The posterior maxilla has traditionally presented a challenge for successful placement of dental implants due to a combination of poor bone quality, ridge atrophy, and pneumatization of the sinus floor following tooth extraction. However, with the successful and predictable surgical outcomes reported in the literature, more clinicians and patients are choosing an implant-supported restoration in the edentulous posterior maxilla. Consequently, sinus elevation and augmentation have gained more popularity. Extensive research has been conducted on types of bone graft materials and implants, less-invasive techniques to perform sinus augmentation, and timing for implant placement for sinus grafting. Despite the predictability of the techniques and biomaterials employed in sinus grafting procedures, intra- and postoperative complications are common. Much of the current literature discusses the local risk factors related to sinus augmentation, with few studies focusing on the patient-related risk factors. The purpose of this review is to identify, evaluate, and discuss the possible management of patient-related risk factors to allow for more predictable maxillary sinus floor augmentation outcomes.


The posterior maxilla has traditionally presented a challenge for successful placement of dental implants. This is due to a combination of poor bone quality, ridge atrophy, and pneumatization of the sinus floor following tooth extraction. With the successful and predictable surgical outcomes reported in the literature, more clinicians and patients are choosing an implant-supported restoration in the edentulous posterior maxilla. Consequently, sinus elevation and augmentation have gained more popularity. The conventional sinus augmentation approach includes preparation of a lateral wall window through which the sinus membrane is carefully elevated, then the created space is filled with a bone graft or bone substitute material. Implant placement can then be performed with a delayed or simultaneous protocol. In 1996, the Sinus Consensus Conference concluded that sinus augmentation should be considered a highly predictable and effective therapeutic modality. Extensive research has since been conducted on types of bone graft materials and implants, less invasive techniques to perform sinus augmentation, and timing for implant placement for sinus graft. Implant survival rates have been reported to range from 81% to 95%, depending...
on the combination of graft materials and implant surfaces. The Sinus Consensus Conference was revisited in 2016 and reaffirmed the validity of the sinus graft. It concluded that noninductive materials with slow resorption might be superior than inductive materials in forming and maintaining bone.

Despite the predictability of the techniques and biomaterials employed in sinus graft procedures, intra- and postoperative complications are common, like sinusitis, rhinosinusitis, fistulae, migration of the implant into the maxillary sinus, infection, sinus membrane perforation, excessive bleeding, and perforations in the buccal flap (Figs 1 and 2). Much of the current literature discusses the local risk factors related to sinus augmentation, with few studies focusing on patient-related risk factors.

The purpose of this review is to identify, evaluate, and discuss the possible management of patient-related risk factors that can contribute to intra- and extraoperative complications, allowing for more predictable maxillary sinus floor augmentation outcomes.

Material and Methods

The patient-related risk factors evaluated in this study include the following: cardiovascular disease and anticoagulant drugs; diabetes; osteoporosis and antiresorptive drugs; organ transplant and immunosuppressive therapy; cigarette smoking/vaping; antibiotic allergy; thickened sinus membrane; age; and gender.

An electronic search was performed in Medline (PubMed) for articles published from 1993 to 2020. The search was limited to the English language. Terms included were “maxillary sinus augmentation” combined with each of the following terms: “cardiovascular disease,” “anticoagulants,” “diabetes,” “osteoporosis,” “antiresorptive drugs,” “organ transplant,” “immunosuppression,” “smoking,” “vaping,” “antibiotic allergy,” “Schneiderian membrane,” “flap attachment,” “gender,” and “age.” To be included in the study, publications needed to be either human or relevant animal studies, reviews (including systematic reviews and meta-analyses), clinical studies with at least a 2-year follow-up, clinical trials, controlled clinical studies, comparative studies, and congress/consensus reports. In vitro and preclinical studies, reports based on questionnaires, studies not meeting the inclusion criteria, studies not available in English, and studies published before 1993 were excluded. The keyword search revealed 799 articles. Of these, 52 articles were selected that best described patient-related risk factors.

Results

Cardiovascular Disease and Anticoagulant Drugs

Cardiovascular disease combined with anticoagulation drug therapy is a risk factor for sinus augmentation procedures due to the patient’s increased risk of bleeding. With an aging population and high incidence of cardiovascular diseases in developed societies, there is an increased prevalence of patients taking some form of anticoagulant therapy. The main objective of this therapy is to reduce the occurrence of thromboembolism. The medications
are divided into two predominant groups: anticoagulants and antiplatelet drugs.

Anticoagulant medications work by interfering with specific clotting factors on the pathway of hemostasis. Although warfarin is the gold standard for anticoagulant therapy and is still widely prescribed, direct-acting anticoagulants (DOAGs) such as dabigatran (Pradaxa), rivaroxaban (Xarelto), and apixaban (Eliquis) are preferred due to the equal or superior efficacy and an improved safety profile.\(^{12,13}\) However, DOAGs lack standardized laboratory monitoring, such as international normalized ratio (INR), and lack anticoagulation reversal agents except for dabigatran. Prothrombin time and thrombin time blood tests are ineffective for DOAGs as they can only be used as qualitative tests to confirm if there is an anticoagulant effect.\(^{12}\) Furthermore, it has been established that anticoagulation therapy is a risk factor for major oral surgery procedures. According to Scully et al,\(^{14}\) a procedure is considered to be major oral surgery if it involves harvesting of autogenous bone grafts, the raising of extensive flaps, or placing an implant in sites where there is a risk of extending outside the bony envelope during osteotomy preparation. As such, anticoagulant medication is a risk factor for maxillary sinus augmentation.

Antiplatelet medications such as aspirin and clopidogrel (Plavix) are commonly prescribed to prevent thrombosis in patients with ischemic heart disease or a history of coronary angina, myocardial infarction, or stent implantation.\(^{15}\) Careful consideration must be given to the management of these medications before commencing sinus augmentation.\(^{15}\) The risk of a patient with coronary heart disease developing an ischemic stroke must be weighed against the risk of postoperative bleeding in such patients. Studies have shown no relevant increase in the rate of postoperative bleeding for implant placement procedures in patients continuing antiplatelet medication.\(^{16-18}\) However, withdrawal of such medications seriously increases the risk of adverse cardiac and brain ischemic events.\(^{19,20}\) As maxillary sinus augmentation is more complex in nature than dental implant placement, consultation with the patient’s cardiovascular physician is necessary to properly manage the antiplatelet regime prior to sinus augmentation surgery. Furthermore, platelet aggregation and bleeding time typically do not return to baseline levels until 10 days after sinus augmentation and/or implant placement and cannot be measured with a diagnostic parameter such as INR, as they do not inhibit the coagulation pathway.

For patients taking anticoagulant and antiplatelet medications, medical clearance from the treating physician outlining the need for a “drug vacation” is essential prior to treatment, in conjunction with the availability of coagulation laboratory tests such as INR if applicable. INR values should be obtained within 24 hours before the dental procedure.\(^{11}\) Values of 2.0 to 3.5 are usually considered appropriate for surgical clearance for sinus augmentation. However, medical clearance is still the deciding factor. One method of determining the risk of a patient taking an anticoagulant during a sinus augmentation procedure is to perform, when necessary, a smaller surgical procedure; if this is not needed, thorough scaling and root planing can be done to assess the bleeding tendency prior to sinus augmentation surgery.

**Diabetes Mellitus**

Diabetes mellitus is a relative risk factor for maxillary sinus augmentation procedures. Uncontrolled diabetes has been associated with an increased susceptibility to infection because of a compromised host response contributing to postoperative infection, a decrease in graft turnover, and creating incisions in the line opening.\(^{21}\) Mareno Varquez et al\(^{22}\) found that 30 out of 147 diabetic patients developed postoperative complications with sinus augmentation procedures. Another study found that diabetes demonstrated a four-fold increase in risk of postoperative swelling using a transcrestal sinus approach.\(^{23}\) This was further influenced by the antibiotic regimen, whereby amoxicillin reduced the probability of incidence by 60%.\(^{23}\) In the same study, looking at lateral window sinus augmentation, diabetes was observed as a factor in developing postoperative swelling, mild postoperative bleeding, delayed wound healing, membrane exposure, and flap dehiscence.\(^{23}\)

On the molecular level, the mechanism by which this may occur...
has been described in the literature as physiologic alteration induced by a hyperglycemic state (uncontrolled diabetes). Such events have been implicated in causing modifications in (1) the function of neutrophils, monocytes, and macrophages, (2) connective tissue metabolism, (3) normal osseous healing, (4) the formation of advanced glycation end products, and (5) the production of proinflammatory cytokines such as IL-1β and TNF-α.23

To manage diabetic patients, sinus augmentation surgery should be scheduled after proper medical clearance and acceptable glycemic control.21 The measure for glycemic control is an HbA1c less than 7%.

**Osteoporosis and Antiresorptive Drugs**

The condition of osteoporosis alone is not an absolute risk factor for sinus augmentation procedures. It has been observed that fractures in patients with osteoporosis heal similarly to healthy patients. The assumption that a decrease in bone mineral density and altered bone mineral metabolism affects sinus healing and implant osseointegration is controversial due to the lack of quality studies available.24

However, antiresorptive drugs (ARDs) are often prescribed for osteoporotic patients. These medications alter bone metabolism and as such are a relative risk factor for sinus augmentation procedures. Furthermore, they are used in the management of skeletal metastases of malignancies, to prevent events like fractures, and to limit pain and metastatic spread. Use of ARDs has traditionally been divided according to the route of administration (ie, oral, subcutaneous, intravenous). The current understanding, however, is that dose is more important than route of administration.25 Thus, low- and high-dose ARDs can be administered today through all three routes. Primarily, a low dose is used for osteoporosis treatment, whereas a high dose is used in cancer patients with bone metastases. Patients on ARD have a risk of developing medication-related osteonecrosis of the jaw (MRONJ), a specific complication directly related to these types of drugs that can have devastating consequences for the individual patient.25 Despite this theoretical risk, clinical studies have demonstrated contrary results. In a study that evaluated sinus augmentation with guided bone regeneration in patients on bisphosphonates, 47 mandibular bone blocks were grafted using the split bone block technique and 14 maxillary sinus augmentations were implemented. A total of 71 implants were placed and restored after 4 months. Of the 47 grafted bone sites, 45 healed without complication with successful integration of all implants.26

Nonetheless, individual patient assessment is important and must be carried out before a sinus augmentation procedure. For example, the risk of MRONJ increases with dose and duration of ARD intake.26 The benefits of the “drug holiday” concept in implant therapy are unclear.26 A drug holiday should be only considered after consultation with the treating physician. Sinus augmentation procedures are currently not recommended in patients on high-dose ARD intake.26 Prophylactic use of antibiotics and postoperative antiseptics (eg, chlorhexidine) are recommended when sinus augmentation procedures are performed in patients with low-dose ARD intake.26

A suggested method to assess the risk of MRONJ is to measure the C-terminal telopeptide of collagen (CTX) as described by Marx et al.27 CTX is a metabolic product from normal bone turnover and can be measured in the blood. As bone turnover is decreased with antiresorptive agents, the CTX value will also decrease, indicating a high risk for MRONJ.28,29 However, meta-analyses have not indicated CTX as a valid predictive value for risk of MRONJ due to a lack of evidence from multiple studies.30

As such, for this group of patients, a medical consultation with the treating physician and medical clearance is essential prior to conducting sinus augmentation procedures.

**Organ Transplant and Immunosuppressive Therapy**

Traditionally, patients with immuno-compromised conditions are often contraindicated for sinus augmentation because of the risk of infection, impaired wound healing, and altered bone metabolism.31 The medications used to treat these patients have evolved over time to reduce comorbidity. A case report
describing ridge augmentation and extended bilateral sinus elevation procedures in a liver-transplant patient with a 28-month follow-up suggests that the class of immunosuppressant therapy may make a difference. By using tacrolimus combined with mycophenolate mofetil instead of cyclosporin A with prednisone, the patient did not show any clinical or radiologic signs of preoperative bone impairment. Furthermore, this drug protocol may reduce complications, including renal toxicity and those related to bone metabolism.

In managing patients on immunosuppressive therapy, a medical consultation with the treating physician and medical clearance are essential prior to conducting sinus augmentation procedures.

**Cigarette Smoking/Vaping**

Cigarette smoking has been established as a risk factor for complications of sinus augmentation surgery. The negative influence of smoking has been attributed to decreased tissue oxygenation capacity, alterations in microcirculation, effects on fibroblasts and connective tissue, and effects on chemotaxis and adherence in leukocyte phagocytosis.

Complications rates have been found to increase in situations where guided bone regeneration is performed simultaneously with sinus augmentation. However, few studies evaluated complication rates with sinus augmentation procedures alone. Cigarette smoking has been widely associated with an impact on host response by decreasing neutrophil and phagocytosis functions. Moreover, the risk of subgingival infection in individuals with a current smoking habit is 2.3 × greater than in nonsmokers or individuals with a past history of smoking. Smoking was also associated with a higher membrane exposure rate, flap dehiscence, and excessive pain in guided bone regeneration procedures. Further studies are required to confirm the detrimental effect of smoking on incidence of sinus membrane perforation and bleeding during sinus elevation procedures.

There are no clinical studies assessing the effect of electronic cigarette smoking on periodontal and peri-implant bone and soft tissues. From the experimental evidence currently available, it seems that electronic cigarette smoking may negatively influence the outcome of dental implant therapy in a manner similar to conventional smoking by enhancing oxidative stress in periodontal and peri-implant tissues and augmenting alveolar bone loss. Thus, well-designed clinical studies are needed in this regard.

**Antibiotic Allergy**

Amoxicillin allergy has been suggested as a contraindication for sinus augmentation procedures. When a patient demonstrated an allergy to amoxicillin, traditionally clindamycin was prescribed as the alternative. However, a recent study showed that sinus augmentation failure occurred in patients who received prophylactic clindamycin therapy. In the retrospective observational study, 1,874 patients received sinus augmentations prior to dental implant placement, and 9 patients developed infection of the sinus graft material. A common trait observed with these 9 patients was a reported penicillin allergy, and all had been prescribed clindamycin.

The primary alternative antibiotic recommendation has changed for patients with a true penicillin allergy. It is recommended that azithromycin be given with a loading dose of 500 mg, then 250 mg for an additional 4 days. The U.S. Food and Drug Administration recently placed a black box warning on clindamycin for risk of *Clostridium difficile* infection. Therefore, clindamycin should only be prescribed if the patient cannot take penicillin or azithromycin.

**Sinus Membrane Thickness**

The thickening of the sinus membrane as identified on radiographs is commonly associated with sinusitis (Fig 3). Mild mucosal thickening is often asymptomatic and considered a normal radiographic finding. However, mucosal thickening > 2 mm is indicative of sinusitis. Patients requiring implant placement with sinus augmentation often present with a thickened membrane. Studies have found a mucosal thickening of > 2 mm in 62.6% of patients presenting for implant placement in the posterior maxilla.

If the sinus membrane is too thick, it can block the osteomeatal
process when elevated (Fig 3). The patency of the osteomeatal complex is essential for overall sinus health. Any blockage of the complex can lead to major complications, such as rhinosinusitis. Studies have shown a significantly greater risk for obstruction of the osteomeatal process where mucosal thickening is > 5 mm.

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Gender/Age

Although gender and age cannot be considered risk factors for sinus augmentation procedures, their relationship with sinus membrane thickness has been investigated. The thicker membrane will allow for greater ease in membrane elevation from the sinus cortical floor and less risk of membrane perforation. In a study by Zimmo et al., age was found to be a factor influencing membrane thickness, with younger patients exhibiting thicker membranes. Two studies demonstrated that gender influenced the dimension of the sinus membrane, with females having healthier membranes. This was refuted in a study by Lim et al., which found that sinus membrane thickness was not influenced by age or gender. Further studies are required to confirm the validity of these trends.

Discussion

Having cardiovascular disease and taking anticoagulants, uncontrolled diabetes, antiresorptive drugs, immunosuppressive therapy, amoxicillin allergy, and cigarette smoking have been identified as patient-related risk factors for sinus augmentation procedures. Where the patient has a pre-existing condition (such as cardiovascular disease and diabetes mellitus) or has had an organ transplant, management of these patients requires a consultation with the treating physician and medical clearance prior to commencing sinus augmentation procedures. Cigarette smoking is an established risk factor for sinus augmentation procedures and should be ceased by the patient prior to treatment. Where the patient has an amoxicillin allergy, azithromycin is considered the alternative antibiotic of choice.

Trends between gender/age and sinus membrane thickness have been studied, but they are not considered to be established risk factors for sinus augmentation procedures. A thickened sinus membrane of > 5 mm is a risk factor, as it can block the osteomeatal process when elevated, causing major complications.

Despite the current understanding of patient-related risk factors, there are a low number of clinical studies relating to sinus augmentation procedures alone. These studies often focus on establishing risk for implant therapy or bone augmentation procedures. Further studies are required to evaluate patient-related risk factors for sinus augmentation procedures.

Conclusions

Predictable outcomes in maxillary sinus augmentation procedures not only require consideration of local factors but also on identification, evaluation, and management (where possible) of patient-related risk factors. Based on a systematic review of the literature, established patient-related risk factors include cardiovascular disease, diabetes mellitus, immunosuppression from organ transplantation, cigarette smoking, amoxicillin allergy, and a thickened sinus membrane. Due to the low number of clinical studies, further research is required to evaluate patient-related risk factors for sinus augmentation procedures.

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References


2. Fugazzotto PA. Success and failure rates of 1,344 6- to 9-mm-length rough-surface implants placed at the time of transalveolar sinus elevations, restored with single crowns, and followed for 60 to 229 months in function. Int J Oral Maxillofac Implants 2017;32:1359–1363.


