

# Osteomyelitis Arising Around Osseointegrated Dental Implants: A Systematic Review

Sergio V. Kellesarian, DDS,\* Fawad Javed, BDS, PhD,\* and Georgios E. Romanos, DDS, PhD†

ental implants are a modern and reliable treatment strategy for the replacement of missing teeth in partially and completely edentulous individuals.<sup>1,2</sup> Although dental implants have demonstrated success and survival rates of up to 100%,3,4 occurrence of complications such as periimplant mucositis, periimplantitis, and loss of osseointegration cannot be overlooked.<sup>5</sup> Risk factors that have been associated with periimplant diseases have broadly been classified as local and systemic risk factors. The local risk factors associated with periimplant complications encompass poor bone quality and quantity, surgical trauma, bacterial contamination, overload during the healing phase and tobacco exposure; and an immunosuppressed health status (such as among patients with acquired immune deficiency syndrome and poorly controlled diabetes mellitus)<sup>4,6–8</sup> and exposure to irradiation therapy and/or bisphosphonates are the common systemic risk factors for periimplant diseases and loss of osseointegration.7-10

\*Post-Doctoral Fellow, Department of General Dentistry, Eastman Institute for Oral Health, University of Rochester, NY. †Professor, Department of Oral Surgery and Implant Dentistry, Dental School, Johann Wolfgang Goethe, University of Frankfurt, Frankfurt, Germany, Professor, Department of Periodontology, School of Dental Medicine, Stony Brook University, Stony Brook, NY.

Reprint requests and correspondence to: Georgios E. Romanos, DDS, PhD, Department of Periodontology, Stony Brook University, School of Dental Medicine, 106 Rockland Hall, Stony Brook, NY 11794-8700, Phone: +1 (631) 632-8755, Fax: +1 (631) 632-8670, E-mail: georgios.romanos@stonybrook.edu

ISSN 1056-6163/18/02701-001 Implant Dentistry Volume 27 ● Number 1 Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved. DOI: 10.1097/ID.0000000000000715 **Objective:** The past few years have seen a progressive increment in the number of osteomyelitis cases associated with dental implants, raising the interest of a possible role of implant therapy in the development of osteomyelitis. The aim of the present study was to systematically review the association between dental implant therapy and occurrence of osteomyelitis.

Data Sources: The focused question addressed was "What is the risk to develop osteomyelitis among patients receiving dental implants?" Indexed databases were searched without language restrictions up to January 2017 using various key words including: "osteomyelitis"; "dental implants"; "osseointegration"; and "risk factors."

**Results:** Fourteen studies reporting cases of 39 patients who developed osteomyelitis after dental implant placement were identified. Among the 39 patients, 66.6% were women and 28.2% were men. The overall mean age was 60.26 years. Thirty-six patients had osteomyelitis of the mandible; 2 cases were reported in the maxilla, whereas, 1 case reported vertebral osteomyelitis associated with implant therapy.

**Conclusion:** The knowledge of the real impact of osteomyelitis on the outcome of implant therapy and the identification of risk factors associated with this infectious and life-threatening condition are essential for the development of prevention protocols and treatment strategies. (Implant Dent 2018;27:1–10)

Key Words: mandible, risk factors, survival, infection, inflammation

Osteomyelitis is an inflammatory condition of the bones, which begins as an infection of the medullary cavity, which may progress rapidly to the haversian systems and the periosteum of the affected area thereby jeopardizing the local blood supply. Ischemia induces necrosis of the bone and leads to sequester formation.<sup>11</sup> The presence of osteomyelitis in the mandible or maxilla is rare; however, a limited number of cases<sup>12–25</sup> have shown the development of osteomyelitis in the jaws after the placement of dental implants. In 1993, Sussman and Moss<sup>23</sup> reported

for the first time a case of localized osteomyelitis in the anterior mandible secondary to implant placement. In the following 20 years, only 6 cases<sup>13,15,18-20,24</sup> of osteomyelitis secondary to implant placement were reported. However, in the past 4 years (2013 - 2016),more than 30 cases<sup>12,14,16,17,21,22,25</sup> of osteomyelitis associated with dental implants have been reported in the literature, raising the interest of a possible role of implant therapy in the development of osteomyelitis. To our knowledge from indexed literature, a review of literature

investigating the association between dental implant therapy and occurrence of osteomyelitis is not yet available.

With this background, the aim of the present study was to systematically review the association between dental implant therapy and occurrence of osteomyelitis.

### METHODS AND MATERIALS

### **Focused Question**

Based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,<sup>26</sup> a specific question was formulated following the Participants, Interventions, Control, and Outcomes (PICO) format. The addressed focused question was: "What is the risk to develop osteomyelitis (O) among patients (P) receiving dental implants? (I/C)"

#### **Eligibility Criteria**

A study was considered eligible for inclusion if it met the following criteria: (1) original study; (2) prospective and retrospective design; (3) case reports; and (4) case series. The exclusion criteria comprised laboratory (*in vitro*) and experimental (animal models) studies, commentaries, letters to the editor, interviews, updates, and qualitative and/or quantitative reviews.

#### Literature Search Protocol

To identify studies relevant to the focused question, 2 authors (S.V.K. and F.J.) conducted a comprehensive and logical electronic search without language or time restriction, up to and including January 2017 in Google Scholar, Scopus, PubMed (National Library of Medicine), and MEDLINE (OVID). The following Medical Subject Headings (MeSH) were used: (1) osteomyelitis, (2) dental implants, (3) osseointegration, and (4) risk factors. Other related non-MeSH terms were used in the search strategy to detect additional studies reporting the association between dental implants and osteomyelitis. These included: (5) failure; (6) complication, and (7) bone loss. The aforementioned terms were used in the following combinations: 1 and 2 or 3; and 1 and 2 and 3; or 4 or 5 or 6 or 7.

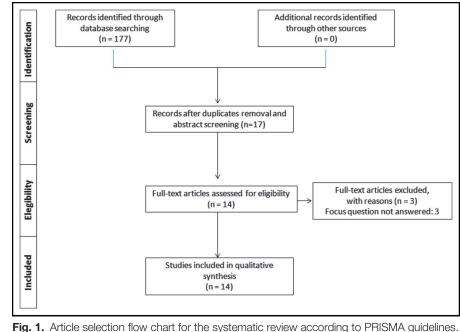
Titles and abstracts of studies identified using the above-described protocol were screened by 2 authors (S.V.K. and F.J.) and checked for agreement to exclude irrelevant articles and duplicates. Full texts of studies judged by title and abstract to be relevant were read and independently evaluated for the stated eligibility criteria. Reference lists of potentially relevant original and review articles were hand searched to identify studies that have remained unidentified in the previous step. Once again, the articles were checked for disagreement by discussion among the authors. Kappa scores (Cohen kappa coefficient) were used to determine the level of agreement between the 2 reviewers (kappa score = 0.88).<sup>27</sup> Figure 1 summarizes the literature search strategies according to the PRISMA guidelines.

### **Quality Assessment**

In an attempt to increase the strength of the present review, the studies with a case report and case series design were assessed qualitatively following the recommendations of Joanna Briggs Institute (JBI) Critical Appraisal Tool for case reports.<sup>28</sup> The JBI tool uses a systematic approach based on 8 specific criteria which are as follows: (1) clear description of

patients' demographic characteristics; (2) clear description of patients' history (presented as a timeline); (3) clear description of current clinical condition; (4) clear description of diagnostic tests and results; (5) clear description of interventions or treatment procedures; (6) clear description of postintervention clinical condition; (7) description of adverse or unanticipated events; and (8) there are important takeaway lessons. Each criterion was given a response of either "Yes," "No," "unclear," or "not applicable." Each study could have a maximum score of 8.

The retrospective studies included underwent a quality assessment with the Critical Appraisal Skills Program (CASP) guidelines.<sup>29</sup> The CASP tool uses a systematic approach based on 12 specific criteria: (1) Study issue is clearly focused; (2) Cohort is recruited in an acceptable way; (3) Exposure is accurately measured; (4) Outcome is accurately measured. (5) Confounding factors are addressed; (6) Follow-up is long and complete; (7) Results are clear; (8) Results are precise; (9) Results are credible; (10) Results can be applied to the local population; (11) Results fit with available evidence; and (12) There are important clinical implications. Each criterion was given a response of either "Yes," "No," or "cannot tell."



Author (Country, y)	Patient	Sex	Age (y)	Medical Background	Site of Infection (Area)	No. of Implants Placed/Failed	Time Before Implantation (y
Sussman and Moss <sup>23</sup> (USA, 1993)	1	Male	52	Systemically healthy	Mandible (anterior)	1/1	Immediate placement
Piattelli et al <sup>19</sup> (Italy, 1995)	2	Female	40	NA	Maxilla (medial)	2/1	10
Esposito et al <sup>13</sup> (Sweden, 1999)	3	Female	54	Cigarette smoking Allergic to penicillin	Mandible (medial and posterior)	3/2	NA
Wiskott et al <sup>24</sup> (Switzerland, 2004)	4	Female	46	Systemically healthy	Mandible (posterior)	1/1	0.5
O'Sullivan et al <sup>18</sup> (England, 2006)	5	Male	72	Myocardial infarction Hypertension Cigarette smoking	Mandible (anterior)	2/1	NA
Kesting et al <sup>15</sup> (Germany, 2008)	6	Female	61	Allergy to penicillin	Mandible (anterior)	2/2	Immediate placement
Rokadiya and Malden <sup>20</sup> (Scotland, 2008)	7	Female	73	Systemically healthy	Mandible (anterior)	2/1	>20
Jacobsen et al <sup>14</sup> (Switzerland, 2013)	8	Female	NA	Mamma carcinoma BP (Zoledronic acid)	Mandible (NA)	NA	NA
	9	NA	NA	Multiple myeloma BP (Zoledronic acid and pamidronate)	Mandible (NA)	NA	NA
	10	NA	NA	Osteoporosis BP (Pamidronate)	Mandible (NA)	NA	NA
	11	Male	NA	Prostate cancer BP (Zoledronic acid)	Mandible (NA)	NA	NA
	12	Female	NA	Mamma carcinoma BP (Zoledronic acid)	Mandible (NA)	NA	NA
Naval et al <sup>16</sup> (Spain, 2014)	13	Male	71	Osteopetrosis	Mandible (posterior)	4/1	NA
Shnaiderman-Shapiro et al <sup>22</sup> (Israel, 2015)	14	Female	68	Diabetes Hypercholesterolemia	Mandible (premolar)	8/1	NA
	15	Male	58	Hypertension	Mandible (posterior)	2/1	Immediate placement
	16	Female	59	Asthma Hypertension	Mandible (medial)	1/1	NA
	17	Female	64	Hypertension Diabetes Hypercholesterolemia	Mandible (medial and posterior)	2/2	NA
	18	Female	75	Hypertension	Mandible (posterior)	1/1	NA
Doll et al <sup>12</sup> (Germany, 2015)	19	Female	64	Noncontrolled diabetes Cigarette smoking Allergic to penicillin Chronic bronchitis and pyrosis	Mandible (anterior, medial, and posterior)	7/7	Immediate placement

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Table 1. (Continued)							
Author (Country, y)	Patient	Sex	Age (y)	Medical Background	Site of Infection (Area)	No. of Implants Placed/Failed	Time Before Implantation (y)
Nazir et al <sup>17</sup> (USA, 2016)			Lumbar spine (L5-S1)	1/NA	Immediate		
				Low back pain			placement
Semel et al <sup>21</sup> (Israel, 2016)	21	Male	65	Cigarette smoking	Mandible (posterior)	1/1	NA
				Asthma			
				Myelodysplastic syndrome			
	22	Female	62	Hypothyroidism	Mandible (posterior)	2/2	Immediate
				Diabetes			placement
	23	Female	50	Systemically healthy	Mandible (anterior and medial)	2/2	NA
	24	Male	54	Diabetes	Mandible (NA)	3/3	NA
				Cigarette smoking			
	25	Female	68	Hypothyroidism and bipolar disorder	Mandible (NA)	4/2	NA
				Cigarette smoking			
Yahalom et al <sup>25</sup> (Israel, 2016)	26	Female	43	Systemically healthy	Mandible	NA	NA
	27	Female	56	Mild neutropenia	Mandible	NA	NA
	28	Male	66	Systemically healthy	Mandible	NA	NA
	29	Male	66	Systemically healthy	Mandible	NA	NA
	30	Male	62	Systemically healthy	Mandible	NA	NA
	31	Female	68	Diabetes	Mandible	NA	NA
	32	Female	70	Systemically healthy	Mandible	NA	NA
	33	Female	55	Systemically healthy	Mandible	NA	NA
	34	Female	44	Systemically healthy	Mandible	NA	NA
	35	Male	67	Systemically healthy	Maxilla	NA	NA
	36	Female	62	Systemically healthy	Mandible (posterior)	2/2	NA
	37	Female	46	Systemically healthy	Mandible (posterior)	2/2	NA
	38	Female	58	Systemically healthy	Mandible	NA	NA
	39	Female	63	Systemically healthy	Mandible	NA	NA

BP, bisphosphonate; NA, not available.

OSTEOMYELITIS ARISING AROUND OSSEOINTEGRATED DENTAL IMPLANTS

				ents With Implant-Associate			
Authors	Patient	Clinical Findings and Reported Symptoms	Radiological Findings	Histology and Microbiological Findings	Time of Implantation (wk)	Pharmacological Treatment	Surgical Treatment
Sussman and Moss <sup>23</sup>	1	Endodontic—implant lesion	PIL	NA	3	NA	Implant removal
Piattelli et al <sup>19</sup>	2	Pain Swelling Suppuration	PIL	Necrotic bone	16	NA	Curettage Implant removal
Esposito et al <sup>13</sup>	3	Pain Swelling Suppuration	PIL	Poor bone formation	9 and 10	NA	Implant removal
Wiskott et al <sup>24</sup>	4	Pain suppuration	Bone sequestrum	NA	2	A+AC Vancomycine	Implant removal Curettage
O'Sullivan et al <sup>18</sup>	5	Pain suppuration mobility	PIL fracture of the mandible	NA	572	Amoxicillin Clindamycin	Curettage Implant removal
Kesting et al <sup>15</sup>	6	Extra- and intraoral abscesses Pain	Moth-eaten lesion	Streptococcus Peptococcus Peptostreptococcus	3	Clindamycin Metronidazole	Implant removal Curettage Hemi- mandibulectomy Fibular bone graft
Rokadiya and Malden <sup>20</sup>	7	Pain suppuration	PIL	Staphylococcus aureus	2.5	Penicillin Flucloxacillin	Implant removal
Jacobsen et al <sup>14</sup>	8	Suppuration	Bone sclerosis and poor bone formation	Necrotic bone Actinomyces	NA	NA	NA
	9	Suppuration	Bone sclerosis and poor bone formation	Necrotic bone Actinomyces	NA	NA	NA
	10	Suppuration	Bone sclerosis and poor bone formation	Necrotic bone Fibrino-leucocytic exudate	NA	NA	NA
	11	NA	Bone sclerosis and poor bone formation	Necrotic bone	NA	NA	NA
	12	Suppuration	Bone sclerosis and poor bone formation	Necrotic bone Actinomyces	NA	NA	NA
Naval et al <sup>16</sup>	13	Pain Suppuration	Bone sclerosis	Necrotic bone >PTH and CK	NA	A+AC	Implant removal Curettage

*Curettage (continued on next page)* 

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<b>Table 2.</b> (0	Continuec

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					Time of		
Authors	Patient	Clinical Findings and Reported Symptoms	Radiological Findings	Histology and Microbiological Findings	Implantation (wk)	Pharmacological Treatment	Surgical Treatment
Shnaiderman- Shapiro et al <sup>22</sup>	14	Pain Suppuration Swelling	PIL bone sequestrum	Necrotic bone	NA	NA	Implant removal Curettage
	15	Pain	Radiolucent-radiopaque lesion	Necrotic bone	8	NA	Implant removal Curettage Bone augmentation
	16	Pain Swelling	Radiolucent-radiopaque lesion	Granulation tissue Hypercellular connective tissue	24	Doxycycline	Implant removal Curettage
	17	Pain Swelling	Radiolucent-radiopaque lesion	Inflammatory infiltrate Atypical osteoblasts	1	NA	Implant removal Partial mandibulectomy
	18	Suppuration Pain	Radiolucent lesion with irregular bone loss	Fibro-osseous lesion High-grade osteogenic sarcoma	260	NA	Reconstruction plate Implant removal Curettage
Doll et al <sup>12</sup>	19	Suppuration	PIL Fracture of the mandible	β-hemolytic streptococcus	1 and 8	Clindamycin Ciprofloxacin Vancomycin	Curettage Implant removal Iliac crest graft
		Cervical fistula		Streptococcus		Voriconazole	Segmentation resection Osteosynthesis
		Submental abscess		intermedius Candida		Rifampicin	Partial mandibulectomy Fibular bone graft
Nazir et al <sup>17</sup>	20	Discitis and osteomyelitis at lumbar (L5-S1) Epidural abscess	NA	Streptococcus viridans	NA	Vancomycin Ceftriaxone	NA

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Authors	Patient	Clinical Findings and Reported Symptoms	Radiological Findings	Histology and Microbiological Findings	Time of Implantation (wk)	Pharmacological Treatment	Surgical Treatment
Semel et al <sup>21</sup>	21	Swelling Suppuration Pain trismus	Radiolucent-radiopaque lesion	Necrotic bone and granulation tissue	32	A+AC	Implant removal Curettage Marginal mandibulectomy Reconstruction plate
	22	Pain	Radiolucent lesion	Necrotic bone	2	Clindamycin	Implant removal Curettage
		Suppuration		Inflammatory infiltrate		Imipenem	Hyperbaric oxygen therapy Segmental mandibulectomy Reconstruction plate
	23	Pain	Radiolucent lesion	Necrotic bone Inflammatory infiltrate	18	Clindamycin	Implant removal Curettage
	24	Swelling	Radiolucent lesion	Candida glabrata	2	Clindamycin Ciprofloxacin	Implant removal Curettage
	25	Pain Swelling Suppuration Parestesia	Bone sequestrum	NA	104	A+AC	Implant removal
Yahalom et al <sup>25</sup>	26	NA	NA	NA	21.1	NA	Implant removal
	27	NA	NA	NA	12.5	NA	Implant removal
	28	NA	NA	NA	20	NA	Implant removal
	29	NA	NA	NA	16.5	NA	Implant removal
	30	NA	NA	NA	18	NA	Implant removal
	31	NA	NA	NA	19.2	NA	Implant removal
	32	NA	NA	NA	20.5	NA	Implant removal
	33	NA	NA	NA	18	NA	Implant removal
	34	NA	NA	NA	22.6	NA	Implant removal
	35	NA	NA	NA	17.5	NA	Implant removal
	36	NA	Radiolucent-radiopaque lesion	NA	26	NA	Implant removal
	37	Pain	Radiolucent-radiopaque lesion	NA	20.6	NA	Implant removal
	38	NA	NA	NA	23	NA	Implant removal
	39	NA	NA	NA	19.5	NA	Implant removal

CK, creatine kinase; NA, not applicable; PIL, periimplant radiolucency; PTH, parathyroid hormone.

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Each study could have a maximum score of 12.

### RESULTS

### General and Demographic Characteristics

One hundred seventy-seven potential articles were initially identified. In the first step, 160 publications which were either duplicates or did not answer the focused question were excluded. In the next step, 3 more articles were excluded. Fourteen studies<sup>12-25</sup> reporting cases of 39 patients who developed osteomyelitis after dental implant placement were identified and processed for data extraction. These pristudies<sup>12-25</sup> were reported marv between 1993 and 2016, in the following countries: England, Germany, Israel, Italy, Scotland, Spain, Sweden, Switzerland, and United States of America. Among the 39 patients, 26 were women (66.6%) and 11 were men (28.2%). In 2 cases, the patients' sex remained unclear. The mean age among women presenting osteomyelitis after dental implant placement was 59 years (range, 40–75 years), whereas the mean age of men was 63.3 years (range, 52–72 years). The overall mean age among patients diagnosed with osteomyelitis after implant rehabilitation was 60.26 years (range, 40-75 years) (Table 1).

# Medical History and Contributing Factors

Sixteen patients were systemically healthy (no medical history, allergies,

or contributing factors). Twenty-two patients had systemic conditions including diabetes mellitus (6 patients) and high blood pressure and/or cardiac disease (5 patients). Six patients were self-reported cigarette smokers and 4 patients reported to be allergic to penicillin. Five patients were under bisphosphonate therapy for the treatment of cancer or osteoporosis.

# Implant Therapy Related Characteristics

In 6 cases, the implant placement was followed immediately after dental extractions (fresh sockets), whereas in 3 cases, the implants were placed in healed bone (range of healing, 6 months-20 years). In 30 cases, the bone condition before implantation was not reported. Regarding the site of osteomyelitis, 36 patients (92.30%) had osteomyelitis of the mandible. Two cases (5.12%) were reported in the maxilla, whereas Nazir et al<sup>17</sup> reported 1 atypical case (2.56%) of vertebral osteomyelitis (L5-S1), with concomiparavertebral and tant epidural abscesses associated with a dental extraction and the placement of an immediate dental implant in the maxilla.

# Osteomyelitis Diagnosis and Management

Implants in the affected areas were removed in 33 of 39 cases, whereas in 6 cases, the implant survival or failure remained unclear. The time since the insertion of the implant until its removal because of complications and/or inadequate healing process (time of implantation) ranged between 1 week and 11 years (mean time of implantation, 40.98 weeks). In 8 cases, the time of implantation was not reported. Histological and/or microbiological findings associated with the failed implants were reported in 21 cases. Microbes identified among patients with osteomyelitis associated with dental implants included Streptococcus, Peptococcus, Peptostreptococcus. *Staphylococcus* aureus. Actinomyces, and Candida. Antibiotic therapy for the treatment of osteomyelitis was recorded in 13 cases. Surgical strategies for osteomyelitis management included curettage (after and/or before implant removal); in 5 cases, mandible resective surgery followed by reconstructive surgery (bone grafts or plates) was completed (Table 2).

#### **Quality Assessment**

Quality score for the retrospective studies<sup>13,14,25</sup> was 12. Quality score of the case report and case series studies<sup>12,15–24</sup> ranged from 5 to 8 (Case report and case series mean quality score: 7.18). Quality assessment identified that in general, the description of patients' demographic characteristics, medical history, and clinical condition were adequately performed in these studies.<sup>12,15–24</sup> The most common limitation was the lack or unclear description of diagnostic tests ordered to confirm osteomyelitis diagnosis. Quality assessment of the individual case report and case series is summarized in Table 3.

Table 3. Quality Assessment of the Included Case Reports Following JBI Critical Appraisal Tool										
Authors	Item 1	ltem 2	Item 3	Item 4	ltem 5	ltem 6	ltem 7	Item 8	Total Quality Score (0-8)	
Sussman and Moss <sup>23</sup>	Yes	Yes	Yes	No	Yes	No	Unclear	Yes	6	
Piattelli et al <sup>19</sup>	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	5	
Wiskott et al <sup>24</sup>	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	7	
O'Sullivan et al <sup>18</sup>	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	7	
Kesting et al <sup>15</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	
Rokadiya and Malden <sup>20</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	
Naval et al <sup>16</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	
Shnaiderman-Shapiro et al <sup>22</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	
Doll et al <sup>12</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	
Nazir et al <sup>17</sup>	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	6	
Semel et al <sup>21</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	

Item 1: clear description of patients' demographic characteristics; item 2: clear description of patients' history; item 3: clear description of current clinical condition; item 4: clear description of diagnostic tests and results; item 5: clear description of interventions or treatment procedures; item 6: clear description of postintervention clinical condition; item 7: description of adverse or unanticipated events; and item 8: there are important takeaway lessons.

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## DISCUSSION

In the present study, a total of 39 cases reported between 1993 and 2016 were assessed. It is noteworthy that the increase of reported cases of osteomyelitis occurred in the period between the years 2013 and 2016. This could be explained by the fact that the popularity of dental therapy and the number of implants placed has raised in the past decade. The authors of the present review speculate that the number of cases of osteomyelitis associated with dental implants might be even significantly higher but influenced by several factors such as publication bias. Welldesigned prospective clinical trials conducted in universities and medical settings are needed to estimate the real prevalence of osteomyelitis secondary to implant therapy.

The literature reviewed and the results of the present study offer important information regarding the demographics of osteomyelitis associated with implant placement. The prevalence of osteomyelitis is higher among women compared with men (2:1) receiving dental implants. Likewise, osteomyelitis onset is higher among women in the sixth decade of life (mean: 60.26 years, range, 40-75 years). These findings are in agreement with studies reporting higher incidence of osteomyelitis among middle-aged female populations.<sup>30,31</sup> Interestingly, the prevalence of osteomyelitis after dental implant therapy was higher in the mandible compared with the maxilla (9:1). It is speculated that the differences in blood supply between the maxilla and mandible play a role in osteomyelitis associated with dental implants. Osteomyelitis spreads mainly by local extension rather than by hematogenous route.<sup>21</sup> The maxilla presents thin cortical bone, less medullary spaces, and high collateral blood supply, which will prevent the infection from being confined to the bone, whereas the mandible presents poor blood supply and thick cortical plates, allowing the local infection to spread.<sup>32</sup>

It is noteworthy that in approximately 57% of the cases, the patients presented concomitant systemic conditions including diabetes mellitus, cigarette smoking, and bisphosphonate treatment for cancer or osteoporosis. Particular mention deserves the case reported by Doll et al<sup>12</sup> in a 64-year-old woman with poorly controlled diabetes and heavy smoking developing refractory osteomyelitis after receiving 7 dental implants in the mandible, which ended after 5 years of multiple surgical treatments in a reconstruction with a fibula-free flap after partial mandibulectomy. It is well established that osteomyelitis is associated with predisposing factors including tobacco use, chronic systemic disorders, and immunosuppression.33 Moreover, inexperienced surgeons and traumatic surgical techniques have also been identified as risks of infection.<sup>20</sup> Several studies<sup>34–39</sup> have reported that chronic hyperglycemia in patients with diabetes mellitus is a significant risk factor for soft tissue inflammation and bone loss around osseointegrated implants and teeth. An explanation in this regard is that chronic hyperglycemia has been associated with an increased formation and accumulation of advanced glycation end products in the systemic and oral tissues, which in turn increase the release of proinflammatory cytokines that enhance bone loss around implants.<sup>40–42</sup> The authors of the present review emphasize the need of a well-designed surgical protocol for implant placement including welltrained surgeons and a thorough study of the patient's medical history.

Among the cases reported, there was not a specific protocol for the treatment of osteomyelitis secondary to implant placement. The treatment should be aggressive and start as soon as possible to prevent the infection from spreading. The main goal is to provide resolution of the infection by removing the infection source.43 From the literature reviewed, approximately 86% of the implants involved with osteomyelitis were removed and the area curettage to remove sequestrum and necrotic bone. Antibiotics that have been recommended for the treatment of osteomyelitis associated with dental implants include amoxicillin with clavulanic acid, clindamycin, and vancomycin.32,43 However, the polimicrobial nature of the odontogenic infection associated with osteomyelitis requires

that antibiotic selection should be ideally based in previous bacterial characterization by culture and sensitivity tests. It is well established in the literature that a longer antibiotic therapy is required; however, the exact duration remains unclear.<sup>43</sup>

## CONCLUSION

The knowledge of the real impact of osteomyelitis on the outcome of implant therapy and the identification of risk factors associated with this infectious and life-threatening condition are essential for the development of prevention protocols and treatment strategies.

# DISCLOSURE

The authors claim to have no financial interest, either directly or indirectly, in the products or information listed in the article.

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