Bedside Electrophysiological Study Using a Temporary Pacemaker May Predict Recurrence of Atrioventricular Block After Transcatheter Aortic Valve Replacement
A Preliminary Report

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Summary
High-degree atrioventricular block (HAVB) or complete heart block (CHB) is a common complication associated with transcatheter aortic valve replacement (TAVR). However, some patients with HAVB/CHB recover with time. The results of electrophysiological studies (EPSs) using permanent pacemaker implantation (PPI) in patients with suspicious HAVB/CHB are considered controversial.

This study aimed to evaluate whether HAVB/CHB induction at the bedside using a temporary pacemaker can predict recurrence in patients who had recovered from HAVB/CHB after TAVR.

We enrolled a total of 11 patients who had recovered from HAVB/CHB and evaluated their electrophysiology using right ventricular pacing and/or procainamide administration.

HAVB/CHB induction was positive. Three patients tested positive for HAVB/CHB, whereas 8 tested negative. The ejection fraction and the interval between HAVB/CHB onset and EPS were found to be significant. HAVB/CHB positive patients underwent PPI. A patient with a balloon-expandable valve tested positive just before recovery of CHB, but tested negative 5 days later and was included in the negative group. The 4 patients who tested negative received a cardiovascular implantable electric device (CIED). We observed HAVB/CHB in 2 patients who had previously tested positive after 3 months. Among those who tested negative, those with CIED had no HAVB/CHB, and others showed neither HAVB/CHB on electrocardiogram nor experienced syncope or sudden death.

Our EPS revealed that HAVB/CHB induction may predict HAVB/CHB recurrence after TAVR. Valve type and EPS timing may affect the results.

Key words: Aortic stenosis, Permanent pacemaker

Transcatheter aortic valve replacement (TAVR) is a well-established therapy for patients with severe aortic stenosis (AS), particularly those with surgical risks.1,2 However, TAVR can cause atrioventricular (AV) conduction disturbances. If conduction worsens, a high-degree AV block (HAVB) or complete heart block (CHB) can occur, which may require permanent pacemaker implantation (PPI).3 Patients with HAVB/CHB undergo a temporary pacemaker (TPM) insertion via a vein until PPI can be performed. However, only some patients with HAVB/CHB can recover. The need for PPI in such patients is highly debated. A study on the management of conduction abnormalities after TAVR was published recently.4 However, it did not provide details regarding patients who recovered from the atrioventricular block (AVB). Another group employed an electrophysiological study (EPS) to examine the recovery of conduction.5 However, EPS can be risky as it requires preparation and can be a burden in patients with severe surgical risks. In this study, we aimed to assess the need for PPI easily in patients who recover from HAVB/CHB. To the best of our knowledge, there are no reports of EPS using TPM after TAVR. The EPS that predict the PPI after TAVR6 needs the electrode catheter and the fluoroscopy. This study does not need them.

EPS has been performed in patients with unexplained syncope.7 Previous studies have reported cases of induced HAVB by pacing or by pharmacological stress (using ajmaline, procainamide, or disopyramide) in patients with a higher risk of developing AVB.8,9,10

We used a “simple” EPS involving AVB induction at the bedside using TPM. This EPS can be performed any
number of times and does not have some of the disadvantages of a "standard" EPS. This study aimed to evaluate whether AVB induction in an EPS by TPM leads to recurrence in patients who recovered from HAVB/CHB after TAVR. These findings may help prevent PPI in such patients who do not need to undergo PPI via an EPS.

Methods

Study design and population: This was a single-center, retrospective study involving patients with severe AS who underwent TAVR from June 2019 to October 2020 at Saiseikai Yokohamashi Tobu Hospital. We enrolled patients who had recovered from HAVB/CHB after TAVR and patients who previously underwent PPI, had no HAVB/CHB, and never recovered (Figure 1). The day of HAVB/CHB recovery depended on the physician’s judgment. This study was approved by the Institutional Review Board of Saiseikai Yokohamashi Tobu Hospital (IRB #20200126) on December 11th, 2020.

Electrocardiographic data: An electrocardiographic analysis was performed using an ECAPS 12C (NIHON KOHDEN Co., Tokyo). Electrocardiographic (ECG) diagnosis depended on the device, and a cardiologist confirmed the diagnosis. HAVB was defined as any of the following: second-degree AVB (Mobitz II); 2:1 AVB; ≥ 2 consecutive P waves at a constant physiologic rate that was not conducted to the ventricle; or transient AVB.4)

Electrophysiological study (EPS): The TPM was placed in the right ventricle apex (RVA) in the fluoroscopy room. EPS was performed at the patient’s bedside. The EPS included the following procedures: (1) pacing at the RVA at

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**Figure 1.** Study flowchart. Eleven patients recovered from AVB; 3 had a positive EPS and 8 had a negative EPS. TAVR indicates transcatheter aortic valve replacement; PPM, permanent pacemaker; AVB, atrioventricular block; TPM, temporary pacemaker; EPS, electrophysiological study; and ILR, implantable loop recorder.
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Figure 2. Atrioventricular block induction. Procainamide (10 mg/kg) administration induced Mobitz type II AVB at 4 minutes (A) which changed to 2:1 AVB at 6 minutes (B). AVB indicates atrioventricular block.

100 per minute for 1 minute; (2) intravenous administration of procainamide (10 mg/kg) for 10 minutes; and (3) pacing after procainamide administration in the same manner. The induction of HAVB/CHB was considered a positive EPS (Figure 2). The TPM was kept in place for at least a day because the procainamide effect may remain.

Enhanced computed tomography (CT): Contrast-enhanced CT was performed before TAVR using a 320-slice system (Aquilion ONE, Canon Medical Systems Corp. Tochigi, Japan). The anatomy of the left ventricle and aortic annulus was constructed using CT data and Ziostation2 Version 2.9.7.1 (Ziosoft, Inc, Tokyo). The length of the membranous septum (MS) was determined in non-reformatted standard coronary view.12)

Transcatheter aortic valve replacement: Patients underwent TAVR after consideration by the cardiology team. The prostheses used in this study were self-expandable valves, including the CoreValve Evolut R and CoreValve Evolut PRO (Medtronic Japan Co., Ltd., Tokyo), and a balloon-expandable valve, specifically the Edwards Sapien 3 (Edwards Lifesciences LLC, CA, USA) valve. Implantation depth was defined as the distance from the native aortic annulus to the implanted valve.13,14) If HAVB/CHB occurred, a TPM was inserted into the vein and placed at the RVA. During hospitalization, the electrocardiographic monitors were assessed, and no AVB occurred after the EPS.

Echocardiographic data: Echocardiography was performed using various devices (Vivid E95, GE Healthcare Japan Corp. Tokyo; APLIO Artida, APLIO 1900, and APLIO 300, Canon Medical Systems Corp. Tochigi, Japan; and iE, Philips Japan Ltd. Tokyo).

Cardiovascular implantable electronic devices (CIEDs): The PPI depended on the TAVR operator. The following permanent pacemakers (PPMs) were used: Medtronic Azure XT DR/SR (Medtronic Japan Co., Ltd., Tokyo) and Evity 8 DR-T ProMRI (Biotronik Japan Co., Tokyo). We also used a Reveal LINQ (Medtronic Japan Co., Ltd.) implantable loop recorder (ILR). The pacemaker modes of the Medtronic and Biotronik PPMs were set in ventricular pacing (MVP) mode and ADI-DDD mode, respectively. If the PPM detected AVB, the DDD mode was activated. If there was no AV conduction in 2 out of 4 beats in PPM with MVP, the AAI mode automatically switches to DDD mode.

Statistical analysis: Continuous data are described as the mean ± standard deviation and categorical data as num-
bers and percentages. The Mann-Whitney U test and Fisher’s exact test were used to compare differences across groups. All tests were two-sided, and a $P$-value of $< 0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Advanced Statistics for Windows, version 24 (IBM Japan, Inc. Tokyo). A multivariable analysis could not be performed due to the small size of the dataset.

### Results

**Atroventricular block after transcatheter aortic valve replacement:** A total of 86 patients underwent TAVR. Of these, 70 (81%, 70/86) had no AVB; 1 (1%, 1/86) previously underwent PPI; and 4 (5%, 4/86) who had never recovered from CHB received a PPI; these patients were excluded from the analysis.

**Results from EPS:** We enrolled the remaining 11 patients (13%, 11/86) with HAVB/CHB who had recovered. These

### Table 1. Characteristics of the Two Groups at Baseline

|                      | Total (n = 11) | Positive EPS (n = 3) | Negative EPS (n = 8) | $P$-value |
|----------------------|---------------|----------------------|----------------------|-----------|
| Age, years           | 86.6 ± 7.6    | 89.7 ± 2.9           | 85.5 ± 8.6           | 0.527     |
| Body mass index      | 21.0 ± 4.1    | 20.0 ± 2.0           | 21.4 ± 4.7           | 0.497     |
| Male                 | 1             | 0 (0)                | 1 (12.5)             | 1.000     |
| AVB onset during procedure | 3            | 1 (33.3)           | 2 (25)               | 1.000     |
| Implantation depth   | 6.7 ± 1.8     | 7.6 ± 2.2            | 6.0 ± 1.5            | 0.297     |
| MS length            | 6.7 ± 1.8     | 5.9 ± 0.3            | 7.0 ± 2.0            | 0.279     |
| Self-expandable valve| 6             | 2 (66.7)             | 4 (50)               | 1.000     |
| Valve pre-dilatation | 6             | 1 (33.3)             | 5 (62.5)             | 1.000     |
| Valve post-dilatation| 3             | 2 (66.7)             | 1 (12.5)             | 0.152     |
| Creatinine           | 1.03 ± 0.42   | 1.23 ± 0.80          | 0.95 ± 0.21          | 0.964     |
| eGFR                 | 45.7 ± 13.1   | 42.3 ± 25.0          | 47.0 ± 16.8          | 0.758     |
| NT-pro BNP           | 2133 ± 2383   | 2826 ± 2662          | 1874 ± 2410          | 0.376     |
| Echocardiographic data |              |                      |                      |           |
| Aortic valve area    | 0.69 ± 0.18   | 0.62 ± 0.12          | 0.72 ± 0.2           | 0.406     |
| Max aortic valve velocity | 4.5 ± 0.7   | 5.1 ± 1.0            | 4.3 ± 0.4            | 0.127     |
| Mean pressure gradient| 50.8 ± 18.1  | 68.4 ± 25.0          | 44.3 ± 10.4          | 0.133     |
| Left ventricular diastolic diameter | 40.5 ± 9    | 39.0 ± 2.9           | 41.1 ± 10.2          | 0.661     |
| Left ventricular systolic diameter | 26.2 ± 5    | 24.5 ± 1.1           | 26.8 ± 5.8           | 0.376     |
| Interventricular septum thickness | 11.5 ± 2.2  | 10.4 ± 2.7           | 11.9 ± 2.1           | 0.891     |
| Posterior wall thickness | 11.7 ± 1.6  | 10.5 ± 2.5           | 12.2 ± 1.1           | 0.261     |
| Left ventricular ejection fraction | 64.7 ± 8.2 | 71.1 ± 4.4           | 62.3 ± 8.2           | 0.048     |
| ECG before TAVR 1st degree AVB | 2 | 1 (33.3) | 1 (12.5) | 0.491 |
| RBBB | 3 | 0 (0) | 3 (37.5) | 0.491 |
| RBBB + hemiblock | 1 | 0 (0) | 1 (12.5) | 1.000 |
| LBBB | 1 | 0 (0) | 1 (12.5) | 1.000 |
| Days From TAVR to AVB onset | 1.4 ± 2.6 | 2.7 ± 4.6 | 0.9 ± 1.6 | 0.661 |
| From AVB onset to recovery | 1.8 ± 2.6 | 4.7 ± 4.0 | 0.8 ± 0.7 | 0.345 |
| From AVB onset to EPS | 3.7 ± 2.3 | 6.7 ± 0.6 | 2.6 ± 1.6 | 0.024 |
| From AVB recovery to EPS | 1.9 ± 2.0 | 2.0 ± 3.5 | 1.9 ± 1.6 | 0.618 |
| Congestive heart failure |              |                      |                      |           |
| NYHA 2 | 5 | 2 (66.7) | 3 (37.5) | 0.545 |
| NYHA 3 | 6 | 1 (33.3) | 5 (62.5) | 0.491 |
| Hypertension | 9 | 2 (66.7) | 7 (87.5) | 0.491 |
| Diabetes | 3 | 0 (0) | 3 (37.5) | 0.491 |
| Chronic kidney disease | 1 | 1 (33.3) | 0 (0) | 0.273 |
| Dyslipidemia | 4 | 0 (0) | 4 (50.0) | 0.236 |
| Atrial fibrillation | 2 | 0 (0) | 2 (25.0) | 1.000 |
| Previous PCI | 3 | 1 (33.3) | 2 (25.0) | 1.000 |
| Beta blocker use | 5 | 2 (66.7) | 3 (37.5) | 0.545 |
| ACEI/ARB use | 5 | 1 (33.3) | 4 (50.0) | 0.182 |
| Loop diuretic use | 6 | 1 (33.3) | 5 (62.5) | 0.545 |
| MRA use | 5 | 0 (0) | 5 (62.5) | 0.545 |

TAVR indicates transcatheter aortic valve replacement; AVB, atroventricular block; MS, membranous septum; NT-pro BNP, N-terminal pro b-type natriuretic peptide; NYHA, New York Heart Association; RBBB, right bundle branch block; LBBB, left bundle branch block; EPS, electrophysiological study; PCI, percutaneous coronary intervention; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; and MRA, mineralocorticoid receptor antagonist.
patients were divided into 2 groups based on the EPS results. There were 3 patients with a positive EPS (27%, 3/11) and 8 patients with a negative EPS (73%, 8/11) (Figure 1).

Patients’ characteristics and list: There was no significant difference between both groups of patients, except in the interval between AVB onset and EPS and their ejection fraction (Table I). Table II shows the baseline characteristics of all patients. Patient #8 had a balloon-expandable valve and was the only patient who underwent EPS twice.

Patients’ schedule: Patient #8 had recovered from CHB just before the EPS and had a positive EPS result 1 day after TAVR, but a negative EPS result 6 days after TAVR (Figure 3). Patients #1, #4, and #11 had a positive EPS result (Table III). Procainamide induced AVB in Patients #1 and #11, and RVA pacing-induced AVB in Patient #4. In Patients #4 and #11, EPS was performed just before recovery from HAVB/CHB. All positive EPS patients underwent PPI. In Patient #10, procainamide was able to induce intermittent left bundle branch block, which appeared as two-to-one beats; this patient was included in the negative EPS group. In the negative EPS group, 2 patients (25%, 2/8) had PPI, and 2 patients, including Patient #8 (25%, 2/8), received an ILR (Table III).

Patients’ follow-up: Over 3 months after TAVR, only Patient #11 in the positive EPS group did not suffer AVB. Patients with negative EPS who had CIED also did not suffer AVB. Other patients with negative EPS showed no signs of AVB on ECG, and no reports of syncope or sudden death were recorded (Table III). The positive predictive value of this EPS was 67%, and the negative predictive value was 100%.

Discussion

This study aimed to evaluate whether inducing atrioventricular block during an electrophysiological study using a temporary pacemaker can lead to a recurrence in patients who have recovered from high-degree atrioventricular block or complete heart block after transcatheter aortic valve replacement. We found that atrioventricular block induction might lead to a recurrence of atrioventricular block in patients who recover from HAVB/CHB.
after transcatheter aortic valve replacement. The positive predictive value of the electrophysiological study was found to be 67%, and the negative predictive value was 100%.

**Recurrence of AVB after TAVR:** Several previous electrophysiological studies have been performed in the past before or after TAVR. However, those studies focused only on the risk of new AVB onset.13-15 There is EPSs that focused on recurrence in patients with TAVR who had recovered from HAVB/CHB.16 This is the first EPS using TPM at the bedside.

**EPS using temporary pacemaker at the bedside:** Our “simple” EPS required only TPM accompanied by an antiarrhythmic drug and could be performed easily by a patient’s bedside. EPS is recommended in patients with unexplained syncope and bundle branch block. The “standard” EPS includes measurement of the His-ventricular (HV) interval at baseline and stress by atrial pacing and pharmacological methods. Ventricular pacing can also induce AVB.26 Incremental atrial pacing can show which site has the disturbance.26 Ventricular pacing only shows disturbance of the His-Purkinje system.26 As this “simple” EPS only used TPM by the bedside, atrial pacing cannot be performed and HV interval cannot be measured. A prolonged HV interval indicates a risk for AVB after TAVR.13-15 By combining a prolonged HV interval and pharmacological stress, a standard EPS had a positive predictive value as high as > 80% and a low negative predictive value.7 However, this “simple” EPS has a high negative predictive value.

**Timing, number of times, and valve type may affect the results of EPS:** In 2 patients with false positives (Patients #8 and #11), EPS was performed just before recovery from AVB (Figure 3). In Patient #8, the first EPS was positive, and the second EPS was negative. The ECG did not change for 6 days, but the AV conduction may have improved. The timing of EPS and valve type may affect EPS results.

There was no significant difference between the EPS positive and negative groups, except in the interval between AVB onset and EPS and ejection fraction. However, the small study size may have influenced our results. In our experience, a long interval between AVB onset and the recovery has relation to PPI.

**Factors affecting recovery of AVB may be different from the new-onset of AVB:** Deeper valve implantation, short MS length, baseline right bundle branch block, balloon pre-dilatation, and a self-expandable valve have been reported to be associated with new-onset AVB.3,12,17-21 In this study, there were no significant differences between the 2 groups. During recovery from AVB, other factors may affect the outcomes and further research is needed to verify our findings.

**Limitations:** There are several limitations to this study. First, it was a single-center observational retrospective study and included a small number of patients. Second,
we could not observe long-term outcomes, and patients with a negative EPS may develop HAVB/CHB in the future. Third, 4 patients with negative EPS (4/8, 50%) received CIED; however, we could not observe the patients with negative EPS without CIED for the presence or absence of an AVB. Finally, the number and timing of EPS were different.

Conclusions

In summary, AVB induction may lead to the recurrence of AVB in patients who recover from HAVB/CHB after TAVR. The positive predictive value of the EPS was 67%, and the negative predictive value was probably 100%. The type of valve used and the timing of the EPS may have influenced our results. Therefore, several EPSs should be performed at different times in patients who receive a balloon-expandable valve and recover from HAVB/CHB. In the future, we hope to determine the indications accurately for PPI with the help of EPS, possibly with the help of a large-scale prospective study.

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Disclosures

Conflicts of interest: There are no conflicts of interest to declare.

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