ORIGINAL RESEARCH

Complications Associated With Catheter Ablation in Patients With Atrial Fibrillation: A Report From the JROAD-DPC Study

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BACKGROUND: Aging is one of the major concerns and determinants of the indications for catheter ablation (CA) for atrial fibrillation. This study aimed to assess the safety of CA in older patients with atrial fibrillation undergoing CA.

METHODS AND RESULTS: The JROAD-DPC (Japanese Registry of All Cardiac and Vascular Diseases-Diagnosis Procedure Combination) is a nationwide claims database using data from the Japanese Diagnosis Procedure Combination/Per Diem Payment System. Among 6,632,484 records found between April 2012 and March 2018 from 1058 hospitals, 135,299 patients with atrial fibrillation (aged 65±10 years, 38,952 women) who underwent CA in 456 hospitals were studied and divided into the following age groups: <60, 60 to 64, 65 to 69, 70 to 74, 75 to 79, 80 to 84, and ≥85 years. The overall in-hospital complication rate was 3.4% (cardiac tamponade 1.2%), and in-hospital mortality was 0.04%. Older patients had a higher prevalence of women, lower body mass index, and a higher burden of comorbidities such as hypertension, and all of those characteristics were predictors for complications in multivariate analysis. A multivariate adjusted odds ratio revealed that increased age was independently and significantly associated with overall complications (60–64 years, 1.19; 65–69 years, 1.29; 70–74 years, 1.57; 75–79 years, 1.63; 80–84 years, 1.90; and ≥85 years, 2.86; the reference was <60 years).

CONCLUSIONS: The nationwide JROAD-DPC database demonstrated that the frequency of complications following CA in patients with atrial fibrillation increased according to age.

Key Words: atrial fibrillation ■ catheter ablation ■ complications ■ older ■ Japanese Registry of All Cardiac and Vascular Diseases

The global population is progressively aging, and the number of people aged 65 years and older in Japan has exceeded 25%, which is larger than in any other country in the world. The number of patients with atrial fibrillation (AF) increases as the older population grows. AF is associated with increased mortality and morbidity, with stroke and thromboembolic events being major complications. Furthermore, symptoms such as palpitations result in a worsening quality of life. Therapy with antiarrhythmic drugs is not effective for survival and has toxicities. Catheter ablation (CA) for AF is widely accepted and has become an effective alternative to drug therapy. It has been shown that CA for AF improves the quality of life and reduces the risk of a stroke, cardiovascular event, and mortality. Indications for CA are based not only on the tachyarrhythmia-related symptoms and the risk of serious consequences of untreated AF.
(eg, heart failure), but they also take into account the risks of the ablation procedure. Recent advance in the ablation technique, better understanding of the electrophysiology and anatomy of the heart, and technological advances have influenced both the safety and success rates of this procedure. There are, however, few safety data on CA for AF in accordance with the detailed age groups and comorbidities.

The JROAD-DPC (Japanese Registry of All Cardiac and Vascular Diseases-Diagnosis Procedure Combination) is a nationwide claims database using data from the Japanese Diagnosis Procedure Combination/Per Diem Payment System. Recently, we analyzed the JROAD-DPC data and reported the current status of cardiovascular medicine in the aging society of Japan. In this study, by using data between April 2012 and March 2018 from the nationwide JROAD-DPC database, we investigated the safety (in-hospital complications and in-hospital mortality) of CA in patients with AF, focusing in particular on the influence of age.

Nonstandard Abbreviations and Acronyms

| Acronym | Definition |
|---------|------------|
| AFL     | atrial flutter |
| AT      | atrial tachycardia |
| AVB     | atrioventricular block |
| CA      | catheter ablation |
| DPC     | Diagnosis Procedure Combination |
| JROAD-DPC | Japanese Registry of All Cardiac and Vascular Diseases-Diagnosis Procedure Combination |

CLINICAL PERSPECTIVE

What Is New?

- In a nationwide claims database, early overall complications among patients undergoing catheter ablation for atrial fibrillation between 2012 and 2018 in Japan was 3.4%, and in-hospital mortality was 0.04%.
- The frequency of complications following catheter ablation in patients with atrial fibrillation increased according to age.
- Furthermore, older patients had a higher prevalence of women, lower body mass index, and a higher burden of comorbidities.

What Are the Clinical Implications?

- It is important to determine the indication and strategies of catheter ablation for atrial fibrillation according to the patients’ characteristics, including age, sex, and comorbidities, to reduce the impact of outcomes.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Data Source

This cross-sectional study used the JROAD-DPC database, which has been described in detail previously. The JROAD-DPC database includes the following information for each patient: patient age and sex, main diagnoses and comorbidities, drugs and devices, diagnostic and therapeutic procedures, length of stay, unique hospital identifiers, and discharge status. The Diagnosis Procedure Combination (DPC) database contains 6 categories of diagnoses based on the International Classification of Diseases, Tenth Revision (ICD-10) codes, each with a limited number of recordable diseases. One diagnosis each is coded for “main diagnosis,” “admission-precipitating diagnosis,” “most resource-consuming diagnosis,” and “second most resource-consuming diagnosis.” A maximum of 4 to 10 diagnoses each can be coded for “comorbidities present at time of admission” and “conditions arising after admission.” The following data can also be extracted from the DPC database: patient age and sex, height, weight, and body mass index. The CHA2DS2-VASc score was calculated for every patient based on a point system in which 2 points are assigned for a history of stroke or transient ischemic attack or age ≥75 years. One point was assigned for age between 65 and 74 years; history of hypertension, diabetes mellitus, heart failure, and vascular disease (prior myocardial infarction or peripheral artery disease); and female sex.

This study received approval from the institutional review board of the National Cerebral and Cardiovascular Center, Japan (R19027, April 25, 2019 and M26-148-9, April 6, 2015) and the Japanese Circulation Society (approval number 2017-14-01). No informed consent was required from participants in this study.

Study Population

The JROAD-DPC database contains 6,632,484 health records from 1058 Japanese Circulation Society-certified hospitals, which were collected between April 2012 and March 2018. Figure 1 shows a flowchart of this study.

Step 1

We extracted patients who were hospitalized for AF identified with a main diagnosis, admission-precipitating diagnosis, most resource-consuming diagnosis, and/or second most resource-consuming diagnosis of I48.
Step 2

We excluded patients with atrial flutter or atrial tachycardia identified with a main diagnosis, admission-precipitating diagnosis, most resource-consuming diagnosis, and/or second most resource-consuming diagnosis, and patients who underwent CA for AF without transseptal puncture.

Step 3

Furthermore, we excluded patients aged <20 years, patients who underwent CA with another CA procedure, and patients who underwent CA for AF other than radiofrequency CA or cryoballoon CA.

Outcome Measurement: Definition of Complications

We identified the common in-hospital complications attributable to CA for AF by using the ICD-10 diagnosis and DPC procedures codes. In-hospital complications were extracted from a maximum of 4 to 10 diagnoses coded for “conditions arising after admission.” Complications were defined on the following ICD-10 diagnosis and DPC procedure codes (Table S1): cardiac complications (cardiac tamponade: I31.9, I97.1, J98.5, and/or pericardial drainage as J048 or J0021; myocardial infarctions: I21$, I22$, or I23$; vasospastic angina: I20.1; complete atrioventricular block: I44.2; and sick sinus syndrome: I45.5 or I49.5), pulmonary complications (pneumothoraces: J930, J931, J938, or J939; hemotherax: J942; and pneumonia: J15.9, J18.9, or J69.0), neurological complications (phrenic nerve palsy: G58.8; stroke and transient ischemic attack [TIA]: G45$ or I63$), vascular access complications (hematoma: S701, S801, T140, or T810 and pseudoaneurysms: I72.4), other complications (thromboembolism: H342, I24, I269, I740, I741, I744, I748, I749, K550, K868, N280, T790; blood transfusion: K920, K9201–K9205; and cardiothoracic surgery: K539), and in-hospital death. Enrolled patients were divided into the following age groups: <60, 60 to 64, 65 to 69, 70 to 74, 75 to 79, 80 to 84, and ≥85 years.

Statistical Analysis

Categorical data are shown as frequencies and percentages. Continuous data are shown using means with the standard deviations when normally distributed, and median (interquartile range) when not normally distributed. The Shapiro-Wilk test was performed for normality test. Uni- and multivariate mixed-effects logistic regression analyses using the institutes as random intercepts were performed to evaluate whether age was independently associated.
with the overall complications. Area under the curve with 95% CI and Hosmer-Lemeshow test for a multilevel mixed model were calculated. Additionally, the Cochran-Armitage trend test category was performed. All analyses were performed using the Statistical Analysis System (version 9.4; SAS Institute, Cary, NC) and Stata 16.0 (StataCorp, College Station, TX).

**Accuracy Validation of JROAD-DPC Database**

We conducted a validation study of patients who were hospitalized at our institute between April 2012 and March 2016. We used 2 databases for this validation study, the DPC database (n=27,889) and AF ablation database (n=903), from our institute (National Cerebral and Cardiovascular Center) between April 2012 and March 2016. The AF ablation database was created based on clinical hospital records, and 2 cardiologists (Y.Y. and K.M.) confirmed the diagnosis and procedure in all 903 patients who underwent CA for AF.

**RESULTS**

**Study Population**

We identified 299,096 hospitalizations for AF identified with ICD-10 codes (I48) between April 2012 and March 2018 (Figure 1, Step 1). We excluded patients with atrial flutter or atrial tachycardia identified with a main diagnosis, admission-precipitating diagnosis, most resource-consuming diagnosis, and/or second most resource-consuming diagnosis (n=36,652) and patients who underwent CA for AF without transseptal puncture (n=126,552) (Figure 1, Step 2). Furthermore, we excluded patients aged <20 years (n=446), patients who underwent CA with another CA procedure (n=141), and patients who underwent CA for AF other than radiofrequency CA or cryoballoon CA (n=6) (Figure 1, Step 3). As a result, 135,299 patients were included in the present study.

The patients’ characteristics are shown in Table 1. The mean age was 64.8 years, and 28.8% of patients were women. A total of 46.7% of patients had hypertension, 15.1% diabetes mellitus, 32.6% heart failure, 14.5% ischemic heart disease, and 1.4% stroke or TIA. The mean CHA\textsubscript{2}-DS\textsubscript{2}-VASc score was 2.05±1.30.

The patients were divided into prespecified groups according to the age at admission (<60, 60–64, 65–69, 70–74, 75–79, 80–84, and ≥85 years) (Table S2). The largest population, except for patients aged <60 years, was patients aged 65 to 70 years (n=30,073), and older patients (aged >70 years) comprised 35.9% (n=48,537) of the study population. Older patients had a higher prevalence of women (P<0.001), a lower body mass index, (P<0.001), a higher burden of comorbidities (hypertension, diabetes mellitus, heart failure, ischemic heart disease, and stroke or TIA; P<0.001), and a higher CHA\textsubscript{2}-DS\textsubscript{2}-VASc score (P<0.001) as shown in Figures 2 and 3.

| Variable                        | Value |
|--------------------------------|-------|
| No. of patients                | 135,299 |
| Age, y, n (%)                  | 64.8±10.4 |
| <60                            | 35,412 (26.2) |
| 60–64                         | 21,277 (15.7) |
| 65–69                         | 30,073 (22.2) |
| 70–74                         | 26,119 (19.3) |
| 75–79                         | 16,459 (12.2) |
| 80–84                         | 5164 (3.8) |
| ≥85                           | 795 (0.6) |
| Sex, women, n (%)              | 38,952 (28.8) |
| Height, cm                     | 163.4±16.9 |
| Body weight, kg                | 65.6±14.0 |
| Body mass index                | 24.2±3.7 |
| Comorbidities, n (%)           |       |
| Hypertension                   | 63,192 (46.7) |
| Diabetes mellitus              | 20,495 (15.1) |
| Heart failure, n (%)           | 44,111 (32.6) |
| NYHA class I                   | 9569 (69.5) |
| NYHA class II                  | 3533 (25.7) |
| NYHA class III                 | 490 (3.6) |
| NYHA class IV                  | 172 (1.2) |
| Stroke or TIA, n (%)           | 1912 (1.4) |
| Ischemic heart disease, n (%)  | 19,600 (14.5) |
| CHA\textsubscript{2}-DS\textsubscript{2}-VASc score | 2 [1–3] |
| CHADS\textsubscript{2} score   | 1 [0–2] |
| Cryoballoon ablation, n (%)    | 18,572 (13.7) |

NYHA indicates New York Heart Association; and TIA, transient ischemic attack.

**In-Hospital Death and Complications**

The in-hospital mortality and complications data in the patients overall are shown in Table 2. The in-hospital mortality was 0.04%, and the overall in-hospital complication rate was 3.4% (cardiac tamponade, 1.2%; stroke or TIA, 1.0%; sick sinus syndrome, 0.36%; pneumonia, 0.28%; vascular access complications, 0.24%; thromboembolism except for strokes/TIA, 0.22%; and myocardial infarction, 0.09%). In-hospital death occurred more frequently corresponding to higher age (P<0.001). Female sex, lower body mass index, and heart failure were also
predictors for mortality in the univariate analysis (Table S3). Similarly, the overall complication rate increased corresponding to age ($P<0.001$) (Table S4). In particular, the following complications occurred more frequently in the older population: cardiac tamponade, $P<0.001$; pneumonia, $P<0.001$; sick sinus syndrome, $P<0.001$; thromboembolism except for strokes/TIA, $P=0.014$; and phrenic nerve palsy, $P=0.037$.

**Figure 2.** Distribution of the CHA$_2$DS$_2$-VASc score in each age group.
The older patients had a significantly higher CHA$_2$DS$_2$-VASc score corresponding to higher age ($P<0.001$).

**Figure 3.** Distribution of sex in each age group.
The older patients had a significantly increased rate of women corresponding to higher age ($P<0.001$).
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Predictors of In-Hospital Complications

The univariate and multivariate predictors for overall complications are shown in Table 3. Older age, female sex, hypertension, diabetes mellitus, heart failure, and hyperlipidemia were predictors for complications in the multivariate analysis. In the multivariate analysis after an adjustment for sex, hypertension, diabetes mellitus, heart failure, and hyperlipidemia showed that increased age remained independently and significantly associated with overall complications (Figure 4). Figures 4 shows a stepwise increase in the odds ratio of developing in-hospital complications with increasing age when compared with the reference group (aged <60 years), even in the 60 to 65 years age group. Figure S1 shows the overall complication rate in each age group according to the CHA2DS2-VASc score. In most of the age groups, the overall complication rate increased as the CHA2DS2-VASc score increased. Table S5 shows the univariate logistic regression analyses of the overall complications for CHA2DS2-VASc score 3, 4, and ≥5. The overall complication rate increased corresponding to the age group who scored 3 (P=0.020 for trend).

Validation of AF and Complication Diagnosis Based on the DPC Database

We examined the accuracy of the DPC database. We extracted patients who underwent CA for AF from 27 889 patients hospitalized at our institute between April 2012 and March 2016 by using the same flowchart as in the present study (Figure S2). As a result, a total of 856 patients were extracted as those who underwent CA for AF. We confirmed that all 856 patients underwent CA for AF by using the institutional AF ablation database. On the other hand, 47 of 903 patients who underwent CA for AF could not be extracted by the DPC database (Figure S2). As a result, the sensitivity of the DPC database to extract patients who underwent CA for AF was 94.7%, and the positive predictive value was 100%.

Next, we examined the accuracy of the DPC database to extract patients who had complications following CA for AF (Figure S3). In 856 patients who were extracted from the DPC database as those who experienced CA for AF (Figure S2), any complications were identified in the DPC database in 22 cases (detailed data are shown in Figure S3). On the other hand, complications following CA for AF were identified with the AF ablation database in 18 cases. As a result, the sensitivity of the DPC database to extract patients who had complications following CA for AF was 100%, and the positive predictive value was 81.8%.

DISCUSSION

The major findings of the present study using the nationwide JROAD-DPC claims database containing >135 000 cases and >450 hospitals between 2012 and 2018 are as follows: (1) the overall complication rate was 3.4% and (2) a multivariate adjusted odds ratio revealed that an increased age was independently and significantly associated with the overall complications (60–65 years, 1.19; 65–70 years, 1.29; 70–75 years, 1.57; 75–80 years, 1.63; 80–85 years, 1.90; and ≥85 years, 2.86; the reference was <60 years).

Validation of the JROAD-DPC Database

There have already been some studies that evaluated the mortality and/or complications following CA for AF by using a nationwide database based on ICD, Ninth Revision or ICD-10 codes, such as the Nationwide Readmissions Database in the United States and the German Diagnosis Related Groups

Table 2. In-hospital Complications

| Variable                                      | Value, N=35 299 | 95% CI   |
|----------------------------------------------|-----------------|---------|
| Overall complications, n (%)                 | 4594 (3.4)      | 3.30–3.50 |
| Cardiac complications, n (%)                 |                 |         |
| Cardiac tamponade                            | 1620 (1.2)      | 1.14–1.26 |
| Myocardial infarction                        | 122 (0.09)      | 0.07–0.11 |
| Vasospastic angina                           | 100 (0.07)      | 0.06–0.08 |
| Complete AVB                                 | 84 (0.06)       | 0.05–0.07 |
| Sick sinus syndrome                          | 491 (0.36)      | 0.33–0.39 |
| Pacemaker implantation                       | 860 (0.6)       | 0.60–0.68 |
| Pulmonary complications, n (%)               |                 |         |
| Pneumothorax                                 | 28 (0.03)       | 0.02–0.04 |
| Hemothorax                                   | 19 (0.01)       | 0.00–0.02 |
| Pneumonia                                    | 378 (0.28)      | 0.25–0.31 |
| Neurological complications, n (%)            |                 |         |
| Phrenic nerve palsy                          | 49 (0.04)       | 0.03–0.05 |
| Stroke or TIA                                | 1325 (1.0)      | 0.93–1.03 |
| Vascular access complications, n (%)         |                 |         |
| Hematoma                                     | 216 (0.16)      | 0.14–0.18 |
| Pseudoaneurysm                               | 107 (0.08)      | 0.06–0.10 |
| Other complications                          |                 |         |
| Thromboembolism, n (%)                       | 299 (0.22)      | 0.20–0.24 |
| Blood transfusion, n (%)                     | 853 (0.6)       | 0.59–0.67 |
| Cardiothoracic surgery, n (%)                | 29 (0.02)       | 0.01–0.03 |
| Length of stay, d                            | 5 [4–7]         |         |
| In-hospital death, n (%)                     | 53 (0.04)       | 0.03–0.05 |

AVB indicates atrioventricular block; and TIA, transient ischemic attack.
These studies are valuable, but they are limited by the accuracy of encoding of the ICD diagnosis and procedure codes, and miscoding and/or overcoding may influence the quality of the study. Hence, we conducted a validation study to examine (1) the accuracy of the DPC database to extract patients who underwent CA for AF and (2) the accuracy of the DPC database to extract patients who had complications following CA for AF. The validation analysis in the present study using the detailed institutional registry data demonstrated that the sensitivity and positive predictive value in extracting both patients who underwent the procedure of CA for AF and those who had complications following CA seemed to be relatively high.

**Comparison With Previous Studies**

There have been previous studies that investigated the safety of CA for AF as shown in Table 4. In Japan, Inoue et al retrospectively studied 3373 patients registered in 3 months (September 2011, March

### Table 3. Univariate and Multivariate Logistic Regression Analyses of the Overall Complications

| Variable                  | Univariate | Multivariate | P Value for Interaction With Age |
|---------------------------|------------|--------------|----------------------------------|
|                          | OR (95% CI)| OR (95% CI)  |                                   |
| Age, y (reference, <60 y)|            |              |                                  |
| 60–64                     | 1.24 (1.11–1.37) | 1.19 (1.07–1.32) | 0.001                            |
| 65–69                     | 1.37 (1.25–1.50) | 1.29 (1.17–1.42) | <0.001                           |
| 70–74                     | 1.70 (1.55–1.87) | 1.57 (1.43–1.73) | <0.001                           |
| 75–79                     | 1.80 (1.62–1.99) | 1.63 (1.46–1.82) | <0.001                           |
| 80–84                     | 2.14 (1.84–2.48) | 1.90 (1.63–2.21) | <0.001                           |
| ≥85                       | 3.24 (2.41–4.36) | 2.86 (2.12–3.85) | <0.001                           |
| Sex, women                |            |              |                                  |
| Hypertension              | 1.23 (1.15–1.31) | 1.14 (1.07–1.21) | <0.001                           |
| Diabetes mellitus         | 1.25 (1.16–1.36) | 1.21 (1.12–1.32) | <0.001                           |
| Heart failure             | 1.25 (1.16–1.34) | 1.22 (1.14–1.32) | <0.001                           |
| Hyperlipidemia            | 1.22 (1.13–1.30) | 1.14 (1.06–1.23) | <0.001                           |
| CHA2DS2-VASc score        | 1.23 (1.20–1.26) | 1.23 (1.19–1.27) | 0.14                             |
| CHADS2 score              | 1.21 (1.17–1.25) | 1.21 (1.17–1.25) | 0.14                             |
| Radiofrequency CA         | 1.02 (0.92–1.12) | 0.769 (0.66–0.89) | <0.001                           |

P<0.001 for trend in each age group. Area under the curve=0.754 (0.746–0.761). Hosmer-Lemeshow test for multilevel mixed model P=0.18.

CA indicates catheter ablation; and OR, odds ratio.

**Figure 4.** Multivariate analysis odds ratio for the overall complications according to the age group after an adjustment for the sex, hypertension, diabetes mellitus, heart failure, and hyperlipidemia.
The data including the age (62.2±0.6 years), prevalence of women (23.9%), and CHADS2 score (1.0±1.0) were comparable with those in the present study. The complication rate was 6.2% in the first period of the survey (September 2011), and it decreased to 4.2% in the third period of the survey (September 2012), which was higher than the complication rate of 3.4% in the present study. The difference in complication rate may be related in part to the study period, 2011 to 2012 versus 2012 to 2018.

There have been large-scale studies using claims databases from the United States (Table 4). Deshmukh et al investigated complications following CA for AF performed between 2000 and 2010 by using a nationwide all-payer inpatient sample conducted in collaboration with the Healthcare Cost and Utilization Project (n=93 801). Approximately 50% of patients were aged ≥50 years, and a majority of participating institutes were characterized with having a large number of hospital beds and were teaching hospitals located in an urban environment. The overall complication rate was 6.29%, and they reported that there was a small (nonsignificant) rise in overall complication rate from 2000 (5.3%) to 2010 (7.5%). Cheng et al investigated complication rates and mortality between 2010 and 2015, and reported that there was a significant increase in quarterly rates of early mortality and procedural complications following CA for AF between 2010 and 2015. It is speculated that these findings of increased mortality and complications may be related in part to a patient population that had more comorbidities (eg, 26.9% having ischemic heart disease).

The strengths of the present JROAD-DPC study are as follows: (1) the nationwide database used covered various cardiovascular hospitals in every region in Japan, (2) there was high accuracy of the DPC diagnoses and procedure codes to extract target subjects, (3) an analysis with detailed age groups (in 5-year increments) was performed, and (4) there was no patient selection bias with a large, unselected, and consecutive patient population. The uniqueness of the nationwide database may enable characterizing Japanese patients in comparison with data from the United States.

The prevalence of risk factors such as ischemic heart disease and female sex is lower in Japanese data compared with data from the United States, which may influence the lower complication rate found in Japan. The present finding of lower ischemic heart disease rates in Asian countries than in Western countries was consistent with a previous study based on statistics of the World Health Organization. It is speculated that the decline in
population blood pressure level, decline in smoking rate, and lower serum total cholesterol level in Japan compared with North America and Europe may be related, in part, to the lower prevalence of ischemic heart disease in Japan. Female sex is associated with lower cardiac mass, which may lead to a higher rate of complications such as cardiac perforation. Racial differences might be also related to the difference in outcomes.

CA for AF in Older Patients

The safety of CA for AF, particularly for older patients, is attracting attention with progressive aging of the global population. There have been some studies (patient numbers of 4000–90 000) focused on the outcomes of AF ablation in older patients by using age cutoff of 70 years, 75 years, and 80 years, and those studies reported that complications following CA for AF was higher in older patients than younger patients. There have been, however, few safety data on CA for AF in accordance with the detailed age groups. In the present study, we assessed the safety of CA for AF based on a real-world nationwide database of detailed age groups containing >135 000 patients. Older age was a particularly strong independent predictor of complications following CA for AF. Furthermore, this study showed that there was a stepwise increase in complication rate across the age groups when compared with the reference group (aged <60 years), and the increase in complication risk was found even in the 60 to 65 years age group. In addition, older patients had a higher prevalence of women, lower body mass index, a higher burden of comorbidities such as hypertension, and all of those characteristics were predictors for complications in the multivariate analysis. We also found that increased age was independently associated with the overall complications. We speculated that structural changes of myocardium with aging, independent of comorbidities, such as a stiffer, less compliant myocardium, made the heart vulnerable and might have influenced the results in this study. From a safety point of view, it is important to determine the indication and strategies of CA for AF according to the patient’s characteristics including age, sex, and comorbidities.

Study Limitations

The present study had some limitations. First, although the DPC data must be confirmed by a doctor and are highly reliable, some of data are based on medical claims. Therefore, there is a possibility that these data may contain certain errors, and some data may be over- or underestimated, although the accuracy of the JROAD-DPC is expected to be high as shown in our validation study (eg, some vascular access complications that have occurred with follow-up examinations might have been underestimated). Second, we investigated only the acute complications of CA; therefore, complications that occurred in the midterm, such as atrioesophageal fistula and pulmonary vein stenosis, could not be identified. As one of the characteristics of the DPC data set, if a patient goes to another hospital, he or she is assigned a different DPC identification. Therefore, it is not possible to follow-up on the same patients across different hospitals. Moreover, data about the technique, procedure time, type of AF (paroxysmal or persistent), time of onset of complications following CA for AF, and medications such as anticoagulants were not available.

CONCLUSIONS

The nationwide JROAD-DPC database demonstrated that the frequency of complications following CA for patients with AF increased according to age.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Tables S1–S5
Figures S1–S3

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SUPPLEMENTAL MATERIAL
### Table S1. ICD-10 Codes.

| Variable                             | ICD-10 Codes                                                                 |
|--------------------------------------|-----------------------------------------------------------------------------|
| Cardiac complications                |                                                                            |
| Cardiac tamponade                    | I31.9, I97.1, J98.5, Procedure Codes: J048, J0021                          |
| Myocardial infarction                | I21$, I22$, I23$                                                           |
| Vasospastic angina                   | I20.1                                                                      |
| Complete atroventricular block       | I44.2                                                                      |
| Sick sinus syndrome                  | I45.5, I49.5                                                               |
| Pacemaker implantation               | Operation Codes: K5971, K5972                                              |
| Pulmonary complications              |                                                                            |
| Pneumothorax                         | J930, J931, J938, J939                                                    |
| Hemothorax                           | J942                                                                       |
| Pneumonia                            | J15.9, J18.9, J69.0                                                        |
| Neurological complications           |                                                                            |
| Phrenic nerve palsy                  | G58.8                                                                      |
| Stroke or transient ischemic attack  | G45$, I63$                                                                 |
| Vascular access complications        |                                                                            |
| Hematoma                             | S701, S801, T140, T810                                                     |
| Pseudoaneurysm                       | I72.4                                                                      |
| Other complications                  |                                                                            |
| Thromboembolism                      | H342, I24, I269, I740, I741, I744, I748, I749, K550, K868, N280, T790     |
| Blood transfusion                    | Operation Codes: K920, K9201-K9205                                        |
| Cardiothoracic surgery               | Operation Codes: K539                                                     |
Table S2. Patient Characteristics in Each Age Group

| Variable (aged)           | <60  | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | ≥85 | P for trend |
|---------------------------|------|-------|-------|-------|-------|-------|-----|------------|
| Number of patients        | 35,412 | 21,277 | 30,073 | 26,119 | 16,459 | 5,164 | 795 |            |
| Age, years                | 50.9±7.1 | 62.2±1.4 | 67.0±1.4 | 72.0±1.4 | 76.7±1.4 | 81.4±1.3 | 86.4±1.8 | <0.001    |
| Sex, female, n (%)        | 5,214 (14.7) | 5,029 (23.6) | 9,099 (30.3) | 9,763 (37.4) | 7,003 (42.5) | 2,442 (47.3) | 402 (50.6) | <0.001    |
| Height, cm                | 169.2±17.0 | 165.5±15.8 | 163.0±15.8 | 159.8±17.0 | 157.9±15.7 | 155.6±16.8 | 152.6±18.8 | <0.001    |
| Body weight, kg           | 72.9±15.0 | 67.7±12.9 | 64.4±12.1 | 61.4±11.7 | 59.4±12.5 | 56.9±10.9 | 54.1±10.7 | <0.001    |
| Body mass index           | 25.2±4.1 | 24.5±3.6 | 24.0±3.4 | 23.7±3.3 | 23.5±3.3 | 23.2±3.3 | 22.8±3.3 | <0.001    |
| Comorbidities             |       |       |       |       |       |       |     |            |
| Hypertension, n (%)       | 14,031 (39.6) | 9,864 (46.4) | 14,665 (48.8) | 12,943 (49.6) | 8,506 (51.7) | 2,751 (53.3) | 432 (54.3) | <0.001    |
| Diabetes mellitus, n (%)  | 4,262 (12.0) | 3,225 (15.2) | 4,900 (16.3) | 4,296 (16.4) | 2,768 (16.8) | 907 (17.6) | 137 (17.2) | <0.001    |
| Heart failure, n (%)      | 11,126 (31.4) | 6,665 (31.3) | 9,621 (32.0) | 8,609 (33.0) | 5,675 (34.5) | 2,040 (39.5) | 375 (47.2) | <0.001    |
| NYHA class I, n (%)       | 2,672 (72.8) | 1,559 (71.4) | 2,152 (71.2) | 1,751 (67.4) | 1,055 (64.6) | 326 (59.0) | 54 (54.0) | <0.001    |
| NYHA class II, n (%)      | 861 (23.4) | 551 (25.2) | 740 (24.5) | 710 (27.3) | 471 (28.8) | 166 (30.0) | 34 (34.0) |            |
| NYHA class III, n (%)     | 104 (2.8) | 57 (2.6) | 96 (3.2) | 103 (4.0) | 78 (4.8) | 44 (7.9) | 8 (8.0) |            |
| NYHA class IV, n (%)      | 35 (1.0) | 17 (0.8) | 36 (1.2) | 33 (1.3) | 30 (1.8) | 17 (3.1) | 4 (4.0) |            |
| Stroke or TIA, n (%)      | 393 (1.1) | 284 (1.3) | 445 (1.5) | 436 (1.7) | 253 (1.5) | 87 (1.7) | 14 (1.8) | <0.001    |
| Ischemic heart disease, n (%) | 3,917 (11.1) | 2,802 (13.2) | 4,427 (14.7) | 4,209 (16.1) | 2,978 (18.1) | 1,098 (21.3) | 169 (21.3) | <0.001    |
| CHA₂DS₂-VASc score       | 1 [0 - 2] | 1 [1 - 2] | 2 [2 - 3] | 2 [2 - 3] | 3 [3 - 4] | 4 [3 - 4] | 4 [3 - 4] | <0.001    |
| CHADS₂ score             | 1 [0 - 1] | 1 [0 - 2] | 1 [0 - 2] | 1 [0 - 2] | 2 [1 - 3] | 2 [2 - 3] | 2 [2 - 3] | <0.001    |
| Cryoballoon, n (%)        | 4,805 (13.6) | 2,620 (12.3) | 4,026 (13.4) | 3,532 (13.5) | 2,450 (14.9) | 947 (18.3) | 192 (24.2) | <0.001    |

TIA = indicates transient ischemic attack, NYHA = New York Heart Association
Table S3. Univariate Logistic Regression Analysis of the Mortality.

| Variable                        | Univariate OR (95% CI) | P value  |
|---------------------------------|------------------------|----------|
| Age                             | 1.05 (1.02-1.09)       | 0.001    |
| Sex (female)                    | 2.21 (1.29-3.80)       | 0.004    |
| BMI                             | 0.86 (0.79-0.94)       | 0.001    |
| Hypertension                    | 0.72 (0.41-1.26)       | 0.249    |
| Diabetes mellitus               | 1.81 (0.96-3.39)       | 0.065    |
| Heart failure                   | 1.90 (1.09-3.30)       | 0.023    |
| Stroke or TIA                   | 2.72 (0.65-11.32)      | 0.169    |
| Prior myocardial infarction     | 1.58 (0.22-11.50)      | 0.649    |

BMI indicates body mass index; TIA, transient ischemic attack; OR, odds ratio; CI, confidence interval
### Table S4. In-hospital Complications in Each Age Group

| Variable / aged | <60 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | ≥85 | P for trend |
|-----------------|-----|-------|-------|-------|-------|-------|-----|-------------|
| Number of patients | 35,412 | 21,277 | 30,073 | 26,119 | 16,459 | 5,164 | 795 |            |
| Overall complications, n (%) | 893 (2.5) | 662 (3.1) | 1,003 (3.3) | 1,060 (4.1) | 678 (4.1) | 244 (4.7) | 54 (6.8) | <0.001 |
| Cardiac complications | | | | | | | | |
| Cardiac tamponade, n (%) | 274 (0.8) | 222 (1.0) | 370 (1.2) | 379 (1.5) | 253 (1.5) | 108 (2.1) | 14 (1.8) | <0.001 |
| Myocardial infarction, n (%) | 23 (<0.1) | 18 (<0.1) | 30 (0.1) | 28 (0.1) | 19 (0.1) | 4 (<0.1) | 0 (0) | 0.108 |
| Vasospastic angina, n (%) | 20 (<0.1) | 13 (<0.1) | 26 (<0.1) | 22 (<0.1) | 14 (<0.1) | 4 (<0.1) | 1 (0.1) | 0.120 |
| Complete AVB, n (%) | 19 (<0.1) | 10 (<0.1) | 20 (<0.1) | 18 (<0.1) | 11 (<0.1) | 4 (<0.1) | 2 (0.3) | 0.133 |
| Sick sinus syndrome, n (%) | 56 (0.2) | 52 (0.2) | 110 (0.4) | 118 (0.5) | 105 (0.6) | 39 (0.8) | 11 (1.4) | <0.001 |
| Pacemaker implantation, n (%) | 58 (0.2) | 89 (0.4) | 205 (0.7) | 243 (0.9) | 177 (1.1) | 74 (1.4) | 14 (1.8) | <0.001 |
| Pulmonary complications | | | | | | | | |
| Pneumothorax, n (%) | 11 (<0.1) | 4 (<0.1) | 6 (<0.1) | 9 (<0.1) | 7 (<0.1) | 0 (0) | 1 (0.1) | 0.591 |
| Hemothorax, n (%) | 5 (<0.1) | 2 (<0.1) | 2 (<0.1) | 4 (<0.1) | 6 (<0.1) | 0 (0) | 0 (0) | 0.365 |
| Pneumonia, n (%) | 89 (0.3) | 55 (0.3) | 61 (0.2) | 79 (0.3) | 64 (0.4) | 20 (0.4) | 10 (1.3) | <0.001 |
| Neurological complications | | | | | | | | |
| Phrenic nerve palsy, n (%) | 10 (<0.1) | 3 (<0.1) | 12 (<0.1) | 12 (<0.1) | 9 (<0.1) | 2 (<0.1) | 1 (0.1) | 0.037 |
| Stroke or TIA, n (%) | 296 (0.8) | 237 (1.1) | 278 (0.9) | 304 (1.2) | 150 (0.9) | 49 (0.9) | 11 (1.4) | 0.052 |
| Vascular access complications | | | | | | | | |
| Hematoma, n (%) | 49 (0.1) | 27 (0.1) | 51 (0.2) | 49 (0.2) | 31 (0.2) | 8 (0.2) | 1 (0.1) | 0.098 |
| Pseudoaneurysm, n (%) | 16 (<0.1) | 17 (0.1) | 24 (0.1) | 23 (0.1) | 22 (0.1) | 4 (0.1) | 1 (0.1) | 0.004 |
| Other complications | | | | | | | | |
| Thromboembolism, n (%) | 68 (0.2) | 36 (0.2) | 67 (0.2) | 77 (0.3) | 31 (0.2) | 14 (0.3) | 6 (0.8) | 0.014 |
| Length of stay, days | 5 [4 - 6] | 5 [4 - 6] | 5 [4 - 6] | 5 [4 - 7] | 5 [4 - 7] | 5 [4 - 8] | 5 [4 - 9] | <0.001 |
| In-hospital death, n (%) | 6 (<0.1) | 6 (<0.1) | 8 (<0.1) | 16 (<0.1) | 11 (<0.1) | 5 (0.1) | 1 (0.1) | <0.001 |

AVB = atrioventricular block, TIA = transient ischemic attack
Table S5. Univariate Logistic Regression Analyses of the Overall Complications for stratified CHA2DS2-VASc score 3, 4, and ≥ 5

| Variable                  | Univariate OR (95% CI) | P value |
|---------------------------|------------------------|---------|
| **CHA2DS2-VASc score = 3**|                        |         |
| Age                       | 1.01 (1.00-1.02)       | 0.007   |
| Age (reference, <60 years)|                        |         |
| 60-64                     | 1.07 (0.76-1.52)       | 0.690   |
| 65-69                     | 0.97 (0.74-1.27)       | 0.825   |
| 70-74                     | 1.21 (0.92-1.58)       | 0.172   |
| 75-79                     | 1.18 (0.89-1.56)       | 0.253   |
| 80-84                     | 1.20 (0.85-1.69)       | 0.307   |
| ≥85                       | 2.32 (1.33-4.04)       | 0.003   |

P=0.020 for trend

| **CHA2DS2-VASc score = 4**|                        |         |
| Age                       | 1.01 (1.00-1.03)       | 0.174   |
| Age (reference, <60 years)|                        |         |
| 60-64                     | 0.45 (0.15-1.37)       | 0.160   |
| 65-69                     | 0.70 (0.35-1.39)       | 0.310   |
| 70-74                     | 0.76 (0.39-1.51)       | 0.441   |
| 75-79                     | 0.69 (0.35-1.35)       | 0.276   |
| 80-84                     | 0.88 (0.44-1.77)       | 0.725   |
| ≥85                       | 1.04 (0.46-2.39)       | 0.918   |

P=0.181 for trend

| **CHA2DS2-VASc score ≥ 5**|                        |         |
| Age                       | 1.00 (0.97-1.03)       | 0.836   |
| Age (reference, <60 years)|                        |         |
| 60-64                     | -                      | -       |
| 65-69                     | 0.83 (0.40-1.73)       | 0.628   |
| 70-74                     | 0.68 (0.32-1.42)       | 0.301   |
| 75-79                     | 0.66 (0.36-1.21)       | 0.178   |
Figure S1. Overall complication rate in each age group according to CHA\(_2\)DS\(_2\)-VASc score.

In most each age group, the overall complication rate increased according to the CHA\(_2\)DS\(_2\)-VASc score.
**Figure S2. Flowchart of the pilot study to examine the accuracy of the DPC database to extract patients who underwent CA of AF.**

DPC indicates Diagnosis Procedure Combination; ICD, International Classification of Disease; CA, catheter ablation; AF, atrial fibrillation; AFL, atrial flutter; AT, atrial tachycardia.
Figure S3. Flow diagram of the pilot study to examine the accuracy of the DPC database to extract patients who had complication following CA of AF.

DPC indicates Diagnosis Procedure Combination; ICD, International Classification of Disease;
CA, catheter ablation; AF, atrial fibrillation; TIA, transient ischemic attack.
| Age Group | OR (CI)       | p-value |
|-----------|---------------|---------|
| 80-84     | 0.75 (0.39-1.42) | 0.374   |
| ≥85       | -             | -       |

P=0.539 for trend

OR, odds ratio; CI, confidence interval