A real-world analysis of the effectiveness, resource use, and costs associated with ventricular tachycardia catheter ablation in Japanese patients aged ≤75 years

Kyoko Soejima, MD,* Akiko Ueda, MD, PhD,* Mami Ogiri, MS,† Yoko Ichishima, BA,† HyeJin Park, MPH,‡ Stephanie Hsiao Yu Lee, PhD§

From the *Division of Advanced Arrhythmia Management, Kyorin University School of Medicine, Tokyo, Japan, †Division of the Chief Medical Officer, Johnson & Johnson K.K., Tokyo, Japan, ‡Health Economics & Market Access, Johnson & Johnson Medical Korea, Seoul, South Korea, and §Health Economics & Market Access, Johnson & Johnson Medical Asia Pacific, Singapore, Singapore.

Introduction
Catheter ablation is important to reduce ventricular tachycardia (VT) or to prevent its recurrence, especially in the setting of structural heart disease (SHD). In idiopathic VT current recommendations place ablation as first-line therapy. In SHD patients it is typically reserved for when antiarrhythmic drugs (AADs) have failed, although multicenter randomized controlled trials have demonstrated ablation to decrease VT burden, painful implantable cardioverter-defibrillator / cardiac resynchronization therapy device (ICD/CRT-D) shocks, and recurrence at 6 months.1–3 Successful VT elimination may also enable patients who frequently have significant pulmonary, renal, and hepatic dysfunction to discontinue long-term pharmacotherapy with poorly tolerated side effects.

Long-term evidence for VT ablation in Asia is relatively sparse.4–7 In the Japanese Catheter Ablation Registry VTs represent just 2% of cases. Studies from highly specialized centers have also found recurrence to range widely, from 13% to 44%, with repeat ablation of 6.7%–26.7% depending on the VT mechanism, substrate, and cardiac site of origin.5–7 As underlying patient characteristics, clinical practice, and health care financing vary by geography, we evaluated pragmatic clinical and economic outcomes associated with VT ablation in Japan.

Methods
Details are described in Supplemental Materials. Briefly, we performed a retrospective analysis using the Japan Medical Data Center (JMDC) dataset, a nationally representative, longitudinal, and de-identified insurance claims database. The population comprised those aged ≥18 years with VT (not including premature ventricular contractions) undergoing ablation between January 2012 and December 2018. Subjects were excluded if they had prior ablation or were diagnosed with supraventricular tachycardia, atrial fibrillation, or atrial flutter in the 6-month pre–index period to ensure treatment was for VT. Based on the Ethical Guidelines for Epidemiological Research issued by the Japanese Ministry of Health, Labor and Welfare, ethics approval and informed consent were not required. Research was conducted following guidelines of the Declaration of Helsinki.

Statistics
Descriptive results were reported using means and standard deviations, or medians and interquartile ranges (IQR) for non-normally distributed continuous variables. Proportions were used for categorical variables. Survival analysis, logistic, or generalized linear regression models were applied to examine outcomes of interest. Significance level was set to $P < .05$.

Results
Utilization of catheter ablation
Of 7807 VT patients, 931 (11.9%) received ablation. Applying our eligibility criteria yielded a final sample of 210 patients (Supplemental Figure S1), with baseline and procedural characteristics in Supplemental Table S1. Cases grew more than 4-fold between 2012 and 2018 and contact force technology reached 83.6% in adoption (Supplemental Table S2).

Acute outcomes
Median length of stay (LOS) was 4 [IQR 3,5] days (Figure 1). Multivariable regression revealed that patients on AADs preablation risked extended stays (hazard ratio...
Follow-up outcomes

Results are described in Table 1. In the index month cardiac, pericardial, and vascular complications occurred in 1.0%, 0.0%, and 1.9% of patients. Hemorrhage requiring transfusion was not observed. Rates of pulmonary embolism and postoperative stroke or transient ischemic attack were 0.5% and 1.4%. Within 1 year 41.4% experienced non-VT arrhythmias, including atrial fibrillation / atrial flutter / supraventricular tachycardia, conduction disorders, and sick sinus syndrome. Seven (3.3%) underwent ICD/CRT-D implantation, with 2 concurrent to ablation. Median arrhythmia-related cost within 1 year was $1162 (IQR $410, $4050).

Readmissions and repeat ablation

Kaplan-Meier survival analyses (Figure 2) showed freedom from all-cause and VT-related readmission at 1 year to be 67.1% (95% CI: 61.1–73.8) and 79.1% (95% CI: 73.7–84.8). Hypertension (HR: 2.050; 95% CI: 1.142–3.680; \( P = .016 \)) was an independent risk factor for all-cause readmission. Freedom from all-cause and VT-related repeat ablation at 1 year was 88.6% (95% CI: 84.4–93.0) and 91.4% (95% CI: 87.7–95.3). Patients with obstructive sleep apnea (OSA) exhibited increased risk of VT-related reablation (HR: 4.460; 95% CI: 1.176–16.909; \( P = .028 \)).

Discussion

This is the first study to report the effectiveness, resource use, and costs for VT ablation in Japan. One-year freedom from VT-related readmissions (79.0%) was lower than a US study stratifying ischemic (83.0%) and nonischemic (92.5%) patients.\(^8\) However, 1-year freedom from all-cause readmission (67.1%) was similar to the THERMOCOOL® postapproval VT trial (69.3%).\(^2\)

Eliminating VT in a single procedure may have significant ramifications for health care systems by preventing downstream economic impact. Three studies (n < 20 subjects) from Japan suggest all-cause reablation rates to be 6.7%–26.7% at 12- to 88-month follow-up.\(^5\)–\(^7\) Here, we found a modest all-cause reablation rate (11.4%) after 1 year. OSA elevated risk for VT-related repeat ablation, in line with research implicating OSA-related autonomic nervous system fluctuations as a stimulant of ventricular arrhythmias.

Only 1.0% of our cohort had an ICD/CRT-D preablation, possibly owing to poor uptake of cardiac implantable devices in the primary prevention of sudden cardiac arrest locally. With 7 patients progressing to implantation within 1 year, our population may have limited prevalence of SHD with compromised ejection fraction. Approximately half of patients were not on AADs at baseline. However, as the 2019 Japanese Heart Rhythm Society guidelines recommend first-line ablation for certain monomorphic indications, this AAD utilization may be reasonable. Younger patients may also choose ablation instead of pharmacotherapy owing to potential side effects or anticipated difficulty with long-term compliance. Consistent with previous studies, a portion (~15%) of patients discontinued AADs postablation.

The index ablation cost was skewed owing to a few patients with protracted LOS or subsequent ICD/CRT-D
implantation. However, overall resource use compared favorably with the US (median LOS: 4.0 vs 4.3 days; index procedure cost: $13,025 vs $28,646). Currently no economic research is published in Japan on VT ablation; more robust resource analyses, projections, and comparative costing to alternative treatments could prove illuminating.

Limitations
JMDC comprises working individuals and their dependents; thus most patients (~97%) were <65 years of age. Using an administrative dataset with limited clinical granularity also prevented us from accounting for operator experience, hospital volumes, determining if procedures were left- or right-sided, or characterizing underlying heart disease sufficiently well. Relying on billing information to define variables may introduce classification errors. For example, although codes existed for heart failure (HF), in contrast to an absence for the New York Heart Association functional class, Japanese physicians routinely code for HF when ordering brain natriuretic peptide tests regardless of suspected HF. We consequently excluded several variables that could have helped with interpretation. Costs were only available at patient level, so economic breakdown by resource type was not possible. Finally, our sample size did not have sufficient power to test many hypotheses of interest, including AAD dose reduction.

Table 1  Follow-up outcomes

| Complications  | Total (N = 210), n (%) |
|----------------|------------------------|
| Cardiac        | 2 (1.0)                |
| Pericardial    | 0 (0.0)                |
| Vascular       | 4 (1.9)                |
| Hemorrhage requiring transfusion | 0 (0.0)                |
| Pulmonary embolism | 1 (0.5)                |
| Postoperative stroke/TIA    | 3 (1.4)                |
| Non-VT arrhythmias† | 87 (41.4)              |
| ICD/CRT-D implantation†      | 7 (3.3)                |
| Beta-blocker use†            | 89 (42.4)              |
| AAD use§         | 75 (35.7)              |
| Class Ia        | 2 (1.0)                |
| Class Ib        | 21 (10.0)              |
| Class Ic        | 10 (4.8)               |
| Class III       | 28 (13.3)              |
| Class IV        | 40 (19.0)              |
| Digoxin         | 1 (0.5)                |
| Number of AADs† | 0 (64.3)               |
|                | 1 (26.7)               |
|                | 2 (6.2)                |
|                | 3 (2.4)                |
|                | 4 (0.0)                |
|                | 5 (0.5)                |

AAD = antiarrhythmic drug; AV = atrioventricular; ICD/CRT-D = implantable cardioverter-defibrillator/cardiac resynchronization therapy device; TIA = transient ischemic attack; VF = ventricular fibrillation; VT = ventricular tachycardia.
†Index month
§Within 12 months.

Figure 2  Kaplan-Meier curves at 1-year follow-up. A: All-cause readmission. B: Ventricular tachycardia (VT)-related readmission. C: All-cause repeat ablation. D: VT-related repeat ablation.
Conclusion
Analysis from the real-world, longitudinal JMDC database revealed an acceptable safety profile, readmission rate, rehospitalization rate, and health care resource utilization for VT ablation.

Acknowledgments
Medical writing services were provided by SBW Medical Writing Inc. Programming and analysis support were provided by Onkar Kakade from Mu Sigma Business Solutions, Bengaluru, India.

Funding Sources: Johnson & Johnson provided funding for this study.

Disclosures: K. Soejima has received lecture honoraria from Abbott and Johnson & Johnson. A. Ueda is a project assistant professor at the Kyorin University School of Medicine’s Division of Advanced Arrhythmia Management, which is affiliated with an Abbott endowment. M. Ogiri, Y. Ichishima, H. Park, and S.H. Lee are employees of Johnson & Johnson.

Authorship: All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent: Based on the Ethical Guidelines for Epidemiological Research issued by the Japanese Ministry of Health, Labor and Welfare, informed consent was not required.

Ethics Statement: Research was conducted following guidelines of the Declaration of Helsinki. Based on the Ethical Guidelines for Epidemiological Research issued by the Japanese Ministry of Health, Labor and Welfare, ethics approval was not required.

Appendix
Supplementary data
Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hroo.2022.02.001.

References
1. Kuck KH, Schaumann A, Eckardt L, et al. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. Lancet 2010;375:31–40.
2. Marchlinski FE, Haftajee CI, Beshai JF, et al. Long-term success of irrigated radiofrequency catheter ablation of sustained ventricular tachycardia: post-approval Thermocool VT trial. J Am Coll Cardiol 2016;67:674–683.
3. Sapp JL, Wells GA, Parkash R, et al. Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs. N Engl J Med 2016;375:111–121.
4. Liu Y, Fang Z, Yang B, et al. Catheter ablation of fascicular ventricular tachycardia: long-term clinical outcomes and mechanisms of recurrence. Circ Arrhythm Electrophysiol 2015;8:1443–1451.
5. Talib AK, Nogami A, Morishima I, et al. Non-reentrant fascicular tachycardia: clinical and electrophysiological characteristics of a distinct type of idiopathic ventricular tachycardia. Circ Arrhythm Electrophysiol 2016;9:e004177.
6. Igarashi M, Nogami A, Kurosaki K, et al. Radiofrequency catheter ablation of ventricular tachycardia in patients with hypertrophic cardiomyopathy and apical aneurysm. JACC Clin Electrophysiol 2018;4:339–350.
7. Igarashi M, Nogami A, Fukamizu S, et al. Acute and long-term results of bipolar radiofrequency catheter ablation of refractory ventricular arrhythmias of deep intramural origin. Heart Rhythm 2020;17:1500–1507.
8. Mehta V, Boo LM, Ghaly N, et al. Real-world characteristics and readmissions among patients undergoing ablation for ventricular tachycardia: a retrospective database analysis of commercially insured patients in the USA. Open Heart 2020;7:e001247.
9. Cheung JW, Yeo I, Ip JE, et al. Outcomes, costs, and 30-day readmissions after catheter ablation of myocardial infarct-associated ventricular tachycardia in the real world. Circ Arrhythm Electrophysiol 2018;11:3006754.