Original Article

Significant Changes in Sexual Behavior After a Diagnosis of Human Papillomavirus-Positive and Human Papillomavirus-Negative Oral Cancer

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BACKGROUND: Sexual behavior and oral human papillomavirus (HPV) infection are risk factors for oral squamous cell carcinoma (OSCC). The effects of OSCC diagnosis and treatment on subsequent relationship stress and sexual behavior are unknown. **METHODS:** Incident cases of HPV-positive or HPV-negative OSCC in patients who had a partnered relationship and partners of patients with oropharyngeal cancer were eligible for a study in which surveys were administered at diagnosis and at the 6-month follow-up time point to assess relationship distress, HPV transmission and concerns about health consequences, and sexual behavior. The frequency distributions of responses, stratified by tumor HPV status, were compared at baseline and follow-up. **RESULTS:** In total, 262 patients with OSCC and 81 partners were enrolled. Among the patients, 142 (54.2%) had HPV-positive OSCC, and 120 (45.8%) had HPV-negative OSCC. Relationship distress was infrequently reported, and 69% of patients felt that their relationship had strengthened since the cancer diagnosis. Both HPV-positive patients (25%) and their partners (14%) reported feelings of guilt or responsibility for the diagnosis of an HPV-caused cancer. Concern over sexual, but not nonsexual, HPV transmission to partners was reported by 50%. Significant declines in the frequency of vaginal and oral sexual behaviors were reported at follow-up, regardless of tumor HPV status. From baseline to 6 months, significant increases in abstinence from vaginal sex (from 10% to 34%; $P < .01$) and oral sex (from 25% to 80%; $P < .01$) were reported. **CONCLUSIONS:** Diagnosis and treatment of OSCC are associated with significant declines in the frequency of vaginal and oral sex, regardless of tumor HPV status. Sexual behavior is an important quality-of-life outcome to assess within clinical trials. [See related editorial on pages 000-000, this issue.] ***Cancer*** **2017;000:000–000.** *© 2017 American Cancer Society.*

KEYWORDS: head and neck cancer, human papillomavirus (HPV) transmission, HPV worries, mouth neoplasm, oral cancer, patient relationships, quality of life, sexual behavior.

INTRODUCTION

Human papillomavirus (HPV) is a common sexually transmitted infection (STI) and is a cause of oropharyngeal and oral cavity squamous cell carcinomas (OSCC).[1] Strong associations are observed between sexual behavior, oral HPV infection, and oropharyngeal cancer.[2] Recently, temporal links between sexual behavior and the risk of acquiring an oral HPV infection have been reported.[3,4] Performing oral sex increases the risk of oral HPV infection, and the risk increases with the number of partners.[3] In addition, oral HPV type 16 (HPV16) infection increases the subsequent risk of oropharyngeal cancer by approximately 22-fold.[4] Awareness of this link between sexual behavior, oral HPV infection, and cancer may cause concern for patients who have HPV-positive OSCC and their partners.

In the case of cervical cancer, it has been demonstrated that the link between sexual behavior and HPV results in stigma and relationship concerns among some women.[5] It remains largely unknown whether or not patients who have HPV-positive OSCC similarly experience stigma or relationship distress or whether they change their sexual behavior as a result of awareness that their cancer is caused by an STI. Cross-sectional studies of patients with head and neck cancer (HNC)

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note reports of intimacy problems because of cancer and/or its treatment at various time points.[6] Approximately 15% of patients with HNC who attended an outpatient clinic reported problems with intimacy at some point from 12 to 48 months after diagnosis.[7] The potential impact of HNC on intimacy and sexual behaviors caused by the loss of tongue and lip function may be underappreciated.[7] Partners of patients diagnosed with HPV-positive OSCC may have concerns about their own health, especially given the rare reports of concurrent diagnoses of HPV-positive OSCC among couples.[8] Although the relative risk of tonsillar cancer among partners of patients who have HPV-positive OSCC is not known, husbands of women with cervical cancer have an approximately 3-fold increase in the risk of tonsillar cancer.[9]

Given the increased incidence of HPV-positive OSCC, especially among younger patients,[10] we designed a study to explore the effects of diagnosis and treatment of HPV-positive and HPV-negative OSCC on subsequent relationship stress and sexual behavior.

MATERIALS AND METHODS

Study Population and Design

Consecutive individuals aged $\geq$ 18 years with an incident diagnosis of histologically or cytologically confirmed OSCC at The Ohio State University from July 2011 through February 2016 were eligible to enroll in a prospective cohort study of the genomics of OSCC. Nested within this cohort was the current pilot study, which was designed to explore the effect of a diagnosis of HPV-positive or HPV-negative OSCC on partnered relationships. Patients who self-described as currently having a partner were eligible to participate. A partner was defined as a spouse, husband/wife, boyfriend/girlfriend, or lover/sexual partner. Partners of patients with oropharyngeal squamous cell carcinoma (OPSCC), but not oral cavity squamous cell carcinoma, were also eligible for enrollment. The study was approved by The Ohio State University Institutional Review Board, and all participants provided written informed consent.

Patients were stratified according to tumor HPV status and were considered positive if both $p16^{INK4a}$ immunohistochemistry and HPV in situ hybridization were positive, as previously described.[11] Patients with unknown tumor HPV status (n = 6) were included in the HPV-negative group. Sensitivity analyses revealed no effect of reclassification of tumor HPV status on sexual behaviors at baseline (Supporting Table 1; see online supporting information).

Patients and partners were separately administered study-specific surveys at enrollment and at 6-month follow-up by means of a computer-assisted self-interview using touchscreen technology on an iPad. A Certificate of Confidentiality was obtained from the National Institutes of Health to protect against the release of data without the participant's consent.

Survey

The study survey was divided into 4 sections: demographic information, relationship stress (the Dyadic Adjustment Scale [DAS]),[12] HPV and health concerns, and HPV and relationships. The last 2 sections were developed by the clinician-scientists for this pilot study based on concerns raised by patients in clinical settings over the previous 20 years. The survey content is summarized in Supporting Table 2 (see online supporting information).

The demographic section of the survey contained 12 items assessing participants' demographic characteristics. The DAS is a validated, 32-item survey designed to measure relationship quality (or level of distress).[12] The 27 items in the consensus, satisfaction, and affectional expression subscales were included in our survey. The cohesion subscale was excluded because of redundancy with questions in the HPV and relationships section.

The HPV and health concerns section of the survey was administered only to partners and contained a 9-item domain that assessed partner worries on a 4-point scale, from 1 (not at all) to 4 (a lot), regarding their risk of being diagnosed with HNC or an HPV infection; concern on a 5-point scale, from 1 (much lower) to 5 (much higher), regarding the comparative risk of HNC and HPV infection; and a single item statement (true, false, don't know) regarding the HPV vaccine.

The HPV and relationship section of the survey was divided into 3 domains containing 54 items. The first, 21-item domain assessed agreement on a Likert scale, from 1 (strongly disagree) to 5 (strongly agree), with statements regarding interpartnership discussions about HPV, lifetime sexual behavior, and history of sexually transmitted infections (part A) and the impact of the HNC diagnosis on their relationship (part B). The second, 11-item, domain assessed agreement on a Likert scale with statements regarding concern over possible mechanisms of HPV transmission. The third, 22-item domain assessed the usual frequency of 9 specific sexual behaviors on an ordinal scale in the 12-month period before the cancer diagnosis and in the 6-month period subsequent to the start of cancer therapy as well as changes in 13 sexual behaviors in this same time frame.

Statistical Analysis

In total, 262 patients with OSCC who were in partnered relationships and 81 partners of patients with OPSCC were included in the analysis. Patients were stratified according to tumor HPV status, and characteristics between groups were compared using the Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. Survey data were summarized with descriptive statistics, including the frequency distribution of responses to survey questions. Variable sample sizes for specific items in the surveys were because of participant nonresponse. For the DAS, T-scores were generated for each subscale as previously reported by Edwards et al.[13] T-scores ≤ 40 were considered indicative of distress in the relationship.[13] Among partner pairs, the Wilcoxon matched-pair signed-rank test was used to evaluate statistical differences in mean DAS subscale scores and in the reported frequency of sexual behaviors. For statistical comparisons of sexual behavior frequencies at baseline and follow-up, the sign test was used. Data analysis was conducted using STATA version 13.1.

RESULTS

Characteristics of the Study Population

In total, 372 patients with OSCC consented to participate in the prospective cohort study of the genomics of OSCC. A Consolidated Standards of Reporting Trials (CONSORT) diagram of the cohort is provided in Supporting Figure 1 (see online supporting information). The 262 patients (70.4%) who self-reported that they were currently in a partnered relationship were eligible for this pilot study. These included 172 patients with oropharyngeal cancer and 90 patients with oral cavity cancer.

Demographic characteristics of the patients are detailed in Table 1. Of the 262 patients, 142 (54.2%) had HPV-positive tumors, and 120 (45.8%) had HPV-negative tumors. As has been previously observed,[10] patients with HPV-positive OSCC were significantly more likely to be male and were younger, had higher educational attainment, reported higher numbers of lifetime vaginal and oral-sexual partners, and had higher overall disease stage (according to the seventh edition of the American Joint Committee on Cancer [AJCC] *Cancer Staging Manual*) compared with HPV-negative patients ($P < .01$ for all). Patients with HPV-negative tumors were significantly more likely to have undergone surgical resection as primary treatment. Of the 262 partnered patients, 10 reported a preference for same-sex partners.

In total, 81 partners (47.1%) of 172 patients with OPSCC (69 HPV-positive and 12 HPV-negative patients) consented to participate. Partners who did not participate in the study (they either refused or did not accompany the patient to the clinic) had unknown characteristics, because refusal to participate precluded the collection of data. However, patients whose partners did and did not complete the survey were similar in age, race, sex, TNM stage, and lifetime sexual partnerships; however, patients with partners who completed the survey were more likely to live with their partners (Supporting Table 3; see online supporting information).

Relationships: The DAS

The DAS was used to assess the level of relationship distress among patients and partners after a diagnosis of OSCC. Overall, few patients or partners reported distressed relationships at baseline or at the 6-month follow-up time point (Supporting Table 4; see online supporting information).

Baseline

A high proportion of patients reported agreement with their partners regarding the majority of consensus subscale topics. Agreement was highest for career decisions (>80%) and lowest for handling family finances (approximately 60%).

A majority of patients also reported high satisfaction with their relationship; they confided in their partner almost always (>85%), rarely/never regretted the marriage/partnership (approximately 95%), and had high confidence in the future of their relationship (>75%). Strong majorities also described their relationships as happy/very happy (>90%).

Regarding demonstrations of affection, a majority of patients agreed with their partner (>70%), including about sexual relations (>65%). The majority stated there were no issues in the relationship with regard to being too tired for sex (>65%) or not showing love (>80%) in the past few weeks.

When evaluated according to T-score criteria, very few patients reported relationship distress (T-score ≤ 40) in any subscale. Distress with regard to consensus in the relationship was reported by 10%, distress regarding relationship satisfaction was reported by only 1.2%, and distress regarding expressions of affection was reported by 5.4% of all patients. No statistically significant differences in levels of relationship distress were observed between HPV-positive and HPV-negative patients in any subscales at baseline. Levels of distress reported by partners at baseline were similarly low.

TABLE 1. Characteristics of Patients With Partners and Partners who Completed the Demographic Survey

Characteristic	No. of Patients (%)			
	HPV+	HPV−	P[a]	No. of Partners (%)
Total no.	142	120		81
Sex			<.01	
Men	125 (88)	88 (73)		9 (11)
Women	17 (12)	32 (27)		72 (89)
Primary tumor[b]			<.01	
Oropharynx	134 (95)	26 (21)		NA
Oral cavity	1 (1)	89 (75)		NA
Unknown	7 (4)	5 (4)		NA
Age, y			.01	
18-39	3 (2)	4 (4)		5 (6)
40-59	84 (59)	59 (49)		56 (69)
60-89	55 (39)	57 (47)		20 (24)
Race			.59	
White	131 (92)	107 (89)		78 (96)
Black/African American	5 (4)	7 (6)		1 (1)
Other	6 (4)	6 (5)		2 (2)
Marital status			.06	
Married/cohabiting	129 (91)	108 (90)		78 (96)
Divorced/separated	9 (6)	5 (4)		3 (4)
Widowed	0 (0)	3 (3)		0 (0)
Never married	4 (3)	4 (3)		0 (0)
Education			.01	
High school/equivalent	39 (28)	38 (31)		17 (21)
<High school	9 (6)	19 (16)		7 (9)
Some college or greater	94 (66)	63 (53)		57 (70)
Employment			.09	
Full time	73 (51)	40 (33)		35 (43)
Part time	8 (6)	6 (5)		11 (14)
Unemployed	15 (11)	19 (16)		17 (21)
Student	0 (0)	1 (1)		0 (0)
Sick leave/disabled	46 (32)	54 (45)		18 (22)
No. of lifetime sexual partners			<.01	
0-1	5 (4)	20 (17)		8 (10)
2-5	31 (22)	37 (31)		34 (42)
6-15	54 (38)	37 (31)		26 (32)
≥16	52 (36)	26 (21)		13 (16)
No. of lifetime oral sex partners			<.01	
0-1	19 (13)	44 (37)		18 (22)
2-5	55 (39)	50 (41)		51 (63)
6-15	45 (32)	19 (16)		9 (11)
≥16	23 (16)	7 (6)		3 (4)
Cancer stage: AJCC seventh edition			<.01	
I	5 (4)	15 (13)		NA
II	7 (5)	26 (23)		NA
III	43 (32)	35 (30)		NA
IV	78 (59)	39 (34)		NA
Primary therapy			<.01	
Surgical resection[c]	45 (32)	96 (79)		NA
Radiation/chemotherapy	89 (62)	18 (15)		NA
Radiation	7 (5)	4 (3)		NA
Chemotherapy	1 (1)	2 (2)		NA
Unknown	1 (1)	1 (1)		NA

Abbreviations: AJCC, American Joint Committee on Cancer; HPV−, human papillomavirus negative; HPV+, human papillomavirus positive; NA, not applicable.
[a] P values here represent the results from Fisher exact tests.
[b] Primary tumor options were oropharynx, oral cavity, and unknown. For the purposes of analysis in this study, patients who had unknown primary tumors were grouped with those who had primary tumors of the oropharynx.
[c] Surgical resection here includes the responses "surgical resection" and "surgical resection before enrollment."

Of the partners who completed the survey, 75 were matched with patients who also completed the survey. Among this subset of 75 matched pairs of patients and partners, there were no statistically significant differences in mean scores on the DAS subscales ($P = .26$ for consensus, $P = .39$ for satisfaction, and $P = .74$ for affectional expression), indicating similar perceptions of the quality of the relationship in patients and their partners.

Follow-up

At the 6-month follow-up time point, DAS scores did not change significantly from baseline for participants on any subscale. However, a trend ($P = .10$) was noted toward higher distress at follow-up in the affection expression subscale for HPV-positive versus HPV-negative patients.

HPV and Relationships

This portion of the survey explored the effect of a diagnosis of an HPV-associated malignancy on relationships among 141 patients with HPV-positive OSCC and 69 of their partners. The majority of HPV-positive patients (71%) reported that they had already talked with their partner about HPV, and an additional 24% reported an intention to do so in the next 30 days (Supporting Table 5; see online supporting information). However, only 56% of patients reported that they subjectively felt they had "enough information" for this discussion. Responses from the participating partners were similar to those of patients (Supporting Table 5; see online supporting information). Most patients and partners (90% and 98%, respectively) reported that they would tell their partner if they had a history of an STI.

Only 38% of HPV-positive patients reported that their relationship with their partner had not changed. However, those who reported a change in their relationship generally perceived it as positive. The majority of patients reported that they felt supported by their partner (92%) and that their relationship had become stronger (69%). Very few patients reported difficulty communicating (3.6%) or more disagreements (2.1%). However, approximately 1 in 4 patients either blamed themselves for their cancer diagnosis (26%) or felt guilty about exposing their partner to HPV (28%).

The majority of partners (approximately 70%) also reported favorable changes in their relationship (Supporting Table 5; see online supporting information) since the patients' HNC diagnosis. However, significantly higher proportions of partners than of patients reported more stress in their relationship since the cancer diagnosis (39% vs 14%; $P < .01$). In addition, 14% of partners either felt guilty that they may have exposed their partner (the patient) to HPV or were concerned that the HPV infection may have occurred as a result of their or their partner's extramarital sexual relationships.

Both patients and partners expressed some concern that HPV infection may be transmitted to them by their partner as a result of sexual behavior. Approximately one-half of patients and partners expressed concern about HPV transmission by sexual intercourse (44.9% and 52.2%, respectively). Significantly more patients than partners were concerned about HPV transmission by oral sex (45% vs 31.3%; $P < .01$). Relatively few were concerned about transmission by kissing (15.3% vs 15.9%, respectively) or by nonsexual contact (Fig. 1).

HPV and Health Concerns

The HPV and health concerns portion of the survey evaluated the impact of the patient's OSCC diagnosis on their partner's perceptions of their own risk of HNC and HPV infection at baseline and 6 months later (Supporting Table 6; see online supporting information).

In the previous 2-week period, 35% and 43% of partners had sometimes or often thought about their chances of getting HNC or HPV, respectively. However, very few partners ($\leq$6%) reported that these thoughts affected their mood or their ability to perform daily activities. Notably, 28% of partners perceived that they were higher risk for HNC, and 25% perceived that they were higher risk for HPV infection compared with other individuals their age. Forty-eight percent believed that they would be less likely to get HNC if they had received the HPV vaccine, but 48% responded "don't know." No statistically significant differences were observed between responses at baseline and at the 6-month follow-up time point.

Sexual Behavior and OSCC Diagnosis

Significant changes in the frequency of sexual behaviors between baseline and follow-up were reported by both HPV-positive and HPV-negative patients (Fig. 2). At baseline, 88% of both HPV-positive and HPV-negative patients reported kissing their partner at least weekly; and 32% and 29%, respectively, reported having sexual intercourse at least weekly. HPV-positive patients performed oral sex significantly ($P < .01$) more frequently than HPV-negative patients. Among HPV-positive patients, 10% and 9% gave and received oral sex, respectively, at least once per week at baseline in contrast to 5% and 4%, respectively, of HPV-negative patients. No other significant differences in frequency of sexual behaviors at baseline were reported.

Kissing was the only sexual behavior without a significant decline in frequency at 6 months. The proportion of patients who reported no sexual intercourse with their partner increased from 10% at baseline to 34% at follow-up. The frequency of sexual intercourse decreased significantly from baseline for both HPV-positive and HPV-negative patients ($P < .01$ for both).

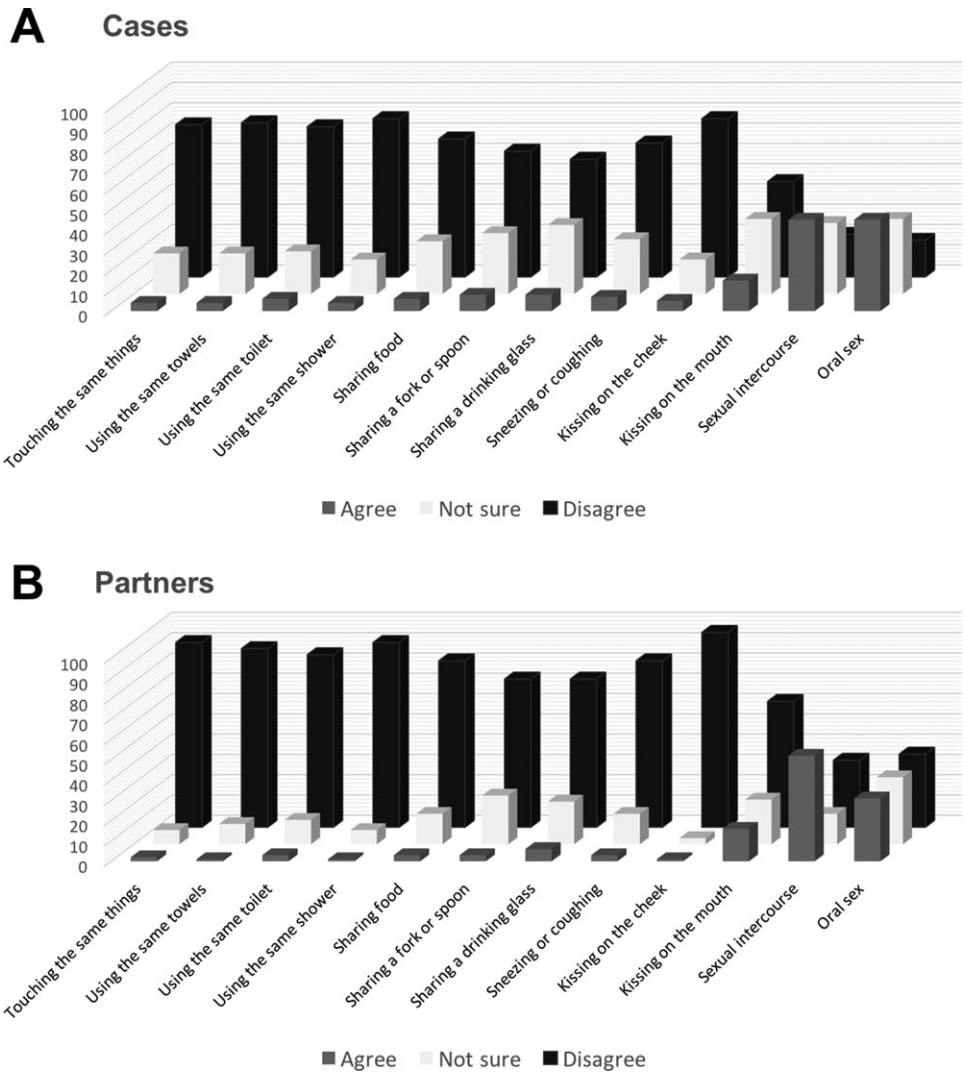

Figure 1. Concerns over possible mechanisms of human papillomavirus (HPV) transmission expressed by (A) HPV-positive individuals and (B) their partners at baseline are illustrated. The frequency distribution for different levels of agreement (1, disagree; 2, not sure; 3, agree) with statements regarding concern over various possible mechanisms of HPV transmission is shown for HPV-positive individuals (n = 141) and their partners (n = 69). Each potential mechanism contained in the survey was preceded by the following statement for patients: "I am concerned that I may transmit HPV to my spouse/partner by…"; and for partners: "I am concerned that my spouse/partner may transmit HPV to me by…."

The sexual behavior with the most pronounced change was oral sex. The proportion of patients reporting that they never performed oral sex on their partner increased from 18% at baseline to 78% at 6 months for HPV-positive patients and from 34% to 85%, respectively, for HPV-negative patients. The proportion of patients reporting that they never received oral sex also increased from 28% at baseline to 68% at 6 months for HPV-positive patients and from 36% to 74%, respectively, for HPV-negative patients. For both performing and receiving oral sex, the change was significant ($P < .01$) regardless of HPV status. The type of primary therapy for the cancer (eg, surgical vs nonsurgical) was not associated with changes in sexual behavior reported at the 6 month follow-up time point (Supporting Table 7; see online supporting information).

Sexual behavioral changes reported by patients were corroborated by their partners. The proportion of partners reporting never having sex increased from 7% at baseline to 32% at 6 months. Corresponding proportions for never performing oral sex were 25% and 59%, respectively; and proportions for never receiving oral sex were 24% and 77%, respectively. The decrease in frequency was statistically significant for having sexual

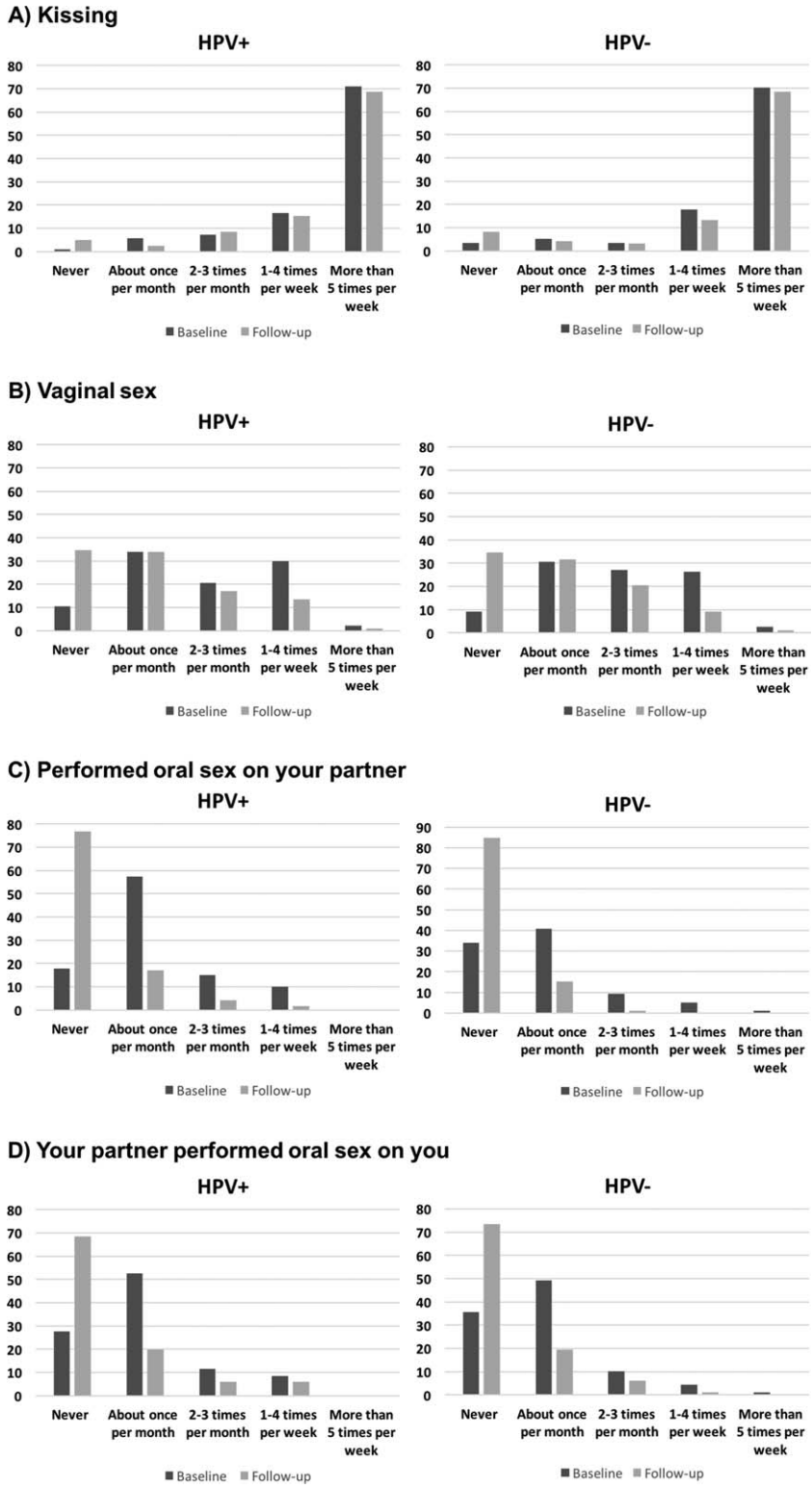

Figure 2. (A-D) The frequency of sexual behaviors is illustrated among human papillomavirus (HPV)-positive (HPV+) and HPV-negative (HPV−) individuals at baseline and at the 6-month follow-up time point. Ordinal categories for the frequency of specific sexual behaviors are shown at baseline and at follow-up for patients with HPV + (baseline, n = 141; follow-up, n = 118) and HPV− (baseline, n = 118; follow-up, n = 94) oral squamous cell carcinoma. With the exception of kissing, all activities declined significantly from baseline to follow-up in all groups ($P < .01$ for vaginal sex, performing oral sex, and receiving oral sex) regardless of HPV status.

intercourse and for performing and receiving oral sex ($P < .01$ for all).

At baseline, frequencies for sexual behaviors reported by patient-partner pairs were similar and not statistically different ($P = .38$ for kissing, $P = .36$ for sexual intercourse, $P = .96$ for performing oral sex, and $P = .71$ for receiving oral sex). At follow-up, the frequency of performing oral sex reported by partners was significantly higher than that reported by their partner (the patient; $P < .01$).

At 6 months, both patients and partners were asked about specific changes in their sexual behaviors since the patient's diagnosis of OSCC (Supporting Table 8; see online supporting information). Patients (65%) and partners (72%) reported that their sex life had changed, and the proportions reporting changes were similar regardless of HPV status. Very few patients reported changes in their use of barrier methods for vaginal (condom use) or oral (dental dam use) sex.

DISCUSSION

This study was designed to evaluate whether a diagnosis of HPV-positive OSCC would be associated with greater relationship stress and changes in sexual behavior than a diagnosis of HPV-negative OSCC. The data suggest little difference in relationship stress or sexual behaviors subsequent to a diagnosis of HPV-positive or HPV-negative OSCC. Sexual behavior changed significantly in the 6 months after a diagnosis of OSCC, regardless of tumor HPV status. This was true, despite the fact that patients and partners generally reported high-quality relationships and a greater appreciation of their partner. The paucity of data on this topic in the medical literature suggests that the HNC community has had little awareness of the major impact of a diagnosis of OSCC on important components of quality of life: sexual function and sexual behavior.

The psychosocial concerns of patients with genital HPV infections and cervical cancer, by contrast, have been extensively studied.[14] An HPV diagnosis has been associated with anxiety, increased concern about sexual relationships, and decreased sexual enjoyment and activity.[14] In a previous qualitative interview study of 10 male HPV-positive OPSCC survivors, similar feelings of guilt and self-blame because of their diagnosis were reported.[15] These findings were confirmed in the current large, prospective study, because approximately 25% of patients with HPV-positive OSCC felt they were to blame for their diagnosis or felt guilty about potentially exposing their partner to HPV. Partners of patients reported similar concerns, although they were less frequent.

Patients and their partners may have concerns about the transmission of HPV infection, because HPV has emerged as an increasingly important cause of OSCC.[16] The existing literature supports a predominantly sexual means of transmission for oral HPV infection. Vaginal, anal, and oral sex and open-mouth kissing all have been linked to an increased risk of HPV infection.[17,18] Approximately one-half of participants in the current study expressed concern about HPV transmission through oral and vaginal sex, but few expressed concern about transmission through kissing or nonsexual contact. A single study observed that oral HPV infection among partners of patients with HPV-positive OSCC was rare, consistent with infrequent transmission, immune protection, or rapid clearance.[19] Although partners of patients with HPV-positive cancers have a significantly increased risk of HPV-associated malignancies (from 2-fold to 6-fold), the absolute risk remains low (approximately 12 per 100,000).[9] Despite concern about sexual transmission, few patients reported increased use of barrier methods for vaginal or oral sex after their diagnosis. It has been demonstrated that barrier methods reduce the risk of genital HPV infection as well as other STIs.[20,21] Additional studies may be warranted to determine whether or not patient and partner anxiety could be reduced through education regarding the low prevalence of oral HPV infection in partners and the protection afforded by barrier methods.

Our most striking finding was a dramatic reduction in the frequency of several sexual behaviors in the 6 months after an OSCC diagnosis. Studies focused on patients who underwent laryngectomy reported considerable impact of the diagnosis and treatment on sexual behavior.[22] Preliminary evidence supports long-term effects of the diagnosis on sexual function[6,23] and indicate that the sexual consequences are both understudied and under-reported by patients.[7,23]

In addition, highly similar declines in the frequency of sexual behaviors in HPV-positive and HPV-negative patients argue against knowledge and concern about HPV transmission through sex as the sole underlying reason for changes in sexual behavior. Our data indicate that the significant changes in sexual behavior are unlikely to be primarily attributable to relationship stress, because very low levels of such distress were reported by participants.

An alternative explanation could be the physical and emotional impact of cancer therapy. Although the type of primary therapy was not associated with changes in sexual behavior, common side effects of head and neck therapy,

such as fatigue and xerostomia, could affect sexual behavior. Vaginal dryness is well recognized as interfering with sexual activity after therapy for cervical cancer.[24] Xerostomia has been studied extensively because of its impact on dysphagia and patient quality of life[25,26]; however, to date, only Rogers et al have associated xerostomia with decreased frequency of oral sex.[7]

A diagnosis of any malignancy may dramatically alter sexuality,[27,28] and sexual function is an important component of survivorship.[29] Most research on the impact of a cancer diagnosis and treatment on sexual function has primarily focused on breast and gynecologic malignancies.[6,30,31] Although studies suggest that care is improving, sexual behavior may be insufficiently addressed even among patients with the most studied cancers.[30,31] Our data indicate that the impact of cancer therapy on the sexual behavior of patients with OSCC warrants further study and should be included as a meaningful endpoint in quality-of-life studies within treatment de-intensification trials.

This study has several potential limitations. The study population may not be representative of all patients with OSCC. In addition, because only one-half of eligible partners of our patients with OPSCC consented to participate, we cannot exclude bias toward less distressed partnerships as a result. Moreover, few partners of HPV-negative patients were recruited. Our data were limited to the 6 months after diagnosis; therefore, the long-term consequences of therapy on sexual behavior require further study. It is possible that sexual behavior could return to baseline with long-term follow-up.

We conclude that changes in sexual behaviors are significant after diagnosis and treatment of OSCC. Care providers should be aware of these changes and their potential impact on patient quality of life. Our data indicate that additional studies are warranted to further clarify the underlying reasons for the higher perceived relationship stress reported by partners versus patients as well as partners' perceptions of increased risk for HNC and HPV. Future studies should also prospectively and longitudinally address changes in sexual behavioral over time and the effects of gender, sexual orientation, side effects of therapy, perceptions of risk, and emotional responses to a cancer diagnosis on these sexual behavioral changes to identify potential means by which to improve upon them.

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CONFLICT OF INTEREST DISCLOSURES

Miren Taberna reports nonfinancial support from Merck and personal fees from Sanofi Pasteur MSD outside the submitted work. Maura L. Gillison reports personal fees from Celgene, Bristol-Myers-Squibb, Lilly, Amgen, Merck, GlaxoSmithKline, and AstraZeneca outside the submitted work. The remaining authors made no disclosures.

AUTHOR CONTRIBUTIONS

Miren Taberna: Study design, questionnaire design, writing–first draft, and approval of final version. **Ronald C. Inglehart**: Statistical analysis, writing–first draft, and approval of final version. **Robert K. L. Pickard**: Study design, questionnaire design, statistical analysis, writing–review and editing, and approval of final version. **Carole Fakhry**: Writing–review and editing and approval of final version. **Amit Agrawal**: Case enrollment, writing–review and editing, and approval of final version. **Mira L. Katz**: Writing–review and editing, and approval of final version. **Maura L. Gillison**: Study design, questionnaire design, writing–first draft, and approval of final version.

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