



Effect of warfarin discontinuation on the incidence of postoperative bleeding in tooth extraction

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Objectives: The number of patients undergoing oral anticoagulant therapy for cardiovascular and cerebrovascular disease is increasing. However, the risk of bleeding after tooth extraction in patients receiving warfarin is unclear. Here, we assess the risk of bleeding after tooth extraction in patients on warfarin.

Materials and Methods: The study included 260 patients taking warfarin who underwent tooth extraction (694 teeth). The patients were divided into those whose teeth were extracted while they were taking warfarin, those who discontinued warfarin before extraction, and those who underwent extraction while receiving heparin bridging therapy. Bleeding complications in the two groups were compared.

Results: Of the 260 patients, 156 underwent extraction while taking warfarin, 70 stopped taking warfarin before extractions, and 34 received heparin bridging therapy and stopped taking either medication before extractions. Bleeding complications occurred in 9 patients (3.5%) and 9 tooth sites (1.3%). Among the 9 patients with bleeding complications, 6 underwent extraction while taking warfarin, 2 stopped warfarin before extraction, and 1 underwent extraction after receiving heparin bridging therapy. No significant difference was seen between patient groups regarding bleeding after extractions ($P=0.917$).

Conclusion: Warfarin use does not increase the risk of post-extraction bleeding and can therefore be continued during tooth extraction.

Key words: Bleeding, Tooth extraction, Warfarin

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I. Introduction

The number of people taking oral anticoagulant therapy for cardiovascular and cerebrovascular disease is increasing worldwide¹. A vitamin K antagonist, warfarin is a commonly used anticoagulant for the treatment and prevention of thromboembolic disease. It prevents blood clotting by inhibiting the synthesis of vitamin K, which is involved in the synthesis of blood coagulant factors II, VII, IX, and X. However, warfarin dosages must be monitored continuously through prothrombin time (PT) and international normalized ratio (INR) tests

as warfarin treatment is associated with an increased risk of bleeding.

Surgical dental treatments that can cause bleeding include periapical, periodontal, and dentoalveolar surgery, as well as extractions. Among these treatments, tooth extractions are performed most often in dental surgery. Like other types of surgeries, in-depth monitoring for bleeding after tooth extraction is necessary for patients on warfarin. Surgeons must consider whether to discontinue warfarin or prescribe an alternate medication before surgery due to the risk of delayed hemostasis after extraction².

Stopping warfarin or substituting it with heparin may increase the risk of other complications, such as thromboembolic diseases³. Considerable research has therefore been undertaken to determine if patients who take warfarin should discontinue use, substitute it for an alternative, or continue warfarin while undergoing an extraction. According to recent reports, local hemostatic methods can be utilized to avoid discontinuing medications such as warfarin (an anticoagulant) or aspirin (acetylsalicylic acid, an antiplatelet agent) in dental treatments, including extractions⁴⁻⁶.

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Currently, clinicians perform extractions while continuing antiplatelet agents such as aspirin. Many dental surgeons are concerned about the possibility of patients bleeding during surgical procedures while they are on warfarin, despite considerable research demonstrating the safety of performing an extraction while continuing warfarin. However, if several teeth need to be extracted and discontinuing warfarin is difficult due to physiological conditions, patients and surgeons should evaluate the risk of bleeding after the extractions.

This study provides a comparative assessment of the effects of dosage controls on bleeding after teeth extractions in patients who are on warfarin.

II. Materials and Methods

Data were collected from the medical records of patients who were administered warfarin and underwent extractions between January 1, 2008, and December 31, 2018 at National Health Insurance Service Ilsan Hospital. Patients were excluded if the specific drug or the duration of administration was not clearly defined in the prescription or they were given warfarin at a different hospital. Only patients who received warfarin at our hospital and were accompanied by a clear record of the prescription were included. Patients were also excluded if they had previously received tumor surgery, radiation therapy in the jaw, or osteomyelitis treatment. A total of 260 patients who satisfied the study conditions were separated into those who had extractions while taking warfarin, those who had extractions after undergoing heparin bridging therapy, and those who had extractions after stopping warfarin a few days beforehand.

1. Extractions

The patients in this study visited the department of oral and maxillofacial surgery in the dental hospital and were taking warfarin. Extractions were performed on patients who first came to our location or were transferred from other departments, such as prosthodontics or periodontics. Panoramic X-rays were taken of the jaws patients who were visiting our hospital for the first time. The medical histories of all patients were assessed, and clinical tests of their main oral problem were performed.

Extractions were performed due to residual roots from previous extractions, incurable severe tooth decay, tooth fractures, severe periodontitis, and pericoronitis. The surgical methods of extraction included the simple extraction of teeth

from the upper or lower jaw under local anesthesia, extractions requiring sutures, and surgical extractions requiring bone resection and root separation. After extraction surgery, no fillers such as bone grafts, collagen, or fibrin were used on the surgical area. Patients took a preventative antibiotic orally 1 hour before extraction. The method of extraction was categorized as a simple extraction or surgical extraction. A simple extraction involved only dental elevators or forceps without the use of a scalpel or bur. This method was mainly used when extracting a tooth that had a whole morphology, as in a case of severe periodontitis or a poor prosthodontic prognosis. Surgical extraction referred to cases in which an osteotomy or odontomy was performed with a fissure bur or when a gum incision was made. This method is commonly used to extract residual roots or impacted teeth. For a simple extraction, a suture was performed if several teeth were extracted or if a primary closure was considered necessary. For sutures, 3-0 black silk (Mersilk 3-0; Ethicon, San Lorenzo, Puerto Rico) was used. For anesthesia before the extraction, lidocaine/epinephrine (1:80,000) 2% local anesthesia (infiltration or inferior alveolar nerve anesthesia) was administered. After extraction, each patient bit down on gauze, and after checking that bleeding had stopped after a few minutes, returned home.

2. Assessment of bleeding after tooth extraction

The reasons patients were taking warfarin included atrial fibrillation, aortic valve replacement, mitral valve replacement, and cerebellar infarction. Medication was prescribed by the cardiothoracic department, neurology department, hematology-oncology department, or the department of thoracic surgery in our hospital or another hospital.

All PT and INR blood test results were checked prior to the extraction. The most recent PT (sec; closest to the date of the extraction) and INR value obtained from a different department were identified. A joint clinical discussion regarding potential warfarin discontinuation was carried out before each extraction by staff of the department that prescribed the warfarin. Depending on the recommendation from the respective departments, warfarin was either discontinued or maintained. If stopping warfarin was impossible, the patient was hospitalized for heparinization bridging therapy before the extraction.

All patients were instructed to take preventative antibiotics before extractions. All patients were also instructed to take pain medications before and after the procedure for a minimum of 3 days and a maximum of 7 days.

For patients who experienced additional bleeding after an extraction, hemostasis was facilitated through gauze pressure or biting down on gauze in the socket. If the bleeding continued, spongostan (an absorbable hemostatic gelatin sponge) was placed in the socket or tranexamic acid was applied to the gauze to promote hemostasis.

3. Statistical methods

A χ^2 test was used to determine the difference in the number of patients who bled after an extraction and continued to take warfarin, stopped warfarin, or underwent heparinization.

Differences in INR and PT values and warfarin dosages between members of the group that continued to take warfarin, those that stopped warfarin, and those who underwent heparinization were tested using ANOVA. Differences in the number of patients who bled after simple extractions and those who bled after surgical extractions were tested using the χ^2 test. Statistical analysis was performed using IBM SPSS Statistics (ver. 23; IBM, Armonk, NY, USA). Significance was set at $P \leq 0.05$.

III. Results

A total of 260 patients were investigated. There were fewer females (n=110) than males (n=150). The mean age was 68.0±11.0 years with standard deviation.

One-hundred and fifty-six patients underwent extractions while continuing on warfarin. Seventy patients underwent extractions after stopping warfarin, and 34 replaced warfarin with heparin during heparin bridging therapy and stopped taking both before the extraction.

A total of 694 teeth were extracted from the 260 patients, with 389 teeth extracted from the upper jaw and 305 from the bottom jaw. In all, 168 anterior teeth, 243 canines and premolars, and 283 molars were extracted. Seventy-two extractions were performed with bone resections.

Post-extraction bleeding complications occurred in 9 (3.5%) of the 260 patients and involved 9 (1.3%) of the 694 teeth extracted. (Tables 1, 2)

Of the 156 patients who underwent extractions while on warfarin, 6 experienced bleeding complications. Among the 70 patients who underwent extractions after stopping warfarin, 2 experienced bleeding complications. Of the 34 patients who underwent extractions after receiving heparin bridging therapy, 1 experienced a bleeding complication. There was

Table 1. Characteristics and incidence of post-extraction bleeding according to the preoperative control of warfarin

Variable	Groups according to preoperative control of warfarin (n=260)			P-value
	Warfarin continuation (n=156)	Warfarin discontinuation (n=70)	Heparinization (n=34)	
Sex (male:female)	91:65	44:26	15:19	0.187
Age (yr)	69.7±10.2	67.0±11.4	62.5±12.2	0.001*
International normalized ratio	2.19±0.55	1.93±0.58	1.72±0.55	<0.001*
Post-extraction bleeding patient	6 (3.85)	2 (2.86)	1 (2.94)	0.917
Daily dosage of warfarin (mg)	3.05±1.33	3.27±1.55	3.82±1.37	0.015*
Surgical extraction with osteotomy	30	12	5	0.802

* $P < 0.05$.

Values are presented as number only, mean±standard deviation, or number (%).

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Table 2. Characteristics of tooth extraction according to the preoperative control method of warfarin

Variable	No. of tooth extractions according to control of warfarin (n=694) (post-extraction bleeding case)		
	Warfarin continuation (n=414)	Warfarin discontinuation (n=175)	Heparinization (n=105)
Maxilla (n=389)			
Anterior:Premolar:Molar=sum	57:79 (1):83 (3)=219 (4)	19 (1):51:38 (1)=108 (2)	14:23:25 (1)=62 (1)
Sim:Sim+Suture:Surgical=sum	119 (1):85 (1):15 (2)=219 (4)	68 (1):35 (1):5=108 (2)	34 (1):25:3=62 (1)
Mandible (n=305)			
Anterior:Premolar:Molar=sum	57:66 (1):72 (1)=195 (2)	12:18:37=67 (0)	9:6:28=43 (0)
Sim:Sim+Suture:Surgical=sum	83 (2):75:37=195 (2)	42:16:9=67 (0)	24:16:3=43 (0)

(Anterior: central and lateral incisor, Premolar: canine and first and second premolar, Molar: first to third molar, Sim: simple extraction without primary closure, Sim+Suture: simple extraction with primary closure, Surgical: surgical extraction with/without osteotomy)

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no significant difference between the groups regarding the number of patients who experienced bleeding after extraction ($P=0.917$).

The mean PT value of the 70 patients who stopped taking warfarin before the extraction was 21.0 ± 6.38 . The mean PT value of the 34 patients who received heparin bridging therapy and stopped both medications before the extraction was 19.2 ± 5.80 . The mean PT value of the 156 patients who continued taking warfarin during the extraction was high, at 24.2 ± 6.39 . The difference in PT values between the groups was significant ($P<0.001$).

The mean INR of the 70 patients who stopped warfarin before extraction was 1.93 ± 0.58 . The mean INR of the 34 patients who received heparin bridging therapy and stopped both medications before extraction was 1.72 ± 0.55 . The mean INR of the 156 patients who continued taking warfarin during extraction was high, at 2.19 ± 0.55 . The difference in INR values between the groups was significant ($P<0.001$).

The daily dose of warfarin for the 156 patients who continued taking warfarin during the extraction was 3.05 ± 1.33 mg. The daily dose of warfarin for the 70 patients who stopped warfarin before the extraction was 3.27 ± 1.55 mg. The daily dose of warfarin for the 34 patients who received heparin bridging therapy and stopped both medications before extraction was 3.82 ± 1.37 mg. A significant difference was evident in the daily doses of warfarin between the heparin bridging therapy group and the group that continued warfarin ($P=0.015$).

The age of the 156 patients who continued warfarin while undergoing an extraction was 69.7 ± 10.2 years. The age of the 70 patients who stopped warfarin before extraction was 67.0 ± 11.4 years. The age of the 34 patients who received heparin bridging therapy and stopped both medications before extraction was 62.5 ± 12.2 years. A significant difference was found between the group that received heparin bridging therapy and the group that continued warfarin ($P=0.001$).

Of the 46 patients who underwent extractions with bone resections, 2 experienced bleeding complications. The mean INR of the 9 patients who experienced bleeding complications was 2.34 ± 0.90 . Three patients had an INR value below 2.2.

IV. Discussion

We found no significant difference in the number of patients who experienced bleeding after extractions among the groups that continued warfarin, stopped warfarin, and under-

went heparin bridging therapy. Bleeding complications after the extractions occurred in 9 (3.5%) of a total of 260 patients, and involved 9 extracted teeth (1.3%) out of a total of 694.

Yoshikawa et al.⁷, in their comparative study of direct oral anticoagulants (DOAC) and warfarin, reported no difference in bleeding after tooth extraction between the two groups. In that study, bleeding complications occurred in 23 (8.8%) of 262 patients who were taking warfarin. This is different from the results of our study, in which post-extraction bleeding complications occurred in 9 patients (3.5%) out of a total of 260. Yagyuu et al.⁸ also conducted a comparative study on post-extraction bleeding while continuing vitamin K antagonists such as a DOAC and warfarin. They reported finding no difference in bleeding between the two groups and that bleeding complications occurred in 12 (12.0%) of 100 extractions. This differs from the results of our study, in which post-extraction bleeding complications occurred in 9 teeth (1.3%), even with a total of 694 extracted teeth.

Moreover, in a study of post-extraction bleeding in healthy patients who did not take warfarin, Rocha et al.⁹ found that 3 (4.3%) of 66 patients who underwent extractions while taking vitamin K antagonists experienced post-surgical bleeding complications and 2 (2.9%) out of 67 patients who were not taking anticoagulants suffered post-surgical bleeding complications. No statistically significant differences in the rates of post-extraction bleeding were found between the two groups, which is similar to the 3.5% rate of post-extraction bleeding found in our study. Similarly, the limited number of bleeding complications may be related to differences in the surgical methods of extraction. Our hospital's practice of returning patients home after checking for bleeding cessation following an extraction may have contributed to the reduction in reported bleeding complications. Svensson et al.⁶ found that, when using absorbent local hemostatic agents such as gelatin sponges or collagen fleece, bleeding complications after extractions occurred in 5 (4.0%) out of 124 patients who were taking warfarin. Considering these findings, post-extraction bleeding complications in patients taking warfarin may be reduced when using less-traumatic extraction methods, hemostatic materials, and hemostatic methods.

Comparing the three groups in our study, 6 patients (3.9%) out of the 156 who continued warfarin experienced post-extraction bleeding complications. Two patients (2.9%) of the 70 who stopped taking warfarin, and one (2.9%) of the 34 in the heparin bridging therapy group experienced post-extraction bleeding complications. The absence of any statistically significant difference between the groups indicates

that bleeding after extraction was no more likely when taking warfarin than after stopping warfarin or undergoing heparin bridging therapy. In a study by Bajkin et al.², 8 (7.3%) of 109 patients who continued oral anticoagulant therapy experienced post-extraction bleeding complications, while 5 (4.7%) of the 105 patients who switched to heparin experienced post-extraction bleeding complications, but the difference was not statistically significant. Considering these findings and those of our study, heparin bridging therapy may not reduce post-extraction bleeding complications.

Multiple studies have reported no statistically significant differences in the rate of post-extraction bleeding between the patients who continued warfarin and those who stopped taking warfarin, which is similar to our findings^{10,11}. Although a large-scale prospective clinical research study may be necessary, even a meta-analysis on continuing oral anticoagulant therapy during extraction concluded that it did not increase post-extraction bleeding complications¹².

Reports have examined the pre-extraction INR values of patients and the likelihood of post-extraction bleeding^{5,10,11}. Most recent studies report no correlation between post-extraction bleeding and INR values, and the risk of bleeding when warfarin is continued in patients with INR values at 4.1 or lower¹⁰, 4 or lower² and 3 or lower¹¹ were not significantly different from the risk in those who stopped taking warfarin. According to Bajkin et al.⁵, extensive surgical methods are feasible if local hemostatic measures are applied without changing medications, even in patients with high INR values (between 3.5 and 4.2).

In our study, the mean INR of the 9 patients who experienced post-extraction bleeding complications was 2.34. The mean INR of the group that underwent extraction while continuing to take warfarin was 2.19. The mean INR for the 6 patients who experienced post-extraction bleeding was lower, at 2.08. However, the mean INR for the group that stopped warfarin before extraction was 1.93. Among those, the mean INR of the 2 patients who had bleeding complications was relatively high, at 3.07. However, one of the two people had a relatively high INR value of 4.49, which increased the mean value. Three patients out of the 9 who had post-extraction bleeding complications had an INR value of 2 or lower, with a mean of 1.56. The relationship between the INR value and post-extraction bleeding complications is therefore weak. Considering that bleeding stopped with local hemostatic treatments when post-extraction bleeding complications occurred, local treatments can be important for reducing bleeding complication risks. Blood coagulations, such as INR,

must be monitored in patients who take warfarin. According to Scully and Wolff³, the therapeutic level of INR values for treatment in patients who take anticoagulants is between 2 and 3.5. As the rate of post-extraction bleeding complications in our study was small, the INR value must be considered when performing extractions.

Research has reported that the interaction between warfarin and ibuprofen (medications in the nonsteroidal anti-inflammatory drug class) increases the likelihood of bleeding¹⁴. Therefore, post-extraction bleeding complications may increase in patients who take warfarin and short-term ibuprofen. Additional research on the effects drug interactions may have on bleeding complications is needed.

A total of 694 teeth were extracted across the three groups. The sockets of 7 (1 anterior, 1 premolar, and 5 molar) of the 389 teeth extracted from the upper jaw and 2 (1 premolar and 1 molar) of the 305 teeth from the lower jaw bled. Research by Febbo et al.¹⁵ found a higher likelihood of bleeding in the lower jaw compared with the upper jaw, and in cases of multiple extractions compared with single extractions in those who take warfarin. Research by Svensson et al.⁶ produced results similar to those of our study, with a higher likelihood of post-extraction bleeding in the upper jaw.

In terms of the difficulty of extraction, 2 of the 46 patients who underwent extractions with bone resections experienced bleeding complications. A higher likelihood of post-extraction bleeding has been reported in those with bone resections compared with simple extractions in patients on warfarin^{1,6}. However, according to Bajkin et al.⁵, extensive surgical treatment is possible if local hemostatic measures are taken appropriately, even without switching or stopping warfarin, when the INR value is high (3.5 to 4.2). Considering that 5 cases of post-extraction bleeding complications occurred after simple extractions in our study, it is difficult to conclude that the number of bleeding complications increases with the difficulty of surgery. Performing local hemostatic treatment may be helpful in patients who take warfarin. As only two cases of bleeding complications occurred in the 252 extractions in which sutures were placed after simple extractions, performing a primary closure even on simple extractions may be recommended.

Our study investigated post-extraction bleeding in patients who took warfarin for a variety of illnesses. The warfarin dosage, INR value, and area of extraction were examined for each patient. The duration over which warfarin was discontinued before the extraction was determined by the primary physician who prescribed the medication. Many cases of

continuing warfarin occurred in older patients, likely because they had physiological conditions that made it difficult to discontinue warfarin. The length of time that warfarin should be discontinued before extraction may vary according to co-diagnoses and the prescribing physician, as definitive evidence may be lacking. The rate of postoperative bleeding may also decrease as extraction techniques and hemostatic materials and methods improve. Previous findings and those of this study suggest that any decision to discontinue warfarin before extraction must be considered carefully.

Our research, a detailed and practical investigation into the risk of post-extraction bleeding depending on the area of extraction, differences in extractions, and simple versus surgical extractions, found no significant difference in the likelihood of post-extraction bleeding for a patient continuing warfarin compared with stopping or replacing the drug. However, the study was limited by the low mean INR value of the patients who took warfarin (2.06), and evaluation of post-extraction bleeding in patients who take warfarin with a high INR value may be lacking. Results from a multi-site study with a larger sample size may be necessary to support these results. Moreover, if the test for PT and INR could be performed immediately before extraction, more accurate INR values could be obtained.

V. Conclusion

The results of the present and similar studies indicate that continuing to take warfarin when undergoing tooth extraction does not increase the likelihood of post-extraction bleeding compared with stopping warfarin or undergoing heparin bridging therapy. Even if multiple extractions are performed on the same patient, bleeding complications occurred in only one area. This suggests that, while the physiological condition of the patients must be considered, local treatment of the extraction area may be an important factor. Recently, the number of cases in which extraction surgery has been performed without discontinuing warfarin due to the severity of the patient's physiological condition has been increasing.

To prevent postoperative bleeding when extracting teeth from a patient taking warfarin, the surgeon must perform an atraumatic surgical procedure, consider using a suture or local hemostatic agent on the extraction site, and evaluate the bleeding tendency during the extraction.

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Authors' Contributions

J.S.L. and S.H.K. obtained data and wrote the manuscript. S.H.K., J.S.L., and M.K.K. drafted the manuscript. S.H.K. and M.K.K. participated in article design and coordination and carefully reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Ethics Approval and Consent to Participate

This retrospective study was approved by the institutional review board of the National Health Insurance Service Hospital (NHIMC 2019-01-038). Because of the retrospective nature of this study, which did not use identifying personal information, the hospital's institutional review board waived the requirement for written informed consent from the study subjects.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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