Head and Neck cancers in young adults

Wojciech Golusiński

Department of Head and Neck Surgery
The Great Poland Cancer Centre, Poznan, Poland
Poznan University of Medical Sciences, Poznan, Poland

Head and Neck cancer in young adults

- DEFINITION
- Epidemiology
- Etiology
- Diagnosis
- Treatment
- Conclusions
Young adult – definition

- Young patients have been defined as patients under ages 35-40 years, with some studies including those younger than 45.


University of Toronto, Department of Otolaryngology-Head and Neck Surgery/Surgical Oncology, Wharton Head and Neck Program, Princess Margaret Hospital, Toronto, Ontario, Canada.

Young adult – definition

- Young patients have been defined as people under 40 or 45 years of age, while the lower limit of age is not defined at all or sometimes it is defined as 15, 18 or 20 years.

Young adults

- **GROUP 1:** patients under age 35 years, with a female predominance, few behavioral risk factors and pathologically more aggressive cancers.

- **GROUP 2:** patients under age 40 with a male predominance, extensive tobacco and alcohol abuse, who present with advanced cancer and a prognosis dependent upon presenting stage.


Young adults

- **GROUP 3:** patients under age 40 with a slight male predominance, roughly half have a history of tobacco use. Predominance of early-stage and well-differentiated cancers as well as better or equivalent response to treatment to that seen in older patients with similar stage disease are noticed.

Head and Neck cancer in young adults

- Definition
- **EPIDEMIOLOGY**
- Etiology
- Diagnosis
- Treatment
- Conclusions

Epidemiology

- A trend for an increasing percentage of younger patients in head and neck squamous cell carcinoma has been noticed in the US, various European countries and China since 1970.
In the Indian sub-continent, where there is a much higher overall rate of head and neck squamous cell carcinoma, a similar trend is occurring.


Epidemiology

Cancer incidence by age

Inherited predisposition

9th International Netherlands Cancer Institute Head and Neck Symposium, Amsterdam, the Netherlands, 16-17 April, 2009
Epidemiology

- 11.3% of all oral cavity and oropharynx cancers and 4.5% of larynx cancers occur in patients under age 45 years.


Epidemiology

- The oral cavity is the most common site for head and neck squamous cell carcinoma in young patients, with the tongue being the most common subsite.

- Oropharyngeal cancer also accounts for a higher percentage of head and neck squamous cell carcinoma in young patients compared with older patients.

  Early stage squamous cell cancer of the oral tongue—clinicopathologic features affecting outcome. Cancer, 2012

### Epidemiology

**DEMOGRAPHICS OF YOUNG PATIENTS**

**SITE**
- Oral Cavity (usually OT) 40-45%
- Oropharynx 20-30%
- Larynx/HP 20-40%
- Missclassification of BOT as "tongue"
- Variation for older cohorts & those with high smoking prevalence

**M:F ratio**
- Oral Cavity - females~males
- Oropharynx - males>females
- Larynx - males>females

**Smoking**
- Oral Cavity - 40-60% never
- Oropharynx - dependent on period of cohort
- Larynx - typical (except children/adolescents)


---

**Site Distribution by Age Category**

(2042 incident patients)

<table>
<thead>
<tr>
<th>Age Category</th>
<th>Oral Cavity Females</th>
<th>Oral Cavity Males</th>
<th>Oropharynx Females</th>
<th>Oropharynx Males</th>
<th>Larynx/HP Females</th>
<th>Larynx/HP Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 yrs</td>
<td>102</td>
<td>364</td>
<td>1270</td>
<td>306</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-69 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70+ yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S 9th International Netherlands Cancer Institute Head and Neck Symposium, Amsterdam, the Netherlands, 16-17 April, 2009
Head and Neck Cancer in young adults

- Definition
- Epidemiology
- **ETIOLOGY**
- Diagnosis
- Treatment
- Conclusions

Etiology

**Potential Etiologic Associations**
- Smoking
- Alcohol
- Other Tobacco Products
- Second-Hand Smoke?
- Asbestos?
- Acid Reflux?
- Nutrition?
- Marijuana?
- HPV?
- Genetics?
Etiology

- Tobacco and alcohol have long been implicated as the traditional risk factors for head and neck squamous cell carcinoma in adults at any age.

- Contrary to older patients, many of the younger patients with oral squamous cell carcinoma have declared never to have smoked or consumed alcohol excessively.


Etiology

- It has been suggested that exposure to carcinogens such as alcohol and tobacco might be of too short a duration for malignant transformation to occur in younger patients.


Etiology

- In the UK, Llewellyn indicates many young patients are heavy smokers and drinkers and although the exposure time still seems short, some have had 20+ years of smoking by their early forties.


- It appears that many in the 40-45 age group have traditional risk factor exposure and represent the tail end of the more usual patient group, whereas patients under 40 years of age are more likely to be non-smokers.

Etiology

- 30% of the young patients claimed not to have used tobacco compared with only 9% of the older patients.
  

- In the West smokeless tobacco has not emerged as a significant factor in young patients.
  

Etiology

- Further epidemiological studies are necessary to determine whether marijuana smoking can cause oral premalignant lesions and cancer, possibly due to field cancerization of the upper aerodigestive tract.
  
## Etiology

- Herpes simplex virus, Epstein-Barr virus and human papilloma virus have been investigated as causes of head and neck squamous cell carcinoma in young patients. An association has been found between HPV-16 and the development of oropharyngeal carcinoma, specifically for cancers of the palatine and lingual tonsils.


### HPV-16 in Tumors

<table>
<thead>
<tr>
<th>Site</th>
<th>HPV16 Tumor Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E6+</td>
</tr>
<tr>
<td>Oral Cavity (No.=256)</td>
<td>46 (18.0%)</td>
</tr>
<tr>
<td>Oropharynx (No.=217)</td>
<td>173 (79.7%)</td>
</tr>
</tbody>
</table>

*9th International Netherlands Cancer Institute Head and Neck Symposium, Amsterdam, the Netherlands, 16-17 April, 2009*
Etiology

Oropharyngeal Cancer Patients
(Segregated by Age, HPV16, & Smoking)

- HPV16 PCR+ NonSmk mean age=51.4
- HPV16 PCR+ Smk mean age=56.2
- HPV16 PCRnegative mean age=56.7

9th International Netherlands Cancer Institute Head and Neck Symposium,
Amsterdam, the Netherlands, 16-17 April, 2009

Etiology

- It has been shown that patients younger than 30 years exhibited a significantly increased chromosome fragility compared to older patients following mutagen exposure. In addition a higher frequency of microsatellite instability has been found in younger patients.

- Conversely, no significant differences were found in the expression of p53, p21, Rb and MDM2 proteins between patients younger than 35 years and older than 75 years.

Goldstein D.P., Irish J.C.
Squamous cell carcinoma in the young.
Etiology

The principal findings in molecular studies of young patients with HNSCC (nonsmokers) is that HNSCC developing in these patients is markedly different, not in any recognizable phenotypic way, but undoubtedly at a genetic level.

Toner M., O'Regan E.M.
Head and Neck Squamous Cell Carcinoma in the Young: A Spectrum or a Distinct Group? Part 2.

---

Proposition of an integrated model of molecular carcinogenesis for head and neck squamous cell carcinoma according to Leemans CR.

Etiology of Malignancies of the Head & Neck Region

9th International Netherlands Cancer Institute Head and Neck Symposium, Amsterdam, the Netherlands, 16-17 April, 2009

Head and Neck cancer in young adults

- Definition
- Epidemiology
- Etiology
- **DIAGNOSIS**
- Treatment
- Conclusions
### Diagnosis

- There are NO SIGNIFICANT DIFFERENCES in the process of the diagnosis of head and neck squamous cell carcinoma in young adults comparing to the group of older patients.

### Clinicopathologic features and outcomes

- Compared to the older group, the younger patients have a significantly worse clinical/radiological N stage in presentation (therefore a more advanced tumour stage: 73% stage 3-4) and more evidence of perineural invasion on histopathological examination.

Clinicopathologic features and outcomes

- Above mentioned differences between young and adult patients may be explained by a delay in diagnosis owing to a lower index of clinical suspicion of tongue squamous cell carcinoma in younger patients or a more aggressive age-related biologic behaviour of the tumour.

- The latter assumption is supported by the significantly higher rate of perineural invasion on histopathological examination in younger group.

- Perineural invasion has been shown to be associated with a high risk of regional metastases, local recurrence and decreased survival. At the same time second head and neck primary tumours develop only in the older patients. These results may suggest that tumour biology might be age-related.


Head and Neck cancer in young adults

- Definition
- Epidemiology
- Etiology
- Diagnosis
- **TREATMENT**
- Conclusions

Treatment

- When pertinent differences in stage, grade and treatment between young patients group and adult patients group are controlled for, outcomes are identical, suggesting that young patients should receive the same therapy that is the standard of care for adult patients.

Traditionally patients with head and neck squamous cell carcinoma are treated with surgical resection and, when indicated, postoperative adjuvant radiotherapy. However such treatment can be functionally debilitating, and radiotherapy may subject the young patient to years of long-term adverse sequelae.


American Society of Clinical Oncology (ASCO) 2012 annual meeting:
neoadjuvant chemotherapy - no survival advantage


Treatment

- Despite encouraging findings according neoadjuvant chemotherapy, it is maintained that the standard treatment of oral tongue cancer in the young adult should remain surgery with adjuvant radiotherapy determined by the surgical pathology results.

Sturgis EM, Moore BA, Glisson BS, Kies MS, Shin DM, Byers RM
Neoadjuvant chemotherapy for squamous cell carcinoma of the oral tongue in young adults: a case series.
Head Neck 2005

Head and Neck cancer in young adults

- Definition
- Epidemiology
- Etiology
- Diagnosis
- Treatment
- CONCLUSIONS
Conclusions

- Young adults are the group of patients with increased incidence of Head and Neck cancer (very important not only for ENT but also for general practitioner!).

- The higher incidence of nonsmokers, lower gender ratio, a greater percentage of oral cavity and oropharynx tumors and lower incidence of second primaries suggest the possibility of different etiologic factors in the younger patient group. Further investigations into genetic factors may yield further insight.

  David P. Goldstein

Conclusions

- Remember about the HPV16 infection in young adults with oral and oropharyngeal cancer.

- During the diagnosis of Head and Neck cancer in young adults especially such features like perineural or vascular invasion should be estimated.

- Do not forget about the patients’ age and future quality of their life when planning the treatment procedures.

- Future