INTRODUCTION

Diabetes mellitus type II has been associated with increased cancer risk and cancer-related mortality, which can be modified by hypoglycemic drugs. Specifically, metformin is considered to have important anticancer properties. However, the effects of metformin on clinical outcomes in oral cavity and oropharyngeal squamous cell carcinoma (OC/OP SCCA) have not been analyzed. We aimed to evaluate the association of metformin use and cancer recurrence or persistence in diabetic patients with OC/OP SCCA.

METHODS

We retrospectively reviewed the clinical data of all diabetic patients with pathologically confirmed OC/OP SCCA treated and followed at our institution from 2001 to 2012.

RESULTS

We identified 77 patients with diabetes mellitus type II and OC/OP SCCA that were treated for their primary or recurrent cancer at our institution from 2001 to 2012. Total follow-up from initial cancer diagnosis until death or last clinical contact was 1 to 288 months (median =33 months). There were no significant clinical differences between patients taking metformin (n=23) and those who were not (n=44) in terms of sex, age, tumor subsite, TNM stage at diagnosis, and smoking or alcohol use.

In the analysis of all 77 patients, metformin does not appear to have a significant effect on disease recurrence, as the hazard ratio was 0.96 (p-value [P]=0.92) (Figure 1). However, 41 of the patients in our cohort had TNM stage III or IV cancer. The HR for metformin in late stage patients was 0.98 (P=0.97). In our cohort, and in the literature, late stage disease is a risk factor for recurrence. In our case, late stage had a significant HR of 2.3 (P<0.02).

DISCUSSION

Over 30,000 new cases of oral and oropharyngeal squamous cancers are expected to be diagnosed each year in the United States, with nearly 8,000 patients dying annually from the disease. Considering that the 5-year survival remains unchanged at approximately 50%, it is critical to identify factors that will improve outcomes for these patients. Our early results suggest that metformin does not seem to have a significant effect in OC/OP SCCA; however, further study is needed to determine the possibility of an effect in early stage (T1/T2 N0) patients.

An Analysis of the Potential Benefit of Metformin in Oral and Oropharyngeal Squamous Cell Carcinoma

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<table>
<thead>
<tr>
<th>Metformin Users</th>
<th>Non-Metformin Users</th>
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<tbody>
<tr>
<td>T1/T2 N0</td>
<td>41</td>
</tr>
<tr>
<td>T1/T2 N1</td>
<td>22</td>
</tr>
<tr>
<td>T1/T2 N2</td>
<td>14</td>
</tr>
<tr>
<td>T1/T2 N3</td>
<td>9</td>
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</tbody>
</table>

DISCUSSION cont.

CONCLUSIONS

There is increasing evidence in the literature that metformin has important anticancer properties resulting in decreased incidence and improved outcomes for certain cancers. Clinical trials have already shown metformin’s benefit with breast cancer, hepatocellular carcinoma, colon cancer, and pancreatic cancer. Vitale-Cross, et al. have had promising results in a mouse oral carcinogenesis mouse model, which were first treated with 4-Nitroquinoline-1-oxide (4NOQ, Sigma-Aldrich), which is a synthetic carcinogen that causes the development of oral cavity tumors. With time, many of these tumors progress to carcinoma. In the animals treated with metformin, there was a significant reduction in the number of overall tumor lesions, as well as a significant decrease in the progression of these tumors to carcinoma.

These laboratory studies are promising and demonstrate the need for clinical studies to determine if there is a clinical benefit for metformin as an adjuvant treatment in H&N SCCA.

REFERENCES

6. Silverman S. Demographics and occurrences of oral and pharyngeal cancers. The outcomes, the issues, the barriers. Annu Am Dent Assoc. 2007;112(Suppl):37-45.