Incidence of Complications in Dental Procedures for Patients on Antithrombotic Therapy: A Single-Institution and National Cohort Study

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Incidence of Complications in Dental Procedures for Patients on Antithrombotic Therapy: A Single-Institution and National Cohort Study

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ABSTRACT

Incidence of Complications in Dental Procedures for Patients on Antithrombotic Therapy: A Single-Institution and National Cohort Study

Introduction

Cardiovascular disease (CVD) is a major cause of death worldwide, and antithrombotic agents such as antiplatelet agents (e.g., aspirin, clopidogrel) and anticoagulants (e.g., warfarin, Direct Oral Anticoagulant [DOACs]) are used in its treatment. Although antithrombotic agents play an important role in preventing thrombosis in patients with CVD, there is a risk of bleeding after dental treatment. Recent studies have recommended continuing antithrombotic agents for patients undergoing dental treatments with a low risk of bleeding, but little is known about dental and systemic complications after invasive dental treatments such as periodontal and implant surgeries.

The aims of this study were (1) to collect factors affecting postoperative bleeding after dental treatment from a single-institution clinical data through the electronic medical records of the Yonsei University Health System, (2) to collect factors affecting systemic complications through the National Health Insurance Service sample cohort database, and (3) to evaluate the effect of antithrombotic agents on postoperative bleeding and systemic complications after dental treatment in patients taking antithrombotic agents using the two datasets.

Body

1) From 2015 to 2019, a total of 1,878 cases were diagnosed with CVD at Severance Hospital and received dental treatment at Yonsei University Dental Hospital. The factors affecting postoperative bleeding were hypertension, diabetes, heart valve surgery, and medications. The results of multivariable logistic regression analysis showed that the odds of postoperative bleeding occurrence were 5.882-fold higher in patients with hypertension. As compared with those not receiving medication, the odds of postoperative bleeding were 3.280-fold higher in patients taking warfarin, and 9.837-fold higher among patients using heparin bridging. The odds of postoperative bleeding were 3.114-fold higher in patients taking DOACs, 2.966-fold higher in those taking single antiplatelet agents, and 2.425-fold higher among patients receiving dual antiplatelet agents. In the case of dental treatment, tooth extraction and implant-related surgery (with bone grafting) affected the odds of postoperative bleeding, and patients in whom four or more teeth were treated had a 7.706-fold higher odds ratio (OR) of postoperative bleeding than patients in whom one tooth was treated.

2) From 2015 to 2019, a total of 714,397 cases were diagnosed with CVD and received dental treatment. Factors affecting systemic complications included sex, age, comorbidities, CVD surgery, medications, and dental treatment. Females had a 1.187-fold higher OR of systemic bleeding than males did. There was an increase in the odds of systemic bleeding and thromboembolic complications with increasing age, and the odds of systemic bleeding were 1.325- and 1.344-fold higher among patients with hypertension and diabetes, respectively. The odds of thromboembolic complications decreased by 0.458-fold in patients who received stent insertion, but the odds of systemic bleeding and thromboembolic complications were 5.688- and 11.204-fold higher in those who received thrombolysis, respectively. Compared with patients who

did not take medication, those receiving both anticoagulants and antiplatelet agents had a higher OR of systemic bleeding and thromboembolic complications. In terms of dental treatment, patients undergoing tooth extraction had a higher odds of systemic bleeding, but those receiving simple extraction and bone grafting had a higher odds of thromboembolic complications.

Conclusion

Patients who took anticoagulants and antiplatelet agents had a higher odds of postoperative bleeding and systemic complications after dental treatment than patients not taking the medications did. In addition, hypertension, tooth extraction, implant surgery with bone grafting, and four or more treated teeth were associated with the odds of postoperative bleeding or systemic complications. Therefore, it is suggested that care be taken to minimize the occurrence of bleeding and complications in patients with these risk factors.

Key Words: Cardiovascular Diseases; Antithrombotic Agents; Anticoagulants; Antiplatelet Agents; Dental Care; Electronic Medical Records; National Health Insurance

1. INTRODUCTION

Cardiovascular disease (CVD) is a group of disorders of the heart and blood vessels.[1,2] These disorders include coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, heart attacks, and stroke. CVD also includes preceding diseases such as hypertension, diabetes, and dyslipidemia. CVD is one of the major causes of death worldwide, and the mortality rate of CVD in Korea is 15.8%.[3] Heart disease ranks second among the causes of death due to CVD, followed by cerebrovascular disease, diabetes, and hypertension, which account for a large proportion of the total causes of death.[3,4]

The use of antithrombotic agents has steadily increased alongside the rise of CVD frequency. Antiplatelet agents and anticoagulants are commonly used in patients with CVD and risk of thromboembolism, and antithrombotic agents should be used appropriately to prevent thrombosis in these patients.[5] Representative antithrombotic agents include antiplatelet agents such as aspirin and clopidogrel and anticoagulants such as warfarin.

Antiplatelet agents commonly used for the primary and secondary prevention of CVD include acetylsalicylic acid (aspirin), clopidogrel, prasugrel, and ticagrelor.[6] Antiplatelet agents prevent the formation of clots by inhibiting blood platelet aggregation. Antiplatelet agents are used as single antiplatelet therapy (SAPT), and in patients undergoing angioplasty and stent implantation, dual antiplatelet therapy (DAPT) is mainly used.[7] If antiplatelet therapy is discontinued within 1 year after stent implantation, there is a risk of stent thrombosis, and in such cases, the risk of death is approximately 40%.[8]

Anticoagulants inhibit blood clotting and prevent thrombus formation.[9] Recently developed direct oral anticoagulants (DOACs) include dabigatran, apixaban, rivaroxaban, and edoxaban.[10] These agents are primarily prescribed for the prevention of thromboembolism or in patients with atrial fibrillation, and careful dose adjustment is essential to minimize bleeding-related side effects.[11]

Many studies have reported on the risk of bleeding after dental treatment in patients taking anticoagulants.[12] Because patients receiving anticoagulant therapy may have an increased risk of bleeding after dental procedures, it is important to consider whether to discontinue medications before treatment. Previous studies have recommended the temporary reduction or discontinuation of antithrombotic agents before dental treatment.[13,14] However, recent studies have reported that antiplatelet agents and warfarin (with an international normalized ratio [INR] <3.5) do not significantly increase the risk of bleeding in patients undergoing general dental procedures or simple tooth extractions, allowing treatment to proceed without discontinuing antithrombotic agents when the risk of bleeding is low.[15-17]

Only limited information is available regarding postoperative bleeding and systemic complications based on the bleeding risk associated with medications and dental treatments. Recent studies have shown that the incidence of bleeding after a dental procedure is similar between patients taking warfarin and those taking dabigatran or apixaban.[18,19] However, these studies did not specify the types of dental procedures performed, the invasiveness of the treatments, or whether the medications were temporarily discontinued before the dental procedures.[20] In addition, researchers have reported that there is no need to discontinue medications before minor surgical procedures (such as simple tooth extractions)[21,22]; however, most reports were based

on extractions, and data on complications following periodontal surgery and implant surgery remain limited. Thus, there remains a need for guidelines on bleeding management before dental procedures in patients on antithrombotic therapy.

In addition, in patients receiving SAPT, the annual incidence of nonmotor bleeding has been reported to be between 0.2% and 3.2%, and the annual incidence of intracranial hemorrhage has been reported to be between 0.02% and 0.47%.[23-25] In patients taking warfarin, the annual incidence of intracranial hemorrhage has generally been between 0.3% and 0.6%,[26,27] but there is a lack of information for DOACs, which have become more common in recent years.[28] Therefore, sufficient numbers of patients are needed to compare systemic complications according to antithrombotic agents.

In this study, we aim to analyze the factors affecting the occurrence of dental and systemic complications in patients taking antithrombotic agents. (1) We aimed to collect factors affecting postoperative bleeding from the single-institution clinical data of the Yonsei University Health System through the electronic medical record (EMR). Although single-institution data offer accuracy in clinical records and detailed information, their representativeness is limited. (2) We aimed to collect factors affecting systemic complications from the National Health Insurance Service sample cohort (NHIS-NSC) database, which is representative of the entire population. Although data from the NHIS-NSC provide broad population coverage, they do not include specific clinical information from each hospital's EMR, accurate diagnoses, or actual prescriptions and are limited to reimbursement. (3) Using the two databases, we aimed to evaluate the risk of postoperative bleeding and systemic complications after dental treatment in patients taking antithrombotic agents.

2. MATERIALS AND METHODS

2.1. Retrospective Single-Institution Study

2.1.1. Ethical considerations

The study protocol was approved by the Institutional Review Board of the Yonsei University Dental Hospital (IRB No. 2-2023-0067). Patient data were anonymized, and the requirement for written informed consent was waived due to the retrospective nature of the study. This study was conducted following the principles of the Declaration of Helsinki.

2.1.2. Data source

This retrospective study used the Severance Clinical Research Analysis Portal (SCRAP 2.0) at Yonsei University Health System. SCRAP 2.0 is a clinical data system that can search information from EMR and order communication systems and can extract data such as diagnosis, surgery, pathology results, imaging tests, prescriptions, clinical observations, and diagnostic tests.

2.1.3 Inclusion/exclusion criteria

This study included patients diagnosed with CVD between January 2015 and December 2019. The study registration date was defined as the date of the initial CVD diagnosis among all diagnostic dates during this period. The CVD diagnosis code was defined as the main and secondary disease claimed based on the *International Standard Classification of Diseases*, 10th Revision (ICD-10) (Table 1).

Table 1. Codes and definitions of the CVD characteristics

Type of CVD	Definition	ICD-10 code
Heart valve disease (HVD)	*Valve disease or disorders*	I05-08, I34-37
Ischemic heart disease (IHD)	*Angina pectoris, myocardial infarction, or other ischemic heart diseases*	I21-25
Stroke	*Hemorrhage, cerebral infarction, or cerebral ischemic attack*	I60, 61, 63, 64, 69, G45.8, G45.9
Peripheral artery disease (PAD)	*Aortic aneurysm and dissection or arterial embolism and thrombosis*	I71, I74
Atrial fibrillation (AF)	*Atrial fibrillation and flutter*	I48
Heart failure (HF)	*Heart failure or heart failure with disease*	I50, 11.0, 13.0, 13.2

CVD, cardiovascular disease; ICD-10, International Standard Classification of Diseases, 10th Revision.

The inclusion criteria were (1) adults older than 30 years and (2) patients with a history of dental treatment after being diagnosed with CVD. Exclusion criteria were (1) patients who died within 1 year of diagnosis; (2) patients with hemophilia, coagulopathy, or liver and kidney dysfunction such as cirrhosis and chronic renal failure; and (3) patients who were prescribed both antiplatelet agents and anticoagulants 6 months prior to dental treatment. In addition, patients were excluded if they underwent two or more dental treatments on the same date (including conservative treatment, periodontal treatment, tooth extraction, and implant-related surgery), had an interval of less than two weeks between dental treatments, or had inaccurate EMR data (Figure 1).

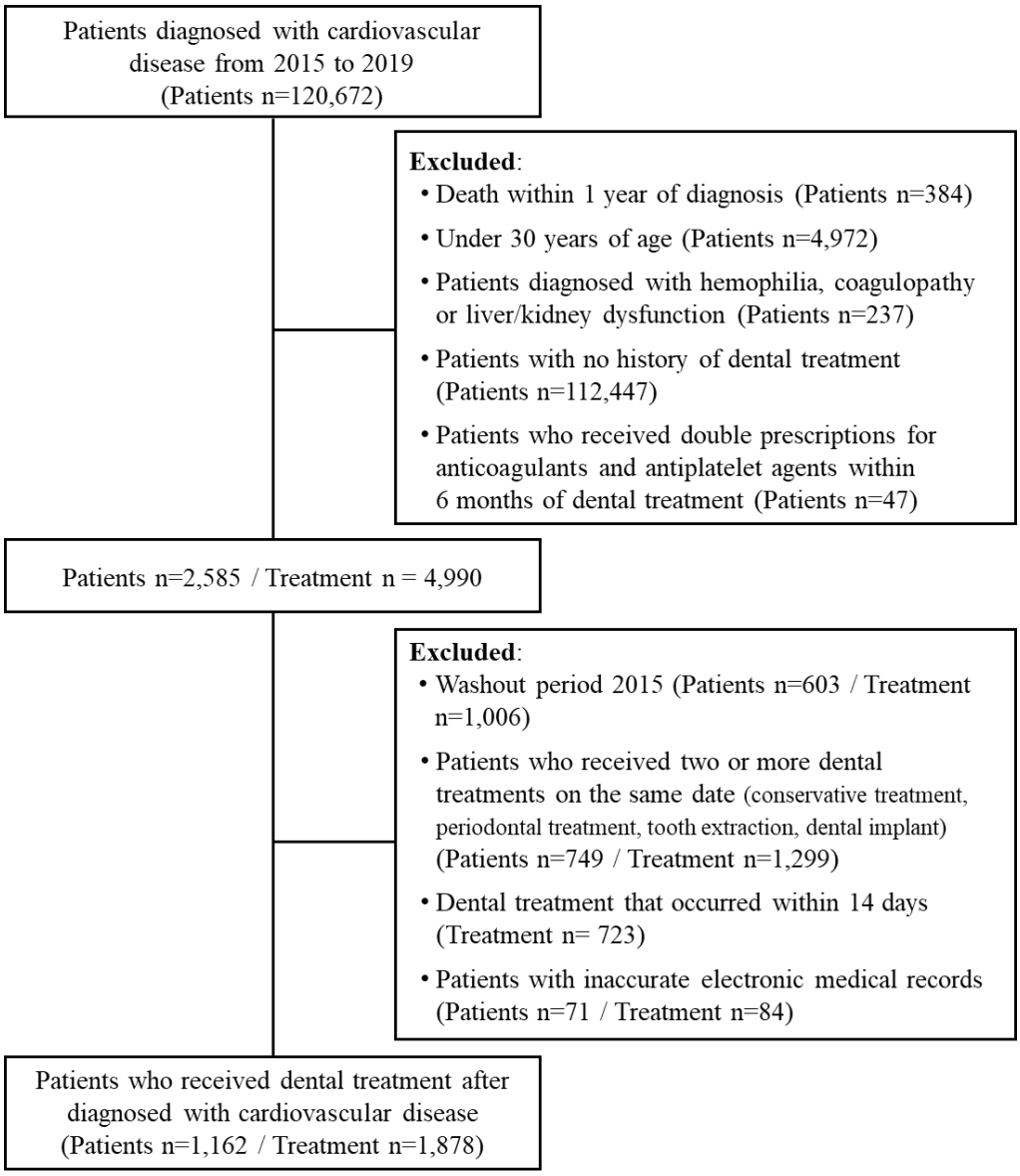

Figure 1. Flowchart of a single-institution, Severance Hospital and Yonsei University Dental Hospital, using SCRAP 2.0

2.1.4 Independent variable

The variables used in this study were categorized into demographic characteristics, medical characteristics, medication characteristics, and dental characteristics.

2.1.4.1 Demographic information

Demographic characteristics included sex and age. Age was grouped into 10-year increments: 30– 39, 40–49, 50–59, 60–69, and ≥70 years.

2.1.4.2 Medical information

Medical characteristics used the procedure codes for stent insertion, coronary artery bypass grafting (CABG), thrombolysis, and heart valve surgery that occurred between the initial diagnosis of CVD and dental treatment (Table 2). Comorbidities were classified based on ICD-10 diagnostic codes for hypertension, diabetes, and dyslipidemia diagnosed between the initial CVD diagnosis and dental treatment.

Table 2. Codes and definitions of the type of CVD surgery and comorbidities characteristics

Type of CVD surgery	Definition	Procedure codes
Stent insertion	*Stent insertion that occurred between the CVD diagnosis and dental treatment*	M6561-6567, M6601-6605, M6611-6613
Coronary artery bypass grafting (CABG)	*CABG that occurred between CVD diagnosis and dental treatment*	O0161-0176, O1640-1649, OA640, OA641, OA647-649
Thrombolysis	*Thrombolysis that occurred between the CVD diagnosis and dental treatment*	M6630, M6632, M6634-6639
Heart valve surgery	*Heart valve surgery that occurred between the CVD diagnosis and dental treatment*	M6531-6533, O1781-1783, O1791-1793
Type of comorbidities	**Definition**	**ICD-10 code**
Hypertension (HTN)	*HTN between the diagnosis of CVD and dental treatment*	I11-13, I15
Diabetes mellitus (DM)	*DM between the diagnosis of CVD and dental treatment*	E10-14
Dyslipidemia	*Dyslipidemia between the diagnosis of CVD and dental treatment*	E78.0-78.5

CVD, cardiovascular disease; ICD-10, International Standard Classification of Diseases, 10th Revision.

2.1.4.3 Medication information

Medication characteristics for anticoagulants and antiplatelet agents prescribed at Severance Hospital within six months prior to dental treatment were investigated. Anticoagulants were classified as warfarin and the DOACs dabigatran, rivaroxaban, apixaban, and edoxaban; antiplatelet agents were defined as cyclooxygenase (COX) inhibitors, phosphodiesterase (PDE) inhibitors, adenosine diphosphate (ADP) inhibitors, 5HT2R antagonists, and DAPT using aspirin and clopidogrel. Patients who were not prescribed antithrombotic agents 6 months before dental treatment were classified as the group. Table 3 shows the list of the main ingredient codes of the drugs. In addition, for patients prescribed antithrombotic agents, we investigated the presence or absence of drug discontinuation and the date of drug discontinuation based on the consultation records to calculate whether the drug was discontinued and, if so, the date on which it was discontinued prior to dental treatment.

Table 3. Codes and definitions of the antithrombotic agent characteristics

Type of antithrombotic agent		Definition	ATC code
Anticoagulant	Warfarin	*Defined from the filled prescription 6 months prior to dental treatment*	B01AA03
	Rivaroxaban		B01AF01, B01AX06
	Apixaban		B01AF02
	Edoxaban		B01AF03
	Dabigatran		B01AE07
Antiplatelet agents	COX inhibitor		B01AC06, B01AC18
	ADP receptor antagonists		B01AC04, B01AC05, B01AC22, B01AC24
	PDE inhibitor		B01AC23
	5HT2R antagonists		B01AC
	Dual antiplatelet		B01AC30, B01AC56

ADP, adenosine diphosphate; COX, cyclooxygenase; PDE, phosphodiesterase.

2.1.4.4 Dental treatment information

Dental treatment was categorized as conservative treatment, periodontal treatment, tooth extraction, or dental implant surgery at Yonsei University Dental Hospital. Conservative treatment included oral cavity preparation, and periodontal treatment included scaling, curettage, root planing, and periodontal flap operation. Tooth extraction included simple extraction, surgical extraction, removal of fractured teeth, and hemisection. Dental implant surgery included implant placement and removal. Table 4 shows the dental treatment procedure codes.

Table 4. Codes and definitions of dental treatment

Type of dental treatment	Definition	Procedure code
Conservative treatment	*Cavity preparation or endodontics*	U0051-3, U0151-4, U0074-79, U151-4 3ZA101-4[a]
Periodontal treatment	*Scaling, curettage, root planing, or related periodontal surgery*	U1010, I1051, U1052, U2232, U2233, U2240 [3DZF041-3, 3DZI702, 3Z3231-4, 3ZB493, 3ZE291-4, 3ZF041, 3ZF051-2, 3ZK211, 3ZK251-2, DU1010F, S0161C, TR004157, TR004686, TR004700, TR004773, TR004775-6, TR004833, YU1051F, YU1052F, YU2232F3, YU2232F6, ZTT0001045-6, ZTT0001082-3, ZTT0001125, ZTT0001312-4, ZTT0001350][a]
Tooth extraction	*Tooth extraction or related tooth extraction*	U0012, U1132, U4411-7 [3ZK224, DU0012E, DU1131-2][a]
Implant-related surgery	*Implant placement, removal, or bone grafting for implant surgery*	U4981, U4982, UB127-8 [OP017093-5, 3Z3131-7, 3Z3141-6, TR003664, TR004125, TR004665, TR004894-6, TR005112, TR005240, TR005550][a]

[a] Nonreimbursement procedure codes at the Yonsei University Health System.

2.1.5 Study endpoints

Post-operative bleeding was investigated based patient-reported occurrences of bleeding after dental treatment and emergency room visits related to bleeding.

2.1.6. Statistical analysis

The number of samples and percentages are presented for categorical variables, while the mean and standard deviation (SD) are reported for continuous variables. Factors affecting postoperative bleeding were analyzed by comparing categorical variables using the chi-square test and continuous variables using the independent Student's t-test. Logistic regression analysis was conducted to evaluate the effects of demographic, medical, medication, and dental characteristics on the occurrence of postoperative bleeding, with the Hosmer–Lemeshow test used to assess the model's goodness of fit. Statistical significance was defined as $P < 0.05$ for all analyses, and all statistical tests were performed using SAS software (version 9.4, SAS Institute, NC, USA).

2.2. National Health Insurance Service Cohort Study

2.2.1. Ethical considerations

The study was approved by the Institutional Review Board of Yonsei University Dental Hospital (IRB No. 2-2022-0072) and the National Health Insurance Service (NHIS) (study No. NHIS-2024-2-040). All NHIS data were anonymized before being provided to the researchers.

2.2.2. Data source

This study used data from the NHIS, a mandatory social health care system in Korea that records all inpatient and outpatient procedures and prescriptions occurring in Korea. The NHIS conducts the National Health Information Sharing Service (NHISS) to provide information supporting policy and academic research (NHIS: https://nhiss.nhis.or.kr). The NHIS database has been widely used for medical and health policy research purposes. This study used the NHIS sample cohort database. This is a population-based cohort, consisting of a representative sample of 2.2% of the Korean population registered in NHIS. NHIS-NSC data consist of the qualification and contribution database, health insurance claiming database (payment specification [20T], consultation statements [30T], diagnosis statements determined by ICD-10 [40T], and detailed statements about prescriptions [60T]), health check-up database, and medical institution database.

2.2.3 Inclusion/exclusion criteria

The inclusion criteria for the national health insurance claim data were patients diagnosed with CVD between January 2015 and December 2019. The study registration date was defined as the date of the initial diagnosis of CVD among all diagnostic dates during this period. The CVD diagnostic code was defined as the main

disease claimed based on the ICD-10 (same as single-institution Table 1). The inclusion criteria were (1) adults older than 30 years and (2) patients with a history of dental treatment after being diagnosed with CVD. The exclusion criteria were (1) patients who died within 1 year of diagnosis; (2) patients with hemophilia, coagulopathy, or liver and kidney dysfunction such as cirrhosis and chronic renal failure; and (3) patients who were prescribed both antiplatelet agents and anticoagulants 6 months prior to dental treatment. In addition, patients who underwent two or more dental treatments on the same date (including conservative treatment, periodontal treatment, tooth extraction, or implant-related surgery) or had less than a two-week interval between dental treatments were also excluded (Figure 2).

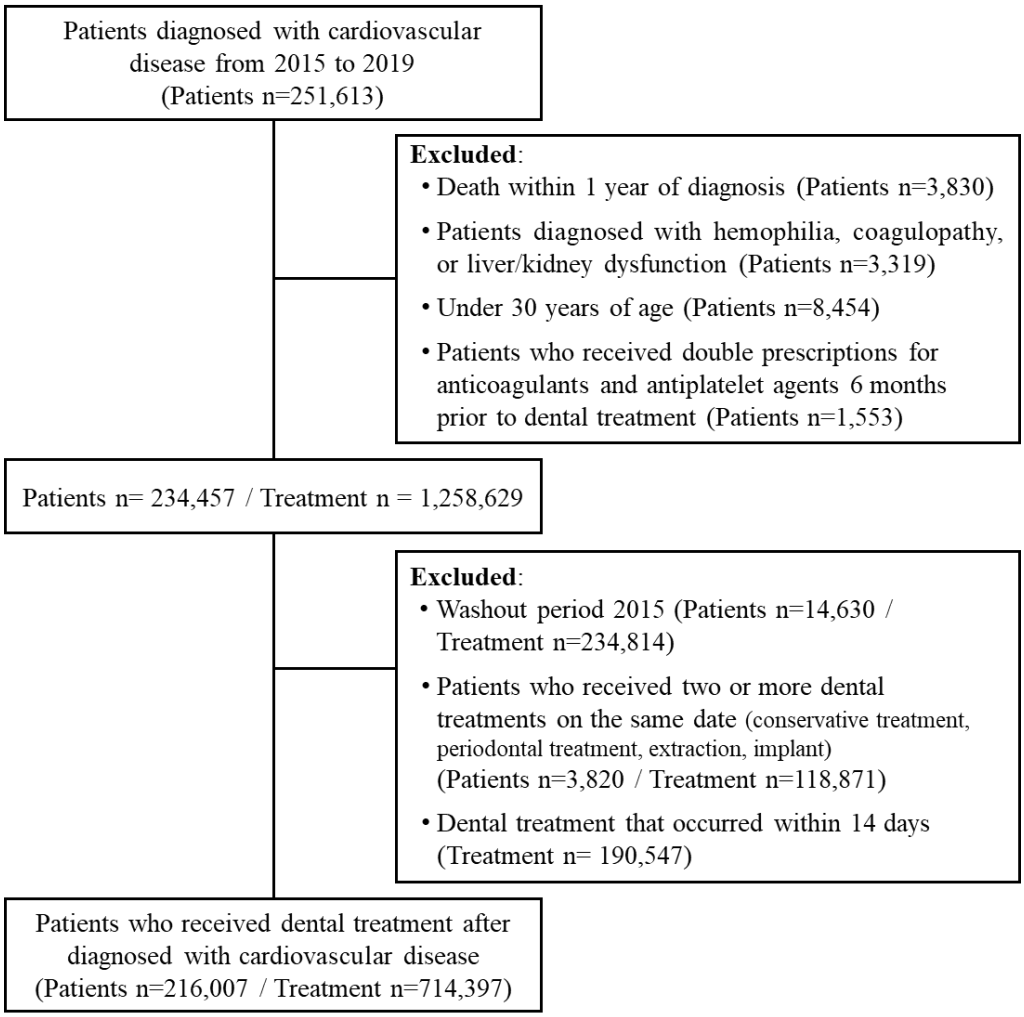

Figure 2. Flowchart of the National Health Insurance Service Cohort Database

2.2.4 Independent variable

The variables used in this study were divided into demographic, medical, medication, and dental characteristics.

2.2.4.1 Demographic information

The demographic characteristics included sex, age, region of residence, and household income level. Age was grouped into 10-year increments: 30–39, 40–49, 50–59, 60–69, and ≥70 years. The region of residence was classified as Seoul metropolitan city, other metropolitan cities (including Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan), and other regions, which were classified as nonmetropolitan areas. Household income levels were classified into medical aid beneficiaries, lower 30%, middle 40%, and upper 30%.

2.2.4.2 Medical information

Medical characteristics used the procedure codes for stent insertion, CABG, thrombolysis, and heart valve surgery occurring between the initial diagnosis of CVD and dental treatment (same as single-institution Table 2). Comorbidities were classified as hypertension, diabetes, and dyslipidemia using the ICD-10 diagnosis codes for main or secondary diseases in the consultation statements between the initial diagnosis of CVD and dental treatment.

2.2.4.3 Medication information

Medication characteristics were analyzed based on the main ingredient codes in consultation statements (30T) and detailed prescription statements (60T) for anticoagulants and antiplatelet agents prescribed within six months prior to dental treatment. Anticoagulants were classified as warfarin and the DOACs dabigatran,

rivaroxaban, apixaban, and edoxaban, and antiplatelet agents were defined as COX inhibitors, PDE inhibitors, ADP inhibitors, 5HT2R antagonists, and DAPT using aspirin and clopidogrel. Patients who were not prescribed antithrombotic agents in the 6 months before dental treatment were classified as the group. The main ingredient codes of the drugs were the same as shown in the single-institution Table 3. In addition, for patients prescribed antithrombotic agents, the presence or absence of drug discontinuation and the discontinuation date were investigated using consultation records to determine whether the drug was discontinued before dental treatment and, if applicable, the specific discontinuation date.

2.2.4.4 Dental treatment information

Dental treatment was defined as conservative treatment, periodontal treatment, tooth extraction, or dental implant surgery, identified based on the procedure codes. Conservative treatment included oral cavity preparation, and periodontal treatment included scaling, curettage, root planing, and periodontal flap operation. Tooth extraction included simple extraction, surgical extraction, removal of fractured teeth, and hemisection. Dental implant surgery included bone grafting, implant placement, and implant removal. Table 5 shows the dental treatment reimbursement procedure codes.

Table 5. Codes and definitions of dental treatment (NHIS-NSC)

Type of dental treatment	Definition	Procedure codes
Conservative treatment	*Cavity preparation or endodontics*	U0051-3, U0151-4, U0074, U0075, U0079
Periodontal treatment	*Scaling, curettage, root planing, or related periodontal surgery*	U1010, U1051, U1052, U2232, U2233, U2240
Tooth extraction	*Tooth extraction or related tooth extraction*	U0012, U1132, U4411-7
Implant-related surgery	*Implant placement, removal, or bone grafting for implant surgery*	U4981, U4982, UB121-129, U1071-1073

2.2.5 Study endpoints

The endpoint for systemic complications was defined as hospital admission or death due to systemic complications within 30 days following dental treatment (Table 6). The primary outcome (systemic bleeding) of complications was hospital admission resulting from intracranial hemorrhage, respiratory bleeding, hematuria, or a diagnosis of anemia due to bleeding. The secondary outcome (thromboembolic complications) was defined as hospital admission or death resulting from CVD combined with stroke, arterial embolism, and thrombosis and complications after acute myocardial infarction.

Table 6. Codes and definitions of outcomes

Systemic bleeding	Definition	ICD-10 code
Hemorrhage from the respiratory passages	*Hospital admission with a diagnosis of hemorrhage from respiratory passages*	R04
Hemothorax or hematuria	*Hospital admission with a diagnosis of hemothorax or hematuria*	N02, R31, J94.2
Hemorrhagic digestive system disorders and ulcers	*Hospital admission with a diagnosis of hemorrhagic digestive system disorders and ulcers*	K25-28, K92
Anemia	*Hospital admission with a diagnosis of anemia or acute posthemorrhagic anemia*	D50, D62
Intracranial hemorrhage or injury	*Hospital admission with a diagnosis of intracranial hemorrhage or Intracranial injury*	I60-62, S06
Thromboembolic complications	**Definition**	**ICD-10 code**
Stroke	*Hospital admission or death with a diagnosis of hemorrhage, cerebral infarction, or cerebral ischemic attacks*	I63, 64, 69, G458, G459
Arterial embolism and thrombosis	*Hospital admission or death with a diagnosis of arterial embolism and thrombosis*	I74
Complications after acute myocardial infarction	*Hospital admission or death with a diagnosis of complications after acute myocardial infarction*	I23

ICD-10, International Standard Classification of Diseases, 10th Revision.

2.2.6. Statistical analysis

The number of samples and percentages were presented for categorical variables, while the mean and standard deviation (SD) were reported for continuous variables. Factors affecting systemic complications were analyzed by comparing categorical variables using the chi-square test and continuous variables using the independent Student's t-test. Logistic regression analysis was conducted to evaluate the effects of demographic, medical, medication, and dental characteristics on the occurrence of systemic complications, with the Hosmer–Lemeshow test used to assess the model's goodness of fit. Statistical significance was defined as $P < 0.05$ for all analyses, and all statistical tests were performed using SAS software (version 9.4, SAS Institute, NC, USA).

3. RESULTS

3.1. Retrospective Single-Institution Study

3.1.1. Demographic and clinical characteristics

A total of 1,878 cases were diagnosed with CVD at Severance Hospital and received dental treatment at Yonsei University Dental Hospital (Table 7). Of the 1,878 cases, 1,037 (55.22%) were male and 841 (44.78%) were female. Most patients were in their 60s (591, 31.47%), followed by their 50s (483, 25.72%). Comorbidities included hypertension in 804 (42.81%) cases, diabetes in 827 (44.04%), and dyslipidemia in 931 (49.57%). Between the diagnosis of CVD and dental treatment, 222 (11.82%) patients underwent stent insertion, 17 (0.91%) underwent CABG, 1 (0.05%) underwent thrombolysis, and 108 (5.75%) underwent valve surgery.

Table 7. Demographic characteristics of patients diagnosed with CVD

Characteristics	Total (N = 1,878)	
	n	%
Sex		
Male	1,037	55.22
Female	841	44.78
Age		
30 to 39	81	4.31
40 to 49	243	12.94
50 to 59	483	25.72
60 to 69	591	31.47
≥70	480	25.56
Comorbidities		
Hypertension		
Yes	804	42.81
No	1,074	57.19
Diabetes mellitus		
Yes	827	44.04
No	1,051	55.96
Dyslipidemia		
Yes	931	49.57
No	947	50.43
CVD surgery		
Stent insertion		
Yes	222	11.82
No	1,656	88.18
CABG		
Yes	17	0.91
No	1,861	99.09
Thrombolysis		
Yes	1	0.05
No	1,877	99.95
Heart valve surgery		
Yes	108	5.75
No	1,770	94.25

CABG, coronary artery bypass grafting; CVD, cardiovascular disease.

There were 1,063 cases (56.60%) without a history of antithrombotic prescription within 6 months of dental treatment (Table 8). Among patients receiving antithrombotic prescriptions, 481 (25.62%) were prescribed antiplatelet agents, including 243 (12.94%) receiving COX inhibitors and 153 (8.15%) receiving DAPT. A total of 334 (17.78%) patients were prescribed an anticoagulant, including 221 (11.77%) receiving warfarin and 113 (6.01%) receiving DOACs.

Table 8. Antithrombotic agent prescriptions in patients diagnosed with CVD

Antithrombotic agent	Total (N = 1,878)	
	n	%
None	1,063	56.60
Antiplatelet agents		
COX inhibitor	243	12.94
ADP receptor antagonists	68	3.62
PDE inhibitor	12	0.64
5HT2R antagonists	5	0.27
Dual antiplatelet therapy	153	8.15
Anticoagulant		
Warfarin	181	9.64
Warfarin (heparin bridge)	40	2.13
DOACs		
Rivaroxaban	47	2.50
Apixaban	38	2.02
Dabigatran	15	0.80
Edoxaban	13	0.69

ADP, adenosine diphosphate; COX, cyclooxygenase; CVD, cardiovascular disease; DOACs, direct oral anticoagulants; PDE, phosphodiesterase.

Conservative treatment was administered in 39 (2.08%) cases, and periodontal treatment was the most common in 1,021 (54.37%) cases (Table 9). Among the periodontal treatments, scaling was the most common in 715 (38.07%), followed by periodontal curettage in 178 (9.48%), root planing in 110 (5.86%), and periodontal flap operation in 18 (0.96%). Tooth extraction was performed in 715 (38.07%) cases, with simple extraction conducted in 540 (28.75%), surgical extraction in 174 (9.27%), and removal of fractured teeth in 1 (0.05%). Implant placement was performed in 78 (4.15%), implant placement with bone graft in 18 (0.96%), and implant removal in 7 (0.37%), with implant-related surgeries in 103 (5.48%) cases.

Table 9. Dental treatment in patients diagnosed with CVD

Dental treatment	Total (N = 1,878)	
	n	%
Conservative treatment	39	2.08
Periodontal treatment		
Scaling	715	38.07
Curettage	178	9.48
Root planing	110	5.86
Periodontal flap operation	18	0.96
Tooth extraction		
Simple extraction	540	28.75
Surgical extraction	174	9.27
Removal of the fractured teeth	1	0.05
Implant related surgery		
Implant placement	78	4.15
Implant placement with a bone graft	18	0.96
Implant removal	7	0.37

CVD, cardiovascular disease.

Demographic and clinical characteristics by antithrombotic agent included 532 (50.05%) males and 531 (49.95%) females in the group with no history of antithrombotic agent prescriptions, 108 (59.67%) males and 73 (40.33%) females in the warfarin group, 19 (47.50%) males and 21 (52.50%) females in the warfarin (heparin bridge) group, and 59 (52.21%) males and 54 (47.79%) women in the DOAC group (Table 10). The single antiplatelet group was composed of 196 (59.76%) males and 132 (40.24%) females; the dual antiplatelet group included 123 (80.39%) males and 30 (19.61%) females. Age was the youngest in the group at 59.64 ± 12.12 years and the oldest in the DOAC group at 66.50 ± 10.49 years. Comorbidities were the lowest in the no prescription group with hypertension, diabetes, and dyslipidemia at 369 (34.71%), 352 (33.11%), and 435 (40.92%), respectively, whereas the DOAC group had the highest frequency of comorbidities at 69 (61.06%), 74 (65.49%), and 76 (67.26%). Among patients who underwent stent insertion and CABG, 102 (45.95%) and 7 (41.18%) were prescribed a single antiplatelet agent, respectively, and in patients who underwent heart valve surgery, 75 (69.44%) were prescribed warfarin.

Table 10. Comparison of characteristics according to antithrombotic agents in patients diagnosed with CVD

Characteristics	None	Anticoagulant			Antiplatelet agents	
		Warfarin	Warfarin (heparin bridge)	DOACs	SAPT	DAPT
Total	1,063 (56.60)	181 (9.64)	40 (2.13)	113 (6.02)	328 (17.47)	153 (8.15)
Sex						
Male	532 (50.05)	108 (59.67)	19 (47.50)	59 (52.21)	196 (59.76)	123 (80.39)
Female	531 (49.95)	73 (40.33)	21 (52.50)	54 (47.79)	132 (40.24)	30 (19.61)
Age, mean±SD, year	59.64±12.12	59.76±12.43	60.00±13.30	66.55±10.49	65.38±10.81	63.12±11.19
Comorbidities (Yes versus no)						
Hypertension	369 (34.71)	96 (53.04)	16 (40.00)	69 (61.06)	173 (52.74)	81 (52.94)
Diabetes mellitus	352 (33.11)	104 (57.46)	19 (47.50)	74 (65.49)	181 (55.18)	97 (63.40)
Dyslipidemia	435 (40.92)	105 (58.01)	19 (47.50)	76 (67.26)	193 (58.84)	103 (67.32)
CVD surgery (Yes versus no)						
Stent insertion	19 (8.56)	1 (0.45)	4 (1.80)	5 (2.25)	102 (45.95)	91 (40.99)
CABG	3 (17.65)	1 (5.88)	1 (5.88)	N/A	7 (41.18)	5 (29.41)
Thrombolysis	1 (100)	N/A	N/A	N/A	N/A	N/A
Heart valve surgery	5 (4.63)	75 (69.44)	6 (5.56)	6 (5.56)	9 (8.33)	7 (6.48)

CABG, coronary artery bypass grafting; CVD, cardiovascular disease; DOACs, direct oral anticoagulants; DAPT, dual antiplatelet therapy; SAPT, single antiplatelet therapy.

The demographic and clinical characteristics by dental treatment included 21 (53.85%) males and 18 (46.15%) females receiving conservative treatment, 391 (54.69%) males and 324 (45.31%) females receiving scaling, 154 (53.47%) males and 134 (46.53%) females receiving curettage/root planing, 7 (38.89%) males and 11 (61.11%) females undergoing periodontal flap surgery, 307 (56.85%) males and 233 (43.15%) females undergoing simple tooth extraction, 98 (56.00%) males and 77 (44.00%) females undergoing surgical extraction, and 59 (57.28%) males and 44 (42.72%) females undergoing implant-related surgery (Table 11). Patients receiving conservative treatment were the youngest at 59.10 ± 13.09 years, and those receiving implant-related surgery were the oldest at 65.17 ± 9.24 years. The frequencies of hypertension, diabetes, and dyslipidemia were the lowest among patients who received scaling, at 298 (41.68%) and 292 (40.84%), respectively. The frequency of hypertension was the highest in patients who received a periodontal flap operation, at 10 (55.56%), and diabetes and dyslipidemia occurred most frequently in patients who received implant-related surgery, at 53 (51.46%) and 61 (59.22%), respectively. Patients who underwent stent insertion comprised the group with the highest proportion of simple extraction at 107 (48.20%), and those who underwent CABG and heart valve surgery comprised the highest proportion of patients undergoing scaling at 8 (47.06%) and 47 (43.52%), respectively.

Table 11. Comparison of characteristics according to dental treatment in patients diagnosed with CVD

Characteristics	Conservative treatment	Periodontal treatment			Tooth extraction		Implant-related surgery
		Scaling	Curettage / Root planing	Periodontal flap operation	Simple extraction	Surgical extraction	
Total	39 (2.08)	715 (38.07)	288 (15.34)	18 (0.98)	540 (28.75)	175 (9.32)	103 (5.48)
Sex							
Male	21 (53.85)	391 (54.69)	154 (53.47)	7 (38.89)	307 (56.85)	98 (56.00)	59 (57.28)
Female	18 (46.15)	324 (45.31)	134 (46.53)	11 (61.11)	233 (43.15)	77 (44.00)	44 (42.72)
Age, mean±SD, year	59.10±13.09	59.79±11.84	59.54±10.97	66.44±15.88	64.12±11.85	59.97±13.91	65.17±9.24
Comorbidities (Yes versus no)							
Hypertension	19 (48.72)	298 (41.68)	127 (44.10)	10 (55.56)	216 (40.00)	79 (45.14)	55 (53.40)
Diabetes mellitus	20 (51.28)	292 (40.84)	135 (46.88)	8 (44.44)	243 (45.00)	76 (43.43)	53 (51.46)
Dyslipidemia	21 (53.85)	335 (46.85)	145 (50.35)	10 (55.56)	276 (51.11)	83 (47.43)	61 (59.22)
CVD surgery (Yes versus no)							
Stent insertion	4 (1.80)	35 (15.77)	21 (9.46)	2 (0.90)	107 (48.20)	24 (10.81)	29 (13.06)
CABG	N/A	8 (47.06)	2 (11.76)	N/A	5 (29.41)	1 (5.88)	1 (5.88)
Thrombolysis	N/A	N/A	N/A	N/A	N/A	1 (100)	N/A
Heart valve surgery	3 (2.78)	47 (43.52)	28 (25.93)	1 (0.93)	17 (15.74)	6 (3.43)	6 (5.56)

CABG, coronary artery bypass grafting; CVD, cardiovascular disease.

3.1.2. Factors associated with postoperative bleeding

Sex and age were not statistically significant factors affecting postoperative bleeding after dental treatment (Table 12). A significantly higher prevalence of postoperative bleeding was observed in patients with comorbidities such as hypertension and diabetes. Stent insertion, CABG, and thrombolysis were not factors affecting postoperative bleeding, but patients with a history of heart valve surgery showed significantly higher rate of bleeding (11%). Among patients with postoperative bleeding, anticoagulants were used in 17 (41.46%), antiplatelet agents in 16 (39.02%), and no medications in 8 (19.51%); however, in those with no postoperative bleeding, anticoagulants were used in 317 (17.26%), antiplatelet agents in 465 (25.31%), and no medications in 1,055 (57.43%), showing a significant difference. However, there was no significant difference in postoperative bleeding due to drug discontinuation, dental treatment, or number of teeth treated.

Table 12. Factors associated clinical characteristics influencing postoperative bleeding

Characteristics	Postoperative bleeding		
	Not occurred (N = 1,837)	Occurred (N = 41)	*P*
Sex			
Male	824 (44.86)	17 (41.46)	0.0536
Female	1,013 (55.14)	24 (58.54)	
Age, mean±SD, year	61.29 ± 12.01	64.34 ± 13.66	0.1900
Comorbidities (Yes versus no)			
Hypertension	778 (42.35)	26 (63.41)	**0.0017****
Diabetes mellitus	802 (43.66)	25 (60.98)	**0.0334***
Dyslipidemia	911 (49.59)	20 (48.78)	0.5269
CVD surgery (Yes versus no)			
Stent insertion	218 (11.87)	4 (9.76)	0.6921
CABG	17 (0.93)	N/A	N/A
Thrombolysis	1 (0.05)	N/A	N/A
Heart valve surgery	101 (5.50)	7 (17.07)	**0.0338***
Medication			
Anticoagulant	317 (17.26)	17 (41.46)	
Antiplatelet agents	465 (25.31)	16 (39.02)	**<.0001*****
None	1,055 (57.43)	8 (19.51)	
Drug discontinuation (n=775)			
Continued	297 (39.76)	15 (53.57)	0.1434
Discontinued	450 (60.24)	13 (46.43)	
Dental treatment			
Conservative treatment	39 (2.12)	N/A	
Periodontal treatment	1,002 (54.55)	19 (46.34)	0.1579
Tooth extraction	697 (37.94)	18 (43.90)	
Dental implant surgery	99 (5.39)	4 (9.76)	
Number of teeth treated			
One tooth	507 (27.60	6 (14.63)	
Two teeth	236 (12.86)	6 (14.63)	0.3947
Three teeth	64 (3.48)	2 (4.88)	
Four or more teeth	1,030 (56.07)	27 (65.85)	

CABG, coronary artery bypass grafting; CVD, cardiovascular disease
*p<0.05; **p<0.01, ***p<0.0001

The rate of postoperative bleeding was higher when warfarin was continued compared with when it was discontinued, but without a statistically significant difference (Table 13). The drug discontinuation date was 3.35 ± 1.94 days in the group without postoperative bleeding and 3.75 ± 2.22 days in the group with postoperative bleeding, with no statistically significant difference. The rate of postoperative bleeding was higher when DOACs were discontinued, but there was no statistically significant difference. The drug discontinuation date was 2.33 ± 1.53 days in the group without postoperative bleeding and 2.22 ± 1.97 days in the group with postoperative bleeding, with no statistically significant difference between the groups. In the single antiplatelet group, the postoperative bleeding rate was higher when the drug was not discontinued but without statistical significance. The drug discontinuation date was was 5.12 ± 2.18 days in the group without postoperative bleeding and 4.00 ± 2.07 days in the group with postoperative bleeding, with no statistically significant difference. In the dual antiplatelet group, the rate of postoperative bleeding was higher when the drug was discontinued, but the difference was not statistically significant. The drug discontinuation date was 4.80 ± 1.49 days in the group without postoperative bleeding and 4.67 ± 0.58 days in the group with postoperative bleeding, with no statistically significant difference.

Table 13. Factors affecting postoperative bleeding according to discontinuation and discontinuation date based on medication

Drug discontinued		Postoperative bleeding		
		Not occurred	Occurred	*P*
Anticoauglant	Warfarin (n=181)			
	Continued	62 (35.63)	4 (57.14)	0.1960
	Discontinued	112 (64.37)	3 (42.86)	
	Discontinuation date, mean ± SD, day	3.35 ± 1.94	3.75 ± 2.22	0.5643
	DOACs (n=113)			
	Continued	63 (58.33)	3 (60.00)	0.9411
	Discontinued	45 (41.67)	2 (40.00)	
	Discontinuation date, mean (SD), day	2.33 ± 1.53	2.22 ± 1.97	0.9164
Antiplatelet agents	SAPT (n=328)			
	Continued	132 (41.77)	8 (66.67)	0.0870
	Discontinued	184 (58.23)	4 (33.33)	
	Discontinuation date, mean (SD), day	5.12 ± 2.18	4.67 ± 1.51	0.5103
	DAPT (n=153)			
	Continued	40 (26.85)	3 (75.00)	0.3058
	Discontinued	109 (73.15)	1 (25.00)	
	Discontinuation date, mean (SD), day	4.80 ± 1.49	4.67 ± 0.58	0.8520

DOACs, direct oral anticoagulants; DAPT, dual antiplatelet therapy; SAPT, single antiplatelet therapy.

3.1.3. Risk factors affecting postoperative bleeding based on logistic regression analysis

Females had a higher OR for postoperative bleeding than males did, but there was no significant difference (Figure 3). The OR increased with age as compared with those in their 30s, but there was no significant difference in the risk of postoperative bleeding.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Sex (ref: Male)				
Male	24	1,037	1	
Female	17	841	0.777 (0.383 - 1.573)	0.4827
Age (ref: 30 to 39)				
30 to 39	2	81	1	
40 to 49	5	243	0.863 (0.147 - 5.048)	0.8700
50 to 59	8	483	0.693 (0.126 - 3.808)	0.6730
60 to 69	11	591	0.907 (0.152 - 4.279)	0.8007
≥70	15	480	1.991 (0.183 - 5.364)	0.9916

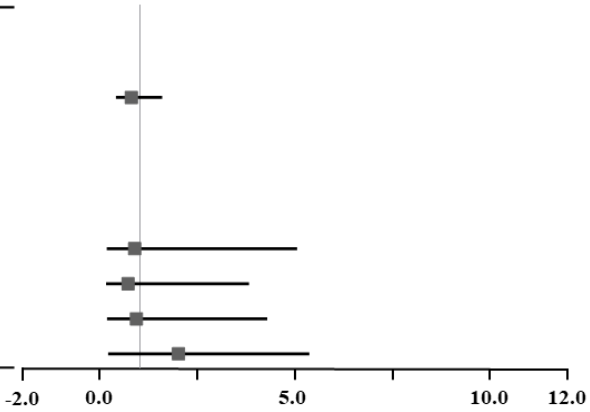

Figure 3. Multivariate logistic regression analysis of postoperative bleeding based on sex and age

Odds ratio of postoperative bleeding after dental treatment for sex and age after adjusting the medications and dental treatment. Male sex and age in the 30s serve as references (the vertical line indicates the reference level).

CI, confidence interval; OR, odds ratio.

The odds of postoperative bleeding were significantly higher in those with hypertension than in those without hypertension (OR, 5.882; 95% confidence interval [CI], 2.202–18.774) (Figure 4). There was no significant difference in the odds of postoperative bleeding in the case diabetes and dyslipidemia. The odds of postoperative bleeding were lower in patients who underwent stent insertion (OR, 0.368; 95% CI, 0.140–0.962). The risk of postoperative bleeding was lower in patients who received stent placement than in those who did not and higher in patients who underwent heart valve surgery, but there was no significant difference.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Comorbidities				
Hypertension (Ref: No)				
No	15	1,074	1	
Yes	26	804	5.882 (2.202 - 18.774)	**0.0287***
Diabetes mellitus (Ref: No)				
No	16	1,051	1	
Yes	25	827	5.691 (0.851 - 18.072)	0.0730
Dyslipidemia (Ref: No)				
No	21	947	1	
Yes	20	931	0.040 (0.010 - 1.152)	0.1325
CVD surgery				
Stent insertion (Ref: No)				
No	37	1,656	1	
Yes	4	222	0.377 (0.112 - 1.274)	0.1165
Heart valve surgery (Ref: No)				
No	34	1,770	1	
Yes	7	108	1.852 (0.618 - 5.543)	0.2709

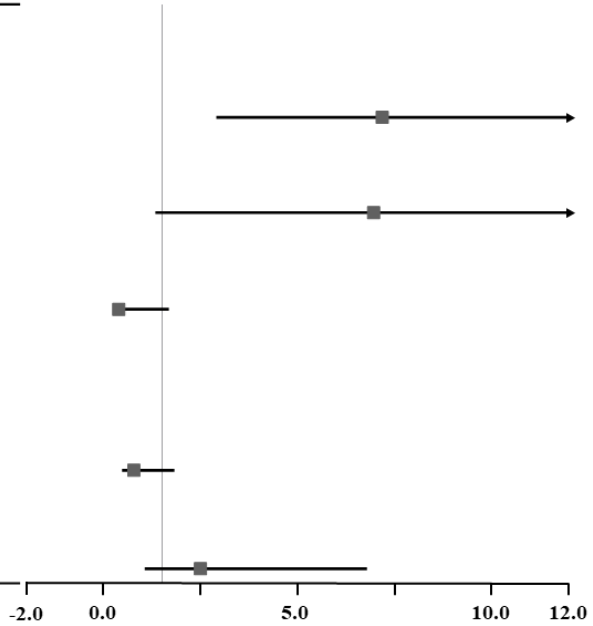

Figure 4. Multivariate logistic regression analysis of postoperative bleeding based on comorbidities and CVD surgery

Odds ratio of postoperative bleeding after dental treatment for comorbidities and CVD surgery after adjusting the medications and dental treatment. The absence of comorbidities and CVD surgery serves as the reference (the vertical line indicates the reference level).

Patients prescribed warfarin (OR, 3.280; CI, 1.058–9.234), warfarin (heparin bridge) (OR, 9.837; CI, 1.276–15.062), and a DOAC (OR, 3.114; CI, 1.852–8.374) had a significantly higher odds of postoperative bleeding compared with patients without a history of drug prescription (Figure 5). Patients prescribed single antiplatelet therapy (OR, 2.966; CI, 1.048–6.396) and DAPT (OR, 2.425; CI, 1.676–6.705) had a significantly higher odds of postoperative bleeding. However, there was no significant difference in the odds of postoperative bleeding according to drug discontinuation by drug type.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Medication (Ref: None)				
None	8	1,063	1	
Anticoagulant				
Warfarin	7	181	3.280 (1.058 ~ 9.234)	**0.0397***
Discontinued	3	115	1	
Continued	4	66	2.409 (0.522 ~ 11.110)	0.2597
Warfarin (heparin bridge)	5	40	9.837 (1.276 ~ 15.062)	**0.0068***
DOACs	5	113	3.114 (1.852 ~ 8.374)	**0.0312***
Discontinued	2	47	1	
Continued	3	66	1.071 (0.172 ~ 6.677)	0.9411
Antiplatelet agents				
SAPT	12	328	2.966 (1.048 ~ 6.396)	**0.0406***
Discontinued	6	190	1	
Continued	6	138	1.394 (0.440 ~ 4.418)	0.5724
DAPT	4	153	2.425 (1.676 ~ 6.705)	**0.0443***
Discontinued	1	110	1	
Continued	3	43	2.726 (0.371 ~ 5.516)	0.3241

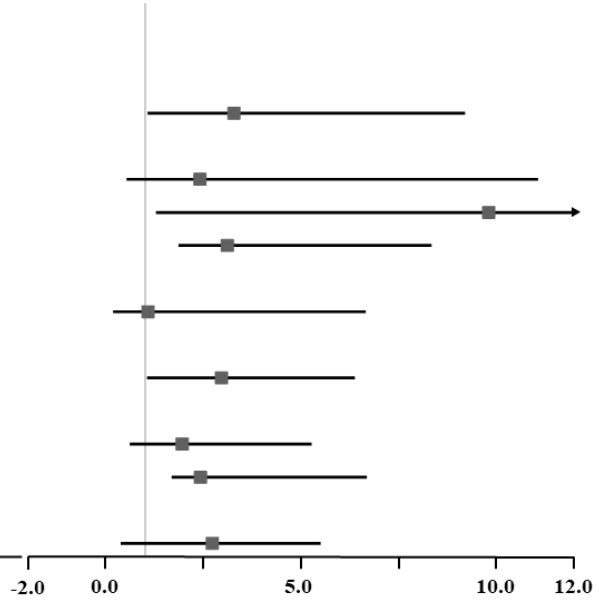

Figure 5. Multivariate logistic regression analysis of postoperative bleeding based on medication characteristics

Odds ratio of postoperative bleeding after dental treatment for medication characteristics after adjusting the demographic and dental treatment. The absence of medication and the discontinuation of drugs serve as references (the vertical line indicates the reference level). CI, confidence interval; DOACs, direct oral anticoagulants; DAPT, dual antiplatelet therapy; OR, odds ratio; SAPT, single antiplatelet therapy. *p<0.05

CVD, cardiovascular disease; CI, confidence interval; OR, odds ratio. *p<0.05

Dental treatment was based on scaling, with zero cases of postoperative bleeding from conservative treatment (Figure 6). Curettage/root planing and periodontal flap surgery had a higher OR of postoperative bleeding than scaling did, but there was no significant difference. Both simple extraction (OR, 6.576; CI, 2.282–8.948) and surgical extraction (OR, 6.566; CI, 1.994–13.936) had a significantly higher OR of postoperative bleeding than scaling did. Implant placement (OR, 4.163; CI, 1.418–9.421) and implant placement with bone grafting (OR, 10.521; CI, 6.168–15.025) had a significantly higher OR of postoperative bleeding than scaling did. When adjusting for dental treatment, the number of teeth treated showed a significantly higher OR of postoperative bleeding when four or more teeth were treated than when one tooth was treated (OR, 7.706; CI, 2.334–10.441).

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Dental treatment (Ref: Scaling)				
Periodontal treatment				
Scaling			1	
Curettage/root planing	7	288	1.771 (0.661 - 4.742)	0.2556
Periodontal flap operation	1	18	2.203 (0.111 - 5.915)	0.6049
Tooth extraction				
Simple extraction	14	540	6.576 (2.282 - 8.948)	**0.0005****
Surgical extraction	4	175	6.566 (1.994 - 13.936)	**0.0173***
Implant related surgery				
Implant placement	1	85	4.163 (1.418 - 9.421)	**0.0238***
Implant placement with bone graft	3	18	10.521 (6.168 - 15.025)	**<.0001*****
Number of teeth treated (Ref: One tooth)				
One tooth	6	513	1	
Two teeth	6	242	2.182 (0.648 - 7.345)	0.2079
Three teeth	2	66	3.872 (0.714 - 8.005)	0.1167
Four or more teeth	27	1,057	7.706 (2.334 - 10.441)	**0.0008****

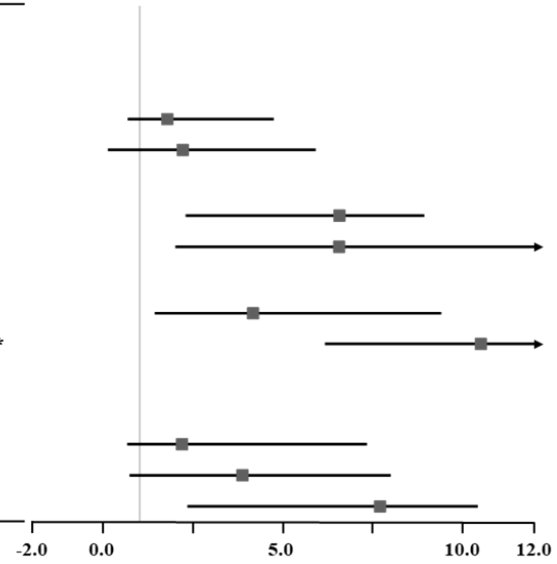

Figure 6. Multivariate logistic regression analysis of postoperative bleeding based on dental characteristics

Odds ratio of postoperative bleeding after dental treatment for dental characteristics after adjusting the demographic and medication characteristics. Scaling as the dental treatment and a one tooth treated serve as references (the vertical line indicates the reference level). CI, confidence interval; OR, odds ratio. *p<0.05; **p<0.01, ***p<0.0001

3.2. National Health Insurance Service Cohort Study

3.2.1. Demographic and clinical characteristics

Between January 2015 and December 2019, a total of 714,397 cases were diagnosed with CVD and received dental treatment (Table 14). Of the 714,397 cases, 371,769 (52.04%) were male and 342,628 (47.96%) were female. Most cases were in their 60s (218,929; 30.65%), followed by their 50s (211,413; 29.59%). Most cases (313,392; 43.87%), had a household income in the highest level (upper 30%). The number of cases receiving dental treatment was 157,119 (21.99%) in Seoul metropolitan city, 182,378 (25.53%) in other metropolitan cities, and 374,900 (52.48%) in nonmetropolitan areas. Comorbidities included hypertension in 414,214 (57.98%), diabetes in 278,305 (38.96%), and dyslipidemia in 467,768 (65.48%). Between the diagnosis of CVD and dental treatment, 5,632 (0.79%) patients underwent stent insertion, 194 (0.03%) CABG, 182 (0.03%) thrombolysis, and 211 (0.03%) valve surgery.

Table 14. Demographic characteristics of patients diagnosed with CVD (NHIS-NSC)

characteristics	Total (N = 714,397)	
	n	%
Sex		
Male	371,769	52.04
Female	342,628	47.96
Age		
30 to 39	28,044	3.93
40 to 49	92,355	12.93
50 to 59	211,413	29.59
60 to 69	218,929	30.65
≥70	163,656	22.91
Household income		
Medical aid beneficiary	21,504	3.01
Lower 30%	157,284	22.02
Mid 40%	222,217	31.11
Upper 30%	313,392	43.87
Region of residence		
Seoul metropolitan city	157,119	21.99
Other metropolitan cities	182,378	25.53
Non-metropolitan area	374,900	52.48
Comorbidities		
Hypertension		
Yes	414,214	57.98
No	300,183	42.02
Diabetes mellitus		
Yes	278,305	38.96
No	436,092	61.04
Dyslipidemia		
Yes	467,768	65.48
No	246,629	34.52

characteristics	Total (N = 714,397)	
	n	%
CVD surgery		
Stent insertion		
Yes	5,632	0.79
No	708,765	99.21
CABG		
Yes	194	0.03
No	714,203	99.97
Thrombolysis		
Yes	182	0.03
No	714,215	99.97
Heart valve surgery		
Yes	211	0.03
No	714,186	99.97

CABG, coronary artery bypass grafting; CVD, cardiovascular disease.

Of the included cases, 553,539 (77.48%) had no history of antithrombotic prescription prior to 6 months of dental treatment (Table 15). The number of cases prescribed antiplatelet agents was 154,006 (21.56%), of whom 88,910 (12.45%) received COX inhibitors and 14,508 (2.03%) received DAPT. A total of 7,051 (0.99%) cases were prescribed anticoagulants, with 1,999 (0.28%) receiving warfarin, 326 (0.05%) warfarin (heparin bridge), and 4,726 (0.66%) DOACs.

Table 15. Antithrombotic agent prescriptions in patients diagnosed with CVD (NHIS-NSC)

Antithrombotic agent	Total (N = 714,397)	
	n	%
None	553,539	77.48
Antiplatelet agents		
COX inhibitor	88,910	12.45
ADP receptor antagonists	26,504	3.71
5HT2R antagonists	12,360	1.73
PDE inhibitor	11,724	1.64
Dual antiplatelet therapy	14,508	2.03
Anticoagulant		
Warfarin	1,999	0.28
Warfarin (heparin bridge)	326	0.05
DOACs[a]		
Rivaroxaban	1,714	0.24
Apixaban	1,154	0.16
Edoxaban	1,096	0.15
Dabigatran	762	0.11

[a] Includes prescription history of two or more main ingredients on the same date
ADP, adenosine diphosphate; COX, cyclooxygenase; CVD, cardiovascular disease; DOACs, direct oral anticoagulants; PDE, phosphodiesterase.

Conservative treatment was performed in 54,448 (7.62%) patients, with periodontal treatment being the most common type of this treatment, administered in 505,409 (70.74%) cases (Table 16). Among the periodontal treatments, scaling was the most common, applied in 375,163 (52.51%), followed by periodontal curettage in 84,273 (11.80%), root planing in 43,379 (6.07%), and periodontal flap surgery in 2,594 (0.36%). Tooth extraction was performed in 131,069 (18.35%) cases, with simple extraction in 127,875 (17.90%), surgical extraction in 1,112 (0.16%), removal of fractured teeth in 1,986 (0.28%), and hemisection in 96 (0.01%). Implant placement was conducted in 21,075 (2.95%), implant removal in 2,243 (0.31%), and bone grafting in 153 (0.02%), with implant-related surgeries occurring in 23,471 (3.28%) cases.

Table 16. Dental treatment in patients diagnosed with CVD (NHIS-NSC)

Dental treatment	Total (N = 714,397)	
	n	%
Conservative treatment	54,448	7.62
Periodontal treatment		
Scaling	375,163	52.51
Curettage	84,273	11.80
Root planing	43,379	6.07
Periodontal flap operation	2,594	0.36
Tooth extraction		
Simple extraction	127,875	17.90
Surgical extraction	1,112	0.16
Removal of the fractured teeth	1,986	0.28
Hemisection	96	0.01
Implant-related surgery		
Implant placement	21,075	2.95
Implant removal	2,243	0.31
Bone graft	153	0.02

CVD, cardiovascular disease.

Demographic and clinical characteristics by antithrombotic agent included 279,140 (50.43%) males and 274,399 (49.57%) females in the no prescription group, 1,097 (54.88%) males and 902 (45.12%) females in the warfarin group, 210 (64.42%) males and 116 (35.58%) females in the warfarin (heparin bridge) group, and 2,688 (59.38%) males and 1,839 (40.62%) females in the DOACs group (Table 17). The single antiplatelet group had 78,365 (56.18%) males and 61,133 (43.82%) females; the dual antiplatelet group had 10,269 (70.78%) males and 4,239 (29.22%) females. Age was the youngest in the no prescription group at 58.78 ± 11.27 years, followed by the warfarin (heparin bridge) group at 63.78 ± 9.69 years, and the warfarin group at 66.10 ± 10.90 years. Comorbidities were the lowest in the no prescription group with hypertension, diabetes, and dyslipidemia at 272,558 (49.24%), 182,880 (33.04%), and 328,066 (59.27%), respectively. Among the cases underwent stent insertion, CABG, and thrombolysis, 3,566 (63.32%), 111 (57.22%), and 93 (51.10%) were prescribed dual antiplatelet agents, respectively, and cases underwent heart valve surgery, 91 (43.13%) were prescribed warfarin.

Table 17. Comparison of characteristics according to antithrombotic agents in patients diagnosed with CVD (NHIS-NSC)

Characteristics	None	Anticoagulant			Antiplatelet agents	
		Warfarin	Warfarin (heparin bridge)	DOACs	SAPT	DAPT
Total	553,539 (77.48)	1,999 (0.28)	326 (0.05)	4,527 (0.63)	139,498 (19.53)	14,508 (2.03)
Sex						
Male	279,140 (50.43)	1,097 (54.88)	210 (64.42)	2,688 (59.38)	78,365 (56.18)	10,269 (70.78)
Female	274,399 (49.57)	902 (45.12)	116 (35.58)	1,839 (40.62)	61,133 (43.82)	4,239 (29.22)
Age, mean±SD, year	58.78±11.27	66.10±10.90	63.78±9.69	71.88±8.43	66.65±9.66	66.98±10.09
Comorbidities (Yes versus no)						
Hypertension	272,558 (49.24)	1,581 (79.09)	279 (85.58)	4,204 (92.87)	122,482 (87.80)	13,110 (90.36)
Diabetes mellitus	182,880 (33.04)	813 (40.67)	186 (57.06)	2,588 (57.17)	82,737 (59.31)	9101 (62.73)
Dyslipidemia	328,066 (59.27)	1,526 (76.34)	294 (90.18)	3,868 (85.44)	120,201 (86.17)	13,813 (95.21)
CVD surgery (Yes versus no)						
Stent insertion	165 (2.93)	8 (0.14)	70 (1.24)	37 (0.66)	1,786 (31.71)	3,566 (63.32)
CABG	15 (7.73)	8 (4.12)	2 (1.03)	N/A	58 (29.90)	111 (57.22)
Thrombolysis	13 (7.14)	13 (7.14)	4 (2.20)	27 (14.84)	32 (17.58)	93 (51.10)
Heart valve surgery	27 (12.80)	91 (43.13)	1 (0.47)	9 (4.27)	72 (34.12)	11 (5.21)

CABG, coronary artery bypass grafting; CVD, cardiovascular disease; DOACs, direct oral anticoagulants; DAPT, dual antiplatelet therapy; SAPT, single antiplatelet therapy.

The demographic and clinical characteristics according to dental treatment were as follows: 28,753 (52.81%) males and 25,695 (47.19%) females received conservative treatment, 189,934 (50.63%) males and 185,229 (49.37%) females received scaling, 67,014 (52.50%) males and 60,638 (47.50%) females received curettage/root planing, 1,417 (54.63%) males and 1,177 (45.37%) females underwent periodontal flap operation, 379,619 (56.12%) males and 56,813 (44.43%) females underwent simple extraction, and 1,891 (59.20%) males and 1,303 (40.80%) females underwent surgical extraction, 11,615 (49.81%) males and 11,703 (50.19%) females received implant surgery, and 83 (54.25%) males and 70 (45.75%) females underwent bone grafting (Table 18). Among the patients, those undergoing bone grafting were the youngest (57.22 ± 8.78 years), whereas the oldest were those undergoing implant surgery (71.09 ± 6.10 years). The lowest frequencies of hypertension and dyslipidemia were observed in patients who underwent implant surgery, at 71 (46.41%) and 94 (61.44%), respectively, and diabetes had the lowest frequency among patients who underwent scaling, at 135,091 (36.01%). Patients who underwent implant surgery had the most common of hypertension (16,846, 72.24%), diabetes (11,386, 48.83%), and dyslipidemia (16,918, 72.55%). Scaling was the most common among patients who underwent stent insertion, CABG, thrombolysis, and heart valve surgery, 2,559 (45.44%), 94 (48.45%), 88 (48.35%), and 107 (50.71%), respectively.

Table 18. Comparison of characteristics according to dental treatment in patients diagnosed with CVD (NHIS-NSC)

Characteristics	Conservative treatment	Periodontal treatment			Tooth extraction		Implant-related surgery	
		Scaling	Curettage / Root planing	Periodontal flap operation	Simple extraction	Surgical extraction	Implant surgery	Bone graft
Total	54,448 (7.62)	375,163 (52.51)	127,652 (17.87)	2,594 (0.36)	127,875 (17.90)	3,194 (0.45)	23,318 (3.26)	153 (0.02)
Sex								
Male	28,753 (52.81)	189,934 (50.63)	67,014 (52.50)	1,417 (54.63)	71,062 (55.57)	1,891 (59.20)	11,615 (49.81)	83 (54.25)
Female	25,695 (47.19)	185,229 (49.37)	60,638 (47.50)	1,177 (45.37)	56,813 (44.43)	1,303 (40.80)	11,703 (50.19)	70 (45.75)
Age, mean±SD, year	62.53±11.32	58.55±11.22	60.26±10.59	59.34±9.69	64.24±11.56	58.90±14.48	71.09±6.10	57.22±8.78
Comorbidities (Yes versus no)								
Hypertension	32,920 (60.46)	203,620 (54.28)	75,203 (58.91)	1,534 (59.14)	82,169 (64.26)	1,851 (57.95)	16,846 (72.24)	71 (46.41)
Diabetes mellitus	22,393 (41.13)	135,091 (36.01)	50,896 (39.87)	1,021 (39.36)	56,261 (44.00)	1,197 (37.48)	11,386 (48.83)	60 (39.22)
Dyslipidemia	82,341 (64.39)	243,589 (64.93)	85,494 (66.97)	1,703 (65.65)	82,341 (64.39)	1,975 (61.83)	16,918 (72.55)	94 (61.44)
CVD surgery (Yes versus no)								
Stent insertion	552 (9.80)	2,559 (45.44)	971 (17.24)	15 (0.27)	1,213 (21.54)	31 (0.55)	291 (5.17)	N/A
CABG	16 (8.25)	94 (48.45)	36 (18.56)	N/A	40 (20.62)	2 (1.03)	6 (3.09)	N/A
Thrombolysis	15 (8.24)	88 (48.35)	33 (18.13)	N/A	40 (21.98)	1 (0.55)	5 (2.75)	N/A
Heart valve surgery	9 (4.27)	107 (50.71)	36 (17.06)	2 (0.95)	48 (22.75)	1 (0.47)	8 (3.79)	N/A

CABG, coronary artery bypass grafting; CVD, cardiovascular disease.

3.2.2. Factors associated with systemic complications

Sex was statistically significant factor affecting the occurrence of systemic bleeding after dental treatment (Table 19). Patients who experienced systemic bleeding or thromboembolic complications after dental treatment were about 5 to 8 years older than patients who did not experience systemic complications, and the difference was significant. A significantly higher prevalence of systemic bleeding or thromboembolic complications was observed in patients with comorbidities as well as in patients with a history of stent insertion or thrombolysis. Among patients with systemic bleeding or thromboembolic complication, the proportion taking anticoagulants and antiplatelet agents was significantly higher, and dental treatment also showed a significant difference in systemic bleeding and thromboembolic complication.

Table 19. Factors associated clinical characteristics influencing systemic complication

Characteristics	Systemic bleeding			Thromboembolic complication		
	Not occurred (N = 712,269)	Occurred (N = 2,128)	*P*	Not occurred (N = 713,935)	Occurred (N = 462)	*P*
Sex						
Male	370,744 (52.05)	1,025 (48.17)	**0.0003****	371,512 (52.04)	257 (55.63)	0.1245
Female	341,525 (47.95)	1,103 (51.83)		342,423 (47.96)	205 (44.37)	
Age, mean±SD, year	60.58±11.44	65.05±11.74	**<.0001*****	60.58±11.44	69.01±11.87	**<.0001*****
Comorbidities (Yes versus no)						
Hypertension	412,723 (57.94)	1,491 (70.07)	**<.0001*****	413,871 (57.97)	343 (74.24)	**<.0001*****
Diabetes mellitus	277,247 (38.92)	1,058 (49.72)	**<.0001*****	278,087 (38.95)	218 (47.19)	**0.0003****
Dyslipidemia	466,288 (65.47)	1,480 (69.55)	**<.0001*****	467,439 (65.47)	329 (71.21)	**0.0095****
CVD surgery (Yes versus no)						
Stent insertion	5,598 (0.79)	34 (1.60)	**<.0001*****	5,619 (0.79)	13 (2.18)	**0.0001****
CABG	193 (0.03)	1 (0.05)	0.4394	194 (0.03)	N/A	N/A
Thrombolysis	176 (0.02)	6 (0.28)	**<.0001*****	175 (0.02)	7 (1.52)	**<.0001*****
Heart valve surgery	209 (0.03)	2 (0.09)	0.1312	210 (0.03)	1 (0.22)	0.1276

Characteristics	Systemic bleeding			Thromboembolic complication		
	Not occurred (N = 712,269)	Occurred (N = 2,128)	*P*	Not occurred (N = 713,935)	Occurred (N = 462)	*P*
Medication						
Anticoagulant	6,795 (0.95)	57 (2.68)		6,831 (0.96)	21 (4.55)	
Antiplatelet agents	153,382 (21.53)	624 (29.32)	**<.0001*** **	153,791 (21.54)	215 (46.54)	**<.0001*** **
None	552,092 (77.51)	1,447 (68.00)		553,313 (77.50)	226 (48.92)	
Dental treatment						
Conservative treatment	54,258 (7.62)	190 (8.90)		54,414 (7.62)	34 (7.36)	
Periodontal treatment	504,066 (70.77)	1,343 (63.11)	**<.0001*** **	505,145 (70.76)	264 (57.14)	**<.0001*** **
Tooth extraction	130,557 (18.33)	512 (24.06)		130,921 (18.34)	148 (32.03)	
Dental implant surgery	23,388 (3.28)	83 (3.90)		23,455 (3.29)	16 (3.46)	

CABG, coronary artery bypass grafting; CVD, cardiovascular disease.
*p<0.05; **p<0.01, ***p<0.0001

3.2.3. Risk factors affecting systemic complications based on logistic regression analysis

There was a significant difference in the OR of systemic bleeding in females compared with males (Figure 7). Although there was no significant difference in the OR of systemic bleeding between those in their 40s and those in their 30s, but there was a significant difference in the OR of systemic bleeding among patients in their 50s (OR 1.397; 95% CI 1.014–1.926), 60s (OR 1.600; 95% CI 1.161–2.205), and 70s and older (OR 2.428; 95% CI 1.758–3.350). The OR of thromboembolic complications increased with age as compared with patients in their 30s, and there was a significant difference of 5.085-fold to 7.978-fold among patients older than their 50s.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Sex (Ref: Male)				
Male	1,025	371,769	1	
	257		1	
Female	1,103	342,628	1.187 (1.080 - 1.282)	**0.0010****
	205		0.892 (0.739 - 1.076)	0.2308
Age (Ref: 30 to 39)				
30 to 39	41	28,044	1	
	2		1	
40 to 49	155	92,355	1.081 (0.766 - 1.527)	0.6573
	20		2.858 (0.887 - 12.282)	0.1573
50 to 59	493	211,413	1.397 (1.014 - 1.926)	**0.0411***
	88		5.085 (1.243 - 20.831)	**0.0236***
60 to 69	633	218,929	1.600 (1.161 - 2.205)	**0.0041****
	111		5.481 (1.348 - 22.928)	**0.0176***
≥70	806	163,656	2.428 (1.758 - 3.350)	**<.0001*****
	241		7.978 (3.193 - 32.752)	**0.0003****

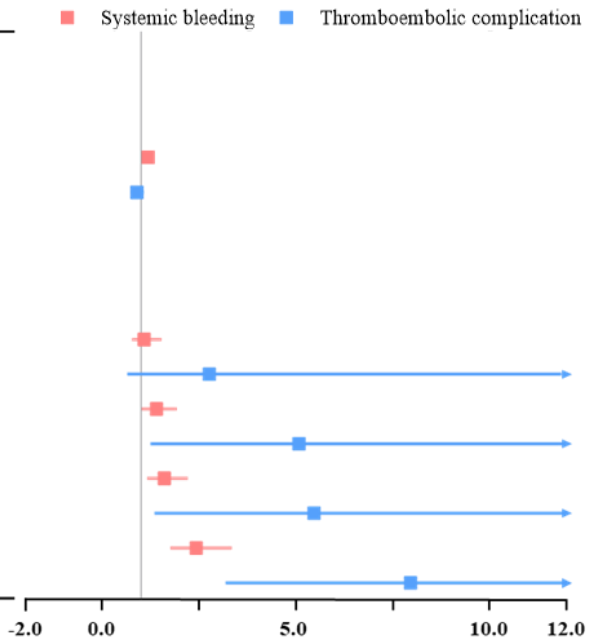

Figure 7. Multivariate logistic regression analysis of systemic complication based on sex and age

Odds ratio of systemic complication after dental treatment for sex and age after adjusting the medications and dental treatment. Male sex and age in the 30s serve as references (the vertical line indicates the reference level).

CI, confidence interval; OR, odds ratio. *p<0.05; **p<0.01, ***p<0.0001

Patients with hypertension had a significantly higher odds of systemic bleeding (OR, 1.325; 95% CI, 1.198–1.489) than those without hypertension (Figure 8). Patients with diabetes had a significantly higher odds of systemic bleeding (OR, 1.344; 95% CI, 1.223–1.476) than those without diabetes. Patients with dyslipidemia had a significantly lower odds of systemic bleeding (OR, 0.864; 95% CI, 0.778–0.989) and thromboembolic complications (OR, 0.795; 95% CI, 0.633–0.996) than those without dyslipidemia.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Comorbidities				
Hypertension (Ref: No)				
No	637	300,183	1	
	119		1	
Yes	1,491	414,214	1.325 (1.198 - 1.489)	**<.0001*****
	343		1.113 (0.880 - 1.407)	0.3710
Diabetes mellitus (Ref: No)				
No	1,070	436,092	1	
	244		1	
Yes	1,058	278,305	1.344 (1.223 - 1.476)	**<.0001*****
	218		0.969 (0.794 - 1.182)	0.7539
Dyslipidemia (Ref: No)				
No	648	246,629	1	
	133		1	
Yes	1,480	467,768	0.864 (0.778 - 0.989)	**0.0058****
	329		0.795 (0.633 - 0.996)	**0.0484***

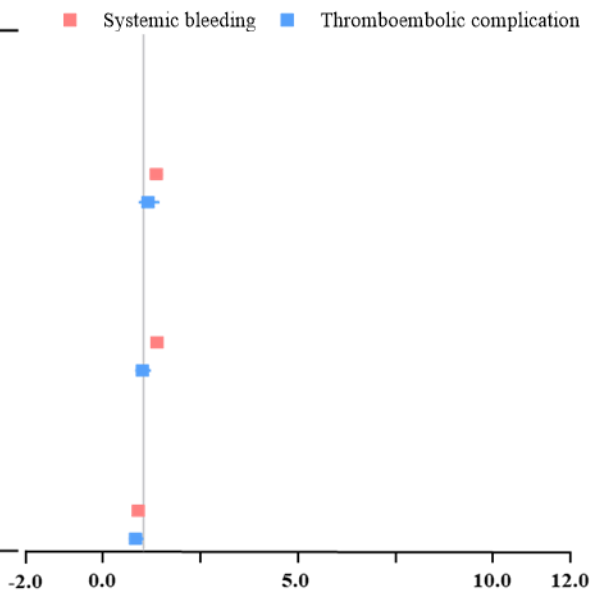

Figure 8. Multivariate logistic regression analysis of systemic complication based on comorbidities

Odds ratio of systemic complication after dental treatment for comorbidities and after adjusting the medications and dental treatment. The absence of comorbidities serves as the reference (vertical line indicates reference level).

CI, confidence interval; OR, odds ratio. *p<0.05; **p<0.01, ***p<0.0001

The odds of systemic bleeding were not significantly different in patients who underwent stent insertion; however, the odds of thromboembolic complications were significantly lower in patients who underwent stent insertion than in those who did not (OR, 0.458; 95% CI, 0.245–0.847) (Figure 9). Patients who underwent thrombolysis had a significantly higher odds of systemic bleeding (OR, 5.688; 95% CI, 2.445–13.229) and thromboembolic complications (OR, 11.204; 95% CI, 7.927–31.808) than those who did not. There was no significant difference in the odds of systemic bleeding and thromboembolic complications between patients who underwent heart valve surgery and those who did not.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
CVD surgery				
Stent insertion (Ref: No)				
No	2,094	708,765	1	
	499		1	
Yes	34	5,632	0.870 (0.584 - 1.274)	0.4760
	13		0.458 (0.245 - 0.847)	**0.0129***
CABG (Ref: No)				
No	2,127	714,203	1	
	462		1	
Yes	1	194	0.835 (0.116 – 6.025)	0.8585
	N/A		N/A	N/A
Thrombolysis (Ref: No)				
No	2,122	714,215	1	
	455		1	
Yes	6	182	5.688 (2.445 - 13.229)	**<.0001*****
	7		11.204 (7.927 - 31.808)	**<.0001*****
Heart valve surgery (Ref: No)				
No	2,126	714,186	1	
	461		1	
Yes	2	211	1.713 (0.414 - 7.082)	0.4573
	1		2.624 (0.352 - 19.583)	0.3469

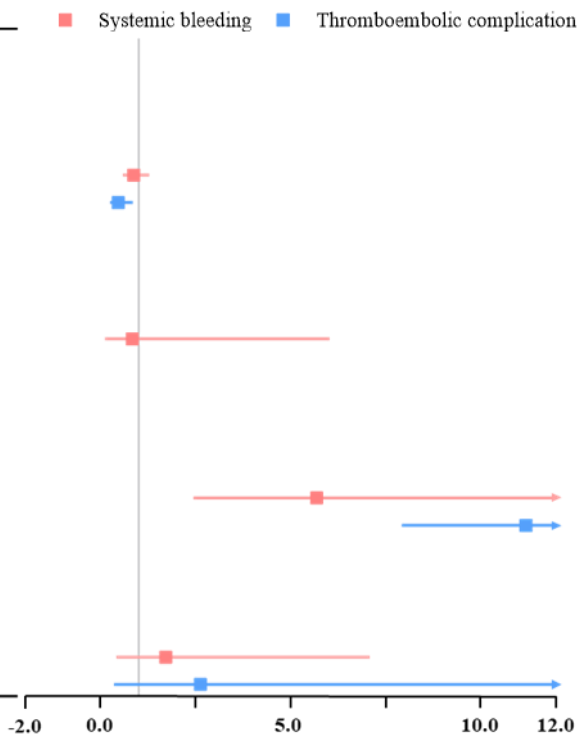

Figure 9. Multivariate logistic regression analysis of systemic complication based on CVD surgery

Odds ratio of systemic complication after dental treatment for CVD surgery after adjusting the medications and dental treatment. The absence of CVD surgery serves as the reference (the vertical line indicates the reference level). CVD, cardiovascular disease; CI, confidence interval; OR, odds ratio. *p<0.05; ***p<0.0001

Patients prescribed warfarin (systemic bleeding OR, 2.419; CI, 1.480–3.953; thromboembolic complication OR, 6.113; CI, 2.938–12.721) and DOACs (systemic bleeding OR, 1.727; CI, 1.209–2.487; thromboembolic complication OR, 3.881; CI, 2.178–6.915) had a significantly higher odds of systemic bleeding and thromboembolic complications as compared with patients without a history of drug prescription (Figure 10). Patients prescribed warfarin (heparin bridge) had a significantly higher odds of systemic bleeding (systemic bleeding OR, 7.734; CI, 3.795–15.762). Patients who were prescribed single antiplatelet therapy had no significant difference in the odds of systemic bleeding as compared with patients without a prescription history, but they had a significantly higher odds of thromboembolic complications (OR, 1.819; CI, 1.439–2.300). Patients receiving DAPT had a significantly higher odds of systemic bleeding (OR, 2.113; CI, 1.692–2.638) and thromboembolic complications (OR, 10.278; CI, 7.895–13.910) as compared with patients without a prescription history.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Medication (Ref: None)				
None	1,447	553,539	1	
	226		1	
Anticoagulant				
Warfarin	17	1,999	2.419 (1.480 - 3.953)	**0.0004****
	8		6.113 (2.938 - 12.721)	**<.0001*****
Warfarin (Heparin bridge)	8	326	7.734 (3.795 - 15.762)	**<.0001*****
	N/A		N/A	N/A
DOACs	32	4,527	1.727 (1.209 - 2.487)	**0.0027***
	13		3.881 (2.178 - 6.915)	**<.0001*****
Antiplatelet agents				
SAPT	517	139,498	1.045 (0.937 - 1.166)	0.4263
	139		1.819 (1.439 - 2.300)	**<.0001*****
DAPT	107	14,508	2.113 (1.692 - 2.638)	**<.0001*****
	76		10.278 (7.895 - 13.910)	**<.0001*****

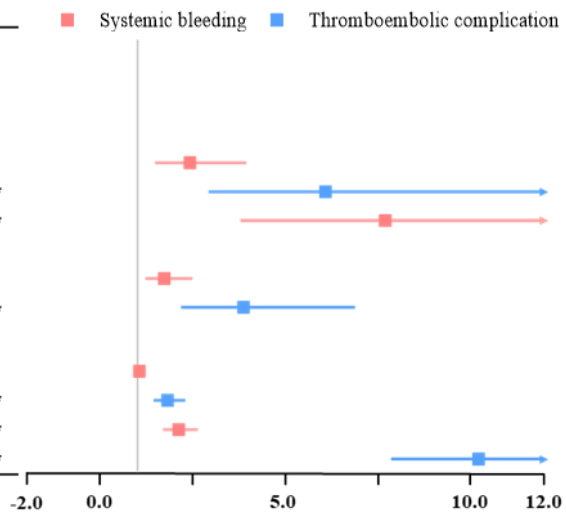

Figure 10. Multivariate logistic regression analysis of systemic complication based on medication characteristics

Odds ratio of systemic complication after dental treatment for medication characteristics after adjusting the demographic and dental treatment. The absence of medication serve as references (the vertical line indicates the reference level).

CI, confidence interval; DOACs, direct oral anticoagulants; DAPT, dual antiplatelet therapy; OR, odds ratio; SAPT, single antiplatelet therapy. *p<0.05; **p<0.01, ***p<0.0001

As with the single-institution study, dental treatment was based on scaling. Conservative and periodontal treatment did not significantly affect the odds of systemic bleeding and thromboembolic complications (Figure 11). Simple extraction had a significantly higher odds of systemic bleeding (OR, 1.206; CI, 1.080–1.347) and thromboembolic complications (OR, 1.545; CI, 1.242–1.928), and surgical extraction had a significantly higher odds of systemic bleeding (OR, 1.770; CI, 1.078–2.906). There was no significant difference in the odds of systemic bleeding in implant-related surgeries; however, the odds of thromboembolic complications were significantly higher (OR, 10.422; CI, 2.141–41.092) among patients receiving a bone graft.

	Events, No.	Sample Size, No.	OR (95% CI)	*P*
Dental treatment (Ref: Scaling)				
Conservative treatment	190	54,448	1.147 (0.981 - 1.341)	0.0858
	34		0.932 (0.648 - 1.343)	0.7038
Periodontal treatment				
Scaling	1,002	375,163	1	
	198		1	
Curettage/root planing	340	127,652	0.944 (0.835 - 1.088)	0.3614
	64		0.865 (0.652 - 1.147)	0.3130
Periodontal flap operation	1	2,594	0.141 (0.020 - 1.005)	0.0506
	2		1.438 (0.388 - 5.778)	0.6128
Tooth extraction				
Simple extraction	496	127,875	1.206 (1.080 - 1.347)	**0.0008****
	145		1.545 (1.242 - 1.928)	**<.0001*****
Surgical extraction	16	3,194	1.770 (1.078 - 2.906)	**0.0240***
	3		1.598 (0.481 - 4.820)	0.4597
Implant related surgery				
Implant surgery	83	23,318	0.924 (0.736 - 1.161)	0.4980
	15		0.663 (0.390 - 1.127)	0.1292
Bone graft	N/A	153	N/A	N/A
	1		10.422 (2.141 - 41.092)	**0.0066****

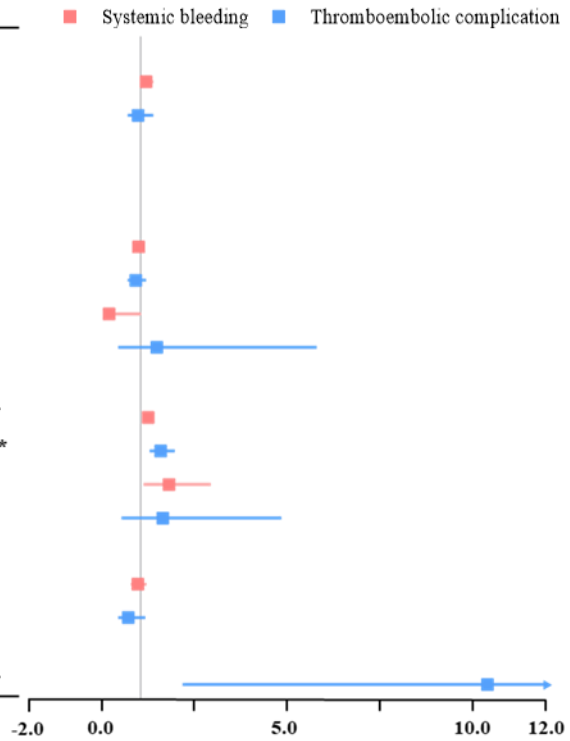

Figure 11. Multivariate logistic regression analysis of systemic complication based on dental characteristics

Odds ratio of systemic complication after dental treatment for dental characteristics after adjusting the demographic and medication characteristics. Scaling as the dental treatment and a one tooth treated serve as references (the vertical line indicates the reference level). CI, confidence interval; OR, odds ratio. *p<0.05; **p<0.01, ***p<0.0001

3.3. Comparison of the Consistency of Single-Institution and NHIS-NSC

The absolute value difference in the gender ratio between the single-institution data and the NHIS-NSC data was 3.18, and the hospital data of NHIS-NSC showed a difference of 0.09 (Table 20). Age showed an absolute value difference between 1.55 in the NHIS-NSC data and 1.20 in the NHIS-NSC hospital data. Household income and region of residence were excluded from the single-institution data as collection variables and could not be compared with the NHIS-NSC data.

Table 20. Ratio differences in demographic characteristics between single-Institution and NHIS-NSC

	Single-Institution	NHIS-NSC, hospital	|%| Difference	NHIS-NSC	|%| Difference
Sex					
Male	1,037 (55.22)	26,544 (55.31)	**0.09**	371,769 (52.04)	**3.18**
Female	841 (44.78)	21,448 (44.69)		342,628 (47.96)	
Age					
30 to 39	81 (4.31)	1,898 (3.95)		28,044 (3.93)	
40 to 49	243 (12.94)	5,783 (12.05)		92,355 (12.93)	
50 to 59	483 (25.72)	13,781 (28.72)	**1.20**	211,413 (29.59)	**1.55**
60 to 69	591 (31.47)	14,713 (30.66)		218,929 (30.65)	
≥70	480 (25.56)	11,817 (24.62)		163,656 (22.91)	
Household income					
Medical aid beneficiary	N/A	1,722 (3.59)		21,504 (3.01)	
Lower 30%	N/A	8,977 (18.71)	N/A	157,284 (22.02)	N/A
Mid 40%	N/A	13,711 (28.57)		222,217 (31.11)	
Upper 30%	N/A	23,582 (49.14)		313,392 (43.87)	
Region of residence					
Seoul metropolitan city	N/A	9,540 (19.88)		157,119 (21.99)	
Other metropolitan cities	N/A	14,002 (29.18)	N/A	182,378 (25.53)	N/A
Non-metropolitan area	N/A	24,450 (50.95)		374,900 (52.48)	

The absolute value differences in the rates of hypertension, diabetes, and dyslipidemia between the single-institution data and the NHIS-NSC data were 15.17, 5.08, and 15.91, respectively, and the NHIS-NSC hospital data showed differences of 16.56, 2.66, and 17.70 (Table 21). The absolute value differences in NHIS-NSC data for stent insertion, CABG, thrombolysis, and heart valve surgery were 11.03, 0.88, 0.02, and 5.72, respectively, and the hospital data of NHIS-NSC showed differences of 10.46, 0.86, 0.01, and 5.67.

Table 21. Ratio differences in clinical characteristics between single-Institution and NHIS-NSC

	Single-Institution	NHIS-NSC, hospital	|%| Difference	NHIS-NSC	|%| Difference
Comorbidities					
Hypertension					
Yes	804 (42.81)	28,493 (59.37)	**16.56**	414,214 (57.98)	**15.17**
No	1,074 (57.19)	19,499 (40.63)		300,183 (42.02)	
Diabetes mellitus					
Yes	827 (44.04)	19,861 (41.38)	**2.66**	278,305 (38.96)	**5.08**
No	1,051 (55.96)	28,131 (58.62)		436,092 (61.04)	
Dyslipidemia					
Yes	931 (49.57)	32,283 (67.27)	**17.70**	467,768 (65.48)	**15.91**
No	947 (50.43)	15,709 (32.73)		246,629 (34.52)	
CVD surgery					
Stent insertion					
Yes	222 (11.82)	651 (1.36)	**10.46**	5,632 (0.79)	**11.03**
No	1,656 (88.18)	47,341 (98.64)		708,765 (99.21)	
CABG					
Yes	17 (0.05)	23 (0.05)	**0.86**	194 (0.03)	**0.88**
No	1,861 (99.09)	47,969 (99.95)		714,203 (99.97)	
Thrombolysis					
Yes	1 (0.05)	27 (0.06)	**0.01**	182 (0.03)	**0.02**
No	1,877 (99.95)	47,965 (99.94)		714,215 (99.97)	
Heart valve surgery					
Yes	108 (5.75)	36 (0.08)	**5.67**	211 (0.03)	**5.72**
No	1,770 (94.25)	47,956 (99.92)		714,186 (99.97)	

CABG, coronary artery bypass grafting; CVD, cardiovascular disease.

The absolute value differences in the ratios of no medication, anticoagulants, and antiplatelet agents between the single-institution data and the NHIS-NSC data were 20.88, 4.09, and 5.61, respectively, and the NHIS-NSC hospital data showed differences of 17.15, 4.31, and 5.37 (Table 22). The absolute value differences in NHIS-NSC data for conservative treatment, periodontal treatment, tooth extraction, and implant-related surgery in dental treatment were 5.54, 5.86, 9.86, and 2.22, respectively, and the NHIS-NSC hospital data showed differences of 1.07, 5.47, 8.11, and 1.03.

Table 22. Ratio differences in medication and dental characteristics between single-Institution and NHIS-NSC

	Single-Institution	NHIS-NSC, hospital	|%| Difference	NHIS-NSC	|%| Difference
Medication					
None	1,063 (56.60)	35,393 (73.75)	**17.15**	553,539 (77.48)	**20.88**
Antiplatelet agents					
SAPT	328 (17.47)	10,199 (21.25)	**4.31**	139,498 (19.53)	**4.09**
DAPT	153 (8.15)	1,588 (3.31)		14,508 (2.03)	
Anticoagulant					
Warfarin	181 (9.64)	314 (0.65)	**5.37**	1,999 (0.28)	**5.61**
Warfarin (heparin bridge)	40 (2.13)	43 (0.09)		326 (0.05)	
DOACs	113 (6.02)	455 (0.95)		4,527 (0.63)	
Dental treatment					
Conservative treatment	39 (2.08)	1,510 (3.15)	**1.07**	54,448 (7.62)	**5.54**
Periodontal treatment					
Scaling	715 (38.07)	24,130 (50.28)	**5.47**	375,163 (52.51)	**5.86**
Curettage / Root planing	288 (15.34)	9,322 (19.42)		127,652 (17.87)	
Periodontal flap operation	18 (0.98)	412 (0.86)		2,594 (0.36)	
Tooth extraction					
Simple extraction	540 (28.75)	10,067 (20.98)	**8.11**	127,875 (17.90)	**9.86**
Surgical extraction	175 (9.32)	416 (0.87)		3,194 (0.45)	
Implant-related surgery					
Implant surgery	103 (5.48)	2,059 (4.29)	**1.03**	23,318 (3.26)	**2.22**
Bone graft		76 (0.16)		153 (0.02)	

DOACs, direct oral anticoagulants; DAPT, dual antiplatelet therapy; SAPT, single antiplatelet therapy.

4. DISCUSSION

This study utilized single-institution clinical data from SCRAP 2.0 at the Yonsei University Health System and the NHIS-NSC database to analyze factors influencing the occurrence of postoperative bleeding and systemic complications in patients taking antithrombotic agents. Patients taking antithrombotic agents had an increased OR of postoperative bleeding and systemic complications compared with patients not taking antithrombotic agents. Among antithrombotic agents, warfarin had a significantly higher OR of postoperative bleeding when heparin bridging was used before dental treatment. In addition, tooth extraction and implant-related surgery (especially bone graft) were dental treatments that affected the occurrence of postoperative bleeding and systemic complications, and hypertension, as a comorbidity, had a significant effect on the occurrence of postoperative bleeding and systemic complications, similar to other studies.

4.1. Anticoagulants: Warfarin and DOACs

Warfarin and DOACs are commonly used to prevent stroke and recurrent myocardial infarction in patients with atrial fibrillation, nonvalvular or valvular atrial disease, and artificial heart valves.[29] Four DOACs, dabigatran, rivaroxaban, apixaban, and edoxaban, are increasingly used as alternatives to warfarin.[30] After dabigatran was approved by the Ministry of Food and Drug Safety in 2010, rivaroxaban, apixaban, and edoxaban were approved in 2011, 2012, and 2015, respectively. Although the number of patients taking DOACs increases every year, warfarin is still prescribed to many patients with contraindications to DOAC treatment (e.g., patients with a high tendency to bleed, resistant hypertension, or atrial valve transplantation).[31]

In this study, the risk of postoperative bleeding was 2.425- to 9.837-fold higher in patients taking antithrombotic agents compared with those not taking them. Among antithrombotic agents, the risk of the anticoagulant was higher than that of the antiplatelet agents, and other studies have also reported that the incidence of bleeding after dental treatment was lower among those taking antiplatelet agents than warfarin.[32] The NHIS-NSC data showed that the average age of patients treated with warfarin was 65.71 ± 10.69 years, and the average age of patients treated with DOACs was 71.77 ± 8.53 years, but the risk of systemic complications was higher for those taking warfarin than for DOACs. Mauprivez et al. reported no significant difference in the number of patients with postoperative bleeding between those taking a DOAC and a vitamin K antagonist (VKA),[9] but other studies reported that DOACs were more successful than warfarin in reducing major bleeding and intracranial hemorrhage.[33,34] In addition, previous studies reported that although patients treated with DOACs were older, the incidence of intracranial hemorrhage and serious bleeding was low,[31] and they confirmed that DOACs had a lower risk of systemic complications than warfarin did.

There have been few studies reporting the occurrence of bleeding after dental treatment with warfarin and heparin bridging. In this study, the odds of postoperative bleeding were higher in those with heparin bridging. These results were similar to the odds of systemic complications. Other studies have also reported that holding warfarin and bridging with heparin/enoxaparin increased not only thrombotic complications but also major and minor bleeding; however, this may be due to the higher anticoagulant effect than desired with low-molecular-weight heparins.[35] Another study reported that the incidence of postoperative bleeding in outpatients who did not discontinue warfarin was 9.1%, which was almost the same as the 8.1% in

inpatients who discontinued warfarin and were bridged with heparin, and heparin bridging therapy may result in similar bleeding rates or thromboembolic events.[32]

For dental procedures with a low risk of bleeding, VKAs can be continued with local hemostatic measures or discontinued 2 to 3 days before surgery if the INR is >3.5 and the bleeding risk is moderate.[36] However, few studies have evaluated the risk of post extraction bleeding in patients taking DOACs, and the need to discontinue DOACs before dental procedures remains controversial. Elad et al. reported that the rate of minor bleeding in patients taking DOACs was similar to or lower than that in patients taking warfarin or enoxaparin.[37] Therefore, these authors recommended that patients requiring tooth extraction or minor dental surgery should not discontinue DOACs but should be considered in the same way as patients taking VKAs with an INR < 3.5. In this retrospective single-institution study, there was no significant difference in the incidence of dental or systemic complications between drug discontinuation and continuation of DOACs. Other studies have found no statistically significant difference between drug discontinuation and continuation, especially for general dental procedures, and reported that postoperative bleeding complications are associated with comorbidities or complex dental procedures such as implant placement.[38]

4.2. Antiplatelet Agents: SAPT and DAPT

Acetylsalicylic acid, a commonly used antiplatelet agent, inactivates COX-1 and prevents the synthesis of thromboxane A2, which has an important role in platelet aggregation and is a representative antiplatelet therapy for the acute and long-term treatment of patients with coronary artery and cerebrovascular diseases.[39] In this study, 26% and 22% of patients were prescribed antiplatelet agents in the single-institution

and NHIS-NSC data, respectively, and approximately 12% were treated with COX inhibitors. Cilostazol is a PDE III inhibitor with antiproliferative and vasodilatory effects and improves endothelial function. Previous studies have reported that cilostazol is effective in the secondary prevention of stroke and in the treatment of intermittent claudication secondary in peripheral arterial disease.[40] Clopidogrel is an effective P2Y12 inhibitor that supports the entire spectrum of acute coronary syndromes, from patients receiving medical management to those undergoing primary percutaneous coronary intervention.[41] DAPT consisting of aspirin and a P2Y12 inhibitor (clopidogrel, ticlopidine, ticagrelor) is recommended after drug-eluting stent implantation unless there is an increased risk of bleeding.[7,42] Antiplatelet agents are mainly used in patients with coronary artery disease, occlusive cerebrovascular disease, and stent insertion.[43]

In single-institution data, the odds of postoperative bleeding were similarly high in patients receiving SAPT (2.966-fold higher) and in patients receiving DAPT (2.425-fold higher) compared with patients not receiving antiplatelet therapy. Yari et al. reported that there was no difference in post-extraction bleeding between the group that took aspirin during the first year after percutaneous coronary intervention and the group that used DAPT,[44] and Lu et al. reported that the incidence of postoperative bleeding in the dual antiplatelet group was higher than that in the single antiplatelet group, but without a significant difference.[45]

In this study, there was no significant association in drug continuation/ discontinuation for both SAPT and DAPT. Previous studies reported that the risk of postoperative bleeding did not increase even if the drug was not discontinued before invasive dental procedures in patients receiving SAPT or DAPT and that local

hemostatic measures were effective in patients with postoperative bleeding.[46] However, in the NHIS-NSC data, the odds of thromboembolic complications in DAPT was significantly higher by 10.278-fold than in patients not taking antithrombotic agents, which was a higher risk compared with the 1.819-fold odds of thromboembolic complications in SAPT. Brown et al. reported that DAPT reduces recurrent ischemic stroke more than SAPT does when initiated immediately after high-risk transient ischemic attack or minor stroke and continued for 21–90 days, but DAPT was associated with an increased risk of major bleeding when initiated within 1–2 months after transient ischemic attack or stroke and continued for 2–3 years.[47] In addition, compared with short-term (≤6 months) DAPT, long-term (>12 months) DAPT was associated with a higher rate of major bleeding and all-cause mortality, and standard-duration DAPT was associated with an increased risk of bleeding. It was reported that the optimal duration of DAPT should take into consideration the individual's ischemic and bleeding risk.[48] However, this study did not include the drug maintenance period of SAPT and DAPT in the investigation. These limitations may have a significant impact on the interpretation of the results of this study, and further research will need to collect specific data on the duration of drug administration and the time of discontinuation.

4.3. Dental Procedures

Most studies have reported on post-extraction bleeding in patients receiving antithrombotic therapy, with incidences ranging from 2% to 26%.[49] Lee et al. reported that extractions with bone grafting and multiple implantations increased the risk of bleeding,[50] and Tang et al. also found that complicated extractions were an independent risk factor for bleeding.[51] Morimoto et al. investigated the incidence of post-operative bleeding in patients receiving warfarin and antiplatelet agents and

reported that surgical extractions with vertical incisions or osteotomies were more likely to cause postoperative bleeding.[15]

This study included conservative treatment with little risk of bleeding, periodontal treatment, simple or surgical tooth extraction, and implant surgery with a risk of bleeding. Tooth extraction, implant surgery, and implant surgery with bone grafting were associated with significantly higher risks of postoperative bleeding and systemic complications. In the single-institution data, both simple extraction and surgical extraction were significantly associated with the odds of postoperative bleeding, whereas in the NHIS-NSC data, simple extraction was significantly associated with a higher risk of systemic bleeding and thromboembolic complications, whereas surgical extraction was significantly associated with a higher risk of systemic bleeding but no significant difference in thromboembolic complications. In this study, simple extraction was defined as tooth extraction without flap elevation, while surgical extraction was defined as tooth extraction with flap elevation. In the case of single-institution data, simple extraction and surgical extraction can generally be distinguished through the EMR and radiograph images, but in the case of the NHIS-NSC data, the distinction can be made only by the procedure code, which may lead to an inaccurate distinction between simple extraction and surgical extraction.

Previous studies have reported a significant correlation between the number of teeth extracted and postoperative bleeding in patients receiving anticoagulant therapy and that the extraction of multiple teeth (two or more) was a risk factor for postoperative bleeding.[49,52] Scully et al. reported that the extraction of up to three teeth was safe if the PT-INR was <3.5 in the absence of other bleeding risk factors. In this study, there was no significant difference in the number of teeth treated and the

occurrence of postoperative bleeding in patients who received dental treatment in the chi-square analysis. However, because scaling with a low risk of bleeding mostly treats at least one-third of the jaw or all teeth, the process of adjusting dental treatment variables was necessary, and the multivariate logistic regression analysis showed that the risk of postoperative bleeding was higher when four or more teeth were treated.

4.4. Comorbidities and CVD Surgery

Previous studies reported that four clinical characteristics, 1) previous stroke or transient ischemic attack, 2) older age, 3) hypertension, and 4) diabetes, are independent risk factors for the development of thromboembolism in patients with atrial fibrillation.[53] The risk factors for postoperative bleeding and systemic complications were also hypertension and diabetes. In the single-institution and NHIS-NSC data, patients receiving antithrombotic therapy had higher rates of hypertension and diabetes compared with patients not receiving antithrombotic therapy. However, when adjusting for drug effects, patients with hypertension had a 5.882-fold higher odds of postoperative bleeding and a 1.325-fold higher odds of systemic bleeding. Patients with diabetes had a 1.344-fold higher risk of systemic bleeding. Hypertension and diabetes may increase the risk of postoperative and systemic bleeding after dental procedures in patients not receiving antithrombotic therapy; therefore, caution is recommended regarding the occurrence of complications.

Patients who underwent stent insertion mainly used aspirin or DAPT. It is recommended to take antiplatelet agents for at least 1 month and up to 1 year after stent insertion, after which antiplatelet agents can be discontinued or adjusted.[54] In this study, it was found that patients who underwent stent insertion had a 0.458-fold

lower risk of thromboembolic complications. This may be because the outcome variable of this study, thromboembolic complications, was defined as bleeding. In most studies, major adverse cardiac events were defined as readmission for acute coronary syndrome or coronary revascularization and death.[54,55] Wijeysundera et al. reported that noncardiac surgery can be safely performed in carefully selected patients in whom at least 6 months had elapsed since drug-eluting stent implantation,[54] and similarly, Graham et al. reported that in patients who received bare metal stents, a similar trend was found for both myocardial infarction and all-cause mortality, with most deaths being cardiac.[55] Patients with PCI stents were reported to have a significantly increased risk of bleeding with triple antithrombotic therapy,[56] but this study excluded triple antithrombotic therapy. Patients who underwent coronary stent insertion were likely to have a lower OR of thromboembolic complications if they were taking anticoagulants or single/dual antiplatelet agents.

Thrombolysis is the use of thrombolytics to destroy or dissolve a blood clot and is indicated for a variety of thrombotic or embolic CVDs, ranging from venous thromboembolism, to acute ischemic stroke, to acute myocardial infarction, to prosthetic valve thrombosis.[57] Thrombolysis and interventional therapy (thrombectomy and stent implantation) are mainly performed.[58] In this study, thrombolysis was found to significantly increase the OR of systemic complications by 5.688- to 11.204-fold. In a previous study, the thrombolysis group was reported to have a 3% higher rate of death due to ischemic heart disease and stroke than the primary PCI group.[59] In addition, Chatterjee et al. reported that thrombolysis had a 5.8% higher rate of major bleeding compared with anticoagulant therapy and a higher rate of intracerebral hemorrhage occurrence.[60] Therefore, during dental treatment, careful attention may be required for bleeding management depending on the patient's

cardiovascular-related clinical characteristics and medications. These clinical characteristics might be carefully considered when establishing a treatment plan before dental procedures.

This study was a large-scale study investigating anticoagulants including warfarin and DOACs, antiplatelet agents including single and dual antiplatelet agents, and a large number of patients who underwent various dental treatments including conservative treatment. This study was conducted using single-institution clinical data and NHIS-NSC data to complement the strengths and limitations of each data source.

Single-institution clinical data are highly reliable and based on EMR and systematically recorded detailed patient diagnosis information, treatment procedures, and posttreatment progress, allowing analysis of each patient's condition, posttreatment complications, and medication discontinuation and resumption. However, the data are limited by the dependence on EMRs, incomplete data in health records, and the possibility that postoperative bleeding occurred in an environment other than the study site.

The NHIS-NSC data include data from various regions and multiple hospitals, allowing research results to be derived and generalized to a broad population without being restricted by the characteristics of a specific institution. However, because the data are based on reimbursement codes and lack specific clinical details, the risk of systemic bleeding and thromboembolic complications according to various factors may be overinterpreted, and the exact causal relationship could not be determined.

Another major limitation of this study was that although VKA triple therapy was associated with a three-fold higher risk of major bleeding compared with VKA monotherapy,[28] but this study focused on individual anticoagulants and antiplatelet agents and did not address triple therapy.

In addition, dental diseases were not included because NHIS-NSC data could only extract diagnostic codes for reimbursement. Periodontal disease has been reported to be associated with an increased risk of CVD, peripheral vascular disease, and stroke, and a history of inflammation or acute infection at the extraction site was reported to be a risk factor for post extraction bleeding in patients receiving anticoagulant therapy.[61,62] Therefore, the exclusion of dental disease information from this study is one of its major limitations.

Finally, the variables between the single-institution data and the NHIS-NSC data could not be directly compared. The two data sets used different collection methods and closed clouds, making it difficult to interpret the research results. For this reason, the results of each dataset could be compared only in absolute values, and there were limitations in confirming the trends between the two sets of data.

Further study will involve a linked analysis of single-institution data from Yonsei University Dental Hospital and public big data, integrating clinical data, including drug use and dental diseases, with public datasets to address the limitations of both sources. This approach will enable a more accurate evaluation of factors contributing to complications in patients using anticoagulants and antiplatelet agents during dental treatments and could suggest clinical guidelines for preventing such complications through long-term follow-up.

5. CONCLUSION

Patients taking anticoagulants and antiplatelet agents were found to have a higher risk of postoperative bleeding and systemic complications compared with those not taking these medications. In particular, the risk was higher in patients taking warfarin when heparin bridging was used before dental treatment; thus, it is recommended that a treatment plan be established according to the condition of each patient to minimize complications after dental treatment in those taking antithrombotic agents.

In addition, factors such as hypertension, tooth extraction, implant surgery with bone grafting, and the treatment of four or more teeth were associated with an increased risk of both postoperative bleeding and systemic complications. These findings suggest that attention might be given to patients with these risk factors to minimize the occurrence of bleeding events.

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Appendix 1. Codes and names of diagnosis

	Code	Name of diagnosis
Heart Valve Disease (HVD)	I05	Rheumatic mitral valve diseases
	I06	Rheumatic aortic valve diseases
	I07	Rheumatic tricuspid valve diseases
	I08	Multiple valve diseases
	I34	Mitral (valve) insufficiency
	I35	Nonrheumatic aortic valve disorders
	I36	Nonrheumatic tricuspid valve disorders
	I37	Pulmonary valve disorders
Ischemic Heart Disease (IHD)	I21	Acute myocardial infarction
	I22	Subsequent myocardial infarction
	I23	Certain current complications following acute myocardial infarction
	I24	Other acute ischaemic heart diseases
	I25	Chronic ischaemic heart disease
Stroke	I60	Subarachnoid haemorrhage
	I61	Intracerebral haemorrhage
	I63	Cerebral infarction
	I64	Stroke, not specified as haemorrhage or infarction
	I69	Sequelae of cerebrovascular disease
	G45.8	Other transient cerebral ischaemic attacks and related syndromes
	G45.9	Transient cerebral ischaemic attack, unspecified

Peripheral Artery Disease (PAD)	I71	Aortic aneurysm and dissection
	I74	Arterial embolism and thrombosis
Atrial Fibrillation (AF)	I48	Atrial fibrillation and flutter
Heart Failure (HF)	I50	Heart failure
	I11.0	Hypertensive heart disease with (congestive) heart failure
	I13.0	Hypertensive heart and renal disease with (congestive) heart failure
	I13.2	Hypertensive heart and renal disease with both (congestive) heart failure and renal failure

Appendix 2. Codes and names of CVD surgery

	code	Name of CVD surgery
Stent insertion	M6561	Percutaneous Transcatheter Placement of Intracoronary Stent-Single Vessel
	M6562	Percutaneous Transcatheter Placement of Intracoronary Stent-Additional Vessel
	M6563	Percutaneous Transcatheter Placement of Intracoronary Stent
	M6564	Percutaneous Transcatheter Placement of Intracoronary Stent
	M6565	PCI of culprit lesion in acute myocardial infarction
	M6566	PCI of Chronic total occlusion
	M6567	Percutaneous Transcatheter Placement of Intracoronary Stent
	M6601	Percutaneous Intravascular Installation of Metallic Stent-Cerebral
	M6602	Percutaneous Intravascular Installation of Metallic Stent-Carotid
	M6603	Percutaneous Intravascular Installation of Metallic Stent-Aortic
	M6604	Percutaneous Intravascular Installation of Metallic Stent-Pulmonary
	M6605	Percutaneous Intravascular Installation of Metallic Stent-Others
	M6611	Percutaneous Intravascular Installation of Stent Graft-Aortic
	M6612	Percutaneous Intravascular Installation of Stent Graft-Aortic And Iliac
	M6613	Percutaneous Intravascular Installation of Stent Graft-Others

Coronary artery bypass grafting (CABG)	O0161	Vascular Bypass Operation (Femoral-Femoral, Clavicle-Clavicle Or Axilla-Axilla), Autologous Vessel
	O0162	Vascular Bypass Operation (Femoral-Femoral, Clavicle-Clavicle Or Axilla-Axilla), Artificial Vessel
	O0163	Vascular Bypass Operation (Femoral-Popliteal[Above Knee Joint]), Autologous Vessel
	O0164	Vascular Bypass Operation (Femoral-Popliteal[Knee Joint Upper]), Artificial Vessel
	O0165	Vascular Bypass Operation (Femoral-Popliteal[Below Knee Joint]), Autologous Vessel
	O0166	Vascular Bypass Operation (Femoral-Popliteal[Below Knee Joint]), Artificial Vessel
	O0167	Vascular Bypass Operation (Femoral-Tibia,Fibula), Autologous Vessel
	O0168	Vascular Bypass Operation (Femoral-Tibia,Fibula), Artificail Vessel
	O0169	Vascular Bypass Operation (Popliteal-Tibia,Fibula), Autologous Vessel
	O0170	Vascular Bypass Operation (Popliteal-Tibia,Fibula), Artificial Vessel
	O0171	Vascular Bypass Operation (Axilla-Femoral), Artificial Vessel
	O0172	Vascular Bypass Operation (carotid-carotid, carotid-subclavian, carotid-innominate artery)
	O0173	Vascular Bypass Operation (Aorto to carotid and subclavian artery)
	O0174	Vascular Bypass Operation (Aorta-innominate, carotid and subclavian arteries)
	O0175	Vascular Bypass Operation (Artery)-Aorta-Renal, Thoracic Aorta-Femoral, Abdominal Aorta-Femoral, Aorta-Splanchnic-Artificial Vessel
	O0176	Vascular Bypass Operation (Artery)-Aorta-Renal, Thoracic Aorta-Femoral, Abdominal Aorta-Femoral, Aorta-Splanchnic-Artificial Vessel

Coronary artery bypass grafting (CABG)	O1640	Vascular Bypass Operation (Aorta-Coronary)-Simple
	O1641	Vascular Bypass Operation (Aorta-Coronary), Simple
	O1643	Vascular Bypass Op (Aorta-Renal,Thoracic,Abdominal Aorta-Femoral,Aorta-Splanchnic), Autologous Vessel
	O1644	Vascular Bypass Op (Aorta-Renal,Thoracic,Abdominal Aorta-Femoral,Aorta-Splanchnic), Artificial Vessel
	O1645	Vascular Bypass Operation (Artery-Others), Autologous Vessel
	O1646	Vascular Bypass Operation (Artery-Others), Artificial Vessel
	O1647	Vascular Bypass Operation (Aorta-Coronary), Complex
	O1648	Vascular Bypass Operation (Aorta-Coronary)-Simple
	O1649	Vascular Bypass Operation (Aorta-Coronary)-Simple
	OA640	Vascular Bypass Operation (Aorta-Coronary)-Simple (Off Pump CABG)
	OA641	Vascular Bypass Operation (Aorta-Coronary), Simple
	OA647	Vascular Bypass Operation (Aorta-Coronary), Complex
	OA648	Vascular Bypass Operation (Aorta-Coronary)-Simple (Off Pump CABG)
	OA649	Vascular Bypass Operation (Aorta-Coronary)-Simple (Off Pump CABG)

Thrombolysis	M6630	Percutaneous Thrombus Removal-Thrombolysis (Intracranial vessel)
	M6632	Percutaneous Thrombus Removal-Thrombolysis-Others
	M6634	Percutaneous Thrombus Removal-Thrombolysis-Coronary Artery
	M6635	Percutaneous Thrombus Removal-Thrombolysis (Extracranial cervical vessel)
	M6636	Percutaneous Thrombus Removal-Mechanical thrombectomy (Intracranial vessel)
	M6637	Percutaneous Thrombus Removal-Mechanical thrombectomy (Extracranial cervical vessel)
	M6638	Percutaneous Thrombus Removal-Mechanical thrombectomy (Coronary Artery)
	M6639	Percutaneous Thrombus Removal-Mechanical thrombectomy (Others)
Heart valve surgery	M6531	Percutaneous Valvuloplasty-Mitral Valve
	M6532	Percutaneous Valvuloplasty-Aortic Valve
	M6533	Percutaneous Valvuloplasty-Pulmonic Valve
	O1781	Valvuloplasty-Tricuspid Valve
	O1782	Valvuloplasty-Mitral Valve
	O1783	Valvuloplasty-Aortic Valve
	O1791	Valve Replacement-Tricuspid Valve
	O1792	Valve Replacement-Mitral Valve
	O1793	Valve Replacement-Aortic Valve

CVD, cardiovascular disease

Appendix 3. Codes and names of comobidity

	code	Name of comobidity
Hyprtension (HTN)	I10	Essential (primary) hypertension
	I11	Hypertensive heart disease
	I12	Hypertensive renal disease
	I13	Hypertensive heart and renal disease
	I15	Secondary hypertension
Diabetes mellitus (DM)	E10	Type 1 diabetes mellitus
	E11	Type 2 diabetes mellitus
	E12	Malnutrition-related diabetes mellitus
	E13	Other specified diabetes mellitus
	E14	Unspecified diabetes mellitus
Dyslipidemia	E78.0	Pure hypercholesterolaemia
	E78.1	Pure hyperglyceridaemia
	E78.2	Mixed hyperlipidaemia
	E78.3	Hyperchylomicronaemia
	E78.4	Other hyperlipidaemia
	E78.5	Hyperlipidaemia, unspecified

Appendix 4. Codes and names of dental treatment

	Code	Name of dental treatment
Conservative treatment	U0051	Access Cavity Preparation
	U0052	
	U0053	
	U0151	Cavity Preparation
	U0152	
	U0153	
	U0154	
	U0074	One Visit Endodontics-Deciduous Tooth
	U0075	
	U0079	
Periodontal treatment	U1010	Subgingival Curettage
	U1051	Periodontal Flap Operation-Simple
	U1052	Periodontal Flap Operation-Complicated
	U2232	Scaling
	U2233	
	U2240	Root Planing
Tooth extraction	U0012	Removal of Fractured Tooth Fragment
	U1132	Hemisection
	U4411	Extraction-Deciduous Tooth
	U4412	Extraction-Anterior Tooth
	U4413	Extraction-Posterior Tooth
	U4414	Extraction-Complicated Extraction
	U4415	Extraction-Impacted Tooth-Simple
	U4416	Extraction-Impacted Tooth-Complex
	U4417	Extraction-Impacted Tooth-Complete

Implant related surgery	U4981	Dental Implant Removal-Simple
	U4982	Dental Implant Removal-Complex
	UB121	Dental Implant-Fixture Placement Operation
	UB122	
	UB123	
	UB124	
	UB125	
	UB126	
	UB127	
	UB128	
	UB129	
	U1071	Allogenic, Xenogenous or Substitute Bone Graft for Alveolar Bone Defects
	U1072	Autogenous Bone Graft for Alveolar Bone Defects
	U1073	Autogenous Tooth derived Bone Graft

Appendix 5. Codes and names of outcomes

	Code	Name of outcomes
Hemorrhage from Respiratory Passages	R04	Haemorrhage from respiratory passages
Hemothorax or Hematuria	N02	Recurrent and persistent haematuria
	R31	Unspecified haematuria
	J94.2	Haemothorax
Hemorrhagic Digestive System Disorders and Ulcers	K25	Gastric ulcer
	K26	Duodenal ulcer
	K27	Peptic ulcer, site unspecified
	K28	Gastrojejunal ulcer
	K92	Other diseases of digestive system
Anemia	D50	Iron deficiency anaemia
	D62	Acute posthaemorrhagic anaemia
Intracranial Hemorrhage or Injury	I60	Subarachnoid haemorrhage
	I61	Intracerebral haemorrhage
	I62	Other nontraumatic intracranial haemorrhage
	S06	Intracranial injury

Stroke	I63	Cerebral infarction
	I64	Stroke, not specified as haemorrhage or infarction
	I69	Sequelae of cerebrovascular disease
	G45.8	Other transient cerebral ischaemic attacks and related syndromes
	G45.9	Transient cerebral ischaemic attack, unspecified
Arterial embolism and thrombosis	I74	Arterial embolism and thrombosis
Complications after acute myocardial infarction	I23	Certain current complications following acute myocardial infarction

Abstract in Korean

항혈전제를 복용하는 환자의 치과 치료에 따른 합병증 발생: 단일 기관 및 국민건강보험공단 표본 코호트 연구

서론

심혈관질환은 전 세계적으로 사망의 주요 원인이며, 항혈소판제 (예: 아스피린, 클로피도그렐) 및 항응고제 (예: 와파린, 직접 경구용 항응고제 (DOAC))와 같은 항혈전제가 치료에 사용되고 있다. 항혈전제는 심혈관질환 환자의 혈전 예방에 중요한 역할을 하지만, 치과 치료 후 출혈이 발생할 위험이 있다. 최근 연구에서는 출혈 발생 위험이 낮은 치과 치료의 경우 항혈전제를 중단하지 않고 계속 사용할 것을 권고하고 있지만, 치주 및 임플란트 수술과 같은 보다 침습적인 치과 치료 후 치과 및 전신 합병증에 대해서는 알려진 바가 적다.

본 연구의 목표는 (1) 연세대학교 의료원의 전자의무기록을 통해 단일 기관 임상 데이터에서 치과치료 후 출혈에 영향을 미치는 요인을 수집하고, (2) 국민건강보험공단 표본 코호트 데이터베이스를 통해 전신 합병증에 영향을 미치는 요인을 수집하였다. (3) 두 데이터를 활용하여 항혈전제를 복용하는 환자에서 치과 치료 후 발생하는 출혈 및 전신 합병증 발생에 미치는 영향을 평가하는 것을 목적으로 하였다.

본론

1) 2015 년부터 2019 년까지 세브란스병원에서 심혈관질환을 진단받고 연세대학교 치과 대학병원에서 치과치료를 받은 케이스는 1,878 케이스였다. 수술 후 출혈에 영향을 미치는 요인으로는 고혈압, 당뇨, 심장 판막 수술, 약물이였다. 다변량 로지스틱 회귀분석 결과 고혈압이 있는 경우 수술 후 출혈 발생 위험도는 5.882 배 높았다. 약물을 복용하지 않은 환자에 비해 와파린을 복용한 환자는 수술 후 출혈 발생 위험도가 3.280 배 더 높았으며, 헤파린 브리징한 환자는 9.837 배 더 높았다. 수술 후 출혈 위험은 DOAC 을 복용한 환자 3.114 배, 단일 항혈소판제 2.966 배, 이중 항혈소판제 2.425 배 출혈 발생 위험도가 높았다. 치과 치료의 경우, 발치와 임플란트 관련 수술 (골이식 포함)이 수술 후 출혈 발생 위험에 영향을 미쳤으며, 4 개 이상의 치아를 치료한 환자는 1 개의 치아를 치료한 환자에 비해 수술 후 출혈 발생 위험이 7.706 배 높았다.

2) 2015 년부터 2019 년까지 심혈관질환으로 진단받고 치과치료 받은 케이스는 714,397 케이스였다. 전신 합병증에 영향을 미치는 요인으로는 성별, 연령, 동반질환, 심혈관 수술, 약물 및 치과 치료였다. 여성은 남성에 비해 전신 출혈 발생 위험이 1.187 배 더 높았다. 연령이 증가함에 따라 전신 출혈 및 혈전색전성 합병증 발생 위험이 증가하였으며, 고혈압과 당뇨가 있는 환자에서 전신 출혈 위험이 각각 1.325 배, 1.344 배 높았다. 스텐트 삽입술을 받은 환자는 혈전색전성 합병증 발생 위험이 0.458 배 감소하였으나 혈전용해술을 받은 환자는 전신 출혈 및 혈전색전성 합병증 발생 위험이 각각 5.688 배, 11.204 배 높았다. 약물을

복용하지 않은 환자에 비해 항응고제와 항혈소판제를 복용하는 환자는 전신 출혈 및 혈전색전성 합병증 발생 위험이 높았다. 치과 치료의 경우, 발치가 전신 출혈 발생 위험이 높았으나, 단순 발치와 골이식 수술이 혈전색전성 합병증 발생 위험이 높았다.

결론

항응고제 및 항혈소판제를 복용한 환자는 약물을 복용하지 않은 환자에 비해 치과 치료 후 출혈 및 전신 합병증 발생 위험도가 높았다. 또한, 고혈압, 치아 발치 및 골이식을 동반한 임플란트 수술, 4 개 이상의 치료 치아 수는 치과 치료 후 출혈 또는 전신 합병증 위험에 관련이 있었다. 따라서, 출혈 및 합병증 발생을 최소화하기 위해 이러한 위험 요소가 있는 환자에게 주의를 기울여야 함을 시사한다.

핵심되는 말: 심혈관 질환; 항혈전제; 항응고제; 항혈소판제; 치과치료; 전자 의무 기록; 국민 건강 보험