Changing Trends in Smoking and Alcohol Consumption in Patients With Oral Cancer Treated at Memorial Sloan-Kettering Cancer Center From 1985 to 2009

Pablo H. Montero, MD; Purvi D. Patel, MD; Frank L. Palmer, BA; Snehal G. Patel, MD; Jatin P. Shah, MD; Richard B. Hayes, DDS, PhD, MPH; Ian Ganly, MD, PhD

Objective: To describe smoking and alcohol consumption trends in patients with oral cavity cancer over the past 25 years.

Design: Retrospective cohort study.

Setting: Single-institution tertiary care cancer center.

Patients: Patients with oral cancer treated primarily with surgery from 1985 to 2009. Patients with previous head and neck cancer were excluded.

Main Outcome Measures: The medical records of 1617 patients were reviewed. Patient demographics and details on smoking and alcohol consumption were recorded. Patients were divided in 5 different cohorts according to the year of initial surgery.

Results: There were no differences in sex, age, or stage of disease among cohorts. Oral tongue was the most common subsite (49%). There was a progressive decrease in tobacco use; 80% in cohort 1 vs 60% in cohort 5 ($P < .001$). A decrease in the daily amount of tobacco used was also found; 55% of patients in cohort 1 smoked more than 1 pack per day compared with 30% in cohort 5 ($P < .001$). Alcohol consumption decreased from 80% in cohort 1 to 67% in cohort 5 ($P < .007$). The percentage of patients who consumed more than 3 drinks per day decreased from 23% in cohort 1 to 9% in cohort 5 ($P < .001$).

Conclusion: Over the past 25 years there has been a progressive decrease in the prevalence of tobacco and alcohol users in patients with oral cancer.


QUAMOUS CELL CANCER OF the oral cavity comprises cancer of the oral tongue, upper or lower gum, buccal mucosa, floor of mouth, or hard palate. Worldwide, oral cavity cancer represents the eighth most frequent cancer.1 The main etiological factors are smoking and alcohol consumption.2,3 National figures suggest there has been a decline in the use of tobacco and alcohol over the past 25 years in the United States.4 In parallel with this, there has been a decrease in the incidence and an improvement in survival of oral cavity cancer as reported by the Surveillance, Epidemiology and End Results (SEER) database.5 However, major cancer registers, such as SEER, do not collect any information about tobacco and alcohol use in patients with cancer. Current literature in head and neck cancer has not reported on trends in tobacco and alcohol use among patients with oral cancer treated during the past 25 years. This lack of information is important because recent studies of oropharynx cancer have shown a change in the etiology of oropharynx cancer from a cancer caused by smoking and alcohol, to a cancer caused by the human papilloma virus (HPV).6 We therefore examined trends in tobacco and alcohol use in patients treated for oral cavity cancer over a 25-year-period (1985-2009) in a single institution to determine if there has been any similar change in the epidemiology of oral cavity cancer.

METHODS

After institutional review board approval, the medical records of all patients with oral cavity cancer, primarily treated at Memorial Sloan Kettering Cancer Center (MSKCC), from 1985 to 2009 were reviewed. The patients were selected from a preexisting database, following strict inclusion criteria: these were previously untreated patients with invasive squamous cell carcinoma of the oral cavity according to American Joint Committee on Cancer definitions, without history of head and neck cancer, primarily treated with surgery at our institution over a 25-year period of analysis between 1985 and 2009. Ultimately, 1617 patients fulfilled the inclusion criteria, and their data were subsequently analyzed.
Data on 1617 patients were available in a database. Demographic factors, comorbidities, smoking and alcohol use, and treatment outcomes were recorded and subsequently analyzed. Alcohol use was categorized as non-drinker, previous drinker, or current drinker. The drinking habit was graded according to the number of drinks per day, week, or month. Different kinds of drinks were homologized using the definition of a US standard drink by the Centers for Disease Control and Prevention, making them comparable. A standard drink is equal to 0.6 oz (14.0 g) of pure alcohol; this amount of alcohol is found in 12 oz of beer or 5 oz of wine. Smoking status was categorized as never, previous smoker, or current smoker. A previous smoker was defined as a smoker who had quit for more than 4 years prior to a diagnosis of oral cancer. A current smoker was defined as a patient with a history of smoking use in the past 4 years until diagnosis. Information about the type of tobacco used, daily amount consumed, and length of use and year of cessation was recorded. Where information was available, the patients were categorized according to the number of packs per day (PPD) smoked and/or the previous tobacco history in pack-years (PY).

For comparison of the trends in alcohol and tobacco use, the patients were separated into 5 different cohorts according to the date of initial surgery (cohort 1: 1985-1990 [n=274]; cohort 2: 1990-1994 [n=250]; cohort 3: 1995-1999 [n=315]; cohort 4: 2000-2004 [n=356]; and cohort 5: 2005-2009 [n=422]). The mean and percentage comparison was calculated using $\chi^2$ analysis. The database was built using CAISIS software (an open-source, web-based, cancer data management system developed at MSKCC) and ACCESS Software (Microsoft, 2007). The statistical analysis was performed using the statistical software package SPSS (version 19; IBM).

### RESULTS

#### PATIENT AND TUMOR CHARACTERISTICS OVER TIME

Patient and tumor characteristics of patients with oral cancer from 1985 to 2009 are shown in Table 1. The median age of patients was 62.5 years (range, 15.0-97.0 years); 86.5% patients were white and 56.0% male. Oral tongue was the most common subsite (49.0%), and 72.0% had T1 and T2 tumors. Over time, there was no change in sex or age distribution. There was an increase in the percentage of nonwhite patients treated from 9.1% to 16.6%. Over time, there was a small change in subsite classification, with a small increase in buccal mucosa cancer treated and a reduction in floor of mouth cancer treated (Table 1). Overall stage distribution remained similar over time.

### TRENDS IN TOBACCO USE AND ALCOHOL CONSUMPTION OVER TIME

The types of tobacco smoked among current and discontinued smokers were predominantly cigarettes (88.5%), cigars (5.8%), pipe (2.0%), and the combinations of these (3.8%). The prevalence of tobacco use over time is presented in Table 2. A progressive decrease in the amount of tobacco use through the years was observed ($P < .001$). This was also apparent when smok-
ers are separated into current and discontinued, with a greater decrease in the group of present users ($P < .001$) (Figure 1). Analysis of the daily use of tobacco reported also showed a significant reduction in the amount of tobacco use by the patients (current and discontinued), with a significant reduction of the PPD intake. In the study cohort (1985-1989), the proportion of patients who smoked more than 1 PPD was 55.2% compared with 30.4% in the 2005-2009 cohort ($P < .001$). This trend was also reflected when tobacco use was analyzed on a PY basis; there was a significant increase in the number of patients with a history of less than 20 PY and a significant decrease of the heavy smoker of more than 60 PY ($P < .001$ for both comparisons).

The prevalence of alcohol use is presented in Table 2: 61.4% of patients had a history of alcohol use at the time of diagnosis: social or occasionally (24.5%), daily (26.8%), or weekly (7.9%). A decrease in the amount of alcohol use through the years was also found ($P < .007$). This trend was also apparent when drinkers were separated into current and discontinuous users, with a greater decrease in the group of present users ($P < .03$).

The different combinations in tobacco and alcohol consumption are presented in Figure 2. The same significant reduction in alcohol and tobacco use was observed with a decline in the combined use history (1985-1989: 71.4% vs 2005-2009: 49.5%; $P < .001$).
Worldwide, oral cancer incidence remains high, especially in some areas of Oceania, South Central Asia, and Central and Eastern Europe, for both males and females. An increasing incidence has been reported in some developing countries but also in Central and Eastern Europe. In the United States, the incidence has been decreasing; the reported age-adjusted incidence in 1985 was 13.33 per 100 000 inhabitants vs a 10.77 per 100 000 in 2008. However, a more detailed analysis has shown that the incidence of certain oral cavity subsites, namely, tongue cancer, is rising, especially in younger men, despite the decline in tobacco use. In addition, the survival rate has improved; according to the SEER database, the 5-year survival of patients treated in the period 1985 to 1989 was 54.2% compared with 65% for patients diagnosed in 2003. This improvement in survival has been reported for all stages of disease and for all age groups, except for patients older than 75 years. The main etiological factors for oral cavity cancer are smoking and alcohol. Several reports have shown a progressive decline in tobacco use over the past 25 years. One could hypothesize that this decrease in tobacco use accounts for the decrease in incidence and improved survival in oral cancer that has been observed. However, to our knowledge, there have been no reports that have examined the smoking and alcohol characteristics of patients with oral cancer over time. In addition, national cancer registries, such as SEER, do not collect data on smoking and alcohol consumption in patients with cancer. A careful analysis of smoking and alcohol consumption in oral cancer is clearly important because recent studies have shown a dramatic change in the etiology of oropharyngeal cancer from a cancer caused by smoking and alcohol to a cancer now predominantly caused by HPV. The aim of our study was therefore to determine the prevalence of tobacco and alcohol use in patients with oral cancer treated in a single institution over a 25-year period.

Our research showed that there have been no major changes in the demographic characteristics of the patients treated in our institution over this time period. As with other reports, most of the patients were men older than 60 years. There was a slight increase in the proportion of nonwhite patients treated at our center, and this is explained mainly by an increased number of Asian-origin patients. No major changes were observed in the different tumor subsites affected in the oral cavity, although a mild increase in buccal mucosa cancer was noticed, with a slight decrease in floor of mouth cancer. The clinical and pathologic staging did not differ significantly over time period. Despite these observations, there was a significant decrease in patients with a history of tobacco and alcohol use (P < .001 and P < .007, respectively). For smoking, there was an increase in the proportion of patients who had never used tobacco and also an increase in the number of quitters. In addition, there was also a decrease of almost 25% in the percentage of patients who smoked heavily (>1 PPD and >20 PY histories). This information is consistent with previous reports from other institutions and national data that have shown a progressive decrease in tobacco smoking over the past 20 years. It was after World War II, when the prevalence of smoking habit reached its maximum, that the first reports about the potential effect of tobacco use on lung and oral cancer were published. Since then, public health policy has been successful in achieving a progressive decline in the rates of tobacco use. It is likely that the findings summarized in our study reflect the results of public campaigns against tobacco use, with an almost 20% decrease in tobacco ever users from 1985 through 2009. This trend was noted also in the daily amount...
of tobacco use, with a decrease in patients smoking more than 1 pack per day. In addition to the decrease in tobacco use, we report a decrease in alcohol consumption. Alcohol is a well-characterized carcinogenic agent of oral mucosa and is associated with an increased risk of oral and oropharyngeal cancer, especially when it is associated with tobacco use.2,17 National figures show that alcohol consumption in the United States has declined over time. The National Institute on Alcohol Abuse and Alcoholism reports that the per capita consumption of alcohol by Americans 14 years or older has dropped from 2.75 gallons in 1980 to 2.31 in 2007,18 although recent reports have noted an increase among young people19 and in heavy drinkers (National Health Interview Survey, 1997-2010).20 A less sharp fall in the use of alcohol compared with that of tobacco is reported in this study (a 12% decline in the prevalence of ever drinkers). The decline in alcohol consumption was based mainly in current users, with a greater decline in the heavy drinkers (about 15% in drinkers of more than 3 drinks per day). The proportions of patients who were nonsmoking drinkers increased by almost 10%, exceeding the proportion of smoking nondrinkers. The synergistic effect of the combination of alcohol and tobacco is well known. However, patients who are nonsmoking drinkers are still at high risk because tobacco is not an essential cofactor in the oral cancer caused by alcohol.2

The decline in tobacco and alcohol use among patients with oral cavity cancer treated in our institution, together with the increasing number of patients with oral cavity cancer whom we treated from 1985 to 2009, strongly suggests that there are other etiological factors now playing a role in the pathogenesis of oral cancer. This could be explained by changes in the oral microflora or the emerging role of new oral infections, such as HPV. In oropharyngeal cancer, we now know that there has been a shift in etiology from smoking- and alcohol-related cancer to a cancer associated with HPV.15 Even the risk factor profile between HPV-positive and HPV-negative patients with oropharyngeal cancer seems to be different: tobacco and alcohol use is more related to HPV-negative patients, whereas HPV-positive patients with cancer are more likely to be nonsmokers and nondrinkers with a history of higher-risk sexual behavior.21 It is now estimated that up to 70% of all oropharyngeal cancers are caused by HPV infection.22 It is therefore plausible that the reduction in prevalence of smoking and alcohol in oral cavity cancer cases may be related to increasing prevalence of HPV-related disease. However, reports on the relationship between HPV and oral cancer pathogenesis are conflicting. Some authors have dismissed a link between oral cavity cancer and HPV infection, based on the very low prevalence rates reported in some studies.23-25 For instance, in the International Agency for Research on Cancer multicenter study, HPV DNA was detected in biopsy specimens in only 3.9% of 766 cancers of the oral cavity with valid polymerase chain reaction results.23 In contrast, other authors have reported that the infection of oral cavity cells by HPV is not a rare phenomenon. Analysis of reports focused only on oral cavity cancer have reported a prevalence as high as that reported for oropharyngeal cancer, around 60% or 70%,26,27 even in subsites not common for this infection (eg, the gums or floor of mouth). The relationship between oral cavity cancer and HPV infection is therefore not a closed case, and further research is necessary to elucidate its role. In addition, other factors should not be disregarded. Poor dental hygiene and poor diet, especially a diet without fruits and vegetables, have been reported as potential factors related to changes in mortality in oral cancer in Eastern Europe.28

In conclusion, we have shown a significant decrease in the prevalence of smoking in patients treated in our institution over the past 25 years. This is also present, but to a lesser magnitude, for alcohol consumption. This strongly suggests other etiological agents are responsible for a significant percentage of patients we currently see with oral cancer. This change in epidemiology is very similar to that reported for oropharyngeal cancer, a cancer now known to be caused by HPV rather than smoking and alcohol. Further studies on the role of HPV in the etiology of oral cancer in nonsmoking patients are therefore warranted.
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Correspondence: Ian Ganly, MD PhD, Department of Otolaryngology–Head and Neck Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10065 (ganliy@mskcc.org).

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REFERENCES