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REVIEW ARTICLE

Complications and treatment errors in periodontal therapy in medically compromised patients

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1 | INTRODUCTION

In 2019, worldwide life expectancy was estimated at approximately 72 years of age. This has improved dramatically over decades, and is mirrored in childhood survival rates.[1] As a consequence, the number of people presenting with long-term conditions is increasing rapidly, as it is closely related to aging.[2] Multimorbidity in this aging population is common and it has been rising in prevalence over recent years, with one in three adults living with more than one chronic disease.[3,4]

Evidence on the prevalence of systemic diseases in patients presenting for periodontal care suggests that between 40% and 52% of patients have more than one systemic condition, and these estimates increase with age.[5-7] In addition, the type of medical problems patients present with can differ significantly depending upon the facility where periodontal care is provided.[8] Findings from a retrospective analysis demonstrated a lower prevalence of medically compromised patients with periodontitis who attended a private dental practice (28%) compared with those attending a dental school or hospital clinic (46% and 74%, respectively).[8] Differences between participants in terms of age, socioeconomic status, or health awareness could explain these findings.[8] The most frequently reported medical problems in the dental office are allergies to medications followed by cardiovascular diseases (including hypertension) and endocrine disorders (including diabetes mellitus).[5-10]

As a direct consequence of medical comorbidities, a substantial number of patients will be taking multiple medications, which may also have an impact on their periodontal management. Radfar and Suresh[11] observed that of 1041 patients treated in their dental school, 360 (35%) were taking antihypertensives, 202 (19%) painkillers, 181 (17%) antidepressants, 107 (10%) antidyslipidemic agents, and 95 (9%) antiplatelet drugs. This highlights an additional consideration in terms of the potential pharmacologic interactions with anesthetics or other medications that we might need to prescribe for these patients after certain periodontal procedures.

In addition to the systemic pathology inherent to age and polypharmacy, the increased survival of patients with certain congenital diseases with periodontal manifestations has created a growing demand for periodontal treatment. These congenital disorders include

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diseases with a considerable prevalence such as Down syndrome[12] and around 14% of rare disorders with a low prevalence.[13] The provision of dental treatment for these patients is not exempt from some potential complications, because the etiopathogenic mechanisms of these diseases include hemorrhagic diatheses, immunodeficiencies, and alterations in the metabolism of vitamins, minerals, and trace elements.[13]

Treatment of periodontitis is part of routine care of patients attending dental practices, but it may be associated with complications, particularly when invasive/surgical approaches are required. Although the overall incidence of these complications is low, it includes prolonged bleeding (1%-8%),[14-17] infection (1%-4%),[14-16,18-20] swelling (1%-60%),[14-16] pain (4%-49%),[14-17] and delayed wound healing (2.5%).[14] In some lower number of cases, complications linked to specific surgical procedures may occur, such as membrane barrier exposure, flap dehiscence, or graft (soft or hard tissue-derived) necrosis.[14] The variability of complication rates is strictly dependent upon the periodontal procedure performed.[14,16] Askar et al[14] retrospectively evaluated complication rates of different periodontal procedures and found that patients who received osseous surgery more frequently developed some type of complication (in 25% of cases), followed by free gingival graft technique (20%), crown lengthening (16%), guided tissue regeneration (13%), open flap debridement (12%), and connective tissue graft procedures (10%). Gingivectomy appeared to be the surgical periodontal technique with the lowest rate of complications (5%).[14]

The presence of any long-term condition may increase the risk of having a complication during or after treatment of periodontitis, as evidenced by Askar et al,[14] who reported that patients diagnosed with diabetes mellitus were six and 25 times more likely to experienced delayed wound healing after an open flap debridement procedure and mucogingival surgery, respectively.

The aim of this narrative review is to provide a comprehensive overview of the potential complications and treatment errors that can occur in medically compromised patients undergoing both nonsurgical and surgical treatment of periodontitis. Specific risk reduction strategies for these patients are also discussed.

2 | EVIDENCE SEARCH METHODOLOGY

To gather all the evidence published in relation to complications after periodontal treatment in medically compromised patients, a systematic search in Medline OvidSP was carried out from 1946 to 10 July 2020. Three key searchable concepts were identified: “Periodontal Diseases”, “Surgical and Non-Surgical Periodontal Therapies”, and “Systemic Diseases”. Given the broad scope of the concept “Medically Compromised Patients”, a list of all diseases to be included in the review was compiled at the protocol stage and search strategies were created for each disease to be appended to a search including the first two concepts.

We conducted searches for each concept using text word terms and medical subject headings wherever these were available. When we carried out text word searches, synonyms, related terms, and singular/plural forms for each concept were used. This strategy ensured that we retrieved studies where surgical and nonsurgical periodontal therapies for periodontal diseases (including dental extractions as part of the periodontal treatment) were discussed along with each systemic disease of interest. We exported the results for each search to the reference management software Endnote X9, which we used to manage our references. We applied no language or date restrictions and used the high-sensitivity animal filter for Medline OvidSP (exp animals/not humans.sh), which we combined with our search strategy with the use of the Boolean operator NOT to exclude animal studies. No restriction was made in terms of study design (ie, from case reports to randomized clinical trials).

The total number of records retrieved by the electronic database was 9294, and one additional article was obtained via a manual search. After removing duplicates, we screened 6599 titles/abstracts and selected 112 articles for full-text screening. Finally, we chose 20 articles to be included in this narrative review.

3 | COMPLICATIONS AFTER PERIODONTAL THERAPY IN PATIENTS WITH COMORBIDITIES

Most studies reported different complications following nonsurgical and surgical periodontal procedures in medically compromised patients (Table 1). Most of the studies included were case reports.[21-32] Two publications were case series,[33,34] four studies had a cross-sectional design,[35-38] and only two were randomized controlled clinical trials.[39,40] The type of complication reported was related to the modality of periodontal treatment and the patient's systemic condition. In most of the studies, a low complication rate was observed (≈5%). The most frequently reported complication was bleeding in more than half of the studies included in this review.[22,23,25,26,29-33,35-38,40] Other less common oral complications include delayed wound healing,[21,22] barrier membrane exposure,[27,28] infection,[28,39] and medication-related osteonecrosis of the jaw.[24]

3.1 | Bleeding-related complications

Four different groups of patients could be identified when prolonged gingival bleeding was reported as a complication after periodontal treatment: in patients with bleeding disorders, drug-induced gingival overgrowth, those taking antithrombotic medications, and patients with hypertension.

3.1.1 | Bleeding disorders

Bleeding disorders can be congenital or acquired (Table 2). An in-depth review of their relationship with periodontics has been previously published and it is not within the scope of the current review.[41]

TABLE 1 Summary of publications reporting on complications related to periodontal therapy in medically compromised patients

Authors (year)	Country	Study design	Systemic condition	Intervention	Complication	Complication rate	Complication management
Andersen et al. (2003)[21]	Norway	Case report	Crohn's disease	Mucogingival surgery (coronally advanced flap with or without enamel matrix derivative)	Altered and delayed healing	—	0.2% clorhexidine mouthwash + 1% clorhexidine gel (once/d for 3 wk)
Blanco-Carrion et al. (2004)[22]	Spain	Case report	Moderate hemophilia A, HIV infection (B_2 stage), and chronic hepatitis C	Mucogingival surgery (subepithelial connective tissue graft)	Area of necrosis at donor palatal site with spontaneous bleeding 1 wk after procedure	—	Factor VIII concentrate (2500 units twice/d, during 1 wk) + prophylactic Factor VIII concentrate (2500 units once/2 d, for 2 more wk)
Campo et al. (2007)[35]	Spain	Cross-sectional	HIV infection	a. Dental prophylaxis (n = 33) b. Scaling and root planing (n = 8) c. Surgical therapy (n = 3)	a. None b. Prolonged gingival bleeding c. None	a. 0.0% (0/45) b. 5.8% (1/17) c. 0.0% (0/4)	Not reported
Cutler et al. (1991)[23]	USA	Case report	Type 1 diabetes mellitus	Nonsurgical periodontal treatment (scaling and root planing) + dental extractions	Liver clots without clot retraction for up to 10 d postextractions	—	Not reported
D'Aiuto et al. (2018)[39]	UK	Randomized controlled clinical trial (*intensive periodontal therapy vs control periodontal therapy*)	Type 2 diabetes mellitus	a. Intensive periodontal therapy (scaling and root planing + re-instrumentation or modified Widman flap technique) (n = 133) b. Control periodontal therapy (supragingival scaling and polishing) (n = 131)	a. Oral: tooth pain, tooth sensitivity, tooth infection, tooth fracture, tooth restoration and gum swelling b. Systemic: chest infection, headache, influenza, throat infection, foot infection, fainting, dizziness, and back pain	a. Dental pain (4%), sensitivity (3.1%), infection (2.5%), fracture (1.1%), restoration (0.8%), gum swelling (1.1%), chest infection (1.2%), headache (0.8%), influenza (0.7%), throat infection (0.4%), foot infection (0.5%), fainting (0.3%), dizziness (0.4%) and back pain (0.3%) b. Dental pain (3.0%), sensitivity (0.9%), infection (2.6%), fracture (1.6%), restoration (1.1%), gum swelling (0.8%), chest infection (1.0%), headache (0.4%), influenza (0.7%), throat infection (0.5%), foot infection (0.6%), fainting (0.3%), dizziness (0.4%) and back pain (0.5%)	Not reported

(Continues)

TABLE 1 (Continued)

Authors (year)	Country	Study design	Systemic condition	Intervention	Complication	Complication rate	Complication management
Diniz-Freitas et al. (2018)[24]	Spain	Case report	Osteoporosis treated with biannual subcutaneous injections of 60 mg of denosumab	Nonsurgical periodontal treatment (scaling and root planing)	Medication-related osteonecrosis of the jaw (stage I)	—	Extraction of teeth involved in the sequestration + complete surgical debridement of necrotic bone + 0.2% chlorhexidine mouthwash (2/d) and doxycycline (200 mg/d) from the 7 d prior to surgery until 3 wk postsurgery
Deppe et al. (2013)[36]	Germany	Cross-sectional	Prosthetic heart valve surgery *Relevant medication: anticoagulant coumarin drug*	a. Periodontal surgery (modified Widman flap technique) with the use of Nd:YAG laser + dental extractions (n = 24) b. Periodontal surgery (modified Widman flap technique) without the use of Nd:YAG laser + dental extractions (n = 21)	Gingival bleeding within 24 h after postoperative hemostasis	a. 3.7% (2/53) b. 4.5% (2/44)	Local hemostasis with either Nd:YAG laser or conventional methods
Elad et al. (2008)[25]	Israel	Case report	Coronary angioplasty and subsequent drug-eluting stent because of ischemic heart disease and acute myocardial infarct *Relevant medication: aspirin 100 mg and clopidrogrel 75 mg*	Nonsurgical periodontal treatment (scaling and root planing)	Severe gingival bleeding >10 h after postoperative hemostasis	—	4/0 vicril suture + local pressure with gauze soaked with tranexamic acid solution in the bleeding area
Federici et al. (2000)[37]	Italy	Cross-sectional	von Willebrand disease	Resective periodontal surgery + dental extractions (n = 63)	Severe gingival bleeding 6-8 h after postoperative hemostasis	3.1% (2/63)	Local application of fibrin glue in the bleeding area
Franchini et al. (2005)[38]	Italy	Cross-sectional	Severe hemophilia A	a. Nonsurgical periodontal treatment (scaling and root planing) (n = 133) b. Periodontal surgery (n = 19)	Severe gingival bleeding 48 h after postoperative hemostasis	a. 0.7% (1/133) b. 0.0% (0/19)	Factor VIII 2000 + 1500 IU after 12 h

TABLE 1 (Continued)

Authors (year)	Country	Study design	Systemic condition	Intervention	Complication	Complication rate	Complication management
Gregoriou et al. (1996)[33]	USA	Case series	Cerebral palsy with gingival overgrowth *Relevant medication: phenobarbital*	Gingivectomy (n = 2)	Severe gingival bleeding 2-3 h after postoperative hemostasis	—	Transfusion of 250 cc of cross-matched O^+ blood and 1255 cc plasmanate (case 1) 6000 units of topical application of hemostatic agent thrombin powder (case 2)
Jones et al. (1988)[34]	USA	Case series	Cerebral palsy with gingival overgrowth *Relevant medication: dyphenylhydantoin*	Gingivectomy (n = 24)	Slow to start adequate oral food intake	8.3% (2/24)	Not reported
Knapp and Fiori (1984)[26]	USA	Case report	Hypertension	Resective periodontal surgery	Prolonged gingival bleeding + hypertensive crisis	—	a. Gingival bleeding: not reported b. Hypertensive crisis: sodium nitroprusside drip
Lee et al. (2005)[40]	UK	Randomized controlled clinical trial (*active 5% tranexamic acid mouthwash vs placebo*)	Hemophilia A or B	Nonsurgical periodontal treatment (dental scaling) (n = 13)	Prolonged gingival bleeding	61.5% (8/13)	Not reported
Mattson et al. (1998)[27]	USA	Case report	Type 2 diabetes mellitus	Regenerative periodontal surgery (guided tissue regeneration using a collagen resorbable membrane)	Membrane exposure	—	Irrigation of surgical site with 0.12% clorhexidine and diluted salt water
Mullally et al. (1993)[28]	UK	Case report	Type 1 diabetes mellitus	Regenerative periodontal surgery (guided tissue regeneration using a nonresorbable membrane)	Membrane exposure + candida infection	—	100 000 units of Nystatin pastilles (4 times/d for 1 wk) + membrane removal + tooth extraction

(Continues)

TABLE 1 (Continued)

Authors (year)	Country	Study design	Systemic condition	Intervention	Complication	Complication rate	Complication management
Nishide et al. (2005)[29]	Japan	Case report	Chronic renal failure (under hemodialysis) with gingival overgrowth *Relevant medication: amlodipine*	Gingivectomy + periodontal surgery (modified Widman flap technique) + dental extractions	Extensive intraoperative gingival bleeding	—	Acrylic splints containing thrombin powder to cover surgical area + 4 units of concentrated red blood cells transfusion + regional anticoagulation hemodialysis with nafamostat-mesilate
Scheitler et al. (1988)[30]	USA	Case report	Plasminogen activator deficiency	Nonsurgical periodontal treatment (scaling and root planing) + dental extractions	Minimal intraoperative gingival bleeding	—	Direct pressure with gauzes
Shapiro (1993)[31]	USA	Case report	Hemophilia C	Mucogingival surgery (free gingival graft)	Bleeding from the palatal donor site 5 d postsurgery	—	Ligation of lesser palatine artery with 4/0 silk suture and this was repeated on day 8 and 10 after surgery + 11 units of fresh frozen plasma
Thomason et al. (1997)[32]	UK	Case report	Renal transplant with gingival overgrowth *Relevant medication: cyclosporine 450 mg/d, azathioprine 75 mg/d, amlodipine 10 mg/d, and aspirin 150 mg/d*	Gingivectomy	Bleeding 40 min after postoperative hemostasis	—	Local hemostasis by means of pressure and infiltration of anesthetic with adrenaline + 6 units of platelets

Abbreviations: IU, International unit; Nd:YAG, neodymium-doped yttrium aluminum garnet.

TABLE 2 Examples of inherited and acquired bleeding disorders

Classification	Body system	Examples of medical conditions
Congenital	Hematological	A Vascular disorders • Hereditary hemorrhagic telangiectasia B Platelet disorders • Bernard Soulier disease • Idiopathic thrombocytopenic purpura C Coagulopathies • Von Willebrand disease • Hemophilia D Fibrinolytic disorders • Plasminogen activator deficiency
	Cardiac	• Cyanotic congenital heart disease
	Connective tissue	• Ehlers Danlos Syndrome
Acquired	Liver disease	• Liver cirrhosis • Liver malignancy
	Renal	• Chronic kidney disease
	Hematological	• Aplastic anemia - pancytopenia
	Immune	• Systemic lupus erythematous • Antiphospholipid syndrome • HIV • Immune thrombocytopenia purpura
	Malignancy	A Hematological malignancies • Leukemia • Lymphoma • Multiple myeloma • Myelodysplasia B Nonhematological malignancies: • Patients undergoing chemotherapy
	Drugs	• Alcohol • Antiplatelets • Anticoagulants • Nonsteroidal anti-inflammatory drugs • Corticosteroids • Chemotherapy
	Idiopathic	• Disseminated intravascular coagulation

A multicenter retrospective analysis of 247 patients with different bleeding disorders who received a total of 543 dental procedures presented an incidence of 1.9% of bleeding complications. Of those undergoing periodontal procedures (n = 152), only one participant diagnosed with severe hemophilia A experienced a hemorrhagic episode, 2 days after subgingival instrumentation that was treated with factor VIII concentrate.[38] A pilot, randomized, double-blind, placebo-controlled clinical trial testing the use of active 5% tranexamic acid mouthwash before dental scaling in patients with hemophilia A/B reported that 38.5% of those who completed the study did not show any sign of gingival bleeding.[40] Bleeding complications from the palatal donor site when performing mucogingival surgery have been reported.[22,31] Mitigating procedures reported to stop the bleeding include one from Shapiro,[31] described as a ligation of lesser palatine artery with 4/0 silk suture, and this procedure was repeated two more times after surgery together with the use of 11 units of fresh frozen plasma. In the case reported by Blanco-Carrion et al,[22] a combination of 2500 units of factor VIII concentrate twice a day during 1 week with prophylactic factor VIII concentrate (2500 units once every 2 days for two more weeks) was used to manage the same complication. Further, data from 63 consecutive patients with von Willebrand disease receiving dental extractions and surgical periodontal procedures were retrospectively analyzed. Results showed that the complication rate of severe gingival bleeding was 3.1% and this was managed through local application of fibrin glue in the bleeding area.[37] However, some case series did not find any bleeding episodes in patients with von Willebrand disease after either nonsurgical[42] or surgical periodontal therapy.[43] Likewise, a low incidence of gingival bleeding in patients with HIV was reported in a cross-sectional study where different periodontal procedures were carried out.[35] When other inherited bleeding conditions such as plasminogen activator deficiency or hereditary hemorrhagic telangiectasia were evaluated, the risk of bleeding was minimal,[30] if any at all.[44]

3.1.2 | Drug-induced gingival overgrowth

Gingival overgrowth may occur in patients taking anticonvulsants (eg, phenobarbital, sodium valproate, and phenytoin) (Figure 1), immunosuppressants (eg, ciclosporin), or calcium channel blocker antihypertensive drugs (eg, nifedipine and amlodipine).[45] Severe cases may require surgical excision of the enlarged gingiva. While a few case reports showed prolonged intraoperative and postoperative bleeding after gingivectomy,[29,32,33] others did not find any bleeding episodes after gingival tissues were treated with both nonsurgical and surgical approaches.[46,47] Jones et al[34] performed 39 gingivectomies in patients with cerebral palsy who presented gingival overgrowth resulting from diphenylhydantoin use and, although they did not observe any bleeding problems, two out of 12 patients had slow resumption of adequate oral food intake.

3.1.3 | Antithrombotics

Patients taking antithrombotic medications may present with extensive bleeding episodes after periodontal therapy. Most of these patients take anticoagulants (eg, warfarin, dabigatran, apixaban, and

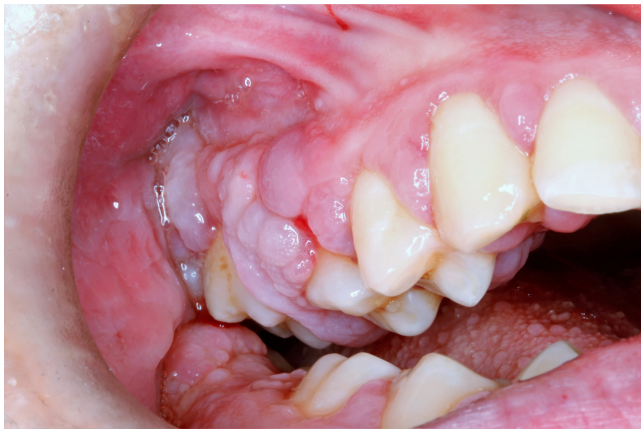

FIGURE 1 Gingival overgrowth and bleeding tendency secondary to the administration of valproate in a patient with severe epilepsy.

rivaroxaban) or antiplatelet (eg, aspirin and clopidogrel) drugs, which makes them more prone to experience bleeding problems in the dental setting. A cross-sectional study of 45 patients who received cardiac valve surgery and were under oral anticoagulation therapy reported a low incidence (<5%) of bleeding independent of using a neodymium-doped yttrium aluminum garnet laser for periodontal surgery.[36] Uncontrolled severe gingival bleeding was also found after delivering scaling and root surface debridement on a patient who was taking aspirin and clopidogrel.[25]

3.1.4 | Hypertension

Knapp and Fiori[26] described a case of prolonged postoperative bleeding and hypertensive crisis associated with resective periodontal surgery. In this case report, a patient diagnosed with hypertension (180/120 mm Hg) underwent periodontal treatment consisting of an initial phase on nonsurgical periodontal therapy followed by two apically repositioned flaps with osseous surgery. Two days after the second surgery, the patient began to bleed spontaneously from the surgical site and was unable to control the local hemorrhage. When the patient attended the emergency room, the amount of blood he had lost was approximately 100 mL/h and at that time the blood pressure was 210/140 mm Hg. He was given his normal dose of clonidine to stop the hypertensive crisis, but no apparent effect was noted. Immediately, a sodium nitroprusside drip was started in the intensive care unit, where his blood pressure dropped to 130/88 mm Hg. Once the blood pressure was stabilized, oral bleeding stopped and healing of the periodontal surgical site was uneventful.

3.2 | Other complications

Soft tissue complications after mucogingival surgery have been described in two case reports.[21,22] The first case consisted of a patient diagnosed with Crohn's disease (a type of inflammatory bowel disease) who presented with multiple Miller's class I gingival recessions. Three different mucogingival surgeries with a 4-week interval difference were carried out using a coronally advanced flap technique and an enamel matrix derivative was used before coronally repositioning the flap in the last two procedures. Two of the three surgeries (one with and another without the use of amelogenins) showed incomplete healing, with a red and swollen appearance of the surgical area that lasted up to 6 weeks. To manage these complications, chlorhexidine gluconate gel and mouthwash were administered. Another study reported a case of a patient with hemophilia and HIV requiring a root coverage procedure of single Miller's class II gingival recession that was carried out by applying a subepithelial connective tissue graft technique. At 1 week postsurgery, the palate (donor site) showed secondary intention healing associated with the necrotic area.[22] Conversely, another case report describes a patient with HIV who received the lateral sliding flap technique and experienced uneventful healing over 8 months.[48] In a case series of 21 patients with HIV, the same authors found no complications (ie, delayed healing or infection) after crown lengthening had been undertaken.[49]

Delayed healing could be expected after periodontal procedures in patients experiencing dystrophic epidermolysis bullosa, as described in two case reports. These cases detail one patient who underwent mucogingival procedures to cover exposed roots by means of a coronally positioned flap combined with a subepithelial connective tissue graft,[50] and another who received an acellular dermal matrix allograft to increase the width of the attached gingiva.[51] Neither patient developed any complications either during or after surgery.

Diabetes mellitus is also known to be associated with impaired wound healing, and patients are more likely to develop infections. Mattson et al[27] treated an intrabony defect with guided tissue regeneration from a patient with type II diabetes mellitus.[25] Resorbable collagen membrane exposure was noticed after 1 week of healing.[27] The membrane was not removed but was irrigated with chlorhexidine and diluted salt water until the soft tissue had healed.[27] Similarly, Mullally et al[28] also reported membrane exposure after a guided tissue regeneration procedure in a patient with diabetes mellitus. Moreover, a fungal infection by *Candida albicans* was diagnosed clinically and confirmed histologically afterwards.[28] In this case, the membrane was removed, the tooth extracted, and antifungal medication was prescribed.[28] Conversely, in a patient with type I diabetes mellitus, the formation of "liver clots" (without clot retraction for up to 10 days) resulting from poor healing 1 week after modified Widman surgery and the extraction of hopeless teeth was observed.[23] However, this finding is not common and results from a recent randomized controlled clinical trial including patients with type II diabetes mellitus and moderate-to-severe periodontitis showed a low incidence of complications after periodontal treatment. D'Aiuto et al[39] did not find any statistically significant differences in terms of oral and systemic complications when intensive periodontal therapy (including subgingival

debridement and modified Widman flap surgery) was compared with a control treatment (only supragingival scaling) over a period of follow-up lasting 1 year.

There are some medications such as antiresorptives and antiangiogenics that could also interfere in both soft and hard tissue healing. A case has been published reporting osteonecrosis of the jaw after nonsurgical periodontal therapy on a patient who was receiving subcutaneous injections of denosumab every 6 months (Figure 2).[24] The complication was managed by means of administration of chlorhexidine mouthwash and systemic antibiotics (doxycycline) together with removal of the affected teeth, sequestrectomy, and surgical debridement of necrotic bone.

4 | RISK ASSESSMENT FRAMEWORK AND APPROPRIATE TREATMENT MODIFICATIONS

When planning treatment for periodontal therapy in patients who are medically compromised, it is important to consider additional factors to provide holistic care. In addition to clinical and radiographic examination, a thorough medical, social, and dental history will enable a comprehensive risk assessment (Table 3). This will ensure that appropriate modifications can be implemented prior to commencement of periodontal therapy, thereby reducing complications and treatment errors. The ACCESS mnemonic[52,53] is a systematic approach to treatment modification, considering six domains that address different aspects of care:

1. **A**ccess
2. **C**ommunication
3. **C**onsent
4. **E**ducation
5. **S**urgery
6. **S**pread of infection

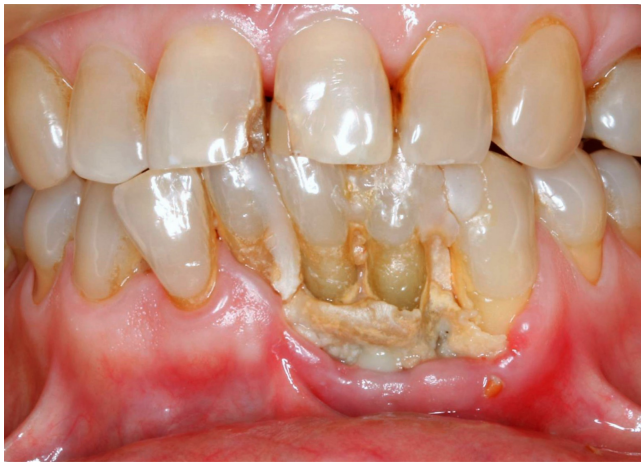

FIGURE 2 Medication-related osteonecrosis of the jaw after nonsurgical periodontal therapy on a patient under antiangiogenics (denosumab).

These domains will be explored further throughout this review with specific examples (Table 4).

5 | PREVENTION AND MANAGEMENT OF COMPLICATIONS AND TREATMENT ERRORS IN PERIODONTAL THERAPY

Complications and treatment errors may occur when providing periodontal therapy in patients who are medically compromised. These will be presented in relation to pain control, bleeding, infection, and wound healing.

5.1 | Analgesia and pain control

Effective pain control is essential for delivery of invasive periodontal procedures. Adaptations may be required in relation to certain medical conditions, operator skills, and availability of equipment, for instance, a computer-controlled local anesthetic delivery system.

The type, dose, and technique for local anesthetic administration may need consideration. For example, patients may have resistance to local anesthetic, as in the case for the hypermobile type of Ehlers Danlos Syndrome. These patients require a systematic approach to the type of local anesthetic selected.[54] It may be administered in order of potency[55] or in combination, for instance lidocaine could be administered first, followed by articaine and then bupivacaine. A retrospective survey of 980 people with Ehlers Danlos Syndrome reported the highest success rate of 30% with articaine, followed by bupivacaine at 25%.[56] When it is not possible to achieve adequate local anesthesia, alternative anesthetic modalities should be considered.

Allergy to local anesthetic and its constituents is rare, and is estimated to have an incidence of less than 1%.[57,58] Further information should be sought to determine the nature of the reported allergy, and, where appropriate, the patient should be referred for formal allergy testing.[59] The most commonly reported reaction to local anesthetics is vasovagal syncope, which the patient may report as an allergy.[60]

The dose of local anesthetic solution may need to be administered with caution in patients with a severe cardiac condition. Good pain control is essential to minimize stress on the myocardium secondary to pain sensation. The local anesthetic should be administered slowly with an aspirating syringe to assess the physiological response and reduce the risk of cardiovascular toxicity.[58] There is insufficient evidence to suggest that local anesthetic with or without adrenaline as a vasoconstrictor poses a risk to patients with hypertension or other cardiomyopathies.[61] However, anesthetics with adrenaline should be avoided in patients with severe hypertension and it is not recommended to use more than two anesthetic cartridges with adrenaline at 1:100 000 (0.04 mg) in patients with certain cardiac conditions, such as those with coronary stents or those with a history of myocardial infarction.[58]

TABLE 3 Examples of potential medical, social, and dental risks

Category	Potential risks
Medical	Aspiration Bleeding Delayed healing Local infection Infective endocarditis Hypoglycemia Trismus
Social	Ability to attend appointments Timing of appointments Communication aids Lack of capacity to consent to periodontal therapy Reduced mobility
Dental	Periodontal disease Reduced cooperation Reduced manual dexterity

Patients with long-term use of opioids, for instance, because of chronic pain syndrome, may present with increased tolerance to local anesthetic. Studies on nondental procedures showed that a higher dose of local anesthetic solution was required to achieve the same efficacy.[62] An increased amount of local anesthetic solution may be required for dental procedures.

Modification of the technique used to deliver local anesthetic may be required in relation to the underlying medical condition. For example, patients with severe bleeding disorders require careful assessment if inferior alveolar nerve blocks or lingual infiltrations are planned, as hematological support (eg, coagulation factor replacement) will be needed.[63] The risks of proceeding without this in place are significant and include hematoma formation and potential risk to the airway. Buccal infiltration has been reported as a safe technique in patients with differing severity of hemophilia, without the need for additional factor cover.[64] Preoperative tests may be required for patients on anticoagulants such as warfarin for whom inferior alveolar nerve blocks are required. The clinician should confirm that the patient's international normalized ratio readings are generally stable. For patients with unstable international normalized ratio profiles, it has been proposed that the international normalized ratio should be checked preoperatively if block injections are planned and given cautiously with a self-aspirating syringe.[65,66]

In patients with trismus, alternative techniques to the conventional inferior alveolar nerve block may be indicated. Gow-Gates and Akinosi techniques deliver the local anesthetic solution higher than the conventional technique and have similar anesthetic efficacy.[67-69] These may be considered in patients with trismus or when the conventional technique fails. Both alternative techniques should be used with caution, and each carries a higher risk of complications.[67] Intraligamentary and intraosseous anesthesic injection techniques may be used as alternatives to mandibular nerve blocks.[70]

Computer-controlled local anesthetic delivery systems can be utilized in patients with needle phobia, especially if there are additional medical comorbidities that contraindicate alternative anesthetic modalities.[71,72] The technique can be used in children and adults, and has been found to reduce the perceived pain on administration, and to achieve greater efficacy compared with the conventional local anesthetic technique.[71,73] It has been suggested that a computer-controlled intraosseous anesthesia system may be useful for root planing procedures because it reduces the pain of the injection and provides a larger area of anesthesia with a single puncture.[74] In a randomized split-mouth study in patients with chronic periodontitis who underwent open-flap debridement on premolars and molars, the authors reported substantial relief from injection pain with a computer-controlled anesthetic delivery system compared with a conventional local anesthetic technique.[75]

An aspirating local anesthetic syringe should always be used.[58] The local anesthetic solution should be delivered in areas without localized inflammation and/or infection, as the presence of inflammation may affect the success of local anesthesia. Block techniques are useful adjuncts in these instances, as the local anesthetic solution is deposited at a site away from inflammation and infection.[76]

In patients with fragile mucosa surfaces, as in the case of epidermolysis bullosa, the technique may need to be altered. Depending on the severity, the local anesthetic solution should be deposited slowly and deeply in the tissues to avoid mechanical separation of the mucosal layer and the formation of blisters.[77] If iatrogenic blisters appear as a result of the injection of local anesthesia, they must be drained to prevent the lesion from expanding (puncturing with a needle or cutting the blister with scissors).[78] Postoperatively, patients should also be instructed to take extra care to avoid traumatizing the mucosa.[77]

If adequate local anesthesia is not achievable, alternative anesthetic modalities may need to be considered, such as conscious sedation and general anesthesia. In patients who are medically compromised, preoperative anesthetic assessment may be required to assess their suitability.[52] Postoperative pain is common among patients undergoing periodontal treatment, and it has been suggested that it is conditioned by variables such as age, the degree of patient anxiety, and the type of procedure performed.[79] Scaling and root planing can cause considerable pain in terms of intensity and duration,[80] although the magnitude of pain is generally greater after surgical periodontal treatment.[16] Acetaminophen (paracetamol) and

TABLE 4 The ACCESS risk assessment and treatment modification framework

Domain	Considerations		Examples of conditions that may require adaptations	Examples of treatment modification
Access	Appropriate dental setting	Bleeding	Low platelets (eg, secondary to chemotherapy, platelet disorders)	Patients requiring platelet support should ideally be seen in a hospital setting
	Access to the dental surgery	Timing of appointment	Antithrombotic medications (eg, oral anticoagulants, antiplatelets)	Appointments early in the day and week for invasive dental procedures
			Chronic kidney disease and dialysis	Appointment the day after dialysis
			History of myocardial infarction	Avoid elective dental procedures within 6 mo of myocardial infarction
		Escort	Learning disability, dementia	Depending on severity, may require family member and/or carer to accompany the patient
		Transport	Frailty, physical disability	Hospital transport
		Wheelchair access	Wheelchair user	Wheelchair recliner if unable to transfer to the dental chair
	Access to the patient's mouth	Aspiration	Dysphagia	Semisupine or upright position in the dental chair
		Involuntary movement	Movement disorders (eg, Parkinson's disease)	Vacuum cushion and/or clinical holding to support the head and neck to minimize trauma
		Temporomandibular dysfunction	Ehlers Danlos Syndrome	Mouth prop, frequent breaks, and shorter appointments
		Trismus	Head and neck cancer therapy	Pediatric handpieces, mouth prop
		Fragile oral mucosa	Epidermolysis bullosa	Lubrication and careful handling of soft tissues
		Altered anatomic landmarks	Obesity, previous surgery to the head and neck	Alternative technique to deliver local anesthetic may be required
Communication	With the medical team		Immunosuppression (eg, transplant)	The ideal timing for elective periodontal therapy should be consulted with the medical team
	With the laboratory		Low neutrophils (eg, secondary to chemotherapy)	Timely reporting of urgent blood tests prior to invasive periodontal therapy
	With social care professionals		Learning disability, mental health conditions	Assistance in organizing appointments for patients who require additional social support
	With patients		Nonverbal communication (eg, stroke, learning disability)	Communication aids (eg, Makaton, pictures, and easy read patient information leaflets)
Consent	Capacity to consent		Learning disability, mental health conditions, dementia	Undertake capacity assessment, if lacks capacity to consent to specific periodontal therapy, involve family and/or carers in the decision-making process
	Fatigue		Fatigue related to the medical condition	Undertake capacity assessment, avoid early morning appointments
	Implications in relation to medical health		Infection risk in patients who are immunocompromised (eg, cancer)	Extraction of teeth with infection risk because of the potential impact on their systemic condition
	Long-term implications		Neurodegenerative conditions (eg, dementia, Parkinson's disease)	Discuss the patient's ability to maintain oral hygiene as the condition progresses

(Continues)

TABLE 4 (Continued)

Domain	Considerations		Examples of conditions that may require adaptations	Examples of treatment modification
Education	Relationship between medical conditions and dental disease		Diabetes mellitus	Patient informed of the bidirectional relationship between periodontal disease and diabetes mellitus, and the importance of managing good periodontal health
	Education of family and/or carers		Learning disability, neurodegenerative conditions (eg, dementia, Parkinson's disease)	Oral hygiene instructions to the family and/or carers for patients who are partly or fully dependent on others for activities of daily living
	Reduced manual dexterity		Cerebral palsy, multiple sclerosis	Adaptation of oral hygiene tools (eg, toothbrush handle holder, and long-handled interdental brushes)
	Dental team		Unstable asthma, angina, epilepsy	Medical emergency training
Surgery	Preoperative	Blood test	Low neutrophils (eg, chemotherapy)	Full blood count may be required within 24 h prior to invasive periodontal therapy
		Blood test	Warfarin	INR test within 24 h (or 72 h if stable) prior to invasive periodontal therapy
		Antibiotics	Special consideration group for infective endocarditis (eg, prosthetic heart valve, previous infective endocarditis)	Antibiotic cover 1 h before invasive periodontal therapy may be required after consulting the patient and their cardiologist
	Perioperative	Local anesthesia	Resistance to local anesthesia (eg, Ehlers Danlos Syndrome)	Select the most appropriate local anesthetic agent
		Monitoring vital signs	Moderate to severe respiratory condition	Monitoring of vital signs
		Oxygen	At risk of hypoxia (eg, sickle cell disease)	Supplemental oxygen via nasal cannula during invasive periodontal therapy
	Postoperative	Prescription	Patients on warfarin	Avoid prescribing metronidazole because of drug interactions
		Follow-up	At risk of osteoradionecrosis (eg, head and neck cancer)	Review 8 wk after invasive periodontal therapy
		Emergency access	Bleeding disorders	Details of emergency services for patients at higher risk of bleeding
Spread of infection	Patients who are immunocompromised		Patients undergoing chemotherapy	May require prophylactic antibiotics; consult the medical team

Abbreviation: INR, international normalized ratio.

nonsteroidal anti-inflammatory drugs are the agents of choice to tackle postoperative pain in dentistry,[81] but they are not exempt from adverse effects and should be administered with caution in patients with certain systemic diseases.[82] The interval between acetaminophen intakes should be adjusted in patients with chronic kidney disease and the total daily dose should be limited in patients with liver disease.[83] Most nonselective cyclooxygenase-1 and cyclooxygenase-2 inhibitor nonsteroidal anti-inflammatory drugs should be avoided in patients with a history of peptic ulcer or gastroesophageal bleeding, in patients receiving anticoagulants, lithium, or methotrexate, with uncontrolled hypertension and chronic kidney disease, or with severe liver failure.[84] Nonsteroidal anti-inflammatory drugs that act as preferential cyclooxygenase-2 inhibitors have also been used to control postoperative pain after periodontal procedures.[85,86] Cyclooxygenase-2 inhibitors reduce the incidence of gastrointestinal side effects and have little or no effect on platelet function, so the risk of bleeding is minimal. However, most selective cyclooxygenase-2 inhibitors have been withdrawn from the market because of the risk of serious cardiovascular events,[87] and nimesulide is also not marketed in some countries because of the risk of acute hepatotoxicity and should not be administered to patients with liver failure.[88]

5.2 | Bleeding

There are congenital and acquired bleeding conditions that may increase the risk of bleeding perioperatively and postoperatively (Table 2). Treatment modifications will be explored to reduce the risk of bleeding resulting from periodontal therapy.

The dental setting should be selected based on the risk of bleeding in relation to the medical condition, dental procedure, and experience of the operator.[89] The clinician should establish whether the patient is under the care of a medical team and consult with them to confirm the severity of their condition and management plan. This will aid in determining the level of risk of bleeding as a complication and/or treatment error in periodontal therapy. For instance, patients who are undergoing chemotherapy for the management of malignant conditions can receive different types of agents. Some agents will predispose the individuals to chemotherapy-induced thrombocytopenia, and others will impact platelets to a lesser degree.[90] Patients with severe risk of bleeding who require onsite medical support for invasive periodontal therapy are more appropriately managed in a secondary care setting.[91]

If the planned periodontal therapy has an increased risk of bleeding, the appointment should be timed earlier in the day and the week, so that postoperative complications can be managed accordingly.[66] The timing of appointments should be in line with the medical management of each patient's condition. For instance, patients who are taking direct oral anticoagulants should provide information about the time of the scheduled dose so as to minimize interruption to the drug regime.[66] The risk of thrombosis outweighs the potential risks of postoperative bleeding from dental procedures.[66] Similarly, single or dual therapy antiplatelets should not be interrupted for dental procedures,[92] including periodontal therapy.[66] However, in patients with a high risk of bleeding and dual therapy, some guidelines have recommended suspending one of the antiplatelet agents before the procedure (5 days in the case of clopidogrel), generally maintaining the administration of aspirin.[93] For patients with hemophilia who have regular prophylactic factor replacement, the dental procedure should be timed as close to the time of administration to avoid the need for additional factor replacement, and thus maximizing therapeutic effects, and reducing risks and overall treatment costs.[63,89,94,95] Patients undergoing renal dialysis should not be seen on the dialysis day because of fatigue and an increased risk of bleeding secondary to heparin and abnormal platelet function.[96]

Depending on the underlying cause of the increased bleeding risk, special investigations may be indicated. Appropriate blood tests such as full blood counts, clotting screen, and liver function tests should be arranged as part of the preoperative assessment depending on the medical condition and its stability[91] (Figure 3). The timing of the blood test needs to reflect the underlying medical condition and its treatment regime. For example, it is acceptable to use a 72-hour international normalized ratio test on patients on warfarin who are stable, but for those with an unstable international normalized ratio, it should be undertaken within 24 hours.[65,66] Point-of-care tests for international normalized ratio are available and can be used

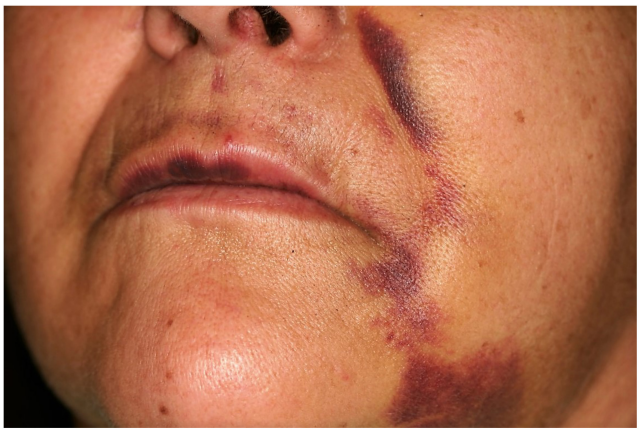

FIGURE 3 Multiple hematomas following scaling and root planing in a patient with liver cirrhosis.

in the dental setting. The international normalized ratio should be <4 to undertake periodontal therapy.[65,66] Morimoto et al[97] undertook a retrospective study on periodontal therapy in patients taking warfarin. They confirmed that nonsurgical periodontal therapy can be safely performed when the international normalized ratio is <4, and that surgical periodontal therapy surgery can be safely performed when the international normalized ratio is <3. These international normalized ratio values are applicable in patients without other concomitant factors that may favor bleeding, such as liver failure or uncontrolled hypertension.[58]

Furthermore, for patients having pharmacotherapy that affects their blood counts, they may require a blood test on the day of the procedure or within the last 24-48 hours to account for more frequent fluctuations in blood counts.[98] It may also be necessary to liaise with the laboratories regarding specific requirements and timely reporting of the investigation results.

Additional hematological support may be required in patients with thrombocytopenia. This will be dependent on the planned periodontal procedure, as well as a preoperative blood test and liaison with the medical team to determine the requirements for platelet transfusions. The most accepted threshold for platelet counts is $\geq 50 \times 10^9$/L for invasive dental procedures, which includes periodontal surgery or tooth extractions. Patients with platelet counts of $<50 \times 10^9$/L are at an increased risk of experiencing perioperative and postoperative bleeding.[99] Platelet transfusion may be indicated preoperatively, perioperatively, and/or postoperatively. Karasneh et al[100] systematically reviewed the evidence on a platelet count threshold of $<50 \times 10^9$/L for platelet transfusions for invasive dental procedures. Two out of nine studies included patients with thrombocytopenia who underwent scaling. One of these studies had a lower threshold of $\leq 30 \times 10^9$/L for prophylactic platelet transfusion for three patients who required scaling. Overall, there was insufficient evidence to suggest that a platelet count of $\geq 50 \times 10^9$/L or prophylactic platelet transfusions prevented significant postoperative bleeding. Local measures were sufficient in managing bleeding. The studies included in the review were small cohort studies that were heterogenous. Another retrospective cohort study

investigated bleeding complications in patients with mild to severe thrombocytopenia after extractions.[101] Over half of the patients displayed evidence of chronic periodontitis, although the reasons for the extractions were not specified. Only four out of 89 (4.4%) patients experienced postoperative bleeding. Prophylactic platelet transfusions did not reduce the risk of bleeding. Inherited qualitative platelet disorders are a broad spectrum of diseases characterized by platelet dysfunction in the early phases of hemostasis (eg, Bernard-Soulier syndrome or Glanzmann's thrombasthenia). Traditionally, the treatment of these patients has been carried out under platelet transfusion.[102] However, based on the high rate of alloimmunization to platelet surface antigens and human leukocyte antigens, recent guidelines recommend the use of tranexamic acid and desmopressin, avoiding prophylactic platelet transfusions, and restricting their therapeutic administration only for severe inherited functional platelet disorders and unresponsive cases.[103]

In relation to patient education and the risk of bleeding, patients should be informed of possible minor bleeding related to the planned periodontal therapy. There is a tendency for patients with bleeding conditions to use soft toothbrushes, which may not effectively remove plaque deposits. In addition, patients may have been advised by their doctors to avoid brushing their teeth or to undertake interdental cleaning measures when they have thrombocytopenia. There is a lack of evidence to suggest the benefits of such an approach.[104] A study conducted by Padrón et al[105] concluded that patients under anticoagulation therapy had greater accumulations of dental plaque, more gingival bleeding, and deeper periodontal pockets than healthy controls, and approximately 17% of them never brushed their teeth compared with 3% of the control group. It has been suggested that fear of gingival bleeding could induce patients using anticoagulants to brush their teeth less.[105] A lack of good oral hygiene measures may predispose the patient to dental disease, and possibly progress to infection, which may compromise their medical health. Dental professionals should consider the risk of bleeding before advising on the most appropriate oral hygiene measure.

For all types of procedures, general precautions should be followed, including gentle handling of the oral mucosa, instruments, and equipment.[106] For pain and anxiety control, appropriate selection of local anesthetic solution and technique is required. Factor replacement may be required for patients with hemophilia in relation to the local anesthetic technique and proposed procedure.[91] The site of surgery helps to determine an appropriate local anesthetic technique for treatment. In patients with hemophilia and other severe bleeding conditions, inferior alveolar nerve blocks and lingual infiltrations pose a risk of airway obstruction, caused by hemorrhage into musculature and the formation of hematomas in retromolar and pterygoid spaces.[107] Factor replacement decreases the risk of bleeding.[94] On the contrary, infiltrations (with the exception of lingual), as well as intraligamentary, intraosseous, and intrapulpal injections, do not require factor replacement.[108] Articaine infiltrations may be used in the mandible to avoid block techniques[109,110] and eliminate the need for factor cover.[111]

Low-risk procedures for bleeding include nonsurgical periodontal therapy.[112] No additional hematological cover is necessary, provided local anesthesia principles are followed.[113] Although routine scaling is unlikely to cause significant bleeding, the overall periodontal condition must be assessed, as hematological support may be indicated in selected cases.[89] High-risk procedures consist of extractions and periodontal surgery.[112] The degree of prophylaxis cover is determined by the hematologist. Local hemostatic measures should be followed, including closure of surgical sites and the use of hemostatic agents.[114] The use of a surgical splint has been suggested to protect the surgical site.[94]

Initially, the treatment area should be limited and staged to assess the bleeding risk, and reassessed before proceeding.[66] Surgical trauma should be minimized where possible, with closure of the wound. At the end of the procedure, the procedural site should be observed for an extended period of time to ensure that there is hemostasis. If there is evidence of bleeding, the site should be compressed with a damp gauze dressing for 10-15 minutes. Consider the use of topical coagulating agents such as oxidized cellulose and gelatin foam to aid hemostasis.[66,115] Rubino et al[115] undertook a retrospective analysis of patients who had invasive periodontal therapy and were on antithrombotic medications (antiplatelets and anticoagulants). The drug regime was not interrupted for most participants (99.6%), and local hemostatic measures were followed. Postoperative bleeding was only observed in three out of 867 procedures (0.35%).

A prescription for tranexamic acid 5% mouthwash, an antifibrinolytic agent, may be considered for use up to four times a day as required. This is a nonformulary preparation and therefore may not be readily accessible in primary care dental services. Successful use of a 2-day course of tranexamic acid 4.8% mouthwash in the management of postoperative bleeding was reported for patients taking warfarin who received tooth extractions because of severe periodontal disease and the results were similar to those obtained for a 5-day course.[116] To manage the bleeding, participants were initially asked to use compression with a gauze pad for 20 minutes, and if the bleeding persisted, the tranexamic acid mouthwash was applied via a gauze pad for a further 20 minutes. Systematic reviews of the evidence on the use of topical tranexamic acid for dental procedures showed successful hemostasis for patients on vitamin K antagonists,[117] and inconclusive evidence for congenital bleeding disorders.[118] If local measures are insufficient to achieve adequate local hemostasis, the appropriate medical team should be contacted to assess the need for systemic agents.

Postoperatively, the dental practitioner should ensure that patients have access to dental emergency services to minimize distress for the patient and facilitate timely access if required.[66] Prescription should be administered with caution. Nonselective cyclooxygenase-1 and cyclooxygenase-2 inhibitor nonsteroidal anti-inflammatory drugs for pain control should be avoided in patients at risk of bleeding, as this may exacerbate the risk of bleeding.[66,119] Acetaminophen is the preferred analgesic.

5.3 | Infection

Infection may occur following periodontal therapy in patients who are medically compromised. This will be discussed in relation to immunosuppression, infective endocarditis, aspiration pneumonia, blood-borne viruses, and wound healing.

5.3.1 | Immunosuppression

Patients who have immunosuppression are at an increased risk of infection after invasive periodontal therapy. The causes of immunosuppression can be categorized into congenital and acquired (Table 5).

The timing of the dental appointment should be made taking into consideration the cause, severity, and the likely duration of the immunosuppression. For example, nonurgent periodontal therapy should be postponed for patients undergoing active chemotherapy.[98,120,121] Patients may have bone marrow suppression, and resultant low white cell count and neutrophils, which predisposes them to infections. Acute periodontal infection should be treated in a timely manner as it poses a risk of bacteremia and sepsis in patients with neutropenia.[122] The ideal treatment window period should be determined after consultation with the oncology team,[98] for instance between chemotherapy cycles.

Another group of patients for which the timing of dental treatment is important consists of those who have had solid organ transplantation. This cohort receive long-term immunosuppressants, with a lower maintenance dose after approximately 6 months. Therefore, elective periodontal therapy should be delayed for 3-6 months after the transplant.[123,124] Georgakopoulou et al[123] reported an increased level of risk of severe oral infections in patients who have undergone renal transplantation. The recommendation for routine periodontal therapy 6 months posttransplant is that scaling can be undertaken in a staged manner, with a small number of teeth cleaned at a time. Invasive periodontal therapy may require further preoperative investigations and close liaison with the patient's physician. To minimize the risk of infection when patients are immunosuppressed, a pretransplant dental assessment should be undertaken.[124,125] Periodontal health should be stabilized, and the source of infection eliminated.[124]

For patients who require regular blood transfusions (eg, thalassemia major) or red cell exchange transfusions (eg, sickle cell anemia), the dental visit should be scheduled soon after their routine transfusions.[126,127] Treatment on the same day should be avoided as the patients are fatigued.[127] In addition, patients with hemoglobinopathies (eg, thalassemia, sickle cell disease) may have either nonfunctional or absence of spleen. This predisposes individuals to infections, and potential sources of periodontal infection should be managed in a timely manner.[127,128]

Preoperative investigations may be required to determine the severity of immunosuppression including complete blood count with differential, coagulation assessment and liver and kidney function tests, to evaluate whether the procedure should be delayed, if it can be done in an outpatient setting, the need for antibiotic prophylaxis, the risk of bleeding, and the dosage of prescriptions. For example, for patients at risk of neutropenia, a preoperative full blood count should be undertaken prior to invasive periodontal procedures. If the neutrophil count is $<1\times10^9$/L, periodontal probing and elective invasive periodontal therapy should be postponed because of an increased risk of infection.[104] In an observational study, 10 out of 116 patients (8.6%) with mild ($1.00\text{-}1.50\times10^9$/L), moderate ($0.50\text{-}0.99\times10^9$/L), and severe ($<0.0\text{-}0.49\times10^9$/L) neutropenia who had extractions presented with one or more complications.[129] The most common complication was delayed healing,[7] followed by postoperative pain[6] and surgical site infection.[3] The likelihood of complications was not associated with the severity of neutropenia. The preoperative management was variable, with some participants receiving preoperative, perioperative, and/or postoperative antibiotics and granulocyte colony-stimulating factor to increase neutrophil levels.

Prophylactic administration of antibiotics may be indicated in patients who are immunosuppressed.[130] For example, in patients who have had a splenectomy (eg, thalassemia and sickle cell disease), antibiotic cover should be considered for invasive dental

TABLE 5 Examples of congenital and acquired immunosuppressive disorders

Classification	Body system	Example of conditions
Congenital	Syndromes	• Down syndrome • Kostmann syndrome • Chediak Higashi syndrome
	Metabolic	• Glucose-6 phosphate dehydrogenase deficiency
Acquired	Endocrine	• Diabetes mellitus • Addison's disease
	Liver disease	• Liver cirrhosis
	Renal	• Chronic kidney disease
	Hematological	• Aplastic anemia • Thalassemia • Sickle cell disease
	Immune	• HIV • Rheumatoid arthritis • Systemic lupus erythematous
	Malignancy	• Hematological (secondary to the malignancy and treatment; eg, chemotherapy, radiotherapy, transplant) • Nonhematological (secondary to treatment; eg, chemotherapy, radiotherapy, transplant)
	Drugs	• Corticosteroids • Immunosuppressants (calcineurin inhibitors, antimetabolite agents, polyclonal and monoclonal antibodies, mTOR inhibitors)

procedures.[127,131,132] Those who are on immunosuppressive therapy constitute another cohort of patients. The American Association of Pediatric Dentistry advises that antibiotic coverage may be required for patients with a neutrophil count of $<2\times10^9$/L, and should be discussed with the medical team.[133] The suggested antibiotic regime is that used for infective endocarditis,[134] although in some cases it is necessary to consult with the medical team (eg, patients with severe immunosuppression, solid organ transplant recipients, or those who have received multiple antibiotic regimens).

The risk of developing systemic infection from a dental source has been reported to be associated with the presence of preexisting infection.[130] A timely and more aggressive antibiotic regime may reduce the risk of infection and its impact on the general health of patients who are immunosuppressed.[130,133]

On the contrary, the British Society for Antimicrobial Chemotherapy do not recommend routine use of prophylactic antibiotics for dental procedures in patients who are immunosuppressed.[135] This is supported by the antimicrobial dental guidelines for immunocompromised patients, including diabetes mellitus, HIV, chemotherapy, solid organ transplants, and hematological malignancies.[136] The case-specific decision is advised by consulting with the medical team, as there may be additional medical factors that indicate the use of antibiotics (Figure 4).

Corticosteroids can cause immunosuppression, predisposing an individual to infections. Patients on a higher dosage of corticosteroids and who have Addison's disease are at an increased risk of adrenal crisis when exposed to stress. A literature review found that adrenal crisis related to dental procedures is rare.[137] The risk is increased in the presence of pain and infection, in addition to invasive procedures, and treatment under general anesthesia. Steroid cover is indicated for patients taking ≥7.5 to 10 mg prednisolone for longer than 3 months and undergoing invasive periodontal therapy and/or treatment under general anesthesia.[138,139] If the patient is on other corticosteroids, the equivalent dose to prednisolone should be calculated, and advice followed accordingly. Patients taking above 50 mg prednisolone are close to the innate maximum cortisol level seen in patients when stressed and may not require further supplementation.[139]

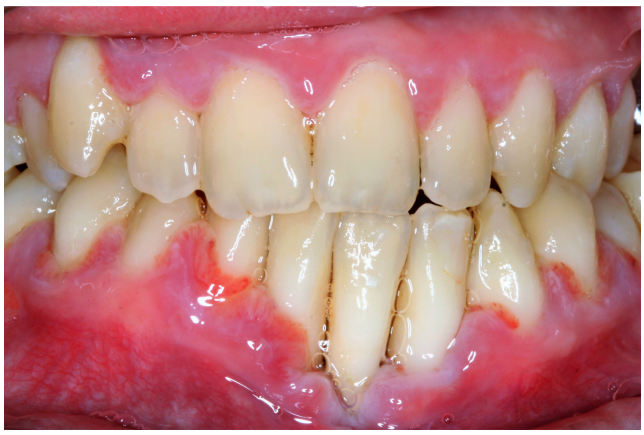

FIGURE 4 Patient with severe primary immunodeficiency who has received several antibiotic regimens. Before carrying out periodontal treatment, the medical team was consulted, who recommended microbiologic and antimicrobial susceptibility testing.

In recent years there have been great advances in targeted anticancer therapies, including monoclonal antibodies, fusion proteins, tyrosine kinase inhibitors, and mammalian target of rapamycin inhibitors, among others.[140] The indications for biologic response modifiers, and in particular monoclonal antibodies, have been extended to numerous cardiovascular and inflammatory diseases (eg, rheumatoid arthritis, psoriasis, or Crohn's disease), transplant rejection, multiple sclerosis, and viral infections.[82] In addition to the immunosuppressive effect, these molecules can cause thrombocytopenia, wound delayed healing, and medication-related osteonecrosis of the jaw.[140]

5.3.2 | Infective endocarditis

Patients with susceptible cardiac conditions are at an increased risk of infective endocarditis following invasive dental procedures. Oral pathogens have been implicated in infective endocarditis, namely, viridans streptococci.[141-143] Periodontal bacterial species such as *Aggregatibacter actinomycetemcomitans* have been detected in specimens from damaged heart valves and aortic aneurysm walls.[144] Dhotre et al[142] reported, in a series of confirmed cases of infective endocarditis undergoing dental extractions, that more than 40% had periodontitis, suggesting that periodontal disease enhances *viridans streptococcal* bacteremia. The prevalence of bacteremia resulting from periodontal pathogens is probably underestimated because of the limitations of microbiologic detection techniques.[145]

Bacteremia may result from noninvasive dental procedures. Toothbrushing has been reported as a potential risk factor for infective endocarditis.[146,147] A randomized controlled trial reported a lower incidence of infective endocarditis with toothbrushing compared with extractions.[148] However, as toothbrushing is performed more frequently on a daily basis, over time it may potentially have a comparable or higher cumulative risk. Patients should be informed of the importance of maintaining good oral hygiene,[149] which will subsequently reduce the incidence of bacteremia as well as the need for invasive dental procedures.[143]

Invasive periodontal treatment can cause bacteremia leading to the development of endocarditis, although the relationship between dental treatment and infective endocarditis remains a controversial issue.[150] Transient bacteremia following dental procedures depends on the state of oral health and the treatment modality, estimating after scaling and root planing in 25%-61%.[151] The rationale for antibiotic prophylaxis prior to invasive procedures is to reduce the bacteremia and subsequently the presumed reduced risk of infective endocarditis. For patients requiring invasive dental procedures, antibiotic prophylaxis is not routinely recommended by the National Institute for Health and Care Excellence (UK) guidelines.[141] There are patient cohorts that are more susceptible to infective endocarditis, requiring special consideration.[149] In these patients, European and American expert committees agree that when high-risk heart conditions are specified in

these patients, it is essential to discuss with them, and eventually their cardiologists and/or surgeons, whether they should receive antibiotic prophylaxis for invasive periodontal procedures, including full periodontal examination, root surface debridement, and surgery.[134,149,152]

5.3.3 | Aspiration pneumonia

Dysphagia (or difficulty in eating, drinking, or swallowing) has a prevalence of up to 16% in the general population.[153] Patients with dysphagia are at risk of aspiration, which may progress to pneumonia, which carries a significant risk of morbidity and mortality. There are multiple causes of dysphagia, including cerebral palsy, learning disability, stroke, and previous head and neck cancer therapy.[153-155]

Periodontitis represents a potential risk factor for the development of aspiration pneumonia in the elderly.[156] Dental plaque has been suggested as a risk factor for healthcare-associated pneumonia in patients who are hospitalized, with an increase in dental plaque levels with longer hospital stays.[157] Good oral hygiene is one of the most effective interventions in reducing the risk of aspiration pneumonia.[158] This includes toothbrushing and denture hygiene, as well as professional cleaning. In relation to toothbrushing, depending on the severity of dysphagia, it should be undertaken in an upright position using a nonfoaming toothpaste.[154,159]

When delivering periodontal care, there are several strategies that can be implemented to reduce the risk of aspiration. Depending on the severity of dysphagia, patients may need to be kept in an upright or semisupine position of no more than 45° if the airway is compromised.[154,155,159,160] The airway may be protected with a gauze trap.[155] In addition to frequent breaks during treatment, ultrasonic scalers should be used with caution with high volume suction.[154] It is important to note that some patients will be at risk of silent aspiration during procedures, without any signs or symptoms of protective reflexes.[155]

5.3.4 | Blood-borne viruses

Patients who received inactivated blood products up to the 1990s may have contracted transfusion-transmitted infections, including HIV and hepatitis.[127,161] This risk is increased in patients who are likely to have received transfusions multiple times, including transfusion-dependent thalassemia, sickle cell disease, hemophilia, and hematological malignancies.[162] Complications of blood-borne viruses include liver disease and, depending on its severity, will have additional considerations for the management of this cohort.[163,164] Current procedures for blood products with virus deactivation processes have reduced the prevalence of transfusion-related infections.[165] The transmission rate of hepatitis viruses to dental professionals is low and is concentrated in developing countries with a higher prevalence of hepatitis-infected individuals,[166] and probably in those who do not have direct access to antiviral agents that cure HIV infection in more than 95% of patients. The risk of HIV transmission in the dental setting is also low, especially when rapid HIV testing of the source patient is available and, if necessary, access to postexposure prophylaxis.[167] Standard infection prevention and control procedures, careful history taking, appropriate immunization of the dental team, and sharps injury protocol should be in place to minimize the risk of transmission.[168] Applying these measures, periodontal treatment is effective in patients with virologically controlled HIV infection and can be performed safely in the dental clinic.[169] The potential complications of dental treatment of patients with viral hepatitis include the potential transmission of the infectious agent and those derived from hepatic dysfunction that favor the appearance of hemorrhages because of coagulation factor deficiency and requires restricting the prescription of hepatic metabolism drugs.[170]

5.4 | Wound healing

Wound healing after periodontal therapy may be impaired in patients with medical comorbidities. For example, patients with poorly controlled diabetes mellitus are at an increased risk of delayed wound healing because of impaired immunity.[27,28] The severity of the condition and related comorbidities should be assessed, and where appropriate by consulting with the medical team. Prior to invasive periodontal therapy, the blood glucose level should be measured using point-of-care tests meters for safe management.[171] A determination of HbA1c (ie, glycated hemoglobin) performed in the last 3 months provides information on the degree of control of diabetes and indirectly on the risk of postoperative complications.[58] There is insufficient evidence to support the use of routine prophylactic antibiotics in patients with diabetes mellitus to reduce the risk of delayed healing and infection.[136,172] The procedural site should be limited and healing monitored closely.[171]

The medical management of conditions may affect wound healing. For example, patients who have had radiotherapy to the head and neck region are at risk of osteoradionecrosis of the jaw. Schuurhuis et al[173] followed up patients who had dental assessment and treatment prior to radiotherapy for head and neck cancer over a 2-year period. Compromised extraction site healing was observed more frequently in patients who had periodontal pockets of ≥6 mm at the assessment prior to radiotherapy (19%) compared with those who had pockets of <6 mm (4%). However, this was not statistically significant. Another study reported that the presence of severe periodontitis postoperatively had the strongest correlation for development of osteoradionecrosis.[174] Patients should have a detailed dental assessment prior to commencing cancer therapy to remove teeth with poor prognosis and severe periodontal involvement.[98] Maintenance of periodontal health postcancer therapy is essential in reducing the risk of compromised healing and the need for invasive procedures. When surgical periodontal procedures are indicated in areas of irradiated bone, these should be undertaken with caution after liaising with the patient's medical team.[175]

Medications can impact wound healing after periodontal therapy. Among patients taking corticosteroids, immunosuppressants,

biologic agents, and disease-modifying antirheumatic drugs, there is a lack of delayed wound healing and medication-related osteonecrosis of the jaw.[161] An association between medication-related osteonecrosis of the jaw and periodontitis has been described, although neither the direction of this association nor predisposing factors have been definitively clarified.[82] Paradoxically, medication-related osteonecrosis of the jaw can occur following periodontal therapy,[24] although it is more commonly associated with dental extractions. Prevention is key in the management of medication-related osteonecrosis of the jaw, and a dental assessment should be undertaken prior to commencement of antiresorptive therapy.[176] For established areas of osteonecrosis, it should be managed conservatively, with symptomatic control and management of infections.[176,177] The Faculty General Dental Practice (UK) guidelines[136] support the use of antibiotics when there is the presence of secondary infection. For extensive areas, surgery may be indicated.[177,178]

In all patients who are medically compromised and at risk of delayed wound healing, a strict follow-up protocol should be in place. For instance, following invasive periodontal procedures, patients at risk of osteoradionecrosis or medication-related osteonecrosis of the jaw should be reviewed to assess the healing.[98,176] In addition, a regular recall interval is essential in maintaining their oral health and reducing the risk of complications.[176,178] This should be agreed for individual patients.[179]

6 | CONCLUSIONS

A complication in medicine is an unanticipated problem that arises following, and is a result of, a procedure, treatment, or illness. Complications may adversely affect the prognosis or outcome of a disease. On the other hand, errors are part of our professional lives. Dentists, as well as physicians, are prone to errors in their profession that can impact on their patients' health and quality of life. The main difference between an adverse event and a complication is that the former is the consequence of a treatment while the latter is a consequence of the disease process.

In this review we have summarized the most common complications reported in patients with systemic comorbidities undergoing periodontal therapy. A framework for risk assessment was provided, including aspects of preoperative planning and intraoperative performance, which we hope will help colleagues prevent and minimize the incidence of treatment complications.

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The authors report no conflict of interest in connection with this review.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available because of privacy or ethical restrictions.

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