Study Finds Gender Disparities in Head and Neck Cancer Treatment and Outcomes

Summary includes data not in the abstract

ASCO Perspective

“We don’t know why women are getting less treatment and having worse outcomes, and we need to find out. Though these findings are specific to California, the disparities we see are startling and worth considering in treatment discussions in everyday practice,” said ASCO Expert Joshua A. Jones, MD, MA.

CHICAGO – An analysis of cancer registry data from a California hospital system shows that women with head and neck cancer were less likely to receive intensive chemotherapy (35% vs. 46%) and radiation (60% vs. 70%) compared to men. Controlling for factors such as age and serious medical conditions, a mathematical model also shows that the ratio of cancer to non-cancer mortality was two times higher for women than the ratio for men. When taken collectively, the findings raise the possibility women with head and neck cancer may be undertreated. The authors explain that there are some confounding factors, so further prospective investigation is necessary to fully address this possibility.

The study will be featured in a press briefing today and presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

“We weren’t looking for gender differences, so the results were really surprising. Besides undertreatment, there are a number of factors that could contribute to the differences in outcomes between women and men with head and neck cancer, and it’s clear we need further investigation,” said senior study author Jed A. Katzel, MD, a medical oncologist at Kaiser Permanente in Santa Clara, CA. “With this mathematical model, we have a tool that can help us identify patients likely to benefit from more intensive treatment, as well as those more likely to die from other non-cancer related causes. The hope is that by integrating this model into our care, we can improve the care of all patients with head and neck cancer.”

Head and neck cancers account for approximately 4% of all cancers in the United States and are more than twice as common among men as they are among women.1
When considering treatment, oncologists take into account a patient’s activity level and other medical problems. Patients with head and neck cancer who have good performance status (a measure of overall well-being) may be offered more intense treatments, including platinum-based chemotherapy with radiation therapy. Patients who cannot tolerate intensive chemotherapy may be offered less intensive treatments, such as targeted therapy cetuximab (Erbitux) with radiation, radiation alone, or even no cancer treatment at all.

Another factor influencing head and neck cancer treatment and outcomes is whether the cancer is caused by the human papillomavirus (HPV). HPV-related head and neck tumors are more responsive to treatment, and people with such cancers generally have a better prognosis. HPV-related head and neck cancer is more common in men than in women. In the authors’ prior analysis of patients in Northern California, for example, they found that only about 22.6% of HPV-related cancers occurred in women, compared with 77.4% in men.²

**About the Study**

Researchers evaluated health outcomes for 223 female and 661 male patients with stage II-IVB head and neck cancer treated at Kaiser Permanente Northern California. The odds of receiving intensive cancer treatment were estimated using logistic regression models and adjusting for factors such as age, gender, tumor stage, Charlson Comorbidity Index, and history of smoking and alcohol use. A mathematical tool called the generalized competing event (GCE) model was used to compare the risk of dying from cancer to the risk of dying from other causes. The GCE model controls for differences in age, gender, tumor site, and Charlson score. In this analysis, the researchers did not control for differences in tumor type with respect to HPV status.

**Key Findings**

Overall, the study identified several differences by gender:

- Treatment: The odds of receiving intensive chemotherapy were 35% for women versus 46% for men, and the odds of receiving radiation were 60% for women and 70% for men.
- Mortality: At a median follow up of 2.9 years, 271 patients died of cancer and 93 from other causes. While both men and women were more likely to die of cancer than of other causes, the ratio of cancer deaths versus non-cancer deaths was 1.92 times higher for women than for men.
- HPV-related cancers: Fewer women than men had oropharyngeal cancers (38% vs. 55%). While further analysis is ongoing, this may also be a factor driving higher cancer-related mortality rates in women, as HPV-related cancers occur most frequently in the oropharynx.

**Next Steps**

Researchers plan to conduct a more detailed review of treatments that women in the study received. They’re also interested in determining causes for the gender differences in survival, such as if the findings reflect the difference in the rate of HPV-related head and neck cancers between women and men.

Additionally, “the GCE model will be further evaluated in the NRG-HN004 trial that is currently enrolling patients,” said Dr. Katzel. “It is a trial that we will be participating in.”

This study received funding from Kaiser Permanente Northern California Graduate Medical Education Department.
Study at a Glance

<table>
<thead>
<tr>
<th>Disease</th>
<th>Head and neck cancer</th>
</tr>
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<tbody>
<tr>
<td>Patients on Trial</td>
<td>884</td>
</tr>
<tr>
<td>Intervention Tested</td>
<td>Cancer treatment use; cancer vs. non-cancer mortality</td>
</tr>
<tr>
<td>Primary Finding</td>
<td>Women less likely to receive intensive treatment than men; ratio of cancer death vs. non-cancer death higher for women than for men</td>
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View the disclosures for the 2018 ASCO Annual Meeting News Planning Team.

ATTRIBUTION TO THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING IS REQUESTED IN ALL COVERAGE.

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2018 ASCO Annual Meeting: Presentation Information

<table>
<thead>
<tr>
<th>Head and Neck Cancer Oral Abstract Session</th>
<th>Annie Park</th>
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<tbody>
<tr>
<td>Sunday, June 3, 2018: 8:24-8:34 a.m. CT</td>
<td>Kaiser Permanente</td>
</tr>
<tr>
<td>McCormick Place, E451</td>
<td>Santa Clara, California</td>
</tr>
</tbody>
</table>

Abstract LBA6002: Are women with head and neck cancer undertreated?

Authors: Annie Park, Amy Albaster, Hanjie Shen, Loren K. Mell, Jed Abraham Katzel; Kaiser Permanente, Santa Clara, US; Kaiser Permanente Division of Research, Oakland, US; UCSD, La Jolla, US; University of California San Diego Moores Cancer Center, La Jolla, CA; Kaiser Permanente, Santa Clara, CA

Background: Generalized Competing Event (GCE) models have been used to stratify patients with cancer according to their relative hazard for cancer death versus death from other causes. We evaluated outcomes for head and neck cancer (HNC) patients treated at Kaiser Permanente Northern California (KPNC) based on demographic data and comorbidities using a GCE model. Methods: We
identified 884 HNC patients diagnosed 2000-2015 from the KPNC cancer registry, age 18-85 and stage II-IVB by AJCC 7th edition. Using the GCE proportional relative hazards model, controlling for age, sex, tumor site, and Charlson comorbidity index (CCI), we identified associations between these factors and the relative hazard for HNC-specific mortality (ω+ ratio, ‘gcerisk’ package in R). Death, disenrollment, and end of study (12/31/2016) were used as censoring events. Logistic regression models estimated the odds of receiving intensive treatment (platinum based regimen), adjusting for the same covariates plus stage, smoking, and alcohol abuse history. **Results:** With a median follow-up of 2.9 years, 271 patients died of cancer, and 93 of non-cancer causes. Compared to male, females were less likely to receive intensive chemotherapy (35% vs. 46%, \(p = 0.006\)) and radiation (60% vs. 70%, \(p = 0.008\)). On GCE analysis, female patients had an increased relative hazard ratio (RHR) for death from HNC vs. other causes (adjusted \(RHR\) 1.92; 95% CI 1.07-3.43), indicating they may be relatively undertreated. **Conclusions:** Female patients in our cohort may be undertreated in clinical practice, potentially missing the opportunity to aggressively treat their HNC. This study supports the use of a GCE methodology to objectively identify patients more likely to benefit from treatment intensification. These findings may help guide future research in health disparities. **Table 1:** ω+ ratio and odd ratio for select variables

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Adjusted RHR (ω+ ratio) for cancer vs. non-cancer mortality (95% CI)</th>
<th>Intensive chemotherapy OR (95% CI)</th>
<th>Radiation OR (95% CI)</th>
<th>Surgery OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1.92 (1.07-3.43)</td>
<td>0.68 (0.48, 0.98)</td>
<td>0.79 (0.56, 1.11)</td>
<td>1.04 (0.72, 1.53)</td>
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<tr>
<td>CCI &gt; = 1</td>
<td>0.75 (0.46-1.24)</td>
<td>0.78 (0.68-0.89)</td>
<td>0.96 (0.86-1.07)</td>
<td>1.02 (0.91-1.15)</td>
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<tr>
<td>Age (per 10 years)</td>
<td>0.78 (0.62-0.99)</td>
<td>0.88 (0.75-1.02)</td>
<td>0.90 (0.77-1.05)</td>
<td>0.70 (0.59-0.82)</td>
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**Disclosures:** Amy Albaster, Research Funding (Institutional) from Bayer; Loren K. Mell, MD, Consulting or Advisory Role with Bristol-Myers Squibb, Speakers’ Bureau for Merck, Travel, Accommodations, Expenses from Bristol-Myers Squibb, Honoraria from Varian Medical Systems, Research Funding from Merck, AstraZeneca.