Opportune Time of Tooth Extraction in Individuals Requiring Ventricular Assist Device Implantation: A Retrospective Cohort Study

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Opportune Time of Tooth Extraction in Individuals Requiring Ventricular Assist Device Implantation: A Retrospective Cohort Study

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Purpose: Individuals with implantable ventricular assist devices (VADs) are at extremely high risk of bleeding, thromboembolism, and infection after undergoing invasive dental procedures. This study aimed to investigate the systemic and local complications of tooth extraction before and after VAD implantation.

Patients and Methods: This retrospective cohort study was conducted at a single center. Oral surgical procedures were performed in patients before and/or after left VAD implantation for bridge-to-heart transplantation between April 2013 and December 2017. In this study, the medical charts of the patients were retrospectively reviewed. Data about pre-extraction complete blood count, coagulation profile, biochemical profile, and incidence of local and systemic complications were compared in patients undergoing tooth extraction before VAD implantation (b-VAD group) versus after VAD implantation (a-VAD group).

Results: In total, 28 inpatients underwent 36 oral surgical procedures before and/or after VAD implantation. Moreover, 24 tooth extractions were performed in the b-VAD group, and 12 were performed in the a-VAD group. The incidence of post-extraction bleeding was higher in the a-VAD group (P = .001, Mann-Whitney U test), and a significant difference was observed in terms of activated partial thromboplastin time (P = .010, Mann-Whitney U test). Systemic complications associated with VADs included cerebral infarction (n = 2) and driveline infection (n = 1). Post-extraction bleeding was observed within 90 days after VAD implantation in all patients who underwent tooth extraction.

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Conclusions: The risk of bleeding after tooth extraction was higher in the a-VAD group (67%) than in the b-VAD group (13%). In 3 cases, VAD-related systemic complications developed within a short period after tooth extraction. The extraction management in the b-VAD group could be controlled without causing any problem. Hence, the opportune time of tooth extraction is before VAD implantation.

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The use of a ventricular assist device (VAD) is one of the most promising strategies for the management of end-stage heart failure. Currently, the proportion of individuals with VADs is rapidly increasing. In Japan, the VAD is used for bridge-to-heart transplantation in individuals with end-stage heart failure, and the average duration of using this device is longer in patients in Japan (1,079.4 days) than in those in other countries.[1] At present, the use of this device as destination therapy is being considered, and the prolonged use of VADs and an increase in the number of individuals with VADs are expected.[2] The source of infection must be removed before VAD implantation.[3] However, it is difficult to completely eliminate the source of infection before VAD implantation and to maintain a healthy oral condition during the prolonged period of VAD implantation. Thus, the requirement of invasive dental treatment during VAD implantation will increase.

Individuals with implantable VADs are at an extremely high risk of bleeding, thromboembolism, and infection. Dental treatment during VAD implantation should be avoided because of such risks.[4-6] The common VAD-related infections are driveline and pump pocket infections attributed to seeding from skin flora, and dental bacterial infections pose a serious risk of the development of endocarditis in the population with VADs. Therefore, dental treatment, including tooth extraction, is required before VAD implantation when the cause of oral infection is identified.

Only a few studies have focused on tooth extraction in individuals with VADs. Moreover, the sample sizes of these studies were small because of the limited number of individuals with VADs and specific facilities.[4,7-9] Most clinicians were concerned about the incidence of post-extraction bleeding caused by anticoagulation therapy. However, only a few performed systemic evaluations. In addition, the incidence of post-extraction bleeding and the management methods used (eg, tooth extraction under sedation, heparin bridging, and withdrawal of antithrombotic agents) were not similar in these studies.[4,7-9] Moreover, cautious management is required for invasive dental procedures before VAD implantation owing to the risk of end-stage heart failure. However, no study has been conducted in individuals with this condition. Even though there are high risks associated with invasive dental procedures both before and after VAD implantation, guidelines about oral management, including tooth extraction, have not been established.[10] Thus, this study aimed to investigate the systemic and local effects and complications of tooth extraction by comparing the condition of patients before and after VAD implantation. Moreover, the opportune time of tooth extraction was investigated.

Patients and Methods

STUDY DESIGN

This retrospective cohort study was conducted at a single center. Between April 2013 and December 2017, patients underwent oral surgical procedures before and/or after left VAD implantation for bridge-to-heart transplantation at Kyushu University Hospital Geriatric Dentistry and Perioperative Medicine in Dentistry. VAD implantation was performed in our hospital. The inclusion criteria were *1)* patients admitted to the hospital for about 1 week, *2)* those who did not undergo invasive procedures other than tooth extraction during the period from the day of tooth extraction until 1 week later, and *3)* those with available data about the results of blood examination conducted within 24 hours before tooth extraction. All VADs after implantation were continuous-flow left VADs.

In this study, a retrospective review of the medical charts of the patients was conducted to obtain data such as pre-extraction complete blood count, coagulation profile, biochemical profile, and incidence of local and systemic complications. This study was approved by the institutional review board for clinical research of Kyushu University (approval No. 2019-399). The purpose of this study and the exclusion criteria were presented. In addition, a sufficient opt-out period was set up. The analysis was performed using anonymized data to prevent patient identification.

SURGICAL PROCEDURE

The surgeons in our facility had more than 3 years of clinical experience. Tooth extraction was performed because of severe dental caries and periodontitis. Standard tooth extraction was performed in individuals

with residual caries, apical lesions greater than 5 mm in diameter, abscesses with drainage, periodontal pockets greater than 8 mm, teeth with mobility of 3° (Miller classification), and third molars with a history of infection.

Tooth extraction involved the following procedures: Before tooth extraction, patients were instructed to rinse the mouth with 0.2% benzethonium chloride solution, and the oral mucosa was wiped with 0.025% benzalkonium chloride solution. In all cases, the tooth was extracted while the patients were under local anesthesia. The anesthetics used were 2% lidocaine containing 1:8 epinephrine, 1:40 lidocaine containing 1:24 epinephrine, and 3% prilocaine containing 0.054 IU of felypressin. By use of dental forceps and an elevator, the teeth were extracted with rotation and traction movements. A complicated tooth extraction was defined as the elevation of a mucoperiosteal flap, osteotomy, or odontotomy. After tooth extraction, suturing with No. 3-0 silk and compression hemostasis using a gauze were performed in all cases. All patients underwent suturing and received antithrombotic therapy and insertion of hemostatic agents (atelocollagen sponge material). Moreover, the wounds were protected by a surgical splint. An electrocautery knife and carbon dioxide laser were used in cases in which hemostasis was difficult to achieve.

The patients were followed at the cardiovascular department of our hospital for at least 1 week from tooth extraction to suture extraction. If bleeding from the socket, incomplete healing, or infection was observed, the dentist examined the patient daily. If there was no problem, the dentist examined the patient only on the following day and after 1 week. In patients at risk of infective endocarditis before and after VAD implantation, we administered amoxicillin, 30 mg/kg, 1 hour before surgery according to treatment guidelines.[11] After tooth extraction, 250 mg of amoxicillin was administered 4 times per day for 3 days. Loxoprofen or acetaminophen was administered as an analgesic. The use of antithrombotic drugs was regulated to achieve a prothrombin time–international normalized ratio (PT-INR) of 2 to 3 after VAD implantation. If further treatment of postoperative infection and pain was required, the duration of antibiotic and analgesic use was extended at the discretion of the medical and dental clinicians.

STUDY VARIABLES

Characteristics of Participants and Systemic Assessment

We assessed the following characteristics of the participants: gender, age, primary disease, type of antithrombotic agent used, blood test values obtained within 24 hours before tooth extraction, body temperature, blood pressure, and pulse rate on the day of tooth extraction. Moreover, the following variables were investigated after VAD implantation: number of days from VAD implantation to tooth extraction, presence or absence of systemic complications correlated to VAD implantation after tooth extraction, and number of days from tooth extraction to the onset of systemic complications. Peripheral blood test values (red blood cell count, white blood cell count, hematocrit level, hemoglobin level, and platelet count), biochemical test values (urea nitrogen, total protein, albumin, creatinine, aspartate aminotransferase, alanine aminotransferase, total bilirubin, alkaline phosphatase, γ-glutamyl transferase, lactate dehydrogenase [LDH], and C-reactive protein [CRP] levels), and coagulation test values (PT-INR, prothrombin time, and activated partial thromboplastin time [APTT]) were evaluated and recorded.

Oral Assessment

In the oral assessment, the following variables were evaluated: number of extracted teeth, dental disease, degree of tooth extraction invasion (simple or complicated), and local complications after tooth extraction. Regarding post-extraction bleeding, any bleeding observed during or after postoperative day 1 was diagnosed as post-extraction bleeding. Exudative bleeding requiring no treatment other than the application of pressure was defined as mild bleeding; bleeding requiring treatment other than pressure application was considered severe bleeding. None of the patients required blood transfusions or treatment with coagulation factors.

STATISTICAL ANALYSIS

The categorical variables were presented as frequency and percentage and were compared before and after VAD implantation using the Fisher exact test. Meanwhile, the Mann-Whitney *U* test was used to compare consecutive variables. Body temperature, blood pressure, pulse rate, and pre-extraction blood test values were compared using the Mann-Whitney *U* test in the groups undergoing tooth extraction before and after VAD implantation. The incidence of local complications was compared using the Fisher exact test. $P < .05$ was considered statistically significant. Two patients from both groups provided data such as baseline characteristics, in addition to vital signs, local complications, and blood parameters before and after VAD implantation. However, because the conditions before and after VAD implantation were different, the cases were treated independently without any relationship. SPSS software (version 26.0; IBM Japan, Tokyo) was used for all analyses.

Results

In total, 28 patients underwent 36 oral surgical procedures before and/or after VAD implantation for bridge-to-heart transplantation. Of the 28 patients, 17 (12 male and 5 female patients) and 11 (7 male and 4 female patients) underwent surgery before and after VAD implantation, respectively, which included the same patients who underwent tooth extraction both before and after VAD implantation.

Table 1 shows the characteristics of the patients who underwent tooth extraction before VAD implantation (b-VAD group) and those who underwent tooth extraction after VAD implantation (a-VAD group). The median ages of the patients in the b- and a-VAD groups were 47.0 years (interquartile range, 29.0 to 57.0 years) and 51.0 years (interquartile range, 46.0 to 59.0 years), respectively. The patients in the b-VAD group received either anticoagulants or antithrombotic agents, whereas combination therapy was provided to all patients in the a-VAD group. A total of 67 tooth extractions were performed during 36 oral surgical procedures. Moreover, 42 teeth were extracted during 24 procedures in the b-VAD group, and 25 teeth were extracted during 12 procedures in the a-VAD group. The median number of extracted teeth was 1.5 teeth per person (interquartile range, 1.0 to 2.8 teeth per person) in the b-VAD group and 1.0 teeth per person (interquartile range, 1.0 to 2.8 teeth per person) in the a-VAD group.

Table 2 shows the vital signs of the b- and a-VAD groups. The a-VAD group had a higher diastolic blood pressure (P = .001) and mean arterial blood pressure (P = .003) and lower pulse pressure (P = .001) than the b-VAD group.

In terms of complications, post-extraction bleeding was more commonly observed in the a-VAD group than in the b-VAD group (P = .001). No significant difference was observed in terms of the incidence of alveolar osteitis (P = .061). All local complications of tooth extraction were more commonly observed in the a-VAD group than in the b-VAD group (P < .001) (Table 3).

Table 4 shows the pre-extraction blood test values between the b- and a-VAD groups. In terms of blood coagulation test findings before extraction, only

Table 1. BASELINE CHARACTERISTICS OF PARTICIPANTS

	Before VAD Implantation	After VAD Implantation
Patients, n	17	11
Age, yr	47.0 (29.0-57.0)	51.0 (46.0-59.0)
Gender (male/female)	12 (71)/5 (29)	7 (64)/4 (36)
Cardiac diagnosis		
Dilated cardiomyopathy	12 (71)	8 (73)
Dilated-phase hypertrophic cardiomyopathy	3 (18)	0 (0)
Ischemic cardiomyopathy	1 (6)	1 (9)
Doxorubicin-induced cardiomyopathy	1 (6)	0 (0)
Other	0 (0)	2 (18)
Antithrombotic therapy		
Antiplatelet and warfarin	0 (0)	11 (100)
Antiplatelet	1 (6)	0 (0)
Warfarin	8 (47)	0 (0)
DOAC	2 (12)	0 (0)
None	6 (35)	0 (0)
Degree of tooth extraction invasion	24	12
Simple tooth extraction	22 (92)	9 (75)
Complicated tooth extraction	2 (8)	3 (25)
Cause of tooth extraction	42	25
Dental disease		
Dental caries	12 (28)	12 (48)
Apical periodontitis	8 (19)	4 (16)
Marginal periodontitis	20 (48)	9 (36)
Partially impacted third molar	2 (5)	0 (0)

Note: Data are presented as number (percentage) or median (25th percentile to 75th percentile).
Abbreviations: DOAC, direct oral anticoagulant; VAD, ventricular assist device.

Table 2. COMPARISON OF PRE-EXTRACTION VITAL SIGNS BETWEEN GROUPS UNDERGOING TOOTH EXTRACTION BEFORE AND AFTER VAD IMPLANTATION

	Before VAD Implantation (24 Tooth Extractions)	After VAD Implantation (12 Tooth Extractions)	*P* Value*
Body temperature, °C	36.3 (36.0-36.6)	36.2 (35.8-36.3)	.054
Pulse rate, beats/minute	72.5 (67.0-80.8)	72.5 (62.3-79.5)	.48
Blood pressure, mm Hg			
Systolic	83.0 (78.5-91.3)	84.5 (81.0-95.8)	.36
Diastolic	54.0 (48.8-61.5)	67.5 (64.3-74.5)	.001
Mean arterial	63.2 (60.2-71.4)	72.2 (68.8-80.6)	.003
Pulse pressure, mm Hg	29.0 (24.5-32.8)	19.0 (12.3-25.0)	.001

Note: Data are presented as median (25th percentile to 75th percentile).
Abbreviation: VAD, ventricular assist device.
* Mann-Whitney *U* test.

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APTT was significantly higher in the a-VAD group than in the b-VAD group ($P = .010$). Significant differences were observed in terms of bilirubin ($P = .034$), LDH ($P = .013$), and CRP ($P = .033$) levels. The bilirubin level was within the normal range. Meanwhile, the LDH and CRP levels were elevated in the a-VAD group.

The b-VAD group did not present with clinically significant systemic complications after tooth extraction. None of the patients in the b-VAD group presented with exacerbation of heart failure after tooth extraction according to body weight and oxygen saturation. No significant differences were noted on the day of and 1 week after tooth extraction in the median body weight (63.5 kg and 63.9 kg, respectively) and oxygen saturation (98% and 98%, respectively). However, 1 patient with severe invasion and perforation of the maxillary sinus after tooth extraction had a fever (38.4°C), which resolved within 2 days.

Table 5 shows the clinical data of the patients in the a-VAD group. In terms of systemic complications, cerebral infarction and driveline infection were observed within 1 month after tooth extraction. Of 12 patients, 8 were monitored for post-extraction bleeding, which is considered a local complication. In terms of the device used, the EVAHEART device (Sun Medical Technology Research Corp, Suwa-shi, Nagano, Japan) was used in 1 of 4 patients and the HeartMate II device (Abbott Labs, Lake Bluff, IL) was used in 7 of 8 patients. Post-extraction bleeding occurred in 3 patients who had their teeth extracted within 90 days of VAD implantation, with mild bleeding in 2 and severe bleeding in 1.

Table 3. COMPARISON OF LOCAL COMPLICATIONS AFTER TOOTH EXTRACTION BETWEEN GROUPS UNDERGOING PROCEDURE BEFORE AND AFTER VAD IMPLANTATION

	Before VAD Implantation (24 Tooth Extractions)	After VAD Implantation (12 Tooth Extractions)	*P* Value*
Incidence			
No	20 (83)	1 (8)	<.001
Yes	4 (17)	11 (92)	
Local complications			
Post-extraction bleeding			
No	21 (88)	4 (33)	.001
Yes	3 (13)	8 (67)	
Alveolar osteitis			
No	23 (96)	9 (75)	.061
Yes	1 (4)	3 (25)	

Note: Data are presented as number (percentage).
Abbreviation: VAD, ventricular assist device.
* Fisher exact test.

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Table 4. COMPARISON OF PRE-EXTRACTION BLOOD PARAMETERS

Parameter	Before VAD Implantation (n = 24)	After VAD Implantation (n = 12)	*P* Value*
WBC count, $\times 10^3/\mu L$	5.60 (4.32-7.02)	6.64 (5.44-7.06)	.31
RBC count, $\times 10^6/\mu L$	4.24 (3.71-4.60)	3.64 (3.41-4.35)	.06
Hb level, g/dL	12.7 (11.8-14.2)	11.7 (10.5-13.3)	.10
HCT count, %	38.0 (35.5-41.7)	34.3 (31.3-39.7)	.050
PLAT count, $\times 10^3/\mu L$	194 (158-232)	192 (161-210)	.99
PT time, seconds	27.1 (19.7-27.9)	31.0 (24.6-35.0)	.12†
PT-INR	2.25 (1.69-2.37)	2.59 (1.97-3.17)	.14†
APTT, seconds	40.2 (35.5-46.8)	50.6 (42.7-57.2)	.010†
TP level, g/dL	6.5 (6.2-7.0)	6.7 (6.2-7.2)	.45
Alb level, g/dL	3.9 (3.5-4.4)	4.1 (3.7-4.3)	.83
UN level, mg/dL	20 (13-31)	16 (13-23)	.23
CRE level, mg/dL	1.07 (0.78-1.38)	0.92 (0.72-1.07)	.23
T-Bil level, mg/dL	1.3 (0.6-1.7)	0.6 (0.4-1.3)	.034
AST level, IU/L	26 (22-31)	27 (19-30)	.63
ALT level, IU/L	20 (14-27)	17 (13-23)	.36
LDH level, IU/L	204 (173-238)	261 (208-375)	.013
ALP level, IU/L	236 (180-354)	294 (184-419)	.42
γ-GTP level, IU/L	41 (31-92)	54 (32-72)	.76
CRP level, mg/dL	0.12 (0.03-0.33)	0.52 (0.11-1.81)	.033

Note: Data are presented as median (25th percentile to 75th percentile).

Abbreviations: Alb, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; CRE, creatinine; CRP, C-reactive protein; γ-GTP, γ-glutamyl transferase; Hb, hemoglobin; HCT, hematocrit; LDH, lactate dehydrogenase; PLAT, platelet; PT, prothrombin; PT-INR, prothrombin time–international normalized ratio; RBC, red blood cell count; T-Bil, total bilirubin; TP, total protein; UN, urea nitrogen; VAD, ventricular assist device; WBC, white blood cell count.

* Mann-Whitney *U* test.

† The coagulation parameters in the group undergoing tooth extraction before VAD implantation were the data of 12 cases administered warfarin.

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Discussion

This study aimed to investigate the systemic and local complications of tooth extraction before and after VAD implantation. This study compared not only the INR value but also various blood test values that are indicators of post-extraction bleeding. Moreover, the opportune time of tooth extraction in patients with VADs was assessed by obtaining and analyzing multifaceted information, such as vital data and device type.

The results showed that the incidence of post-extraction bleeding was higher in the a-VAD group than in the b-VAD group. In the a-VAD group alone, post-extraction bleeding was observed in approximately 67% of the patients. In our study, the combination of warfarin and antiplatelet drugs was used in all patients in the a-VAD group. By contrast, in the b-VAD group, none of the patients received combination therapy. This combination therapy was found to be a risk factor for post-extraction bleeding,[12] and it might have been responsible for post-extraction bleeding in our study. However, in another study conducted from June 2016 to January 2019, we observed post-extraction bleeding in only 1 of 29 patients who received the combination therapy (excluding patients with VADs; unpublished data). Therefore, the combination of anticoagulant and antiplatelet agents may not have been the main cause of post-extraction bleeding in the a-VAD group. In patients who are routinely receiving anticoagulation drugs (including warfarin), such as those with VADs, the PT-INR is used as an indicator of the risk of post-extraction bleeding.[13] No significant difference was noted in terms of the PT-INR between the b- and a-VAD groups; this finding indicates that it might not have been an indicator in our study. It is interesting to note that the APTT was higher in the a-VAD group than in the b-VAD group. Hemorrhage caused by the destruction of von Willebrand factor (vWF) multimers in the pump after VAD implantation has been reported (acquired von Willebrand syndrome [AVWS]).[14-16] A study has shown that the APTT is

Table 5. CLINICAL DATA OF PATIENTS IN GROUP UNDERGOING TOOTH EXTRACTION AFTER VAD IMPLANTATION

Case No.	Gender	Age, yr	Cardiac Diagnosis	LVAD	No. of Extracted Teeth (Complicated Extraction)	Event After Extraction	Days From VAD Implantation to Tooth Extraction	Systemic Complication Associated With VAD	Days From Tooth Extraction to Systemic Complication
1	M	51	Cardiac sarcoidosis	EVAHEART	2 (1)	Alveolar osteitis	438	Cerebral hemorrhage	332
2	M	52	Cardiac sarcoidosis	EVAHEART	2	Alveolar osteitis	634	Cerebral hemorrhage	136
3	M	58	Dilated cardiomyopathy	EVAHEART	2 (2)	Alveolar osteitis	704	—	—
4	M	60	Dilated cardiomyopathy	HeartMate II	1	None	531	Subdural hematoma	507
5	M	51	Dilated cardiomyopathy	HeartMate II	1	Mild bleeding	857	Cerebral infarction	70
6	M	46	Dilated cardiomyopathy	HeartMate II	1	Mild bleeding	31	—	—
7	F	59	Ischemic cardiomyopathy	HeartMate II	5	Mild bleeding	59	—	—
8	M	34	Cardiac sarcoidosis	EVAHEART	1	Severe bleeding	708	—	—
9	M	37	Dilated cardiomyopathy	HeartMate II	1	Severe bleeding	67	Driveline infections	7
10	F	59	Dilated cardiomyopathy	HeartMate II	5	Mild bleeding	580	—	—
11	F	50	Dilated cardiomyopathy	HeartMate II	1 (1)	Mild bleeding	788	Cerebral infarction	23
12	F	49	Dilated cardiomyopathy	HeartMate II	3	Mild bleeding	784	—	—

Abbreviations: F, female; LVAD, left ventricular assist device; M, male; VAD, ventricular assist device.

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prolonged in patients with AVWS even if the prothrombin time is within normal range. The significant difference in APTT is not contradictory. Because the quantification of vWF is extremely laborious, a simple APTT level may be a useful indicator of the risk of postoperative bleeding.[17] Compared with other data about blood test values, significant differences in terms of LDH and CRP levels were observed between the b- and a-VAD groups. The LDH and CRP levels were elevated in the a-VAD group. The former was correlated to the result of hemolysis with the use of the VAD, and the latter might indicate an inflammatory reaction after VAD implantation. However, neither was correlated to the event after tooth extraction.

Significant differences were observed in terms of the important blood examination values. The high diastolic blood pressure and mean arterial blood pressure and low pulse pressure in the a-VAD group were partly attributed to the mechanical properties of continuous-flow VADs. After VAD implantation, the cardiac output of the patients was more likely to mainly depend on the continuous-flow pattern of the VAD, not the heartbeat. Our results showed that the mean arterial blood pressure eventually increased and pulse pressure decreased in patients with VADs. A higher mean arterial blood pressure, which is an indicator of tissue perfusion pressure, can cause post-extraction bleeding.[18] Angiogenesis and the consumption of vWF caused by decreased pulse pressure have been reported,[18] and a lower pulse pressure may be associated with post-extraction bleeding.

Post-extraction bleeding was observed in 1 of 4 patients with the EVAHEART device and 7 of 8 with the HeartMate II device. Some studies have shown that the incidence of AVWS owing to the destruction of vWF multimers is relatively low in patients undergoing EVAHEART implantation[19,20] whereas the use of the HeartMate II device was associated with AVWS.[21] Moreover, the structure of the device indicates that blood damage, including destruction of vWF, occurs more frequently in axial flow pumps than in centrifugal pumps.[22] This result is consistent with the findings of our study, and it indicates that AVWS might be associated with post-extraction bleeding. Hamzah et al[9] found that although all patients with VADs had AVWS, a significant difference was not observed in the incidence of post-extraction bleeding between VAD patients and patients receiving anticoagulants but without VAD implantation. In a previous study,[9] post-extraction bleeding was observed in 2 of 20 patients (10%) in the groups before and after VAD implantation. Moreover, most VADs were HVADs (Medtronic Inc, Minneapolis, MN), with a centrifugal pump. The difference in the results between the previous studies and current study might be associated with the predominance of the HeartMate II, with an axial flow pump.

Adequate hemostatic procedures at the time of tooth extraction can prevent post-extraction bleeding after VAD implantation,[7,9,23] or caution is required given the frequent occurrence of post-extraction bleeding.[4,8] All studies differed in terms of the management of tooth extraction. Therefore, the incidence of post-extraction bleeding is challenging to compare. On the basis of the results of this study, post-extraction bleeding occurred more frequently after VAD implantation. In the a-VAD group, the causes include the combined use of anticoagulant and antiplatelet drugs, prolonged APTT, high mean arterial pressure, low pulse pressure, and presence of axial flow pumps.

In the a-VAD group, post-extraction bleeding was observed in 8 of 12 cases. However, bleeding could be inhibited with local hemostatic treatments, including the application of pressure. Notably, 3 patients who underwent tooth extraction within 90 days after VAD implantation had post-extraction bleeding. Moreover, bleeding after extraction was severe in 1 case. When the duration of VAD implantation is shorter, the incidence of hemorrhagic events is higher,[24,25] indicating a high risk of bleeding after tooth extraction.

None of the patients in the b-VAD group presented with exacerbation of heart failure after tooth extraction. We investigated the body weight and oxygen saturation of the b-VAD group to determine whether there were signs of worsening heart failure after tooth extraction. The results showed no significant differences in terms of median body weight and oxygen saturation on the day of and 1 week after tooth extraction. The brain natriuretic peptide level could not be obtained during the same period. These results indicate that there was no worsening of heart failure after tooth extraction in the patients in the b-VAD group and that this procedure could be safely performed. However, there were complications associated with VADs after tooth extraction. The typical complications associated with VAD implantation are bleeding and/or embolism, VAD-related infection, and neurologic dysfunction due to massive bleeding, and these conditions are sometimes life-threatening.[24] After tooth extraction, 2 patients and 1 patient in the a-VAD group presented with cerebral infarction (after 23 and 70 days) and driveline infection (after 7 days), respectively. After VAD implantation, the coagulation-fibrinolysis system may be affected by tooth extraction. Moreover, this procedure may cause serious complications. For example, in cases of bacteremia or sepsis caused by oral diseases, the adjustment of antithrombotic therapy and administration of antibiotics are considered important factors. In case of driveline

infection, infection in the tooth extraction wound was suspected during the state of incomplete healing. Thus, amoxicillin was continuously administered. The presence of oral bacteria was not observed in the driveline infection site. However, the administration of amoxicillin might have affected the flora.[26,27] The direct relationship between tooth extraction and such complications in 3 cases cannot be explained. Thus, tooth extraction after VAD implantation is considered a high-risk procedure.

This study had several limitations: It was a single-center study conducted in Japanese patients only. Therefore, the results cannot be generalized to other populations. In addition, the statistical analyses were limited by the small number of patients. Thus, a larger cohort must be included, and vWF levels must be analyzed. Moreover, a longer study period is required to confirm the initial findings of this study.

In conclusion, the a-VAD group had a higher risk of bleeding after tooth extraction than the b-VAD group (67% vs 13%). In 3 patients, VAD-related systemic complications developed within a short period after tooth extraction. The extraction management in the b-VAD group could be controlled without causing any problem. Hence, the opportune time of tooth extraction is before VAD implantation.

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