



Laser-assisted Oral and Maxillofacial Surgery for Patients on Anticoagulant Therapy in Daily Practice

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Purpose: In general clinical practice, the oral and maxillofacial surgeon is frequently required to treat patients on anticoagulant therapy. The purpose of this paper is to review the literature in order to provide evidence-based guidelines for the management of anticoagulated patients undergoing oral and maxillofacial surgery.

Materials and Methods: Literature published over the past 40 years was reviewed. The management of patients on anticoagulant therapy as well as laser-assisted oral and maxillofacial surgery is discussed.

Results: Currently, the continuation of anticoagulant therapy is strongly encouraged when INR is within the therapeutic range and meticulous local hemostatic measures are taken.

Conclusion: It may be concluded that the risk of postoperative bleeding is outweighed by the higher risk of thromboembolism after withdrawal of the anticoagulant therapy and thus continuation of the anticoagulant regimen is encouraged. Laser-assisted oral and maxillofacial surgery in daily practice has enabled surgeons to achieve controlled hemostasis and minimize intra- and postoperative hemorrhage without discontinuing anticoagulants.

Keywords: hemostasis, CO₂, diode, Nd:YAG, Er:YAG-YSGG, anticoagulants, oral and maxillofacial surgery.

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In general clinical practice, it is very common for the oral and maxillofacial surgeon and even for the general dental practitioner to deal with patients on anticoagulant therapy for prophylaxis against thrombosis and embolism. The currently recognized indications for antithrombotic therapy include coronary artery disease, vascular thromboembolism and myocardial infarction, cerebrovascular ischemic attacks, valvular disorders and prosthetic heart valves, atrial fibrillation, deep vein thrombosis, and pulmonary embolism.¹ The most commonly used anticoagulants are coumarin drugs, heparins, anti-platelet drugs, and thrombolytic agents. Hemorrhage is the principal adverse effect of oral anti-

coagulants, and obviously these drugs present management problems especially in daily clinical practice of oral surgery during and after surgical procedures.^{2,3}

Several authors have published guidelines for the management of patients on anticoagulant therapy.⁴ Traditionally, anticoagulated patients who are to undergo oral surgery are managed according to the following protocols: discontinuation of the anticoagulation regimen 2 days before surgery, provided the INR measured on the day of the operation is within therapeutic range (INR < 4), modification of medication intake and "bridging" therapy either with intravenous infusion of heparin in the hospital environment or subcutaneous



infusion of low molecular-weight heparins (LMWH) for outpatients, and finally, continuation of the anticoagulation regimen throughout surgery with application of local hemostatic agents and minimally invasive techniques. Consultation with the patient's cardiologist is always incumbent on the oral surgeon, and the final treatment plan should always be formulated in collaboration with the prescribing physician. A wide range of variables should be taken into consideration, such as the medical indications for anticoagulation, the therapeutic status of anticoagulation, and the risk of thromboembolic events. Other factors affecting treatment plan by increasing the risk of hemorrhage are cardiovascular disease, liver disease, renal disease (uremia), gastrointestinal disease (diarrhea), blood disturbances (thrombocytopenia), hyperthyroidism, cancer and HIV infection. On the other hand, the nature of the surgical procedure as well as its potential for bleeding, inflammation of the surgical site (potentiates fibrinolysis), and risk of intra-operative infection should also be assessed before surgery, since they increase the risk of postoperative bleeding. Therefore, the surgeon faces the dilemma of whether to discontinue the anticoagulation regimen before surgery or not. Stopping or continuation of the anticoagulant therapy bears the risk either of thromboembolism in the first case or uncontrolled postoperative hemorrhage in the latter. Immune-suppressed patients with systemic diseases and INR above therapeutic range requiring emergency oral surgery are preferably treated in hospital settings, while those patients requiring less complicated oral surgery can be treated in private practice under local anesthesia.

Promulgated guidelines concerning oral and maxillofacial surgery in relation to anticoagulated patients have been controversial. Since there is still no consensus about the INR threshold below which it is safe to perform this kind of oral surgery, therapeutic management should be balanced according to the patient's condition profile, the status of patient's coagulation expressed with INR value, the nature of oral surgical procedures to be carried out, and the type of anticoagulant medication.⁵

Laser applications represent a new tool available to the surgeon for the management of patients undergoing oral and maxillofacial surgery. Lasers can achieve controlled hemostasis, enhance visibility in the operation field, improve wound healing, and diminish postoperative hemorrhage, swelling, and pain. Laser-induced hemostasis enhances current surgical options for the treatment of patients on anticoagulant therapy without alteration of the medication regimen.

The aim of this review article is to discuss the currently used anticoagulant drugs, the management of anticoagulated patients undergoing oral and maxillofacial surgery, and the applicability of lasers in this field.

DRUGS WITH ANTICOAGULANT EFFECT

Anticoagulants are divided into 3 subcategories according to their mechanism of action: a) anticoagulants, b) anti-platelet drugs c) thrombolytic agents.^{5,6}

Anticoagulants

Anticoagulants are subcategorized as coumarins (vitamin-K antagonists), heparins, and heparins of low molecular weight (LMWH).

Coumarins (dicoumarol, warfarin) are used therapeutically to induce hypocoagulability and are competitive inhibitors of vitamin K. Warfarin sodium and acenocoumarol are the most widely used coumarins, because they have predictable onset and duration of action as well as excellent bioavailability. Warfarin has a plasma half-life of 36 to 42 h and is administered orally. Coumarin derivatives are indicated for the prevention of venous thromboembolism, systemic embolism in patients with atrial fibrillation or prosthetic heart valves, and for the prevention of stroke and pulmonary embolism.

Heparin is a fast-acting anticoagulant drug that is administered by intravenous or subcutaneous injection and inhibits the coagulation properties of thrombin. Heparin's half-life is very short with a range of 2 to 4 h, depending on the concentration of the dose and the patient.^{6,7} Heparin strongly inhibits the recurrent formation of thrombi and is effective in the prevention and treatment of deep venous and pulmonary thromboembolism as well as in the treatment of patients with acute myocardial infarction.

Low molecular-weight heparins have become quite popular and tend to replace heparin. They offer the advantages of outpatient self-administration of fixed doses without laboratory monitoring, and at the same time have rapid action and improved bioavailability. The patient does not need to enter the hospital. The most common LMWH is enoxaparin and is administered with subcutaneous injection to prevent deep venous thromboembolism. Their improved bioavailability also leads to a more predictable anticoagulation effect.⁷



Anti-platelet Drugs

Platelets participate in the blood clotting mechanism with platelet adhesion, activation, and finally aggregation. Anti-platelet drugs (aspirin, clopidogrel, dipyridamole, ticlodipin) are used to prevent platelet thrombus formation and blood clotting. Clinical indication for anti-platelet drugs administration is the prevention of transient ischemic attacks, myocardial infarction and occlusion of coronary grafts.⁶ The most commonly used anti-platelet drug is aspirin. Cyclooxygenase initiates the biosynthesis of thromboxane A₂. Aspirin irreversibly acetylates cyclooxygenase, thus resulting in inhibition of biosynthesis of platelet thromboxane A₂. This aspirin-induced inhibition prevents thromboxane A₂-mediated platelet plug formation. Since platelets lack a nucleus, they do not have the ability to synthesize new proteins/enzymes and consequently the deficiency induced by aspirin cannot be reversed during their life span of 3 to 7 days.^{6,7} Hemostasis slowly recovers 2 days after the withdrawal of aspirin, because during this time, new platelets are produced and enter the circulation.⁷

It has been reported that postoperative bleeding in patients under low-dose aspirin therapy undergoing oral surgery should not be of major concern for the dental practitioner.^{5,9}

Thrombolytic Agents

Thrombolytic agents (streptokinase, urokinase, alteplase t-PA) are used in the treatment of deep venous thromboembolism, and pulmonary and coronary artery embolism. These agents catalyze the conversion of plasminogen to plasmin, a fibrinolytic enzyme which dissolves the thrombus. These drugs are always administered in a hospital environment within the first 6 hours from the ischemic attack to prevent irreversible damage. They are used in the treatment of acute myocardial infarction, stroke, and pulmonary embolism.⁶ Since this category of patients will not undergo oral surgery in daily clinical practice, this review article will mainly focus on patients under anticoagulant or anti-platelet medication.

MANAGEMENT OF PATIENTS ON ANTICOAGULANTS IN ORAL AND MAXILLOFACIAL SURGERY

Several protocols for the management of oral surgical patients on anticoagulant therapy have been reported.⁵ Some suggest the anticoagulation regimen be discontinued or modified, while others propose the continuation of the anticoagulation therapy.

Oral anticoagulation therapy status was initially monitored by the one-stage prothrombin time (PT). In 1985, the INR (International Normalized Ratio) was introduced to standardize the PT reports by converting the PT ratio into INR according to the formula: $INR = (f\Delta \text{ Ratio})^{ISI}$. Hence, the intensity of anticoagulation therapy is safely and accurately measured by this new calibration method.^{7,9,10} The INR should be assessed preferably the day of the operation or up to 24 hours prior to the dental procedure.

For most therapeutic indications, ie, atrial fibrillation, myocardial infarction, and deep venous thromboembolism, the targeted goal is to attain an INR with a therapeutic range between 2 and 3. The recommended INR range for patients with prosthetic heart valves or recurrent deep venous thrombosis lies between 3 and 4.^{11,12}

PATIENTS ON ORAL ANTICOAGULANTS OR ANTI-PLATELET DRUGS

Discontinuation or Modification of the Anticoagulation Regimen

Customary practice has been to discontinue or reduce the anticoagulation therapy. In 1957, Ziffer et al reported on serious postoperative bleeding after oral surgery in anticoagulant patients.¹³ Since then, common practice is to stop warfarin or aspirin intake 2 to 3 days prior to the surgery, according to the drug's half-life, and re-instate them within 24 hours after surgery.¹⁴⁻²¹ The INR is measured the day of the surgery or the day before, and must be below 3 (INR < 3) in order to minimize the risk of hemorrhage. Consultation with the patient's physician is incumbent on the oral and maxillofacial surgeon, and the warfarin dosage should never be altered without the agreement of the prescribing physician.

It should be noted that the reduction in PT and INR values takes 3 to 5 days to be accomplished after withdrawal of oral anticoagulants.⁵ Bleeding is the main adverse effect of these drugs. By stopping the anticoa-



gulant medication intake, coagulation activity is normalized and the risk for postoperative bleeding is minimized.^{5,22-24} However, discontinuing anticoagulant medication does not always accomplish predictable reduction in the INR value, and it is possible that rebound phenomena of hypercoagulability occur after discontinuation of the drugs.²⁵⁻³¹ Although some people can stop taking antithrombotic medication before dental surgery without developing serious effects,³² others have suffered complications.³³ Several incidences have been reported in the literature, including deaths after stopping anticoagulants.³⁴⁻³⁷ For this reason, anticoagulation therapy should be re-instituted as soon as possible after oral surgery in order to reduce the risk of serious thromboembolic events.

Replacement of Oral Anticoagulants with Low Molecular-weight Heparins

An alternative way to handle patients on warfarin or aspirin is to replace the oral anticoagulants with low molecular-weight heparins (LMWH). The dosage of LMWH required for antithrombotic effect is less than conventional heparin and they can be administered once a day. Patients can safely undergo oral surgery without dose modification, and their previous anticoagulant therapy is re-instituted after the surgery. Bleeding is manageable with local measures. An advantage of this tactic is the fact that there is no need for monitoring the anticoagulation levels with clotting tests.

However, precaution should be taken when replacing an anti-platelet drug such as aspirin with LMWH. Owing to the fact that anti-platelet drugs need 2 to 3 days to reach the therapeutic range of anticoagulation level, the doctor needs to administer both anti-platelet and LMWH for 2 to 3 days until therapeutic levels are attained.

If the patient receives high doses of LMWH, the physician can stop the medication intake for 1 day prior to oral surgery and continue it afterwards.⁵

Continuation of Anticoagulation Regimen

Currently, many clinicians advocate the performance of routine oral surgery without reducing the dose of oral anticoagulants. Many studies have demonstrated that oral surgical procedures can be performed safely if the INR is within therapeutic range ($INR < 4$) and local hemostatic agents are applied afterwards to prevent postoperative bleeding.^{4,22,25,33,38-48}

Despite the risk of postoperative hemorrhage, several reports support that antithrombotic medication dosages should not be altered when scheduling patients for oral surgery.⁴⁴ When the anticoagulant regimen is modified to prevent the risk of bleeding, this at the same time predisposes the patient to risks of thromboembolic complications. Local antifibrinolytic therapy with tranexamic acid mouthwash can be used to control hemorrhage. Several authors recommend rinsing with a 4.8% or 5% tranexamic acid mouthwash for 2 min, 4 times per day for 5 to 7 days to reduce post-extraction bleeding.⁴⁹⁻⁵³ Carter et al⁵² illustrated that a 2-day regimen is as satisfactory as the 5-day regimen, with concurrently better patient compliance.

Consistent with the above studies are the guidelines promulgated in 2001 by the North West Medicines Information Centre⁵⁴ of the National Health System (NHS) of the United Kingdom:

- Stopping oral anticoagulants 2 days prior to routine oral surgery increases the risk of thromboembolic events.
- Withdrawal of anticoagulants does not guarantee that the risk of postoperative bleeding is minimized, since even healthy patients can develop bleeding complications after oral surgery. Bleeding, although it can be troublesome, does not place patients at the same risk as a serious thromboembolic event does.
- Routine oral surgery for patients on continuous anticoagulants bears the risk of postoperative hemorrhage that may need local hemostatic measures to be controlled.
- Published studies suggest that dental surgery for patients on continuous anticoagulant therapy can be safely performed when $INR < 4$.

The 2005 updated guidelines on oral anticoagulation (warfarin) of the British Committee for Standards in Haematology (BCSH) and of the British Society for Haematology (BSH) recommend that anticoagulation therapy does not need to be stopped for dental extraction in patients within therapeutic range, ie, $INR < 3$.¹² The October 2002 Dental Practitioners' Formulary gives a threshold INR of 3 ($INR < 3$);⁵⁵ this supercedes the value of 4 ($INR < 4$) given in the North West Medicines Information Centre guidelines in July 2001.^{54,56} Patients who require dental surgery and have an $INR < 3$ should continue warfarin therapy without dose adjustment. Under these circumstances, bleeding is easily controlled with local measures. The risk of thromboembolism after warfarin withdrawal greatly outweighs the risk of bleeding.



HEPARINIZED PATIENTS

Heparin is the main medication for management of the chronically anticoagulated, high-risk patient, and the most common route of administration is continuous intravenous infusion. In hospital patients under heparinization, only emergency treatment should be undertaken and that as conservatively as possible. Nevertheless, dental treatment should be completed prior to scheduled general medical procedures. Heparinized patients can safely undergo an oral surgical procedure after 6 hours from the latest administration of heparin, because of heparin's short half-life (1 to 2 hours). Its optimal anticoagulation action is immediately initiated but wears off after 4 to 6 hours and the dose has to be repeated.³ The scheduled operation can then take place, and provided there is no spontaneous bleeding, heparin will be re-administered later on the same day.

INTRAOPERATIVE CARE

It is well known that no vasoconstrictors (epinephrine) should be used in the anesthetic solution for cardiovascular patients. Mepivacaine 3% or prilocaine 3% with felypressin can be safely administered in these patients. As far as anesthesia is concerned, local infiltration is preferred but the inferior nerve regional block can also be used by means of an aspirating syringe.³³ Intraligamentary or intrapapillary injections are safer than regional blocks.

The minimally invasive surgical technique is of paramount significance in oral surgery. The less traumatic the procedures are, the better and more uneventful the healing process will be. The compression of trauma for 30 min with a gauze pack upon the surgical area is the common practice to prevent bleeding after every extraction. Meticulous suturing with nonabsorbable silk sutures is highly recommended when treating anticoagulated patients; sutures are carefully removed after 8 to 10 days.

Local hemostatic agents help control intra- and postoperative hemorrhage from small blood vessels by causing an artificial clot to form or by creating a mechanical matrix, which facilitates blood clotting.⁷ Such hemostatics are collagen and fibrin sponges, fibrin glue, absorbable gelatin sponges, and oxidized regenerated cellulose.^{53,57,58} According to Blinder et al,^{48,53} the utilization of absorbable gelatin sponges and sutures is adequate to control hemorrhage in cases of extractions.

POSTOPERATIVE CARE

Once the operation is completed, the patient is given oral and written postoperative instructions. It is safer for the patient to remain for observation for approximately 20 minutes and be dismissed only after the bleeding is controlled.⁵⁹ Family members are also provided with postoperative instructions. In case of emergency, a telephone number is given. Traditionally, the patient is instructed to avoid smoking, coffee, tea, alcohol, hard and hot food on the 1st postoperative day. Unless the doctor prescribes a mouthwash, the patient should not rinse the first few days because the blood clot may be disturbed.

Local antifibrinolytic therapy with tranexamic acid as a mouthwash significantly reduces the incidence of postoperative bleeding. Several double-blind randomized controlled studies have demonstrated the efficacy and safety of tranexamic acid 4.8% or 5% mouthwashes when used to achieve hemostasis.⁴⁹⁻⁵³

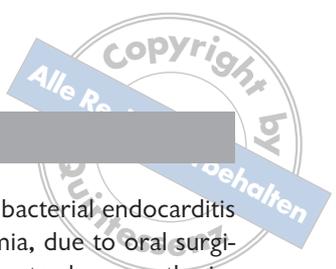
Paracetamol is the analgesic of choice for short-term use in anticoagulated patients and is preferred over non-steroid anti-inflammatory drugs (NSAIDs) since it does not affect platelets. A possible postsurgical sedative medication should consist of diazepam and its derivatives, because these drugs do not cross-react with anticoagulants. Drugs such as NSAIDs, acid reducers (simetidin), sulphonamides, metronidazole, selective COX-2 inhibitors, and broadband antibiotics can inhibit the metabolism of warfarin, and due to that mechanism, reduce the activity of warfarin.⁶

LASER-ASSISTED ORAL SURGERY

Oral surgery has a broad spectrum of applications in soft and hard tissues. In all cases, one of the major concerns of the surgeon is to minimize bleeding in order to achieve a clear overview of the surgical field and more importantly, to minimize risks for the patient.^{60,61}

In oral and maxillofacial surgery, electrocauterization has been used for coagulation of blood vessels and capillaries. Moreover, hemostatic agents such as fibrin glue have also been applied for management of minor postoperative hemorrhage. In postsurgical sockets, gelatin sponges have been utilized.

With the advent of lasers in the field of dentistry in the mid 1960s, a new treatment modality is at the oral surgeon's disposal. Inherent advantages of lasers are hemostasis, decreased charring, and diminished postoperative pain.⁶²⁻⁶⁴ Laser application could be the key



for diminution of intra- and postoperative hemorrhage and decrease in postoperative symptoms, offering an alternative or even the best possible solution in the oral surgery management of anticoagulated patients. Laser-assisted oral surgery can be performed regardless of the variation of INR values, ie, 3 or 3.5, due to the excellent hemostasis achieved with the surgical laser systems. Thus, there is no need to discontinue or reduce the anticoagulant medication intake and expose the patient to the risk of thromboembolic complications.

The hemostatic nature of lasers, which is based on the photothermal or photochemical interaction of light and matter, is of great value in oral surgery. It allows surgery to be performed more precisely and accurately because the surgeon has increased visibility of the surgical site. Consequently, operation time is reduced and postoperative hemorrhage is minimized.⁶⁵ The latter is crucial when dealing with anticoagulated patients on continuous therapy and enables surgery without withdrawal of the anticoagulant medication. The utilization of lasers as a hemostatic tool is well documented in the scientific literature. Since the medical indications for continuous anticoagulant intake are growing, the number of such patients will continue to rise. Laser-induced hemostasis offers an alternative solution in the controversial issue of intra- and postoperative bleeding control in patients on anticoagulant therapy.

Decreased postoperative swelling is also achieved with laser applications.^{66,67} The subsequent reduction in swelling after laser application in oral surgical procedures seems to be related to the sealing of the lymphatic vessels.⁶⁸ Tissue healing and scarring are also improved with utilization of lasers.^{67,69} Zeinoun et al⁷⁰ found that laser wounds featured significantly fewer myofibroblasts – the cells responsible for wound contraction – than scalpel wounds and this may be the reason for the minimal contraction of laser wounds. Crespi et al⁷¹ presented a case series showing that CO₂ laser enhances wound healing after periodontal surgery. Wound healing after laser application is excellent with decreased charring and increased function due to less invasive surgery, minimum collateral trauma, less scarring, and presence of fewer myofibroblasts than scalpel wounds.

Furthermore, there is a significant reduction in bacterial populations due to the bactericidal effect lasers possess. Since they do not cause implant surface alterations, the efficacy of the diode laser systems in the treatment of peri-implantitis has made them valuable tools in this field.⁷² The bactericidal effect of lasers is paramount when treating patients with heart-valve dis-

ease, due to the increased risk of bacterial endocarditis associated with transient bacteremia, due to oral surgical procedures. The ability of lasers to decrease the incidence of transient bacteremia due to oral surgical procedures was shown in an in vivo study by Pinhero,⁷³ who performed laser curettage before operation. Patients treated with laser showed 0% bacteremia post extractionem or after periodontal surgery compared to 52% positive blood cultures in the non-lased control group. Specific guidelines on antibiotic chemoprophylaxis already exist and have shed light upon the medical indications for endocarditis prophylaxis prior to oral surgery. Further double-blind, controlled studies are needed to determine whether laser-assisted oral surgery may put an end to antibiotic chemoprophylaxis in patients at risk for bacterial endocarditis.

Decreased postoperative pain is another positive effect attained with surgical laser application. The physiology of this effect remains unknown. According to one theory, pain reduction is attributed to the protein coagulum formed on the wound surface after laser irradiation, thus acting as a biological dressing and sealing sensory nerve fibers.⁶⁷

Moreover, the decreased tissue trauma is considered to contribute to the reduction of postoperative pain. It must be emphasized that the claim that laser surgery results in less postoperative pain has not been proven scientifically, but merely relies on case reports and observations as well as subjective patient reports.

Finally, one of the greatest advantages of laser use is high patient acceptance. The patient's confidence is increased by seeing the pioneer oral surgeon utilizing the most contemporary and advanced methods of dental treatment.

DISCUSSION

The performance of oral and maxillofacial surgery on patients who are taking oral anticoagulants remains quite a controversial issue. Especially in routine oral surgery, the formation of a coagulum is *conditio sine qua non* for the postoperative differentiation of cells and hence for the healing pattern of the intraoral wounds. In contrast, the formation of a clot in the periphery of the cardiovascular system has to be inhibited in order to minimize the possibility of an ischemic episode. Postoperative bleeding occurs even in healthy individuals, let alone in the compromised anticoagulant patient. Hence, both the physician and oral and maxillofacial surgeon face a dilemma.^{23,24} Should one risk postoperative bleeding by continuing the anticoagulant

regimen during surgery, or a life threatening thromboembolic event if medication is discontinued prior to oral surgical procedures?

Alteration of the regimen is associated with an increased risk of thromboembolism.^{29,42,44} Many studies have demonstrated that oral surgical procedures can be performed safely if the INR is within therapeutic range (INR < 4), and local hemostatic agents such as sutures and Surgicel are applied afterwards to prevent postoperative bleeding.^{4,22,25,33,38-48} Today, there is a growing tendency among dental surgeons not to alter the medication routine.

Wahl^{25,42} conducted a thorough retrospective study of the literature focusing on oral surgery (extractions) in patients who either stopped or continued the anticoagulant intake. He concluded that there is no need to discontinue the anticoagulation therapy, because the risk of postoperative hemorrhage is greatly outweighed by the risk of life-threatening thromboembolic events. However, Wahl's conclusions were based on case reports and case series rather than on controlled clinical trials. Despite the criticism of this good review article¹⁸ and the author's argument against reduction of anticoagulant medication routine, it is obvious that the risk of hemorrhage is outweighed by the risk of thromboembolism.

Campbell et al²² evaluated the amount of bleeding during oral surgery in patients on either continuous or discontinued anticoagulant therapy and reported that there was no statistically significant difference in intraoperative bleeding between the two groups.

In another study, Blinder et al placed 246 patients who underwent 543 dental extractions during continuous anticoagulation therapy in five groups according to INR values. They found no statistically significant correlation between postoperative values of INR within the therapeutic range and the incidence of bleeding, and concluded that local hemostatic measures are sufficient to control hemorrhage in orally anticoagulated patients.⁴⁸

In a review article, Scully et al⁷⁴ recommended that minor oral surgical procedures, such as uncomplicated forceps extraction, can be safely carried out with INR of less than 3.5. In addition to this, they suggested that when there is need of more than simple oral surgery or with INR of more than 3.5, the patient should be referred to a hospital. Nonetheless, referring the anticoagulated patient to a hospital in order to undergo minor oral surgery may not be easily implemented in daily clinical practice.

After completing a randomized, controlled study of 109 patients, out of which 57 continued warfarin in-

take and 52 stopped warfarin (control group), Evans et al suggested that oral surgical procedures can be safely performed even when INR < 4.1 in a hospital setting.⁴³ The difference in bleeding between the two groups was not statistically significant and hemorrhage was controlled successfully with local measures.

It must be highlighted that these studies were carried out in hospital settings. Further evidence is required to establish whether this is also the case in private practice. Published data demonstrate that when comparing postoperative hemorrhage in both normal and anticoagulated patients, there is no statistically significant difference between the two groups.⁷⁵

In an editorial, Butchart⁷⁶ characterized the practice of withdrawing anticoagulants before noncardiac surgery as being based on "folklore" rather than science. In a previously published survey among North American physicians, it was concluded that 73% and 51% of the physicians would alter warfarin and aspirin therapy, respectively, for at least one oral surgical procedure.⁷⁷ Although many studies have repeatedly shown that patients who continuously take anticoagulants can safely undergo oral surgical treatments,^{20,78} many physicians suggested alteration of the anticoagulation regimen before the procedures. Nonetheless, endodontic treatment causes little or no bleeding compared to professional cleaning. Wahl interpreted this as an indication that physicians may misunderstand the nature of oral surgical procedures. A similar study assessing the management of patients on warfarin by dentists in southwest Wales showed that there was a significant variation in the management protocols implemented by these general dental practitioners.⁷⁹ What can easily be inferred is that physicians have little knowledge about the nature of dental procedures and the associated risk of hemorrhage, and should be informed about it.²⁵ Likewise, consultation with the patient's prescribing physician is incumbent on the dental surgeon. Assessing the risk factors for bleeding tendency in conjunction with the interdisciplinary cooperation of the dentist and physician are paramount to formulating the optimal treatment plan.

In a case report, a high risk thromboembolic patient with severe inflammation of blade implants who did not discontinue nifedipin or dicumarol dosages throughout major oral surgical procedures, such as explantation of all implants, guided bone regeneration (GBR) with allograft bone or inserting of fixtures (implants) post-explantation, developed no postoperative bleeding thanks to laser-assisted surgery and proper suturing.^{80,81}

The wavelengths of lasers used in medicine and dentistry generally range from 193 nm to 10,600 nm and



the choice of the wavelength for specific surgical procedures is crucial for the success of the procedure. In medicine, the use of lasers is well documented and currently common practice in ophthalmology, dermatology, otolaryngology, and endoscopic urology; laser use is also in accordance with the contemporary principles of minimally invasive surgery. The evolution and incorporation of lasers in the field of dentistry have led to significant advances in oral surgery and improved patient care.

Lasers in oral surgery are a valuable tool, which effectively addresses the ambiguous and controversial issue of management of anticoagulated patients. Laser-assisted oral surgery can be performed regardless of the variation of INR values (3 or 3.5) due to the excellent hemostasis achieved with most lasers. Thus, the concern of the surgeon about adjusting the warfarin dosage may no longer be of relevance during laser-assisted oral surgery in anticoagulated patients, as there is no need to alter the anticoagulant medication intake and expose the patient to the risk of thromboembolism associated with the withdrawal of anticoagulants. Hence, the scope of oral surgery in anticoagulated patients is expanded, and more extended surgical procedures than simple extractions can be performed. Oral soft tissues have a large amount of rather small vessels and capillaries which are traumatized during surgery. Hemorrhage of these vessels can easily be controlled with local hemostatic measures, while accidental damage of larger vessels is considered to be a common troublesome complication, regardless of anticoagulant intake. The reliable hemostasis attained with lasers has made them valuable tools, especially when treating patients with blood clotting disturbances.

Apart from the applicability of lasers in oral surgery, they have been suggested to enhance wound healing (biostimulation effect) as well.⁸²⁻⁸⁴ Irradiation of oral tissues at low power settings with soft lasers is supposed to accelerate wound healing, reduce pain, and promote differentiation and proliferation of connective tissue cells. However, the mechanism of action of low-level laser therapy (LLLT) is still unknown.

Studies concerning the speed of healing of laser wounds compared with scalpel wounds are inconclusive. Some claim faster healing of laser wounds, while others suggest there is no difference.⁷⁵ However, evidence from studies demonstrates that the duration of healing is prolonged compared with other types of wounds.^{85,86} This delay in healing is due to the sealing of blood and lymphatic vessels and the subsequent need for neo-vascularization for healing. Further randomized, controlled clinical trials and subsequent meta-analyses are needed to elucidate this issue.

Hemostasis, bactericidal effect at the surgical site, and decreased postoperative swelling, pain and discomfort along with enhanced wound healing are inherent advantages of lasers. In dentistry, their use is growing exponentially both in private practices and hospital settings. Advances in laser technology will undoubtedly yield new procedures and have a major role in the future of minimally invasive oral surgery.

The quantum leaps of progress in every aspect of contemporary dentistry and medicine have enhanced the clinician's ability to confront demanding cases and offer the best to the patients. As a conclusion, based on published data, we suggest the following guidelines:

- The risk of postoperative bleeding when continuing the anticoagulation regimen is outweighed by the risk of a potentially life-threatening thromboembolic event if the anticoagulant therapy is withdrawn. The anticoagulation regimen should not be altered if INR is within therapeutic range.
- Oral surgery for patients on continuous anticoagulant therapy can be safely performed when INR < 3, provided that local hemostatic measures are taken.
- Lasers are adequate tools assisting the oral surgeon in performing major oral surgical procedures without altering the anticoagulation regimen. Utilized laser systems can achieve hemostasis and prompt formation of a coagulum. The spectrum of outpatient intraoral surgical procedures is broadened by laser-assisted oral surgery.

REFERENCES

1. Tierney LM, McPhee SJ, Papadakis MA. *Current Medical Diagnosis & Treatment*, ed 44. Lange, 2005:282-286.
2. Hirsh J, Fuster V, Ansell J, Halperin JL. American Heart Association/American College of Cardiology Foundation. Guide to warfarin therapy. *Circulation* 2003;107:1692-1711.
3. Opie LH. *Drugs for the Heart*, ed 2. G & S Inc, 1988:299-340.
4. Cohen SG, Glick M. Anticoagulant therapy. In: Rose LF, Kaye D, eds. *Internal medicine for dentistry*, ed 2. St. Louis: Mosby, 1990:374.
5. Little JW, Miller CS, Henry RG, McIntosh BA. Antithrombotic agents: Implications in dentistry. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;93:544-551.
6. Harvey RA, Champe PC. *Pharmacology*, ed 2. Philadelphia: Lippincott, 1997:219-227.
7. Terezhalmay GT, Lichtin AE. Antithrombotic, anticoagulant and thrombolytic agents. *Dent Clin North Am* 1996;40:649-664.
8. Ardekian L, Gaspar R, Peled M, Brenner B, Laufer D. Does low-dose aspirin therapy complicate oral surgical procedures? *J Am Dent Assoc* 2000;131:331-335.

9. Loeliger EA, van den Besselaar AM, Lewis SM. Reliability and clinical impact of normalization of prothrombin times in oral anticoagulant control. *Thromb & Haemost* 1985;53:148-154.
10. Hirsh J, Poller L. The International Normalized Ratio: a guide to understanding and correcting its problems. *Arch Intern Med* 1994;120:552-558.
11. Hirsh J, Fuster V. Guide to anticoagulant therapy. Part 2: oral anticoagulants. *Circulation* 1994;89:1469-1480.
12. British Committee for Standards in Haematology (BCSH). Guidelines on Oral Anticoagulation (warfarin), ed 3. 2005 update, p. 12.
13. Ziffer AM, Scopp IW, Beck J, Baum J, Berger AR. Profound bleeding after dental extractions during coumarol therapy. *N Engl J Med* 1957;256:351-353.
14. Russo G, Corso LD, Biasiolo A, Berengo M, Pengo V. Simple and safe method to prepare patients with prosthetic heart valves for surgical dental procedures. *Clin Appl Thromb Hemost* 2000;6:90-93.
15. Saour JN, Ali HA, Mammo LA, Sieck JO. Dental procedures in patients receiving oral anticoagulation therapy. *J Heart Valve Dis* 1994;3:315-317.
16. DeClerck D, Vinckier F, Vermynen J. Influence of anticoagulation on blood loss following dental extractions. *J Dent Res* 1992;71:387-390.
17. Dugdale M, Smith RM. The patient with bleeding problems. *Dent Clin North Am* 1983;27:271-278.
18. Todd DW. Anticoagulant therapy: consideration of modification in conjunction with minor surgery. *J Oral Maxillofac Surg* 2003;61:1117-1118.
19. Todd DW. Evidence to support an individualized approach to modification of oral anticoagulant therapy for ambulatory oral surgery. *J Oral Maxillofac Surg* 2005;63:536-539.
20. Kearon C, Hirsh J. Management of anticoagulation before and after elective surgery. *N Engl J Med* 1997;336:1506-1511.
21. Mulligan R. Response to anticoagulant drug withdrawal. *J Am Dent Assoc* 1987;115:435-438.
22. Campbell JH, Alvarado F, Murray RA. Anticoagulation and minor oral surgery: should the anticoagulation regimen be altered? *J Oral Maxillofac Surg* 2000;58:131-135.
23. Herman WW, Konzelman JL, Sutley Sh. Current perspectives on dental patients receiving coumarin anticoagulant therapy. *J Am Dent Assoc* 1997;128:327-335.
24. Weibert RT. Oral Anticoagulant therapy in patients undergoing dental surgery *Clin Pharm* 1992;11:857-864.
25. Wahl MJ. Myths of dental surgery in patients receiving anticoagulant therapy. *J Am Dent Assoc* 2000;131:77-81.
26. Palareti G, Legnaci C, Guazzaloca G, Frascaro M, Grauso F, De Rosa F, et al. Activation of blood coagulation after abrupt or stepwise withdrawal of oral anticoagulants: a prospective study. *Thromb & Haemost* 1994;72:222-226.
27. Genewein U, Haerberli A, Straub P, Beer JH. Rebound after cessation of oral anticoagulant therapy: the biochemical evidence. *Br J Haematol* 1996;92:479-485.
28. Grip L, Blomback M, Schulman S. Hyper coagulate state and thromboembolism following warfarin withdrawal in post myocardial-infarction patients. *Eur Heart J* 1991;12:1225-1233.
29. Poller L, Thomson J. Evidence for rebound hypercoagulability after stopping anticoagulants. *Lancet* 1964;2:62-64.
30. Sise HS, Moschos CB, Gauthier J, Becker R. The risk of interrupting long-term anticoagulant treatment. *Circulation* 1961;24:1137-1142.
31. Harenberg J, Haas R, Zimmerman R. Plasma hypercoagulability after termination of oral anticoagulants. *Thromb Res* 1983;29:627-633.
32. Mulligan R, Weitzel KG. Pre-treatment management of the patient receiving anticoagulant drugs. *J Am Dent Assoc* 1988;117:479-483.
33. Devani P, Lavery KM, Howell CJ. Dental extractions in patients on warfarin: is alteration of anticoagulant regime necessary? *Br J Oral Maxillofac Surg* 1998;36:107-111.
34. Akbarian M, Austen WG, Yurchak PM, Scannell JG. Thromboembolic complications of prosthetic cardiac valves. *Circulation* 1968;37:826-831.
35. Marshall J. Rebound phenomena after anticoagulant therapy in cerebrovascular disease. *Circulation* 1963;28:329-332.
36. Behrman SJ, Wright IS. Dental surgery during continuous anticoagulant therapy. *J Am Dent Assoc* 1961;62:172-180.
37. Cosgriff SW. Chronic anticoagulant therapy in recurrent embolism of cardiac origin. *Ann Intern Med* 1953;38:278-287.
38. Dodson TB. No need to routinely discontinue anticoagulants before dental extractions. *Evidence-based Dentistry* 2002;3:100-101.
39. Zanon E, Martinelli F, Bacci C, Cordioli G, Girolami A. Safety of dental extraction among consecutive patients on oral anticoagulant treatment managed using a specific dental management protocol. *Blood Coagul Fibrinolysis* 2003;14:27-30.
40. Benoliel R, Leviner E, Katz J, Tzukert A. Dental treatment for the patient on anticoagulant therapy: prothrombin time value - what difference does it make? *Oral Surg Oral Med Oral Pathol* 1986;62:149-151.
41. Beirne OR. Evidence to continue oral anticoagulant therapy for ambulatory oral surgery. *J Oral Maxillofac Surg* 2005;63:540-545.
42. Wahl MJ. Dental surgery in anticoagulated patients. *Arch Intern Med* 1998;158:1610-1616.
43. Evans IL, Sayers MS, Gibbons AJ, Price G, Snooks H, Sugar AW. Can warfarin be continued during dental extraction? Results of a randomized controlled trial. *Br J Oral Maxillofac Surg* 2002;40:248-252.
44. Jeske AH, Suchko GD. Lack of scientific basis for routine discontinuation of oral anticoagulation therapy before dental treatment. *J Am Dent Assoc* 2003;134:1492-1497.
45. Webster K, Wilde J. Management of anticoagulation in patients with prosthetic heart valves undergoing oral and maxillofacial operations. *Br J Oral Maxillofac Surg* 2000;38:124-126.
46. Souto JC, Oliver A, Zuazu-Jausoro I, Vives A, Fontcuberta J. Oral surgery in anticoagulated patients without reducing the dose of oral anticoagulant: a prospective randomized study. *J Oral Maxillofac Surg* 1996;56:27-32.
47. Beirne OR, Koehler JR. Surgical management of patients on warfarin sodium. *J Oral Maxillofac Surg* 1996;54:1115-1118.
48. Blinder D, Manor Y, Martinowitz U, Taicher S. Dental extractions in patients maintained on oral anticoagulation therapy: comparison of INR value with occurrence of postoperative bleeding. *Int J Oral Maxillofac Surg* 2001;30:518-521.
49. Sindet-Pedersen S. Haemostatic effect of tranexamic acid mouthwash in anticoagulated treated patients undergoing oral surgery. *N Engl J Med* 1989;320:840-843.
50. Ramstrom G, Sindet-Pedersen S, Hall G, Blomback M, Alander U. Prevention of post-surgical bleeding in oral surgery using tranexamic acid without dose modification of oral anticoagulants. *J Oral Maxillofac Surg* 1993;41:1211-1216.

51. Borea G, Montebugnoli L, Capuzzi P, Magelli C. Tranexamic acid as a mouthwash in anticoagulant-treated patients undergoing oral surgery: an alternative method to discontinuing anticoagulant therapy. *Oral Surg Oral Med Oral Pathol* 1993;75:29-31.
52. Carter G, Goss A. Tranexamic acid mouthwash- a prospective randomized study of a 2-day regimen vs 5-day regimen to prevent post-operative bleeding in anticoagulated patients requiring dental extractions. *Int J oral Maxillofac Surg* 2003;32:504-507.
53. Blinder D, Manor Y, Martinowitz U, Taicher S. Dental extractions in patients maintained on continued oral anticoagulant: comparison of local haemostatic modalities. *Oral Surg Oral Med Oral Pathol* 1999;88:137-140.
54. Randall CJ. Surgical management of the primary care dental patient on warfarin. North West Medicines Information Centre. Available at: www.ukmi.nhs.uk/med_info/documents/Dental_Patient_on_Warfarin.pdf
55. Dental Practitioners' Formulary. London. British Dental Association, British Medical Association and Royal Pharmaceutical Society of Great Britain, 2002-2004: D8, p. 117-119.
56. Carruthers S. Chairman BDA Formulary Committee. Letters. *Br Dent J* 2003;194:530.
57. Rakocz M, Mazar A, Varon D, Spierer S, Blinder D, Martinowitz U. Dental extractions in patients with bleeding disorders. The use of fibrin glue. *Oral Surg Oral Med Oral Path* 1993;75:280-282.
58. Halfpenny W, Fraser J, Adlam DM. Comparison of 2 hemostatic agents for the prevention of post extraction haemorrhage in patients on anticoagulants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;92:257-259.
59. Petersen LJ, Ellis E, Hupp JR, Tucker MR. Postoperative instructions. In: Petersen LJ, Ellis E, Hupp JR, Tucker MR (eds). *Contemporary oral & maxillofacial surgery*, ed 2. St. Louis: Mosby, 1993:772.
60. Aoki A, Sasaki KM, Watanabe H, et al. Lasers in non surgical periodontal surgery. *Periodontol* 2000 2004;36:59-97.
61. Rossmann JA. Lasers in Periodontics. Position paper by the American Academy of Periodontology. *J Periodontol* 2002;73: 1231-1239.
62. Gaspirc B, Scaleric U. Lasers in periodontics. *J Oral Laser Applic* 2003;3:135-140.
63. Strauss RA, Fallon SD. Lasers in contemporary oral and maxillofacial surgery. *Dent Clin North Am* 2004;48:861-888.
64. Schwarz F, Sculean A, Rothamel D, Schwenzer K, Georg T, Becker J. Clinical evaluation of an Er:YAG laser for nonsurgical treatment of peri-implantitis. A pilot study. *Clin Oral Impl Res* 2005;16:44-52.
65. Darbar UR, Hopper C, Speight PM, Newman HN. Combined treatment approach to gingival overgrowth due to drug therapy. *J Clin Periodontol* 1996;23:942-944.
66. Fisher SE, Frame JW. The effects of the CO₂ laser on oral tissues. *Br J Oral Maxillofac Surg* 1984;22:414-425.
67. Fisher SE, Frame JW, Browne RM, Tranter RM. A comparative histological study of wound healing following CO₂ laser and conventional surgical excision of canine buccal mucosa. *Arch Oral Biol* 1983;28:287-291.
68. Pick PH, Pecaro BC, Silberman CJ. The laser gingivectomy. The use of CO₂ laser for the removal of phenytoin hyperplasia. *J Periodontol* 1985;56:492-496.
69. Roodenburg JL, ten Bosch JJ, Borsboom PC. Measurement of the uniaxial elasticity of oral mucosa in vivo after CO₂ laser evaporation and surgical excision. *Int J Oral Maxillofac Surg* 1990;19:181-183.
70. Zeinoun T, Nammour S, Dourov, Aftimos G, Luomanen M. Myofibroblasts in healing laser excision wounds. *Lasers Surg Med* 2001;28:74-79.
71. Crespi R, Covani U, Romanos G, Barone A. CO₂ laser effects on root surfaces in periodontal treatment. Case reports. *J Oral Laser Applic* 2004;4:109-117.
72. Kreisler M, Gotz H, Duschner H. Effect of Nd:YAG, Ho:YAG, Er:YAG, CO₂ and GaAlAs laser irradiation on surface properties of endosseous dental implants. *Int J Oral Maxillofac Impl* 2002; 17:202-211.
73. Pinhero J. Nd:YAG assisted periodontal curettage in the prevention of bacteremia prior to cardiovascular surgery [abstract]. *Lasers Surg Med* 1997;20(Suppl 9):13.
74. Scully C, Wolf A. Oral surgery in patients on anticoagulant therapy. *Oral Surg Oral Med Oral Pathol Radiol Endod* 2002;94:57-64.
75. Bailey BMW, Fordyce AM. Complications of dental extractions in patients receiving warfarin anticoagulant therapy: a controlled clinical trial. *Br Dent J* 1983;155:308-310.
76. Butchart EG. Anticoagulation management during non-cardiac surgery- time for common sense (Editorial). *J Heart Valve Dis* 1994;3:313-314.
77. Wahl MJ, Howell J. Altering anticoagulation therapy: a survey of physicians. *J Am Dent Assoc* 1996;127:625-638.
78. Rooney TP. General dentistry during continuous anticoagulation therapy. *Oral Surg Oral Med Oral Pathol* 1983;56: 252-253.
79. Muthukrishnan A, Bishop K. An assessment of the management of patients on warfarin by general dental practitioners in South West Wales. *Br Dent J* 2003;195:567-570.
80. Chrysikopoulos SA. Er:YAG and CO₂ lasers in oral implantology. A study on 83 implants. *J Oral Laser Applic* 2003;2:97-103.
81. Chrysikopoulos SA. Er:YAG laser assisted explantation of blade implants and CO₂ laser assisted transmucosal implantation of screw implants to a patient under antithrombotic therapy [abstract 24]. 2nd Laser Congress of the European Society of Oral Laser Applications, Florence 2003.
82. Kreisler M, Christoffers AB, Willerhausen B, d' Hoedt B. Effect of low-level GaAlAs laser on the proliferation rate of human periodontal ligament fibroblasts: an in vitro study. *J Clin Perio* 2003; 30:353-358.
83. Dörtbudak O, Haas R, Mailath-Polorny G. Effect of low power irradiation on bony implant sites. *Clin Oral Impl Res* 2002;13:288-292.
84. Takeda Y. Irradiation effect of low-energy laser on alveolar bone after tooth extraction: An experimental study in rats. *Int J Oral Maxillofac Surg* 1988;17:388-391.
85. Pick RM, McCollum Y, Kaminsky EJ. Comparative wound healing of the scalpel, Nd:YAG laser and electrosurgery in oral mucosa. *Innov Technologie Biologie Med* 1990;11:116-121.
86. Pogrel MA, Yen CK, Hansen LS. A comparison of CO₂ laser, liquid nitrogen cryosurgery and scalpel wounds in healing. *Oral Surg Oral Med Oral Path* 1990;69:269-273.

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