Oral Squamous Cell Carcinoma Arising Around Osseointegrated Dental Implants

Fawad Javed, BDS, PhD,* Mansour Al-Askar, BDS, MSc,* Faisal Qayyum, BDS, MClinDent,† Hom-Lay Wang, DDS, PhD,‡ and Khalid Al-Hezaimi, BDS, MSc§

Purpose: This literature review investigates the occurrence of oral squamous cell carcinoma (OSCC) around osseointegrated dental implants (DI).

Methods: Databases were searched from 1989 up to and including November 2011. The eligibility criteria were as follows: (1) original studies, (2) clinical studies and case reports, (3) reference lists of the relevant original and review articles, (4) intervention: occurrence of OSSC around osseointegrated DI, and (5) articles published only in English language.

Results: Fourteen studies were included. In nine studies, the dental implant patients with diagnosed OSCC had previously been exposed to cancer. In five studies, the patients presented with a history of habitual tobacco smoking and alcohol consumption.

Conclusion: OSCC is more likely to arise around osseointegrated DI in patients with a previous history of cancer. However, the role of other factors including tobacco and alcohol usage cannot be disregarded.

Key Words: cancer, dental implants, osseointegration

Studies have reported that dental implants (DI) can osseointegrate and remain functionally stable over lengthy time periods in healthy as well as medically compromised individuals, including those having undergone oral cancer therapy.1–7 The Kovács study8 investigated the effect of chemotherapy on the survival and success of DI in oral cancer patients. In this study, DI were installed in 30 patients having undergone oral cancer therapy and were followed up for a decade. The results showed that oral cancer therapy did not have detrimental effects on the survival and success of DI, and the overall implant survival rate was reported to be 99.1%.8 Similar results have been reported by other studies.9,10 Although DI have been shown to exhibit high survival rates in patients having undergone oral cancer treatment,11–13 clinical studies14–24 have also reported oral squamous cell carcinoma (OSCC) to arise after installation of DI. In their study, Gallego et al16 presented a case report of an 81-year-old woman who had received dental implant therapy. Nearly 3 years after implant treatment, the patient developed an exophytic mass around DI, which upon biopsy was diagnosed as OSCC.16 In another study, Czeminski et al21 presented a case series of individuals in whom DI were installed as a replacement for missing teeth. The individuals included in these studies developed nonhealing ulcers around the DI after a few years of implant treatment. The ulcerated lesions were subjected to histological assessment, and the results revealed the presence of OSCC around the DI.21

Periimplantitis is a complication of dental implant treatment with a classical sign of alveolar bone loss around DI.25,26 OSCC around DI may present as a red, hyperplastic, and/or ulcerated oral mucosa with alveolar bone loss and hence may be misdiagnosed as “periimplantitis.”27 Under such circumstances, a detailed clinical and radiological evaluation accompanied by a biopsy and histopathologic assessment may be performed to elucidate any diagnostic doubt. Block and Scheufler23 presented a case where the patient demonstrated periodontal bone loss around endosseous DI. Tissues from within the bone were debrided and sent for microscopic evaluation. The histological results showed the presence of a well-differentiated OSCC within the bone tissues.23

As the topic of OSCC arising after installation of DI has received limited attention, this in-depth review addresses the association of OSCC that may arise around osseointegrated DI.

Materials and Methods

Focused Question

The addressed focused question was “Can OSSC arise around osseointegrated DI?”
Eligibility Criteria

The eligibility criteria were as follows: (1) original studies, (2) clinical studies, (3) reference list of relevant original and review articles, (4) intervention: OSSC arising around osseointegrated DI, and (5) articles published only in English language.

Letters to the editor, historic reviews, and unpublished articles were excluded.

Search Strategy

As a first step, the authors searched the MEDLINE/PubMed (National Library of Medicine, Bethesda, MD) and Google Scholar databases for appropriate articles addressing the focused question. Titles and abstracts of articles that abided by the eligibility criteria were screened by the authors and validated for agreement. Databases were explored from 1989 up to and including November 2011 using the following keywords in various combinations: “cancer,” “dental implants,” and “osseointegration.”

As a next step, hand searching of the reference lists of potentially relevant original and review articles was performed, and once again any disagreement between the authors was resolved via discussion. The initial search yielded 28 studies. Fourteen studies, which did not comply by the eligibility criteria, were excluded (see Appendix). In total, 14 studies11–24 were included and processed for data extraction, as shown in Table 1.

RESULTS

Characteristics of Included Studies

The studies11–24 were performed in humans and were either carried out at universities or healthcare centers. Nine studies were case reports,12–14,16–20,23 four were case series,15,21,22,24 and one study11 had a retrospective design. The number of participants ranged between 1 and 21 individuals. The age range of the study participants was between 52 and 90 years. The patients presented in six12–14,16,19,20 out of the nine case reports12–14,16–20,23 were females. There was no significant difference in gender among the participants included in the retrospective study.11 In the case reports,12–14,16–20,23 at least two DI were placed in each subject, whereas in the retrospective study,11 a total of 56 DI were placed in 21 individuals. Characteristics of studies that fulfilled our eligibility criteria are summarized in Table 1.

In five studies12,13,15,21,23 the patients presented with a history of habitual tobacco smoking and/or alcohol consumption. In seven studies,11,14,16–20 there was no evidence of habitual tobacco smoking and alcohol consumption among the subjects. Two of the three cases presented in the Clapp study24 comprised individuals who were nonsmokers.

In nine studies,13,15,16,19–24 the dental implant patients with diagnosed OSCC had a history of either oral or systemic cancers. In three studies,16,22,23 the patient history revealed that these individuals were exposed to precancerous conditions (leukoplakia and oral lichen planus) before the installation of DI. In two,15,19 one,20 one,21 and two studies,23,24 individuals with OSSC after implant therapy also had a history of breast cancer, lung cancer, colon cancer, and verrucous carcinoma of alveolar ridge, respectively.

DISCUSSION

Although the results from this literature review showed that OSCC can arise around osseointegrated DI, it should be noted that in most of the case studies that fulfilled our eligibility criteria the patients already had a history of some form of cancer.13,15,16,19–24 For example, in the study by Dib et al,19 the patient presented with OSCC 7 months after dental implant therapy; however, the patient had a previous history of breast cancer. Likewise, in the case series by Czerninski et al,21 the male patient had a previous history of colon cancer. Although metastasis to the oral cavity and the jaws is uncommon (estimated to comprise about 1% of newly diagnosed oral malignancies),27,28 the possibility of cellular metastasis of systemic malignancies into the oral cavity cannot be disregarded. Trauma has been reported to facilitate the growth of blood-borne tumors.29 This possibility stems from the entrapment of tumor cells during clot formation in fresh wounds and to the fact that malignant cells grow more rapidly in areas of high cellular proliferation, such as regenerating tissue, mediated by host-generated growth factors. This may be an explanation for the metastasis of malignant cells from different locations into the oral cavity. Although malignant cells are known for their ability to invade different anatomical structures of the body, the role of confounding factors that may also participate in inducing or exacerbating OSSC in dental implant patients cannot be overlooked.

Periimplantitis is a chronic inflammatory condition which if left untreated may cause loss of supporting bone in the tissues surrounding a functioning implant. In some instances, OSCC may manifest clinical and radiological features (such as mucosal hyperplasia, mucosal ulcerations, and alveolar bone loss) similar to periimplantitis.30 The gingival attachment around DI is an area that experiences constant inflammation that may in turn affect mucosal stability. This inflammation may play an important role in the development of cancer due to the action of cytokine mediators including interleukin-1, interleukin-6, and tumor necrosis factor.25,30 A biopsy and histopathological assessment is particularly essential when mucosal inflammation and alveolar bone loss rapidly occur around DI without any response to therapy. This may assist in clarifying any diagnostic doubts.

Habitual tobacco and alcohol consumption are significant risk factors for oral inflammatory conditions including periodontal disease and OSCC.6,31,32 Some studies17,22,23 have also discussed the topic of periimplant OSCC which may initially present as periimplantitis and that in patients with a long-standing history of smoking and alcohol abuse, a biopsy of the tissues associated with periimplant inflammation should be taken. Habitual tobacco and alcohol abuse have also been positively associated with the development of oral premalignant

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<th>Number of DI Inserted</th>
<th>Number of Cases/DI Associated With OSSC</th>
<th>Main Results</th>
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<tr>
<td>De Ceulaer et al(^{11})</td>
<td>To underline the phenomenon of tumor recurrence around DI</td>
<td>Retrospective</td>
<td>21 (9 M:12 F)</td>
<td>65.8 (range: 27-77)</td>
<td>56</td>
<td>3 patients</td>
<td>Three patients developed local OSCC recurrence around one of the implants. No recurrence of OSCC was observed in the group implanted in second stage surgery.</td>
</tr>
<tr>
<td>Meijer et al(^{12})</td>
<td>To present a novel surgical treatment of an OSCC in the vicinity of DI</td>
<td>Case report</td>
<td>1 F</td>
<td>65</td>
<td>2</td>
<td>2 DI</td>
<td>Four years after implant therapy, OSCC was observed in the floor of the mouth between the two implants. It extended to the attached keratinized periimplant mucosa of both implants.</td>
</tr>
<tr>
<td>Gulati et al(^{13})</td>
<td>To report the case of a patient who presented with OSCC around DI</td>
<td>Case report</td>
<td>1 F</td>
<td>62</td>
<td>5</td>
<td>2 DI</td>
<td>After extensive oral surgery, the patient suffered from multiple episodes of periimplantitis and later developed OSCC.</td>
</tr>
<tr>
<td>Gallego et al(^{14})</td>
<td>To present a case of OSCC in an edentulous ridge in relation to an implant-supported overdenture</td>
<td>Case report</td>
<td>1 F</td>
<td>70</td>
<td>3</td>
<td>—</td>
<td>After 12 months of follow-up, no evidence of local or cervical recurrence was observed.</td>
</tr>
<tr>
<td>Kwok et al(^{15})</td>
<td>To present a case series where OSCC was associated with DI</td>
<td>Case series</td>
<td>1 M</td>
<td>62</td>
<td>14</td>
<td>—</td>
<td>Three months after implant treatment, a nonhealing ulcer was seen in the periimplant tissue on the lingual aspect of the mandibular right premolar region. On biopsy, it was diagnosed as OSCC.</td>
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<td>Six years after implant treatment, the patient developed inflammatory changes around one implant. Biopsy revealed the presence of a well-differentiated OSCC.</td>
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<tr>
<td></td>
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<td></td>
<td>1 M</td>
<td>71</td>
<td>NA</td>
<td>1 implant</td>
<td>One year after implant treatment, the patient developed an area of papillary hyperplasia on the lower lip. Biopsy revealed the presence of OSCC.</td>
</tr>
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<td></td>
<td></td>
<td>1 F</td>
<td>67</td>
<td>2</td>
<td>1 implant</td>
<td>Three years after implant therapy, the patient developed an exophytic mass around the DI which was diagnosed as OSCC on biopsy.</td>
</tr>
<tr>
<td>Gallego et al(^{16})</td>
<td>To present a case of OSCC adjacent to symphyseal implants</td>
<td>Case report</td>
<td>1 F</td>
<td>81</td>
<td>2</td>
<td>2 DI</td>
<td>The patient presented with a white exophytic lesion (6 mm in diameter), with superficial ulceration. Incisional biopsy showed the presence of a well-differentiated OSCC.</td>
</tr>
<tr>
<td>Eguia et al(^{17})</td>
<td>To present a case of OSCC arising around a dental fixed prosthesis over osseointegrated DI</td>
<td>Case report</td>
<td>1 M</td>
<td>76</td>
<td>2</td>
<td>1 implant</td>
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<th>Main Results</th>
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<tr>
<td>Schache et al[18]</td>
<td>To present a case to suggest that DI provide a route of entry for OSCC to the mandible</td>
<td>Case report</td>
<td>1 M</td>
<td>77</td>
<td>15</td>
<td>1 implant</td>
<td>Five years after implant therapy, the patient developed an exophytic mass around the DI inserted in the left mandible. Biopsy revealed the presence of OSCC.</td>
</tr>
<tr>
<td>Dib et al[19]</td>
<td>To describe a case of a metastatic breast carcinoma to the mandible and the maxilla, around DI</td>
<td>Case report</td>
<td>1 F</td>
<td>67</td>
<td>8</td>
<td>4 DI</td>
<td>Approximately 7 months after implant treatment, inflammatory lesions were seen around the maxillary and mandibular DI. Biopsy confirmed it to be metastatic carcinoma from the breast to jaws.</td>
</tr>
<tr>
<td>Verhoeven et al[20]</td>
<td>To present a case of a patient with OSCC around osseointegrated DI</td>
<td>Case report</td>
<td>1 F</td>
<td>67</td>
<td>2</td>
<td>1 implant</td>
<td>Progressive swelling (35 mm in diameter) developed around the left DI. The associated DI was removed and the swelling was biopsied. It was diagnosed as a metastasis of the lung carcinoma to the mandible. The jaw tumor was treated with local radiotherapy.</td>
</tr>
<tr>
<td>Czerninski et al[21]</td>
<td>To present cases of OSCC adjacent to DI</td>
<td>Case series</td>
<td>1 F</td>
<td>52</td>
<td>3 DI</td>
<td>—</td>
<td>Three years after implantation, a 25-mm ulcer developed on the alveolar ridge posterior to the DI. Upon biopsy, a well-differentiation OSCC was diagnosed. Five years after implant therapy, a 15-mm ulcerated exophytic mass was observed surrounding the DI. Upon biopsy, a poorly differentiated OSCC was diagnosed.</td>
</tr>
<tr>
<td>Shaw et al[22]</td>
<td>To demonstrate clinical cases where malignancy in the periimplant tissues necessitated further major resections</td>
<td>Case series</td>
<td>1 M</td>
<td>67</td>
<td>4 DI</td>
<td>1 implant</td>
<td>Nearly 5 y after implant treatment, an exophytic mass was noticed under the implant-supported dental prosthesis. Biopsy of the mass was diagnosed as OSCC. Nearly 5 y after implant treatment, an exophytic mass was noticed under the implant-supported dental prosthesis. Biopsy of the mass was diagnosed as OSCC.</td>
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white lesions (including leukoplakia and oral lichen planus). It may therefore be argued that such confounding parameters may also play a role in exposing the patients with DI to OSCC. From the literature reviewed, we found it exigent to predict the frequency of tobacco usage that could expose the patient with DI to OSCC. For example, in the study by Gulati et al, the patient with OSCC around DI smoked 20 cigarettes per day for several years, whereas in the Kwok study, the patient smoked 40 cigarettes a day for over 30 years but quitted the habit only 2 months before his attendance to the oral healthcare centre. Further studies are warranted in this regard.

Oral inflammatory conditions have been reported to be significantly higher in immunocompromised females compared to males in the same group. From the literature reviewed, it may be postulated that OSCC develops more frequently in females with DI compared with males; however, it should be noted that patients in nearly 70% of the studies who fulfilled our eligibility criteria were females. Hence, the role of gender in the occurrence of OSCC around DI remains unclear. Further studies with a larger sample size are needed to assess the significance of gender with reference to the development of OSCC around DI. A limitation of the present review is that the study search yielded only case reports or case series; however, further prospective studies are warranted to comprehend the development of OSCC around osseointegrated DI.

**CONCLUSION**

It is concluded that OSSC may arise around osseointegrated DI particularly in patients with (a) a history of oral or systemic malignancy and (b) regular tobacco use and alcohol consumption habits. A detailed review of the patients’ habits and medical and dental history may play an essential role in selecting candidates for future implant treatment. This may also help predict the possible complications that may arise after placement of DI in susceptible individuals.

**APPENDIX: LIST OF EXCLUDED STUDIES**

Main reason for excluding the is shown in parenthesis.
- Blake F, Bubenheim M, Heiland M, et al. Retrospective assessment of the peri-implant mucosa of implants inserted in reanastomosed or free bone grafts from the fibula or iliac crest. *Int J Oral

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### Table 1. (Continued)

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<th>Main Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Block and Scheufler</td>
<td>To present a case report of a patient who developed periimplant bone loss in a span of 5 months</td>
<td>Case report</td>
<td>1 M</td>
<td>72</td>
<td>8 DI</td>
<td>2 DI</td>
<td>Two years after implant treatment, bone loss was observed around two DI. One implant was removed and biopsy of the intraosseous tissues showed a well-differentiated OSCC.</td>
</tr>
<tr>
<td>Clapp et al</td>
<td>To present a case series of patients who developed OSSC in association with osseointegrated DI</td>
<td>Case series</td>
<td>1 F</td>
<td>65</td>
<td>5 DI</td>
<td>5 DI</td>
<td>Three years after implant therapy, the patient developed OSCC of the alveolar ridge around the DI.</td>
</tr>
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<td></td>
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<td></td>
<td>1 M</td>
<td>79</td>
<td>NA</td>
<td>NA</td>
<td>Four years after implant treatment, the patient developed a nonhealing ulcer around the DI. It was diagnosed as OSCC.</td>
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<td></td>
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<td></td>
<td>1 F</td>
<td>90</td>
<td>NA</td>
<td>NA</td>
<td>Three years after implant placement, the patient developed persistent buccal mucosal ulcer around DI. Biopsy of the associated tissues revealed the presence of OSCC.</td>
</tr>
</tbody>
</table>

DI indicates dental implants; NA, not available; OSCC, oral squamous cell carcinoma.
Maxillofac Implants. 2008;23:1102-1108 (Focused question not answered).


**DISCLOSURE**

The authors claim to have no financial interest in any company or any of the products mentioned in this article.

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**REFERENCES**


