REVIEW ARTICLE

Dental Surgery in Anticoagulated Patients

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Continuous oral anticoagulant therapy has been used to decrease the risk of thromboembolism for more than half a century, prolonging the lives of thousands of patients. Many physicians recommend interrupting continuous anticoagulant therapy for dental surgery to prevent hemorrhage. In reviewing the available literature, there are no well-documented cases of serious bleeding problems from dental surgery in patients receiving therapeutic levels of continuous warfarin sodium therapy, but there were several documented cases of serious embolic complications in patients whose warfarin therapy was withdrawn for dental treatment. Many authorities state that dental extractions can be performed with minimal risk in patients who are at or above therapeutic levels of anticoagulation. There are sound legal reasons to continue therapeutic levels of warfarin for dental treatment. Although there is a theoretical risk of hemorrhage after dental surgery in patients who are at therapeutic levels of anticoagulation, the risk appears to be minimal, the bleeding usually can be easily treated with local measures, and this risk may be greatly outweighed by the risk of thromboembolism after withdrawal of anticoagulant therapy.

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Continuous oral anticoagulant therapy has been used to decrease the risk of thromboembolism for more than 50 years, prolonging the lives of thousands of patients. Dental treatment on continuously anticoagulated patients has been controversial,[1-4] and physicians must weigh the risks of hemorrhage from the dental procedure against the risks of emboli from withdrawing anticoagulation treatment. Some recommend no change in anticoagulation for dental treatment.[5,6] Others recommend withdrawal of oral anticoagulant therapy for several days before the procedure and consideration of therapeutic administration of heparin for certain high-risk patients and high-risk dental procedures.[7-11] The focus of this article is to review only surgical dental procedures (extractions, gingival surgery, and alveolar surgery): nonsurgical dental procedures (professional cleanings, fillings, crowns, etc) have been shown not to present a significant bleeding risk.[5]

In a 1995 survey, the majority (73%) of practicing physicians recommended withdrawing therapeutic continuous warfarin therapy in some patients for at least some dental procedures.[12] Instead of changing the patient's prothrombin time, it is time to change the practice of withdrawing anticoagulant treatment for dental surgery.

DENTAL SURGERY IN ANTICOAGULANT-TREATED PATIENTS

In a review of the English-language literature (using computerized searches and au-

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thors' references), there have been more than 2014 dental surgical procedures (including more than 1964 dental extractions) documented in 26 case reports and studies of more than 774 patients receiving continuous oral anticoagulant therapy. These procedures include both single and multiple simple extractions, surgical extractions, full mouth extractions, alveoectomies, and other surgical procedures. Nonsurgical dental procedures were not included in this review. Many of the patients had levels of warfarin above 1992 recommended levels on the day of surgery. In 1992, the American College of Chest Physicians stated that the recommended therapeutic range of warfarin is an international normalized ratio (INR) of 2.0 to 3.0 for all conditions except for patients with mechanical prosthetic valves, for which the INR is 2.5 to 3.5.[13] These recommendations were endorsed by the American Heart Association.[14] Assuming an international sensitivity index between 1.8 and 2.8, the therapeutic prothrombin time (PT) ratio would range from at lowest 1.3 to at highest 2.0. Cannegieter et al[15] have suggested a higher therapeutic range, an INR of 3.0 to 4.0 (PT ratio ≤2.2), for patients with artificial valves. Therefore, for the purposes of this review, the therapeutic level of warfarin in all patients is no higher than an INR of 4.0 or a PT ratio (at highest) of 2.2. The studies of reported cases of dental surgery on patients receiving continuous oral anticoagulant therapy are summarized in **Table 1**.

Because of variations in study designs and differences in measuring the intensity of anticoagulant therapy between the more recent and the older reports, these studies do not lend themselves to a conventional meta-analysis or even systematic review. Still, of the more than 2014 dental surgical procedures reported in more than 774 patients receiving continuous warfarin therapy, the following observations can be made:

1. Although some patients had minor oozing treated with local measures, more than 98% of patients receiving continuous anticoagulation had no serious bleeding problems after dental surgery, with serious bleeding problems defined as bleeding uncontrolled by local measures.

2. Many of these procedures were performed in patients with warfarin levels above present recommended therapeutic levels of anticoagulation.

3. Many procedures were extensive, including multiple and full mouth extractions, alveoectomies, and surgical extractions.

4. Only 12 patients (<2%) had postoperative bleeding problems that were controlled by more than local measures. But after examining these 12 cases closely, none makes a good case for withdrawal of warfarin for dental surgery.

ANALYSIS OF 12 DOCUMENTED CASES OF POSTOPERATIVE HEMORRHAGE TREATED BY MORE THAN LOCAL MEASURES

In 5 of the 12 cases,[30,32,41] the PT ratios were above therapeutic levels. In 3 cases[21,39] in which patients were administered concomitant antibiotics, the preoperative INR was within the therapeutic range, and bleeding was initially controlled in all 3 cases by local measures. After 2 consecutive days (contrary to American Heart Association guidelines to prevent endocarditis[44]) of high-dose prophylactic erythromycin treatment, 1 of these patients developed bleeding 2 days after the extraction (when his INR was 4.3).[39] Another patient had 6 extractions done after prophylactic amoxicillin was administered.[39] Interestingly, although this patient's INR was an astounding 9.1 one week after the extraction, only 1 socket was bleeding, and this bleeding was only described as "oozing," indicating that the hospitalization may have been precautionary for the high INR and not for the oozing. The authors speculated that the antibiotics caused the increase in INR and subsequent bleeding and oozing, although there may have been other causes, including warfarin overdose. In the third case, the patient had a therapeutic preoperative INR of 3.51 for 20 extractions and an alveoplasty, and there was good hemostasis 72 hours postoperatively.[21] Although antibiotic prophylaxis has not been shown to be necessary or effective in preventing postextraction wound infections,[45] prophylaxis with amoxicillin, 500 mg 3 times daily for 7 days after surgery, had been prescribed. On the fourth postsurgical day, the patient was bleeding. The INR was then 9.03. Warfarin (Coumadin) was withheld, and the patient underwent transfusion of fresh-frozen plasma, then packed red blood cells, and ultimately vitamin K. The authors concluded that the elevated PT was from an interaction with amoxicillin, and that the amoxicillin was probably unnecessary.

Ramstrom et al[31] and Sindet-Pedersen et al[34] conducted separate studies comparing results of dental surgery on patients taking anticoagulants who rinsed 4 times a day for 7 days with a tranexamic acid mouthwash with those of patients who rinsed with a placebo mouthwash. Only 1 patient in each study (each in the placebo group) developed postoperative bleeding that was treated by more than local measures. Unfortunately, the authors did not report these patients' INRs, although they reported an INR range of all patients, the upper level of which in the study by Sindet-Pedersen was above recommended therapeutic levels. More important, the study design was poor: patients should not rinse at all after dental extractions until a hemostatic clot has formed.[28,46] Rinsing with a placebo mouthwash after dental extractions could have *created* the bleeding problem by interrupting the formation of a hemostatic clot. A more fair comparison would have been comparing tranexamic acid with no mouthwash at all.

Kwapis[28] reported in 1963 that 3 of 60 treated patients had "prolonged bleeding" after dental extractions. The PT ratio was reported for only 2 of these patients, and it was less than 1.5. These patients were administered vitamin K, but it was not reported if local measures to control hemostasis were at-

Table 1. Reported Cases of Dental Surgery on Patients Receiving Continuous Oral Anticoagulant Therapy*

Source, y	No. of Patients Treated; Total No. of Surgical Procedures (No. of Extractions)	PT or INR†	Comment	Patients With Postsurgical Hemorrhage Treated by More Than Local Measures
Anavi et al,[19] 1981	15; 52 (52)	PT, 19%-36%; mean PT, 27.5% [INR, <2.5 to >3.0]	Gelatin sponges (Gelfoam) used	None
Askey and Cherry,[6] 1956	6; 14 (14)	Prothrombin concentration, 14%-51% [INR, <2.0 to >3.5]	. . .	None
Bailey and Fordyce,[20] 1983	25; 156 (156)	PT ratio, 1.2-4.3; mean PT ratio, 2.4	. . .	None
Bandrowsky et al,[21] 1996	1; 21 (20)	INR, 3.51 preoperatively; INR, 9.03 at 96 h postoperatively	Tranexamic acid	1 patient had good hemostasis 72 h after surgery; amoxicillin, 500 mg 3 times daily for 7 d after surgery was prescribed as prophylaxis against a potential infection; on postsurgery day 4, patient came in with bleeding; warfarin sodium was withheld, and patient underwent transfusion of fresh-frozen plasma, then packed red blood cells, and ultimately vitamin K; authors conclude the elevated PT was from interaction with amoxicillin, and that the amoxicillin was probably unnecessary
Behrman and Wright,[22] 1961	20; 45 (35)	PT ratio, 1.2-2.5	Gelfoam and sutures under tension placed	None
Benoliel et al,[5] 1986	>3 <30; 87 (87)	PT ratio, 1.3-2.5	. . .	None
Borea et al,[23] 1993	15; 15 (15)	INR between 3.0 and 4.5; mean INR, 3.09	Antifibrinolytic mouthwash (tranexamic acid)	None
Borea et al,[23] 1993 (placebo mouthwash)	15; 15 (15)	(Anticoagulation withdrawn for unknown days) INR between 1.5 and 2.5; mean INR, 1.69	Placebo mouthwash	None
Cone,[24] 1993	1; 1 (1)	INR, 1.5	. . .	None
Frank et al,[25] 1963	11; 51 (51)	PT activity, 35%-15% [INR, <2.5 to 3.5]	. . .	None
Greenberg et al,[26] 1972	13; 27 (27)	PT activity, 28%-14% [INR, >2.5 to >3.5]	. . .	None
Kovacs et al,[27] 1976	31; 56 (53)	Prothrombin level, 19%-49% (mean, 33.3%) [INR, <2.0 to >3.0; mean INR, <2.5]	Coagulation-active substance applied	None
Kwapis,[28] 1963	60; >85 (>82)	PT ratios not given	. . .	3 patients (2 of whom had single extractions and PT times <1.5 the control) had "prolonged bleeding" and were administered vitamin K (not known if local measures to control hemostasis were attempted)
Martinowitz et al,[29] 1990	40; 63 (63)	INR, 2.5-4.29; mean INR, 3.25	Biologic adhesive used	None
McIntyre,[30] 1966	106; 636 (636)	Thrombotest generally 15%-7% [INR, 2.1 to 3.6]	. . .	1 patient whose thrombotest was 5% [INR, 4.8] bled for 12 h after 9 teeth were extracted and was administered vitamin K
Ramstrom et al,[31] 1993 (tranexamic acid)	44; ~70 (~66)	INR, 2.1-4.0	Antifibrinolytic mouthwash (tranexamic acid)	None

tempted before administering vitamin K.

Although there is a theoretical risk of hemorrhage after dental surgery, the literature indicates that the risk is very small. Some investigators recommend consideration of replacement heparin for especially high-risk patients undergoing extensive dental surgery. In addition to the high cost-benefit ratio for intravenous administration of heparin,[47] the cases documented above include many extensive surgical procedures and argue against any withdrawal of anticoagulant therapy, including heparin replacement. In reviewing the English-language literature, there are no well-documented cases of serious bleeding problems from dental surgery in patients receiving therapeutic levels of continuous anticoagulant therapy.

Table 1. Reported Cases of Dental Surgery on Patients Receiving Continuous Oral Anticoagulant Therapy* (cont)

Source, y	No. of Patients Treated; Total No. of Surgical Procedures (No. of Extractions)	PT or INR†	Comment	Patients With Postsurgical Hemorrhage Treated by More Than Local Measures
Ramstrom et al,[31] 1993 (placebo mouthwash)	45; ~67 (~67)	INR, 2.1-4.0	Placebo mouthwash	1 patient administered vitamin K (5 mg) after local measures; INR not given
Shira et al,[32] 1962	18; 50 (45)	PT, 16.8-50.7 s [PT ratio, 1.4-4.225]	Gelfoam and sutures placed for most extractions	1 patient: PT, 12.5%; 35.4 s [PT ratio, 2.95] (extraction with suture but no Gelfoam) given vitamin K
Souto et al,[33] 1996	92; 102 (102)	INR, 1.25-5.25	Tranexamic acid mouthwash	None (J.C. Souto, J. Fontcuberta, written communication, August 21, 1996)
Souto et al,[33] 1996	>100; >100 (>100)	INR, 2.0-3.5	Tranexamic acid mouthwash	None
Sindet-Pedersen et al,[34] 1989	19; 63 (60)	INR, 2.5-4.8	Antifibrinolytic mouthwash (tranexamic acid)	None
Sindet-Pedersen et al,[34] 1989 (placebo mouthwash)	20; 56 (52)	INR, 2.5-4.8	Placebo mouthwash	1 patient required hospitalization and fresh-frozen plasma; INR not given
Street and Leung,[35] 1990	12; 12 (12)	INR not reported	Antifibrinolytic mouthwash (tranexamic acid)	None, although 1 patient not compliant with mouthwash who had an impacted infected tooth extraction was admitted to the hospital for observation but not treatment
Tomasi and Wolf,[36] 1974	1; 2 (1)	PT ratio, 1.2	. . .	None
Tulloch and Wright,[37] 1954	1; 1? (1?)	PT ratio, 3.3	. . .	None
Waldrep and McKelvey,[38] 1968	20; 76 (60 both surgical and closed)	Prothrombin activity rate, 30% or less; mean, 20.3% [INR, ≥2.5; mean INR, 3.0]	. . .	None
Wood and Deeble,[39] 1993	2; 7 (7)	INR, 2.3-2.9 preoperatively; INR, 4.3-9.1 postoperatively	Sutures and oxidized regenerated cellulose (Surgicel)	2 patients: after bleeding was controlled by local measures, 1 patient (preoperative INR, 2.3) bled 2 days after extraction when his INR was 4.3, possibly from interaction with concomitant erythromycin; given fresh-frozen plasma and blood. In the second patient (preoperative INR was 2.9 for 6 extractions), no bleeding problem existed until 1 wk later (oozing from 1 socket) when INR was 9.1; given fresh-frozen plasma, blood, and vitamin K
Yoshimura et al,[40] 1987	13; 20 (20)	PT ratio, 1.05-2.1	Alveolar sockets were sutured and generally packed with Oxycel or Oxycel and thrombin	None
Ziffer et al,[41] 1957 and Scopp and Fredrics,[42] 1958	2; 3 (3)	PT ratio, 2.35-2.8	Gelfoam placed	2 patients (PT ratio, 2.8 for 1 patient; PT ratio, 2.35 and 2.4 for other patient): vitamin K administered
Zusman et al,[43] 1992	23; 61 (61)	PT, 50%-19% [INR, <2.0 to 3.2]	Fibrin sealant used	None
Total	>774; >2014 (>1964)	. . .	. . .	12 patients (3 of whose PT ratios or INRs were within or below the therapeutic range) had more than local measures to control hemostasis

**Nonsurgical dental procedures are not included. PT indicates prothrombin time; INR, international normalized ratio; and ellipses, no special methods.*
†Conversion to INR from other monitoring methods is given in brackets. Because international sensitivity indexes were not given, the author converted other monitoring methods to a range of INRs.[16-18]

DENTAL TREATMENT IN PATIENTS DURING WITHDRAWAL OF CONTINUOUS ANTICOAGULATION

Many practitioners believe that there is minimal risk of thromboembolism in patients whose anticoagulant therapy is interrupted for surgery.[48] Warfarin withdrawal may[49] or may not[50] create a transient hypercoagulable state, but if warfarin prevents thromboembolism, then withdrawal of warfarin does not prevent thromboembolism. There have been several documented cases of serious embolic complications, including deaths, after withdrawing continuous warfarin therapy. Cosgriff[51] reported that embolisms occurred in 14 of 17 patients (71% of cases) whose warfarin therapy was withdrawn. Three of these embolisms occurred within 5 days of the interruption of therapy.

Table 2. Reported Cases of Withdrawal of Continuous Oral Anticoagulation for Dental Procedures*

Source, y	No. of Patients; No. of Cessations for Dental Extractions (Time of Cessations)	Complications
Akbarian et al,[52] 1968	1; 1 (not reported)	1 fatal embolism
Anavi et al,[19] 1981	15; 36 (until prothrombin time level was 50%-60%)	None
Behrman and Wright,[22] 1961	1; 1 (not reported)	1 fatal massive cerebral thrombosis 17 d after discontinuing warfarin sodium
Borea et al,[23] 1993 (control)	15; 15 (not reported)	None
Davis and Sczupak,[53] 1979	28; 28? (up to 2 wk) for "dental or surgical procedures"	None
Marshall,[54] 1963	1; 1 (9 d)	Fatal myocardial infarction 19 d after interruption of therapy of 9 d duration
Mulligan,[55] 1987	17; 44 (2-7 d) for dental treatment and for other reasons	None
Ogiuchi et al,[56] 1985	128; 128 (warfarin dose decreased 3-7 days preoperatively, then discontinued the day of the procedure and restarted afterward)	1 fatal cerebral thromboembolism 5 d postoperatively
Saour et al,[57] 1994	240; 240 (2 d or until INR ≤1.5)	None
Sheller and Tong,[58] 1994	1; 1 (2 d)	None
Street and Leung,[35] 1990	2; 2 (not reported)	None
Tulloch and Wright,[37] 1954	12; 13 (4 d in most cases)	1 patient whose therapy was withdrawn for 8 d developed cerebral and brachial nonfatal emboli
Wood and Conn,[59] 1954	5; 5 (7-37 d) for "dental extraction or surgical procedure"	None
Yoshimura et al,[40] 1987	3; 3 (1 withdrawn for 2 d; 2 withdrawn for 1 d before procedure)	None
Ziffer et al,[41] 1957	1; 1 (9 d)	None
Zusman et al,[60] 1993	23; 23 (3-5 d?)	None
Total	**493**; **542**	4 deaths; 1 patient had 2 nonfatal embolisms

**Patients receiving heparin replacement are not included. INR indicates international normalized ratio.*

In 542 documented cases in 493 patients of withdrawing continuous anticoagulation specifically for dental procedures, 5 (1.0% of patients; 0.9% of cases) had serious embolic complications (including 4 deaths). **Table 2** presents the reported cases of withdrawal of continuous oral anticoagulation for dental procedures (patients receiving heparin replacement are not included).

Unfortunately, there are several documented cases of serious embolic complications in patients whose warfarin therapy has been withdrawn for dental treatment.

There are limitations in comparing the results of dental surgery in patients receiving continuous anticoagulant therapy with those of patients whose anticoagulation treatment is withdrawn. There was not necessarily a direct cause-and-effect relationship between the embolic complications and the withdrawal of warfarin therapy for dental treatment since these complications sometimes occur even if the patient continues warfarin therapy. On the other hand, some of the bleeding complications in patients who continued warfarin therapy for dental surgery may have also been coincidental since patients who have normal coagulation sometimes have postoperative bleeding.

Several studies have confirmed that warfarin therapy should not be interrupted for nonsurgical dental procedures.[5,11,57,61] On the other hand, a single dental extraction has been called "a significant stress to the hemostatic mechanisms."[62] Some recommend that anticoagulation therapy be reduced or withdrawn until PT or INR is near normal (PT within 1.5 times control)[63,64] or even normal[65] before dental surgery.

At a minimum, the application of pressure is required immediately after dental extractions, especially in patients receiving anticoagulant therapy. But dental extractions are different from other types of surgery: major vessels are unlikely to be encountered, and postoperative bleeding is usually controlled within minutes by application of pressure (biting on gauze) or, if necessary, additional local measures such as biting on tea bags (which contain tannic acid) or using gelatin sponges, topical thrombin, additional sutures, and even electrocautery. The American Dental Association has stated that for dental treatment, postoperative bleeding is minimal if the PT is close to (or even slightly above, depending on the international sensitivity index) the therapeutic range (PT up to 2 times the control).[66] Several investigators have stated that postoperative bleeding after dental extractions is minimal at or above present therapeutic PT ratios (PT up to 2.5 times the control).[5,67,68]

Since dental extractions have been called a "significant" or even "severe" challenge to hemostasis, some assume that dental extractions in anticoagulant-treated patients present more bleeding problems than in patients not taking anticoagulants. But even patients with normal coagulation undergoing dental surgery may have postoperative hemorrhage. Several studies have compared postoperative bleeding in anticoagulant-treated patients with that of normally coagulated patients. McIntyre[30] compared postoperative bleeding after dental extractions in 106 anticoagulant-treated patients with that of 106 normally coagulated patients and found no difference in postoperative bleeding. Greenberg et al[26] compared blood loss after dental extractions in 13 patients receiving continuous warfarin anticoagulation with that of 7 control patients. Only 2 anticoagulant-treated pa-

tients had significantly greater blood loss per tooth than the control group (in both cases the bleeding was controlled by local measures). Bailey and Fordyce[20] compared the result of extractions in 25 anticoagulant-treated patients with that of 25 control patients and found no difference in immediate postoperative bleeding. There was more "late bleeding" in the anticoagulated group, which was "easily controlled" by local measures.

Even if practicing physicians and dentists are convinced that there are sound scientific and medical reasons to continue therapeutic levels of warfarin for dental surgery, they may decide to interrupt therapy for fear of a lawsuit after complications from postoperative hemorrhage in a patient whose INR was not lowered to below the therapeutic range before dental surgery. These practitioners are actually treating the doctor rather than the patient. The leading cause of lawsuits against physicians is improper prescribing of medications,[69] which may include altering therapeutic levels of anticoagulants. Although theoretically possible, there are no well-documented cases of serious postoperative bleeding complications after dental surgery in patients receiving anticoagulant therapy within the therapeutic range. If a patient whose preoperative PT ratio or INR was within the therapeutic range were to be hospitalized or even die of postoperative hemorrhage after dental surgery, the defendant can show that many authorities state that there is minimal risk of such hemorrhage during dental procedures within the therapeutic range, while pointing out the risks of thromboembolism if therapy is interrupted. On the other hand, if a patient whose warfarin dosage was reduced or withdrawn below therapeutic levels has serious complications or dies of an embolism, the plaintiff can use these same studies to reject the interruption of therapy. In either case, there are good legal reasons to continue warfarin therapy for dental surgery.

CONCLUSIONS

It is time to stop interrupting warfarin therapy for dental surgery. Although there is a theoretical risk of hemorrhage after dental surgery in patients at therapeutic levels of anticoagulation, the risk is minimal, bleeding is usually easily treated with local measures, and the risk may be greatly outweighed by the risk and morbidity of thromboembolism after withdrawal of anticoagulant therapy. There are no well-documented cases of serious bleeding problems from dental surgery in patients receiving therapeutic levels of continuous warfarin therapy. There are several documented cases of serious embolic complications, including deaths, in patients whose warfarin therapy has been withdrawn for dental treatment. Many authorities state that dental extractions can be performed with minimal risk at or above therapeutic levels of anticoagulation. Patients receiving anticoagulant therapy who undergo dental surgery have not been shown to have more bleeding problems than patients with normal coagulation. There are sound legal reasons to continue therapeutic levels of warfarin for dental treatment. Dentists and physicians should collaborate closely in treating their patients who are taking anticoagulants, especially to make sure that the patient's INR is within the therapeutic range before dental surgery. Good surgical technique and local measures to control bleeding are important in all dental surgical patients, especially those receiving continuous anticoagulation.

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