



Review

Flapless Dental Implant Surgery in Bleeding Disorders

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Abstract: Hemostasis disorders require particular attention in dental treatment. Dental implants are a very widespread and valid method for total rehabilitation. Flapless dental implant surgery is a minimally invasive treatment that allows the implants to be placed in the jaw bones with minimal surgical trauma. The aim of this study is to report the bleeding incidence in a group of patients with bleeding disorders treated with flapless implants. A total of 52 patients with bleeding disorders (46 in anticoagulant therapy; 4 with hemophilia; 2 with von Willebrandt disease) were treated with 188 flapless implant surgeries. Anticoagulants were not discontinued. Patients with hemophilia and VWD were treated following specific protocols. Four late, easy to treat bleeding complications were reported (three mild bleeding, one ecchymosis). No additional sutures or other hemostatic measures were taken, no further infusions or transfusions were reported, and no severe bleeding complications requiring more than easy on-chair treatment, were reported. In conclusion, with adequate knowledge of the procedure and the pathology, dental implantology can be safely performed in patients with bleeding disorders.

Keywords: dental implant; flapless implant; anticoagulant; antiplatelet; haemophilia; von Willebrand



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1. Introduction

Bleeding disorders are a group of disorders in which the blood does not clot properly, and such conditions can be congenital or acquired. Congenital diseases are hereditary and quite rare, while acquired diseases can develop from pathological conditions or be caused by the administration of drugs, specifically drugs of the antiplatelet or coagulation factor inhibitor classes.

Von Willebrand disease is the most common of the congenital coagulation disorders and is caused by a reduced number of von Willebrand factors or structural defects [1].

Such a disorder is primarily a genetic disorder, but acquired variants of von Willebrand disease have also been observed. The best-known classification of the disease distinguishes the following three genetic types: Types 1 and 3 include defects in quantitative factors, while Type 2 includes qualitative defects [1,2].

The second most common congenital coagulation disorder is hemophilia, a group of genetic disorders characterized by defects in the proteins involved in the blood clotting process [3,4].

Anticoagulants prevent blood clots from forming by acting selectively on specific clotting factors. These drugs are believed to prevent deep vein thrombosis, venous and arterial thromboembolic disease, pulmonary embolism, atrial fibrillation with a risk of embolism, and to prevent the formation of blood clots on the valve in patients with a mechanical heart valve prosthesis, myocardial infarction, and recurring heart attacks. Anticoagulants are also suitable for managing new cardiovascular events (recurring heart

attack, stroke, etc.), unstable angina, acute peripheral arterial occlusion, and unstable coronary syndrome [5].

The most commonly used anticoagulants are the vitamin K-dependent inhibitors warfarin [6] and acenocoumarol; however, the use of this class of anticoagulants has limitations.

To overcome these limitations, direct thrombin inhibitors and activated factor X inhibitors have recently been proposed as substitutes [7].

Another anticoagulant worth mentioning is heparin; however, it is most commonly used as short-term therapy or to overlap with long-term therapy when interruption of anticoagulant therapy is required [8].

It was once believed that anticoagulation disease patients should receive less invasive dental treatments; however, in recent years, thanks to the therapeutic progress and, above all, to the close multidisciplinary cooperation among the professional figures involved, these patients can be treated securely with proper rehabilitation processes [9].

In dental surgery, the treatments of coagulopathic patients are a much debated topic.

If, on one side, the patient in oral surgery has a relative low risk of bleeding, these are always cases of minor surgery. However, bleeding can be very bothersome for the patient [10].

Moreover, patients require treatment daily, usually at home, which is why very clear postsurgery suggestions must be given.

On the one hand, there is the necessity to manage the thromboembolic risk; on the other hand, there is the necessity to obtain a good hemostasis.

In regard to anticoagulated patients with the inhibitor of Vitamin K, we have gone from the proposal of suspending the medicine [11], to its reduction [12], to bridging, using low-molecular-weight heparin [13].

All these procedures submit the patient to a thromboembolic risk [14].

The current attitude is not to suspend the medicine but to simply control the anticoagulation level through administering prothrombin with an INR (International Normalized Ratio) which must essentially take part in the therapeutic range (usually under INR of 3 [11]; this topic has already been discussed in the literature with a 1966 article [15]).

The same goes for direct inhibitor (whether on the factor II or on the factor X), where it is not necessary to control INR, thanks to their short half-life as their onset time [16,17].

Hemophilic patients (HP) were once treated in oral surgery with plasma transfusions, followed by a purified factor, and currently with a recombinant factor, [18], in some cases with activated prothrombin complex concentrate [19,20] or with desmopressin or infusion of the factor of VW [21].

Desmopressin was first developed in order to treat nocturnal enuresis and has proven to be efficient in the inducing of VWF release.

In the literature, it is possible to find information on congenital diseases [Von Willebrand/Hemophilia A and B] and acquired diseases [liver diseases, thrombocytopenia, prolonged PT (prothrombin time), PTT (activated partial thromboplastin time), and kidney and bone marrow diseases] in regard to the safest protocols involving the use of local hemostatics, the administration of desmopressin [22] and antifibrinolytics [23], or the offsetting missing coagulation factors.

Patients with clotting disorders are one of the most difficult medical cases when it comes to dental implants, which are a proven solution for restoring toothless areas, and the number of these treatments used worldwide is increasing and has also proven to be an effective solution in treating patients with systemic diseases [24].

However, doctors prefer to either send this category of patients to the hospital to undergo these procedures or choose other prosthetic solutions instead of dental implants.

Treatment is not regulated by certified and unanimous guidelines; however, for the management of hemophilic patients (HP), international guidelines have implemented that feature several recommendations for oral therapy [25,26].

Hemostatic processes have been strongly simplified thanks to the clinical use of tranexamic acid, which is able to stabilize factor XIII, ensuring a minor fibrinolysis.

Its use has been validated in oral surgery (even for topic use) by two independent equipes in different geographical areas [27,28], and, thanks its use, implant treatment has also been validated [29].

Additionally, using Autologous Platelet Concentrates (APCs), which are growth factors, so blood products, seem to be a valid solution for reducing post-operative bleeding in dentistry in patients undergoing anticoagulant therapy without its discontinuation [30,31].

In implant surgery, the flapless technique is becoming more popular every year. It consists of placing endosseous implants without the elevation of a mucoperiosteal flap. This type of procedure has been widely validated in literature and allows for a much more conservative approach with a reduction in pain and post-operative swelling, allowing for a quicker recovery time [32].

It is also associated with a lower risk of bleeding, which is why it was chosen in this protocol [33].

The positioning of flapless implant surgery can take place freehand or using stents made with a model or designed in pure digital CAD CAM flow based on radiographic examinations [34].

The method involves either the performance of a minimally circular mucotomy with a diameter either bigger or smaller than that of the implant or performing a mucosa perforation directly with the osteotomy drill.

This method cannot be obviously associated easily with regenerative therapies or with immediate post-extraction implant placement.

On the other hand, it fits very well with tilted implants and direct placement of the healing cup (one stage).

The therapy does not include anticoagulant suspension at any time.

However, it has also been shown that, for patients undergoing VKA therapy, it is recommended that, before dental surgery, they request an INR 2.0 to 3.5 for most indications (with some exceptions requiring higher levels (up to 3.5) [35–41]).

Experts suggest obtaining INR values within 24 h [22] or up to 72 h before dental surgery [42,43].

Instead, DOACs (Direct Oral Anticoagulants) are a class of targeted anticoagulants that can inhibit free factor Xa, clot-bound factor Xa, and factor Xa bound to the prothrombinase complex [44].

The most common ones are rivaroxaban, apixaban, and edoxaban [45].

Dabigatran is also part of DOACs; it binds directly to thrombin and blocks its interaction with its substrates' Direct Thrombin Inhibitors (DTIs) [46].

DOACs have been shown to be safer than VKAs, with equivalent efficacy for stroke or venous thromboembolism prevention [47].

In the existing literature, there is no mention of the need to discontinue anticoagulant use when undergoing dental procedures that may cause bleeding [48,49].

However, it may be important to be aware of the drugs' half-life and the patient's renal conditions (specifically their creatinine clearance) to establish the residual level of DOACs in their blood at the time of surgery and evaluate its level of safety [45].

Such levels can be established by having the patient undergo an aPTT and/or TT before surgery [50].

In the literature, many studies have described that, with a well-known onset time of anticoagulant, without its suspension, and with adjunctive local hemostatic measures being used appropriately, patients who are currently on anticoagulant therapy can undergo dental surgery safely.

The main aim of this retrospective observational study is to evaluate intra-operative and post-operative bleeding (incidence) after implant placement in patients with bleeding disorders and to test the suitability of flapless surgery treatment.

We want to demonstrate that these patients can be treated and rehabilitated as safely as the patients without hemostasis disorders without interrupting anticoagulation therapy. However, we do anticipate post-operative bleeding and complications.

Patients using antiaggregation agents and heparin are excluded because of these substances' mediocre treatment levels, which have been noted in the literature [29,31].

2. Materials and Methods

2.1. Patients

Patients with bleeding disorders such as hemophilia and VWD, as well as vitamin K dependence and use of direct anticoagulants, are included in the study sample, without suspension of anticoagulant therapy, but using local hemostasis, also for hemophilia and VWD.

From the patient population requiring anticoagulant therapy, 46 patients (27 male 19 female) aged 42 to 87 years (mean 59.5 ± 9.66 years) receiving oral anticoagulant therapy (warfarin, apixaban, rivaroxaban, edoxaban, dabigatran) were consecutively recruited. Endosseous dental implant surgery (Group A) at the Department of Neuroscience, Section of Clinical Dentistry, University of Padua.

Patients had to meet the following inclusion criteria: (1) they had to be receiving warfarin and a confirmed INR value between 4 and 1.8, 1 h before surgery, or direct anticoagulants (dabigatran, rivaroxaban, apixaban, edoxaban); (2) anticoagulant therapy for 6 months; (3) partial edentulism requiring placement of at least one dental implant; (4) they had to have a normal hemoglobin level and platelet count.

Implants were placed for overdentures, fixed prosthodontics or full arch treatments, not for fresh socket post extraction implant placements.

Following surgery, either nothing or a a fixed or mobile prosthesis has been placed.

Instructions advised a soft diet, gentle hygiene, compression with gauzes saturated with tranexamic acid, communication of every instance of bleeding to the clinic.

The patient was informed about the nature of the protocol, which was to maintain the patient's usual anticoagulation therapy, unchanged, and to apply local hemostatic measures (gelatin sponge, sutures, tranexamic acid) [51].

The low chance of thromboembolic complications and the putative increased risk of intra- and post-operative bleeding related to this protocol were thoroughly explained.

Before the beginning of the study, all 46 patients signed the informed consent.

The distribution of the patients, according to the indications for anticoagulant therapy and INR value, is presented in Table 1.

Table 1. Indication for anticoagulant therapy in the 46 patients included in the study.

Indication	Number
Myocardial infarction	16
Atrial fibrillation	13
Stroke	6
Prosthetic valve	6
Venous thromboembolism	4
Valvulopathy	1

4 patients affected by hemophilia A were enrolled (male, average age 60 standard deviation 5.9). Where take in consideration 2 patients with VWD (male, 59 and 61 yo, 1 type 1 while 1 type 2B).

This is a retrospective observational study.

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by local ethic committee (5646/A0/23).

2.2. Surgical Procedures and Post-Operative Care

All the procedures were performed in an outpatient setting.

Patients receiving anticoagulant therapy were treated with a non-suspension protocol in accordance with the current literature [24,52–54].

Hemophilia patients (Figures 1 and 2) were treated by replacement therapy of the deficient factor associated with tranexamic acid, as widely documented in the literature [20,55–57].

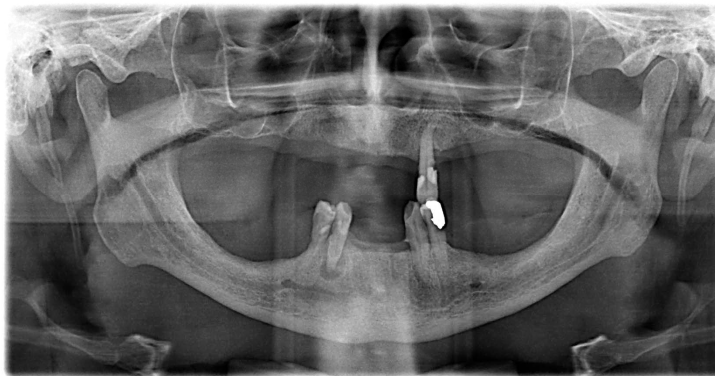


Figure 1. Radiological situation before surgery.

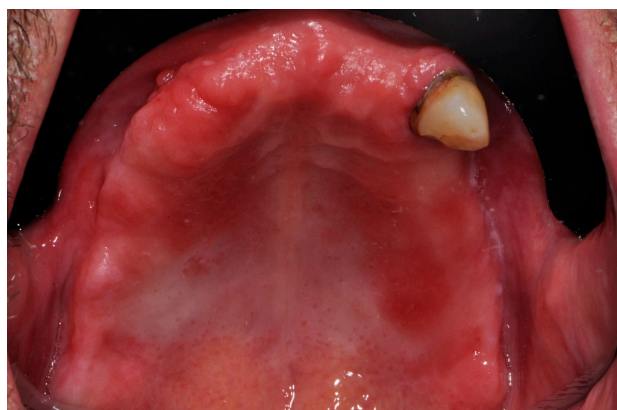


Figure 2. Clinical situation before surgery of patient with HP.

The patient with VWD type 2B was treated with infusion of factor VIII e VWF [23].

The patient with VWD type 1 was treated with desmopressin, subcutaneously, 30 min before the procedure, 0.3 mg per kilo [23,58,59].

Patients were pre-medicated with diazepam 5 mL (Biologici Italia Labs, Milan, Italy).

Vital signs, including oxygen saturation, blood pressure and cardiac electric activity, were monitored throughout surgery. The surgical procedures were performed by three different experienced surgeons using standardized protocols. Local anaesthesia was obtained using mepivacaine 2% with 1:100,000 adrenaline (Carbocainas, AstraZeneca S.p.A., Basiglio, Milan, Italy) and an additional local infiltration of bupivacaine 5 mL (Bupisolver, Solver-Pharma S.r.l., Milan, Italy) to obtain more prolonged analgesia.

The template was designed on the basis of the CBCT (Cone Beam Computed Tomography) or the plaster model with dental or mucosal support. Additionally, no flaps were raised, and the threaded fixture sites (3i, Implant Innovations Inc., Palm Beach Gardens, FL, USA) were prepared according to the standard clinical protocol for the implant system.

Mucosa has been perforated directly with a lance drills (Figure 3), with the osteotomy following afterwards, as indicated (1.2 mm).

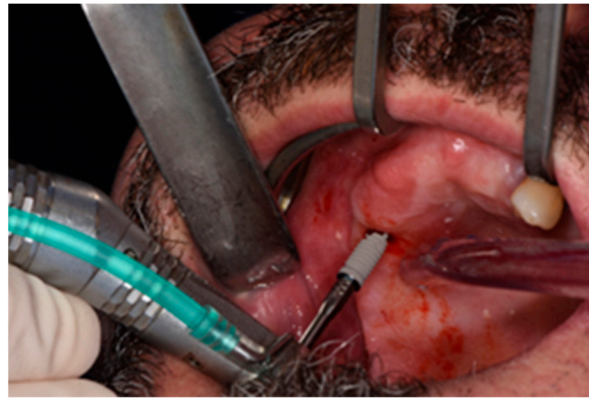


Figure 3. Mucosa perforation directly with a lance drills.

By the producer, with drills, increasing from 2 to 3 mm in diameter. Drills of 3.25 mm and 3.50 mm are used in cases of high bone density in order to place implants of 4.0 mm of diameter (Figures 4 and 5). There are no cases where a bone graft has been attempted (instruments by 3i, Palm Beach, Florida).



Figure 4. Implants position control.

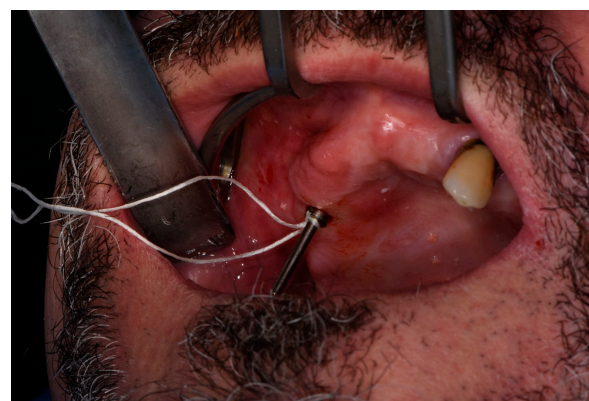


Figure 5. Placement of implants of 4.0 mm of diameter.

A compressive gauze soaked with tranexamic acid (Ugurols, Rottapharm S.r.l., Monza, Milan, Italy) was applied to the site of surgery for 30–60 min post-operatively. Antibiotic treatment (amoxicillin 1 g, 2 b.i.d.) was prescribed for 6 days, and patients received analgesics, such as paracetamol (Efferalgan Laboratories UPSA, Agen, France) or diclofenac (Voltarens, Novartis Farma S.p.A., Varese, Italy), when required. Antibiotic prophylaxis was administered to patients with prosthetic valves, following recommended best practice [60].

Furthermore, we recommend not applying ice after surgery. Applications of it may not adequately slow bleeding and may impair coagulation and hemostasis, which may be more useful in controlling pain [61].

A series of studies conducted on humans and animal models has shown that ice application after surgery can lead to a decrease in platelet aggregation, resulting in an increase in clotting time and clot formation, causing prolonged bleeding and the formation of an unstable clot. Of course, this is an effect with less relevance on the healthy population, but it is relevant when applied in hemophiliac patients (HP) [62–64].

Patients were asked to report any post-operative bleeding.

Follow-Up and Evaluation Parameters

Post-operative visits were scheduled on days 3 (Figure 6) and 8.



Figure 6. Post-operative visits scheduled on day 3.

Patients were evaluated for the presence of swelling, pain, local infection, and bleeding by the same clinician who performed the surgical procedure. The evaluation of post-operative bleeding during the 8-day period following implant insertion was carried out semi-quantitatively, as follows:

- (1) No bleeding;
- (2) Mild bleeding, defined as minor oozing from the wound incision controlled with compressive gauze only;
- (3) Moderate bleeding, associated with the presence of large clots continuously disrupting the surgical area and requiring additional local hemostatic measures and
- (4) Severe bleeding, requiring further medical control of coagulation. Patients were also requested to record the time when bleeding occurred.

3. Results

Patients and implants placed are reported in Table 2.

Table 2. Number of patients and implants placed for each type of hemostatic disease/type of Medicine.

Hemostatic Disease/Type of Medicine	Patients	Implants
Warfarin 5 mg	23	86
Dabigatran 75–110–150 mg	8	26
Apixaban 2.5–5 mg	4	18
Rivaroxaban 2.5–10–15 mg	8	28
Edoxaban 30–60 mg	3	10
HP	4	13
VWD	2	7

Bleeding complications in Table 3.

Table 3. Bleeding complications for every hemostatic disease/type of medicine.

Hemostatic Disease/Type of Medicine	Number of Patients	Bleeding Complications
HP	4	1 (25%) (ecchymosis)
VWD	2	0
Warfarin	23	1 (4.34%)
Dabigatran	8	1 (12.5%)
Apixaban	4	1 (25%)
Rivaroban	8	0
Edoxaban	3	0
Total	52	4

As regards the occurrence of bleeding, four late-bleeding complications were reported 2 days after surgery by patients.

Three mild bleeding complications required a delicate debridement of coagulable and compressive gauze soaked with tranexamic acid, which was applied at the site of the surgical wound for 1 h.

The first appearance was in a patient under warfarin, one under dabigatran, and one under apixaban.

Bleeding was controlled within 1 h and did not require further surgical wound debridement.

An ecchymosis (not requiring any treatment) of the cheek appeared in a patient with hemophilia A.

No additional sutures, other hemostatic measures, or further infusions or any rean-sufusion have been reported, nor have any severe bleeding complications requiring more than easy on-chair treatment.

4. Discussion

There are some papers that sustain the possibility to utilize endosseous implants in patients with high bleeding risks.

A part of the cases described do not detail whether the procedure used involved an access flap. This work has proposed a minimally invasive procedure that can potentially ensure minor post-operative bleeding.

Being clearly an observational trial, in absence of the control group, it is not possible to determine a relative risk.

For this reason, hemorrhagic episodes have to be compared with those reported in the literature.

In 2007, Nkenke supported the use of flapless implant surgery in order to reduce the possibility of bleeding in patients with hemostasis pathology [65]. It can be used in the following two types of approaches: mucosa-supported guided and bone-supported guided.

The first technique could be more appropriate in partially or fully edentulous patients and can be related with flapless surgery, which is associated with lower post-operative pain, less swelling, lower patient morbidity [66], shorter chair-time [67], and reduced risk of post-operative bleeding compared to open flap surgery [68].

The second technique requires a surgical guide supported by the bone surface and a full-thickness flap, necessary in the case of bone augmentation, but is followed by post-op swelling [69–73].

The major limit of flapless techniques compared to open flap surgery is indeed the disponibility of sufficient bone volumes. It is impossible, in fact, to associate flapless surgical techniques with bone grafts and GBR therapies.

Therefore, flapless surgeries should be restricted to a minor amount of cases where a proper clinical and radiological evaluation and planning has been conducted. Patients

treated with anticoagulant drugs or who are medically compromised can equally benefit from this minimally invasive technique [74].

However, blind flapless placement can cause bleeding complications that are more difficult to manage than bleeding with flap implants [53].

It is also important to take into account that there is an increased risk of thromboembolic events in the case of anticoagulant discontinuation. As a result, the continuation of anticoagulant therapy in the case of implant surgery does not cause an increase in the risk of bleeding as long as local hemostatic measures are used [36,40,47,75,76].

In 2006, an article was published investigating bleeding disorders in dentistry. Therefore, protocols used for non-suspension of anticoagulant treatment seem to be safe, as do those for replacement therapy in hemophilia patients and patients suffering from VW disease.

In our cases, we registered minimally post-operative bleedings, which are perfectly managed with local hemostasis.

A future hypothesis could realize a case-control trial comparing patients with hemostasis disorders and healthy patients, or comparing open flap surgery with flapless surgery.

The strengths of this study are that it is a study with a large case series. It is also the first work to report this treatment option in hemophiliac patients (HPs).

The limitation of the study is that it is miscellaneous, as we considered both patients undergoing anticoagulation therapy and patients having true hemostasis pathologies.

5. Conclusions

We have succeeded, through our results, in achieving the purpose of this study. However, given that it is a retrospective observational study, it is not comparable with other types of treatment.

Finally, it can be inferred that the flapless surgery technique can also be evaluated and considered in this category of patients.

In any case, it is always very important that there is cooperation among the different clinicians figures involved in the treatment of these patients. Thanks to the right collaboration and to the correct planning, all kinds of treatments can be successfully performed.

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Informed Consent Statement: Was always obtained.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

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