients compared with older HNSCC patients;[25,25,7,11,26] however, others found no difference in use.[27,22,28]

In a review of risk factors in 116 patients from the south east of England, Llewellyn et al found equal and substantial exposure to tobacco and alcohol in young patients with oral SCC and a control group of patients without cancer (both groups were composed of subjects younger than 45 years).[15] In their analysis, tobacco consumption for greater than 21 years resulted in a significantly elevated risk of oral cancer. Note that patients starting tobacco use in their teenage years reach the 21-year mark prior to their 40th birthday.

In a smaller, more recent series of 56 patients with oral cavity cancer and controls matched for age, Llewellyn and colleagues found an increased risk of cancer in males who started smoking before their 16th birthday, reinforcing that tobacco use can still be a risk factor in the young.[18] Similarly, Lipkin and colleagues found a very high rate of heavy alcohol and tobacco use in an analysis of 39 adults with HNSCC age 40 or younger from the Baylor College of Medicine.[29]

The use of smokeless tobacco has been linked to oral cavity cancer. In an analysis of the SEER database from 1973-1984, Davis and Severson found tongue cancer to increase by 1.8 fold in the 30-39 age group.[19] They juxtaposed their findings to other data that demonstrated an increase in the use of smokeless tobacco among the young. However, as the SEER database did not contain specific data on habits of smokeless tobacco use, the association is conjectural.

Interestingly, a third series on young patients with oral squamous cell carcinoma (SCC) by Lewellyn et al highlighted a caveat regarding the connection between tobacco and cancer: an absence of tobacco use doesn't mean an absence of cancer. They reported that among young patients with cancer, a lack of tobacco use was associated with a delay in seeking medical care for their cancer-related symptoms.[18]

Thus, young patients with no risk factors (and their physicians) may not suspect cancer despite worrisome signs and symptoms. Clearly, subsets of young patients who present without these risk factors (Funk's Groups I and III) exist; in fact, 38% of the young women and 18% of the young males in Llewellyn's larger series had no risk factors.[18] Such patients have been the subject of searches for additional etiologies specific to or present in young patients with HNSCC, as addressed below.

Marijuana

Marijuana use and its association with younger patients has led to suggestions that this may be an unreported risk factor in studies that have found fewer risk factors in younger patients. In the only studies to specifically address marijuana use in young patients, 2 of Llewellyn et al's series both reported similar use of marijuana among young patients with oral SCC and young controls.[15,5]

Zhang and colleagues at Memorial Sloan Kettering Cancer Center looked at the incidence of marijuana use among patients with pathologically confirmed squamous cell carcinoma (all head and neck sites) compared with age-matched and sex-matched controls culled from their blood

bank records.[30] Most marijuana smokers from both groups were under the age of 55. An increased odds ratio for risk of squamous cell carcinoma among marijuana smokers was found, but, as the authors point out, whether their data was biased by the controls being blood donors (and possibly less likely to be users of illegal drugs) was unclear.

In an age- and sex-matched, case control analysis of HPV-positive and HPV-negative HNSCC at Johns Hopkins, Gillison et al found an association of HPV positivity and marijuana use that increased in strength with increasing cumulative marijuana use.[31] In contrast, the HPV-negative group was more strongly associated with traditional HNSCC risk factors (tobacco, alcohol, and poor oral hygiene). No specific analysis of marijuana use and age with respect to HNSCC in this study was found, but the study does provide further evidence for a subgroup of patients who lack traditional risk factors yet share the risk factors of HPV positivity and marijuana use that many have linked to younger patients. Also, the observed cohorts of younger patients with head and neck cancer that have been reported in previous decades are possibly a result of a wave of generations in which marijuana use had become more commonplace during the teenage years.

Diet

In 2 of Llewellyn and colleagues' series, a significant reduction in risk was found in subjects who reported consumption of 3 or more portions of fresh fruit or vegetables per day.[15,5] Generally, a diet high in fruits and vegetables is inversely correlated with a risk of oral cancer,[32] and, based on Lewellyn's studies, this can also be applied to young patients.

Human papillomavirus

Perhaps the most widely studied virus in the head and neck cancer literature in recent years is HPV, a virus initially linked to cervical carcinogenesis that has now gained interest for its connection to cancer of the oropharynx, particularly the lingual and palatine tonsils.[32] The increasing incidence of tongue and tonsil cancer among young patients has led some authors to suggest that HPV may be responsible for this trend;[4,12] although the connection between oral (versus oropharyngeal) cancer and HPV is controversial.[33,34]

In a direct comparison between oral cavity, oropharynx, and larynx squamous cell carcinoma (SCC) samples from young (<50 years) and old (>50 years) patients, Sisk and colleagues found no significant difference by age in the rates of HPV positivity (50% vs 44%, respectively.[35] The authors acknowledge that theirs was a small study that does not allow definitive conclusions on this matter. Similarly, Koch and colleagues did not find an association of HPV positivity with age in 305 patients with HNSCC.[36]

Gillison and colleagues, however, in a case control analysis looking at HPV-16 status of 240 patients with HNSCC at Johns Hopkins, found a higher proportion of young patients (<50 years) in the HPV-16–positive group than the HPV-16–negative group (33% vs 17%, respectively).[31] Additionally, they found a strong association between HPV-16 positivity and oropharyngeal and lingual or palatine tonsil primary sites.

In a multi-institutional, prospective phase II trial of chemoradiation for advanced HNSCC (ECOG 2399) that included analysis of HPV status in the primary biopsy, the mean age of the 38 patients with HPV positive tumors was lower than the 58 with HPV-negative tumors (56 versus 60, respectively), but the difference was not significant.[37] However, this study did find a significantly better response and survival in the HPV-positive group, even when adjusted for age, tumor stage, and performance status.

Sisk likewise found HPV positivity to be linked to a better overall prognosis,[35] and this has been seen in several other studies as well,[32] although none of these studies specifically addressed young patients. Interestingly, improved survival was also seen with increasing copy number of HPV-16 in 35 patients with tonsil carcinoma in one study, suggesting that the connection between HPV status and response to treatment may be quite strong.[38]

The connection between HPV and oropharyngeal cancer combined with the current evidence suggesting a better prognosis with HPV-related tumors may be one explanation for the markedly different subsets of young patients with head and neck cancer. If tongue cancer, for instance, is not related to HPV, but rather a more sinister, as of yet unidentified risk factor, this would explain the reports by Byers and others that describe young women with aggressive and difficult-to-treat disease (Funk's Group I).

The Gillison and colleagues' case control analysis did not address prognosis, but they did find the HPV-16–positive group to be significantly less likely to have the typical risk factors for HNSCC (tobacco, alcohol, poor dental hygiene).[32] Funk's Group III patients fit into this description. Clearly, more research is needed into the role of HPV in HNSCC and its connection to treatment response, as well as into possible chemopreventive strategies (like those developed for cervical cancer).

Human immunodeficiency virus

Infection with the human immunodeficiency virus (HIV) and progression to AIDS is positively correlated with malignancies of the upper aerodigestive tract, particularly Kaposi sarcoma and non-Hodgkin lymphoma and, to a lesser extent, squamous cell carcinoma (SCC).[39] Funk and colleagues reported a very high incidence of Kaposi sarcoma in young African American males between 1985 and 1996, a time when the AIDS epidemic heavily affected that demographic.[14] Other series have not addressed (even indirectly) immunodeficiency due to HIV or other causes in young patients.

Genetics

Some genetic component to cancer development in young patients is likely, particularly in those patients with no recognized risk factors. These patients have been shown to have increased DNA fragility, which may make them more likely to develop genetic abnormalities.[40] However, studies examining specific genetic alterations in HNSCC as a function of patient age, including mutations in *p53, p21, Rb,* and *MDM2,*[23,41] and microsatellite instability,[42] have failed to find an increase in these abnormalities among young patients.

Likewise, Koch and colleagues found tumors of nonsmokers with HNSCC to have fewer genetic abnormalities than those of their smoking counterparts, leading them to conclude that the genetic alterations in tumors from nonsmoking patients remain undiscovered.[36] Llewellyn and colleagues' larger series reported a positive family history of cancer in 75% of female and 59% of male subjects younger than age 45 with HNSCC, suggesting genetics, immunology, or some common environmental exposure may play a role in the development of HNSCC in the young.[15]

A rare inherited cancer syndrome associated with HNSCC is Fanconi anemia (FA), an autosomal recessive syndrome caused by defects in DNA repair. FA carries a high risk of development of malignancy at a young age, with a median age of presentation of 31, and a cumulative incidence of HNSCC of 14% by age 40.[43,44] Patients with FA and HNSCC are more likely to be female (2:1), with very few reporting tobacco use. Oral cavity is the most common site and the outcome is poor, with a 63% rate of second primaries and a 2-year overall survival of 49%.[44]

Workup

No specific additional workup is required for young patients with head and neck squamous cell carcinoma (HNSCC) compared with their older counterparts. However, a young patient presenting with no traditional risk factors may warrant at least a careful history to examine for other possible etiologies, including a familial syndrome or evidence of immunodeficiency. If these etiologies are uncovered, appropriate additional workup should be carried out. In centers with active protocols examining the role of human papillomavirus (HPV) or other genetic abnormalities, eligibility for these studies should be assessed and participation offered. As of yet, no role for HPV serotyping or genetic testing in young patients has been standardized.

Please see sections on specific head and neck subsites for workup of malignancies in these areas.

Treatment

Chemotherapy and radiation therapy

No studies have specifically examined different types or doses of chemotherapy or radiation therapy as a function of age. Most studies using chemotherapy as a modality for head and neck squamous cell carcinoma (HNSCC) fail to stratify age in looking at outcome. Currently, available studies looking at outcomes with regards to patient age give little to no data about specific chemotherapeutic agents or radiation techniques and dosing. Given that less than 2% of HNSCC patients are enrolled in clinical trials nationwide, only future enrollment of all patients into clinical trials can give us knowledge about the role of modality and outcome regarding patient age.

Radiation is used as single modality therapy for early stage disease (stage I-II) and in multimodality therapy for advanced disease (stage III-IV). However, radiation of young patients has specific implications given their potential lifespan. As patients survive longer after radiation treatment for head and neck cancer, the long-term consequences of this treatment become more significant. Difficulties with xerostomia, fibrosis, and swallowing are significant quality of life issues in long-term survivors of head and neck irradiation.[45]

Radiation-induced malignancies, such as sarcoma or thyroid carcinoma, although uncommon, are also a concern in the long-term follow-up of irradiated patients. Young HNSCC patients successfully treated with radiation have longer posttreatment lives in which to potentially develop these malignancies, and this has prompted some authors to suggest surgery as the primary modality for treatment of the young patient.[46]

Conversely, recent evidence suggests that HPV-positive tumors may be more responsive to organ preservation therapy than HPV-negative tumors.[37]This may lead to organ preservation therapy being the preferred modality for both young and old patients who are HPV positive.

Surgical therapy

No studies specifically address the extent of surgical resection in young patients. As discussed in Histology (in the Introduction section) and Outcome and Prognosis, most young patients with HNSCC do not have an inherently more aggressive disease, and, therefore, do not require a departure from standard treatment for any given stage. However, by the same token, efforts should not be made to perform a more limited or less complete resection simply because of a patient's young age. Further research may reveal if young women with aggressive disease (Funk's Group I) warrant more aggressive initial treatment, even when presenting with early disease (stage I-II).[47]

Outcome and Prognosis

Prognosis

The vast majority of publications on young patients with head and neck squamous cell carcinoma (HNSCC) address outcome, and yet debate in the literature continues as to whether age at presentation has any effect on prognosis. Identified papers addressing prognosis in young patients with HNSCC are summarized in Table I below. Many of the studies are smaller, retrospective, matched studies and case series that suffer limitations of this methodology, as well as other methodological issues.[48]Only one study matched patients by treatment and found no difference in survival among 31 patients younger than 40 years and 62 matched controls.[25]

Authors	Year	Site(s) [a]	Age	# Young	# Control	Method [b]	Prognosis for Young [c]
Venables and Craft	1967	T	<30	13	none	Case Series	Worse
Byers	1975	T	<30	11	none	Case Series	Worse
Amsterdam et al	1982	OC	<35	12	none	Case Series	Worse
McGregor et al	1983	OC	<40	27	none	Case Series	Better

Newman et al	1983	T	<30	13	none	Case Series	Similar
Mendez et al	1985	A	<=40	63	none	Case Series	Similar
Son and Kapp	1985	OC, OP	<40	27	none	Case Series	Worse
McGregor and Rennie	1987	OC	<40	13	none	Case Series	Worse
Benninger et al	1988	A	<=40	41	none	Case Series	Worse
Cusamano et al	1988	CO, OP	<=40	23	none	Case Series	Worse
Tsukuda et al	1993	A	<40	48	none	Case Series	Better
Sarkaria and Harari	1994	T	<40	6	none	Case Series	Worse
Atula et al	1996	T	<40	34	none	Case Series	Similar
Martin-Granizo et al	1997	OC	<40	24	none	Case Series	Similar
Pitman et al	2000	T	<40	28	none	Case Series	Similar
Iype et al	2001	OC	<35	264	none	Case Series	Similar
Vermund et al	1982	T	<40	16	384	Institutional Series	Better
Von Doersten et al	1995	A	<40	23	122	Institutional Series	Similar
Siegelmann-Danieli et al	1998	T	<=45	30	57	Institutional Series	Similar
Veness et al	2003	T	<=40	22	142	Institutional Series	Similar
Lipkin et al	1985	OC, OP, L	<=40	39	39	Matched Control (sx, si, st)	Similar
Schantz et al	1988	A	<=40	83	83	Matched Control (sx, st, si, y)	Worse
Kuriakose et al	1992	OC	<35	37	37	Matched Control (random sample)	Similar
Friedlander et al	1998	T	<40	36	36	Matched Control (sx, st, y)	Similar
Verschuur et al	1999	A	<40	185	185	Matched Control (sx, si, y)	Better
Vargas et al	2000	T	<40	17	17	Matched Control (st)	Worse
Pytynia et al	2004	A	<40	31	62	Matched Control (sx, r, si, st, tx)	Similar
Sasaki et al	2005	OC	<40	35	110	Matched Control (random sample)	Similar

Garavello et al	2007	T	<=40	46	92	Matched Control (sx, si, st)	Worse
Lee et al	2007	T	<45	20	20	Matched Control (sx, st)	Better
Ho et al	2008	OC	<45	28	56	Matched Control (sx, si, st)	Better
Lacy et al	2000	A	<=40	40	990	Database Review (Washington University Cancer Registry)	Better
Davidson et al	2001	T	<40	N/A [d]	N/A [d]	Database Review (SEER 1988-1993)	Better
Annertz et al	2002	T	<40	276	4748	Database Review (Scandanavian Cancer Registry)	Better
Funk et al	2002	OC	<35	2,148	56776	Database Review (National Cancer Database)	Better
Schantz and Yu	2002	A	<40	3339	60070	Database Review (SEER 1973-1997)	Better
Kolker et al	2007	PC, OP	<50	1343	9401	Database Review (Michigan State Cancer Registry)	Worse

Table Legend

Table I: Articles addressing prognosis of young patients with head and neck cancer were identified from PubMed searches and from reference lists of primary and review articles.

[a] Site abbreviations are as follows: T=tongue, OC=oral cavity, OP=Oropharynx, L=larynx, A=all head and neck sites.

[b] Matching criteria is as follows: sx=sex, si, site, st=stage, r=race, tx=treatment, y=year at presentation; SEER=Surveillance, Epidemiology, and End Results program.

[c] Relative prognosis of young patients compared with older patients reported here is what was reported by the authors of the identified papers. For all of the case series listed, authors made comparisons to historic "controls" to assign relative prognosis.

[d] Specific numbers are not listed in the paper.

Additionally, remember that young patients are not necessarily free of other medical problems. Singh and colleagues found the presence of advanced comorbidity to diminish disease-free interval and tumor specific survival in an analysis of 70 patients with HNSCC younger than age 45.[44] This remains another element that is not typically accounted for in matched studies.

The larger database studies may be more reliable. Funk and colleagues analyzed the 1985-1996 NCDB, finding an increased 5-year survival rate for patients with HNSCC age 35 or younger compared with patients age 36-65, and for patients age 36-65 compared with patients 65 years and older across all stages, but these differences were only significant for stage I disease.[14] Shiboski and colleagues' analysis of the 1973-2001 SEER database revealed an overall increased 5-year survival for patients with HNSCC who were younger than 45 years.[4] An analysis of Scandinavian cancer registries by Annertz and colleagues similarly found increased 5-year survival among patients younger than 40 years.[9]

Lacy and colleagues reviewed the cancer database of the Washington University School of Medicine from 1980-1991.[48] Forty patients aged 40 years or younger were identified out of 1030 patients with 5-year survival data available. Young patients had a significantly better 5-year

survival than the middle-aged (41-64 y) or old (≥65 y) age groups (65% vs 52% and 35%, respectively). Young patients also had a lower recurrence rate and a lower incidence of second primaries than their older counterparts.

An astute caveat to these reported 5-year survival rates, as pointed out by Vargas and colleagues, is the difference between 5-year overall survival and 5-year disease-free survival. In their series of 17 female patients younger than age 40 with tongue squamous cell carcinoma (SCC) and 17 controls matched for stage, the 5-year overall survival of the study group was 65%, but the 5-year disease-free survival was only 47%.[47] This distinction between "alive with no evidence of disease" and "alive with disease" was not explicitly addressed in the NCDB, SEER, Scandinavian, or Washington University studies above.[14,4,9,48] Young, otherwise healthy patients may be able to survive with incurable disease longer than their older counterparts, and this may confound studies based on cancer databases that do not make this distinction.

Patterns of recurrence

Several small case series have been published reporting young patients with a high rate of locoregional recurrence.[1,49,50,46] These case series may be subject to publication or referral bias but do highlight a subset of young patients that may have more aggressive disease. Another explanation for the higher local recurrence rate could be a lack of appropriate initial surgical treatment. Because of their young age, these patients may not have been as aggressively treated as their older counterparts, although in the absence of details about margin assessment and extent of resection, this would be speculation.

Two small, matched control studies[28,47] and one retrospective institutional series[22] also found high locoregional recurrence in younger patients compared with older patients, but none demonstrated a corresponding difference in 5-year survival. On the contrary, Von Doersten and colleagues did not find age to affect recurrence at all in a multivariate analysis on 155 patients, of whom 23 were under age 40.[51] Thus, whether young patients, or a subset thereof, have a higher propensity for locoregional recurrence has yet to be definitely determined.

Second primary tumors

In patients of all ages who have been treated for HNSCC, the risk of development of second primaries increases over time[52] and is linked to tobacco consumption.[3] In a matched control study, Verschuur and colleagues found a decreased incidence of second primaries among patients younger than 40 years compared with older patients (8% versus 18%) over 10 years, but this may have been confounded by the higher proportion of smokers in the older age group.[3] Similarly, Lacy and colleagues in a retrospective database review in which 40 of the 1030 patients were age 40 or younger, the risk of recurrence or second primary tumors was significantly lower than in the older age groups.[48]

Young patients may have a lower incidence of second primaries, at least in the short term. However, for those young patients who developed cancer in the absence of known risk factors, the continued presence of an unknown risk factor should be assumed. These as-of-yet unidentified risk factors may have long incubation times and patients may not present with another primary for decades after treatment of the first cancer. Only long term-studies on young patients who have been treated for HNSCC will answer these questions. In the meantime, young patients cured of their first primary deserve long-term adherence to routine follow-up and cancer surveillance, regardless of the etiology.

Medicolegal Pitfalls

In Byers's 1975 publication, he wrote, "the failure of physicians to vigorously investigate a persistent ulcer of the tongue in a patient less than thirty years of age resulted in considerable delay in diagnosis of many of these patients." Enough evidence in the literature confirms that young patients can develop malignancy to warrant a high level of suspicion for cancer in any patient with worrying signs and symptoms, regardless of age.

Academic health professionals must continually update and educate our colleagues in the community regarding the identification and appropriate workup or referral for patients presenting with sings and symptoms of head and neck cancer.

In 2006, the Scottish Intercollegiate Guidelines Network published its national clinical guideline for the diagnosis and management of head and neck cancer.[53]

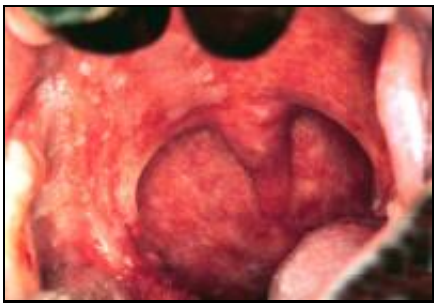
Future Directions and Controversies

More than 3 decades after the first reports focusing on young patients with head and neck cancer, much remains to be learned about this subset of patients. The low incidence of head and neck squamous cell carcinoma (HNSCC) in the young patient has made development of prospective studies and analysis of single-institution data difficult. With the advent of more sophisticated and cooperative multi-institutional cancer databases, further details regarding the prognosis and treatment response of young patients may become available.

As more is learned about the association of human papillomavirus (HPV) with head and neck cancer, screening and chemopreventive strategies may have a larger role in preventing the development of HNSCC in all patients. The young patient may particularly benefit from population-based programs because they may be intercepted at an age prior to infection with HPV.

Finally, an as-of-yet-unidentified genetic defect, error in immune surveillance, or environmental exposure may be implicated in cancer development in the young patient. Future research should be directed toward identifying these risk factors.

Multimedia



Media file 1: Reddening of the soft palate, perhaps with scattered areas of white and velvet red patches, tobacco-induced squamous cell carcinoma involving the tongue base and/or supraglottis, and a firm, mobile mass that is palpable at the left carotid bifurcation.

References

1. Byers RM. Squamous cell carcinoma of the oral tongue in patients less than thirty years of age. *Am J Surg*. Oct 1975;130(4):475-8. [Medline].

2. McGregor GI, Davis N, Robins RE. Squamous cell carcinoma of the tongue and lower oral cavity in patients under 40 years of age. *Am J Surg*. Jul 1983;146(1):88-92. [Medline].

3. Verschuur HP, Irish JC, O'Sullivan B, Goh C, Gullane PJ, Pintilie M. A matched control study of treatment outcome in young patients with squamous cell carcinoma of the head and neck. *Laryngoscope*. Feb 1999;109(2 Pt 1):249-58. [Medline].

4. Shiboski CH, Schmidt BL, Jordan RC. Tongue and tonsil carcinoma: increasing trends in the U.S. population ages 20-44 years. *Cancer*. May 1 2005;103(9):1843-9. [Medline].

5. Llewellyn CD, Johnson NW, Warnakulasuriya S. Factors associated with delay in presentation among younger patients with oral cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. Jun 2004;97(6):707-13. [Medline].

6. Burzynski NJ, Flynn MB, Faller NM, Ragsdale TL. Squamous cell carcinoma of the upper aerodigestive tract in patients 40 years of age and younger. *Oral Surg Oral Med Oral Pathol*. Sep 1992;74(3):404-8. [Medline].

7. Schantz SP, Byers RM, Goepfert H, Shallenberger RC, Beddingfield N. The implication of tobacco use in the young adult with head and neck cancer. *Cancer*. Oct 1 1988;62(7):1374-80. [Medline].

8. Sasaki T, Moles DR, Imai Y, et al. Clinico-pathological features of squamous cell carcinoma of the oral cavity in patients <40 years of age. *J Oral Pathol Med*. 2005;34:129-133.

9. Annertz K, Anderson H, Biorklund A, et al. Incidence and survival of squamous cell carcinoma of the tongue in Scandinavia, with special reference to young adults. *Int J Cancer*. Sep 1 2002;101(1):95-9. [Medline].

10. Kuriakose M, Sankaranarayanan M, Nair MK, et al. Comparison of oral squamous cell carcinoma in younger and older patients in India. *Eur J Cancer B Oral Oncol*. Oct 1992;28B(2):113-20. [Medline].

11. Martin-Granizo R, Rodriguez-Campo F, Naval L, Diaz Gonzalez FJ. Squamous cell carcinoma of the oral cavity in patients younger than 40 years. *Otolaryngol Head Neck Surg*. Sep 1997;117(3 Pt 1):268-75. [Medline].

12. Schantz SP, Yu GP. Head and neck cancer incidence trends in young Americans, 1973-1997, with a special analysis for tongue cancer. *Arch Otolaryngol Head Neck Surg*. Mar 2002;128(3):268-74. [Medline].

13. Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for squamous cell carcinoma of the oral cavity in young people--a comprehensive literature review. *Oral Oncol*. Jul 2001;37(5):401-18. [Medline].

14. Funk GF, Karnell LH, Robinson RA, Zhen WK, Trask DK, Hoffman HT. Presentation, treatment, and outcome of oral cavity cancer: a National Cancer Data Base report. *Head Neck*. Feb 2002;24(2):165-80. [Medline].

15. Llewellyn CD, Linklater K, Bell J, Johnson NW, Warnakulasuriya KA. Squamous cell carcinoma of the oral cavity in patients aged 45 years and under: a descriptive analysis of 116 cases diagnosed in the South East of England from 1990 to 1997. *Oral Oncol*. Feb 2003;39(2):106-14. [Medline].

16. Kolker JL, Ismail AI, Sohn W, Ramaswami N. Trends in the incidence, mortality, and survival rates of oral and pharyngeal cancer in a high-risk area in Michigan, USA. *Community Dent Oral Epidemiol*. Dec 2007;35(6):489-99. [Medline].

17. Slotman GJ, Swaminathan AP, Rush BF Jr. Head and neck cancer in a young age group: high incidence in black patients. *Head Neck Surg*. Mar-Apr 1983;5(4):293-8. [Medline].

18. Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for oral cancer in newly diagnosed patients aged 45 years and younger: a case-control study in Southern England. *J Oral Pathol Med*. Oct 2004;33(9):525-32. [Medline].

19. Davis S, Severson RK. Increasing incidence of cancer of the tongue in the United States among young adults. *Lancet*. Oct 17 1987;2(8564):910-1. [Medline].

20. Frisch M, Hjalgrim H, Jaeger AB, Biggar RJ. Changing patterns of tonsillar squamous cell carcinoma in the United States. *Cancer Causes Control*. Jul 2000;11(6):489-95. [Medline].

21. Levine PH, Connelly RR, Easton JM. Demographic patterns for nasopharyngeal carcinoma in the United States. *Int J Cancer*. Dec 15 1980;26(6):741-8. [Medline].

22. Veness MJ, Morgan GJ, Sathiyaseelan Y, Gebski V. Anterior tongue cancer and the incidence of cervical lymph node metastases with

increasing tumour thickness: should elective treatment to the neck be standard practice in all patients?. *ANZ J Surg*. Mar 2005;75(3):101-5. [Medline].

23. Atula S, Grenman R, Laippala P, Syrjanen S. Cancer of the tongue in patients younger than 40 years. A distinct entity?. *Arch Otolaryngol Head Neck Surg*. Dec 1996;122(12):1313-9. [Medline].

24. Spiro RH, Guillamondegui O Jr, Paulino AF, Huvos AG. Pattern of invasion and margin assessment in patients with oral tongue cancer. *Head Neck*. Aug 1999;21(5):408-13. [Medline].

25. Pytynia KB, Grant JR, Etzel CJ, Roberts D, Wei Q, Sturgis EM. Matched analysis of survival in patients with squamous cell carcinoma of the head and neck diagnosed before and after 40 years of age. *Arch Otolaryngol Head Neck Surg*. Jul 2004;130(7):869-73. [Medline].

26. Siegelmann-Danieli N, Hanlon A, Ridge JA, Padmore R, Fein DA, Langer CJ. Oral tongue cancer in patients less than 45 years old: institutional experience and comparison with older patients. *J Clin Oncol*. Feb 1998;16(2):745-53. [Medline].

27. Ho HC, Lee MS, Hsiao SH, et al. Squamous cell carcinoma of the oral cavity in young patients: a matched-pair analysis. *Eur Arch Otorhinolaryngol*. Jul 2008;265 Suppl 1:S57-61. [Medline].

28. Friedlander PL, Schantz SP, Shaha AR, Yu G, Shah JP. Squamous cell carcinoma of the tongue in young patients: a matched-pair analysis. *Head Neck*. Aug 1998;20(5):363-8. [Medline].

29. Lipkin A, Miller RH, Woodson GE. Squamous cell carcinoma of the oral cavity, pharynx, and larynx in young adults. *Laryngoscope*. Jul 1985;95(7 Pt 1):790-3. [Medline].

30. Zhang ZF, Morgenstern H, Spitz MR, et al. Marijuana use and increased risk of squamous cell carcinoma of the head and neck. *Cancer Epidemiol Biomarkers Prev*. Dec 1999;8(12):1071-8. [Medline].

31. Gillison ML, D'Souza G, Westra W, et al. Distinct risk factor profiles for human papillomavirus type 16-positive and human papillomavirus type 16-negative head and neck cancers. *J Natl Cancer Inst*. Mar 19 2008;100(6):407-20. [Medline].

32. Gillison ML. Current topics in the epidemiology of oral cavity and oropharyngeal cancers. *Head Neck*. Aug 2007;29(8):779-92. [Medline].

33. Miller CS, Johnstone BM. Human papillomavirus as a risk factor for oral squamous cell carcinoma: a meta-analysis, 1982-1997. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. Jun 2001;91(6):622-35. [Medline].

34. Acay R, Rezende N, Fontes A, Aburad A, Nunes F, Sousa S. Human papillomavirus as a risk factor in oral carcinogenesis: a study using in situ hybridization with signal amplification. *Oral Microbiol Immunol*. Aug 2008;23(4):271-4. [Medline].

35. Sisk EA, Bradford CR, Jacob A, et al. Human papillomavirus infection in "young" versus "old" patients with squamous cell carcinoma of the head and neck. *Head Neck*. Oct 2000;22(7):649-57. [Medline].

36. Koch WM, Lango M, Sewell D, Zahurak M, Sidransky D. Head and neck cancer in nonsmokers: a distinct clinical and molecular entity. *Laryngoscope*. Oct 1999;109(10):1544-51. [Medline].

37. Fakhry C, Westra WH, Li S, et al. Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. *J Natl Cancer Inst*. Feb 20 2008;100(4):261-9. [Medline].

38. Cohen PR, Schulze KE, Rady PL, et al. Coincidental consort clear cell cutaneous carcinoma: facial squamous cell carcinoma in situ

containing human papillomavirus and cancer cells with clear cytoplasm in an octogenarian couple. *South Med J*. May 2007;100(5):525-30. [Medline].

39. Epstein JB, Silverman S Jr. Head and neck malignancies associated with HIV infection. *Oral Surg Oral Med Oral Pathol*. Feb 1992;73(2):193-200. [Medline].

40. Schantz SP, Hsu TC, Ainslie N, Moser RP. Young adults with head and neck cancer express increased susceptibility to mutagen-induced chromosome damage. *JAMA*. Dec 15 1989;262(23):3313-5. [Medline].

41. Regazi JA, Dekker NP, McMillan A et al. P53, p21, Rb, and MDM2 proteins in tongue carcinoma from patients <35 versus >75 years. *Oral Oncol*. 1999;35:379-383.

42. Jin YT, Myers J, Tsai ST, Goepfert H, Batsakis JG, el-Naggar AK. Genetic alterations in oral squamous cell carcinoma of young adults. *Oral Oncol*. May 1999;35(3):251-6. [Medline].

43. Kutler DI, Auerbach AD, Satagopan J, et al. High incidence of head and neck squamous cell carcinoma in patients with Fanconi anemia. *Arch Otolaryngol Head Neck Surg*. Jan 2003;129(1):106-12. [Medline].

44. Singh B. Squamous cell carcinoma and FA. In: Owen J, Frohnmayer L, Eiler ME, Eds. *Fanconi Anemia, Standards for Clinical Care*. 2nd Ed. Oregon: Fanconi Anemia Research Fund; 2003.

45. Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, Leemans CR, Aaronson NK, Slotman BJ. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. *J Clin Oncol*. Aug 1 2008;26(22):3770-6. [Medline].

46. Amsterdam JT, Strawitz JG. Squamous cell carcinoma of the oral cavity in young adults. *J Surg Oncol*. Feb 1982;19(2):65-8. [Medline].

47. Vargas H, Pitman KT, Johnson JT, Galati LT. More aggressive behavior of squamous cell carcinoma of the anterior tongue in young women. *Laryngoscope*. Oct 2000;110(10 Pt 1):1623-6. [Medline].

48. Lacy PD, Piccirillo JF, Merritt MG, Zequeira MR. Head and neck squamous cell carcinoma: better to be young. *Otolaryngol Head Neck Surg*. Feb 2000;122(2):253-8. [Medline].

49. Sarkaria JN, Harari PM. Oral tongue cancer in young adults less than 40 years of age: rationale for aggressive therapy. *Head Neck*. Mar-Apr 1994;16(2):107-11. [Medline].

50. Son YH, Kapp DS. Oral cavity and oropharyngeal cancer in a younger population. Review of literature and experience at Yale. *Cancer*. Jan 15 1985;55(2):441-4. [Medline].

51. von Doersten PG, Cruz RM, Rasgon BM, Quesenberry CP Jr, Hilsinger RL Jr. Relation between age and head and neck cancer recurrence after surgery: a multivariate analysis. *Otolaryngol Head Neck Surg*. Sep 1995;113(3):197-203. [Medline].

52. Argiris A, Brockstein BE, Haraf DJ, et al. Competing causes of death and second primary tumors in patients with locoregionally advanced head and neck cancer treated with chemoradiotherapy. *Clin Cancer Res*. Mar 15 2004;10(6):1956-62. [Medline].

53. Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of head and neck cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN). Oct 2006;90 p. (SIGN publication; no. 90).

54. Benninger MS, Roberts JK, Levine HL, Wood BG, Tucker HM. Squamous cell carcinoma of the head and neck in patients 40 years of

age and younger. *Laryngoscope*. May 1988;98(5):531-4. [Medline].

55. Cusamano RJ. Squamous cell carcinoma of the oral cavity and oropharynx in young adults. *Head Neck Surg*. 1988;10:229-134.

56. Davidson BJ, Root WA, Trock BJ. Age and survival from squamous cell carcinoma of the oral tongue. *Head Neck*. Apr 2001;23(4):273-9. [Medline].

57. Garavello W, Spreafico R, Gaini RM. Oral tongue cancer in young patients: a matched analysis. *Oral Oncol*. Oct 2007;43(9):894-7. [Medline].

58. Iype EM, Pandey M, Mathew A, Thomas G, Sebastian P, Nair MK. Oral cancer among patients under the age of 35 years. *J Postgrad Med*. Jul-Sep 2001;47(3):171-6. [Medline].

59. Lee CC, Ho HC, Chen HL, Hsiao SH, Hwang JH, Hung SK. Squamous cell carcinoma of the oral tongue in young patients: a matched-pair analysis. *Acta Otolaryngol*. Nov 2007;127(11):1214-7. [Medline].

60. Llewellyn CD, Linklater K, Bell J, Johnson NW, Warnakulasuriya S. An analysis of risk factors for oral cancer in young people: a case-control study. *Oral Oncol*. Mar 2004;40(3):304-13. [Medline].

61. McGregor AD, Rennie JS. Intra-oral squamous cell carcinoma in patients under 40 years of age. A report of 13 cases and review of the literature. *Br J Plast Surg*. May 1987;40(3):270-3. [Medline].

62. Mendez P Jr, Maves MD, Panje WR. Squamous cell carcinoma of the head and neck in patients under 40 years of age. *Arch Otolaryngol*. Nov 1985;111(11):762-4. [Medline].

63. Newman AN, Rice DH, Ossoff RH, Sisson GA. Carcinoma of the tongue in persons younger than 30 years of age. *Arch Otolaryngol*. May 1983;109(5):302-4. [Medline].

64. Pitman KT, Johnson JT, Wagner RL, Myers EN. Cancer of the tongue in patients less than forty. *Head Neck*. May 2000;22(3):297-302. [Medline].

65. Singh B, Bhaya M, Zimbler M, et al. Impact of comorbidity on outcome of young patients with head and neck squamous cell carcinoma. *Head Neck*. Jan 1998;20(1):1-7. [Medline].

66. Tsukuda M, Ooishi K, Mochimatsu I, Sato H. Head and neck carcinomas in patients under the age of forty years. *Jpn J Cancer Res*. Jul 1993;84(7):748-52. [Medline].

67. Venables CW, Craft IL. Carcinoma of the tongue in early adult life. *Br J Cancer*. Dec 1967;21(4):645-50. [Medline].

68. Vermund H, Brennhovd IO, Harvei S, Kaalhus O, Poppe E, Wiley AL Jr. Carcinoma of the tongue in Norway and Wisconsin. I. Incidence and prognosis related to sex and age. *Acta Radiol Oncol*. 1982;21(3):155-68. [Medline].

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