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Impact of successful restoration of sinus rhythm in patients with atrial fibrillation and acute heart failure: results from the Korean Acute Heart Failure registry

Short title: Restoring sinus rhythm in the setting of AHF

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Abstract

Background: Restoring and maintaining sinus rhythm (SR) in patients with atrial fibrillation (AF) failed to show superior outcomes over rate control strategies in prior randomized trials. However, there is sparse data on their outcomes in patients with acute heart failure (AHF).

Methods: From December 2010 to February 2014, 5,625 patients with AHF from 10 tertiary hospitals were enrolled in the Korean Acute Heart Failure registry, including 1,961 patients whose initial electrocardiogram showed AF. Clinical outcomes of patients who restored sinus rhythm by pharmacological or electrical cardioversion (SR conversion group, n = 212) were compared to those of patients who showed a persistent AF rhythm (AF persistent group, n = 1,662).

Results: All-cause mortality both in-hospital and during the follow-up (median 2.5 years) were significantly lower in the SR conversion group than in the AF persistent group after adjustment for risk factors (adjusted hazard ratio [HR]; 95% confidence interval [CI] = 0.26 [0.08–0.88], p = 0.031 and 0.59 [0.43–0.82], p = 0.002, for mortality in-hospital and during follow-up, respectively). After 1:3 propensity score matching (SR conversion group = 167, AF persistent group = 501), successful restoration of sinus rhythm was associated with lower all-cause mortality (HR [95% CI)] = 0.68 [0.49–0.93], p = 0.015), heart failure rehospitalization (HR [95% CI)] = 0.66 [0.45–0.97], p = 0.032), and composite of death and heart failure rehospitalization (HR [95% CI)] = 0.66 [0.51–0.86], p = 0.002).

Conclusions: Patients with AHF and AF had significantly lower mortality in-hospital and during follow-up if rhythm treatment for AF was successful, underscoring the importance of restoring sinus rhythm in patients with AHF.

Keywords: atrial fibrillation, acute heart failure, cardioversion

INTRODUCTION

Atrial fibrillation (AF) and heart failure (HF) are very prevalent cardiovascular diseases resulting in enormous healthcare expenditures and patient suffering. They share risk factors, often coexist, and affect each other's outcomes [1–3]. Therefore, the importance for the proper management of AF in patients with HF is growing. Rhythm control strategies for

AF management — restoring and maintaining sinus rhythm — failed to show superior outcomes in terms of mortality in prior randomised trials. In the AFFIRM trial, around 4,000 patients with AF and risk factors for stroke or death were randomised and treated either with rhythm control or rate control strategies, and it was suggested that rate control strategies might be potentially advantageous because of their lower risk of adverse drug effects. However, it was also suggested that rhythm control strategies might be beneficial in higher risk patients with AF [4]. In the AF-CHF trial, patients with both AF and chronic HF were enrolled, and it also failed to show a superior impact of rhythm control strategies over rate control strategies [5]. However, there are limited data on the impact of conversion to sinus rhythm from AF in patients with acute heart failure (AHF). The aim of this study was to investigate the outcomes after rhythm treatment in patients with AHF and AF.

METHODS

Study population and Korean Acute Heart Failure registry

The Korean Acute Heart Failure (KorAHF) registry is a prospective multicenter cohort study that is currently ongoing. Patients are consecutively enrolled upon initial hospital admission for AHF syndrome and are followed up accordingly. The registry is accumulating data on individual patients, not individual hospitalizations. Information on the objectives of the study design and study population is provided in the clinical trial registration (ClinicalTrial.gov NCT01389843), and the design and the purpose of the KorAHF registry have been published elsewhere [6, 7]. Among a total of 5,625 patients with AHF enrolled in this registry, the initial electrocardiograms of 1,933 patients showed AF. Excluding 87 patients who spontaneously converted to sinus rhythm (SR) without any rhythm treatment, herein, 212 patients were compared who had restoration of sinus rhythm and its maintenance until discharge (SR conversion group) with 1662 patients who showed a persistent AF rhythm (AF persistent group). The study population flow diagram is presented in Figure 1. The study protocol was approved by the ethics committee or institutional review board at each hospital (IRB No. B-1104-125-014). The need for written informed consent was waived by the institutional review board. The study complied with the Declaration of Helsinki.

Rhythm treatment for atrial fibrillation

Restoration of sinus rhythm as well as the modality of rhythm treatment in patients with AHF and AF were left to the individual physician's choice. Both electrical (n = 38) and pharmacological cardioversion (n = 174) were included as adequate rhythm treatment. When AF spontaneously converted to sinus rhythm, the patient was excluded from the analysis.

Clinical follow-up and endpoints

The attending physician completed a web-based case report form in the Clinical Data Management System (iCReaT) from the Korea National Institute of Health (NIH) with the assistance of a clinical research coordinator. The latest information on patient clinical manifestation, biochemistry, and medication was collected at the first follow-up visit at 30 days and again at follow-up visits at 3, 6, 12, 24, 36, 48, and 60 months. The follow-up data were collected from the patients by the attending physician and stored in the web-based case report form. The outcome data on subjects who were not followed-up were ascertained by telephone interview. In addition, the outcome data on patients lost to follow-up were collected from the National Death Records. The primary endpoint of this study was the all-cause mortality rate. The in-hospital outcomes, especially in-hospital mortality were also evaluated. All deaths were considered cardiac unless a definite non-cardiac cause could be established. All outcome data reported from the participating centers were reviewed by an independent clinical event adjudicating committee.

Statistical analysis

The Student t-test and chi-square or the Fisher exact test were used to compare means and proportions of baseline clinical characteristics between the two groups. To address potential sources of bias and confounding factors in this retrospective study, propensity analysis was performed. Baseline clinical characteristics were incorporated into a non-parsimonious logistic regression model to compute the propensity score for AF rhythm treatment. The included covariates were age, sex, diabetes, hypertension, ischemic heart disease, cerebrovascular disease, chronic kidney disease, malignancy, serum hemoglobin and creatinine levels, high B-type natriuretic peptide (BNP, > 500 pg/mL) or N-terminal pro-BNP

(NT-proBNP, > 1000 pg/mL), left ventricular ejection fraction (LVEF), type of HF (de novo vs. acute decompensated), tachycardia as an etiology of AHF, new-onset AF, admission to the intensive care unit (ICU), and mechanical ventilation support (C-statistics = 0.739). 1:3 propensity score-matching iteration were then performed from the fifth digit to the first digit and 167 patients with restoration of sinus rhythm were matched to 501 patients with persistent AF. Baseline characteristics of the two groups were compared again in this matched population. The Cox proportional hazard model was used to estimate the hazard ratio (HR) and 95% confidence interval (95% CI) for the clinical outcomes of the two groups. All of the statistical analyses were performed using R version 3.6.0, and $p < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

Baseline clinical characteristics of the overall study population and propensity score-matched population are shown in Table 1. An SR was more frequently restored in relatively younger patients with lower CHA_2DS_2-VASc scores. Hypertension and chronic kidney disease tended to be more prevalent in the AF persistent group. The proportion of new-onset AF, de novo HF, and elevated BNP (or NT-proBNP) was higher in the SR conversion group. The SR conversion group included more patients who were admitted to ICU or had mechanical ventilator support. The LVEF was significantly lower and the left atrium (LA) dimension was smaller in the SR conversion group. These parameters were all comparable between the groups after propensity score matching.

In-hospital outcomes

The median duration of hospitalization was 8 days (interquartile range [IQR], 5–13), and overall in-hospital mortality was 4.2% in patients with AHF presenting with AF. The median duration of hospitalization was 11 days (IQR, 7–19) in the SR conversion group and 7 days (IQR, 5–13) when AF persisted. Comparisons of in-hospital outcomes between the SR conversion and AF persistent groups are presented in Table 2. In-hospital all-cause mortality was 4.2% in both groups (unadjusted odds ratio [OR], 95% confidence interval [95% CI] =

1.01 [0.44–2.07], p = 0.982), but after adjustment for age, sex, comorbidities, type of HF, new-onset AF, laboratory tests, echocardiographic parameters, ICU admission, and mechanical ventilation, all-cause mortality was significantly lower in the SR conversion group than in the AF persistent group (adjusted OR [95% CI] = 0.26 [0.08–0.88], p = 0.031). Cardiovascular mortality and cerebral vascular events were not different between the two groups, regardless of the adjustments. After propensity score matching, the overall mortality was 2.4% in SR restored patients and 5.9% in AF persisted patients (OR [95% CI] = 0.39 [0.10–1.00], p = 0.050). Cardiovascular mortality and the incidence of cerebral vascular accident were not significantly different between the SR conversion and AF persistent groups.

Mortality and HF rehospitalization during Follow-up

The overall mortality rates at 1, 2, and 3-year follow-up were 18.9%, 23.6%, and 27.2% when SR was successfully restored, and 22.9%, 31.3%, and 38.2% when AF persisted, respectively. The median follow-up duration was 2.5 years. Univariate survival analysis indicated that old age and various co-morbidities significantly increased the risk of death after AHF. Type of AHF (de novo vs. acute decompensated HF), timing of AF onset (newly diagnosed vs. previously diagnosed), laboratory tests, and discharge medications were also significantly correlated with mortality (Table 3). The SR conversion group showed significantly lower mortality than the AF persistent group in both the unadjusted (unadjusted HR [95% CI] = 0.70 [0.54–0.91], p = 0.007) and adjusted analysis (adjusted HR [95% CI] = 0.59 [0.43–0.82], p = 0.002). HF rehospitalization rate tended to be lower in the SR conversion group (unadjusted HR [95% CI] = 0.60 [0.47–0.77], p = 0.001; adjusted HR [95% CI] = 0.72 [0.49–1.05], p = 0.084). The composite of death and HF rehospitalization rate was lower in the SR conversion group than in the AF persistent group (unadjusted HR [95% CI] = 0.60 [0.47–0.77], p = 0.001; adjusted HR [95% CI] = 0.65 [0.49–0.85], p = 0.002). Kaplan-Meier curves for cumulative incidences of outcome events are presented in Figure 2.

After propensity score matching, all-cause mortality was still significantly lower in the SR conversion group (HR [95% CI] = 0.68 [0.49–0.93], p = 0.015). HF rehospitalization and the composite of mortality and HF rehospitalization were also lower in the SR group than

in the AF persistent group (HF rehospitalization: HR [95% CI] = 0.66 [0.45–0.97], p = 0.032, composite of mortality/HF rehospitalization: HR [95% CI] = 0.66 [0.51–0.86], p = 0.002). (Fig. 3).

In subgroup analysis, successful SR conversion was significantly associated with lower mortality rate in patients with hypertension, in contrast to patients without hypertension, where there was no difference in mortality between the SR conversion and AF persistent group (interaction p = 0.021). Other than hypertension, the beneficial effect of successful SR conversion for patients with AHF and AF did not, in terms of mortality, significantly differ according to age, sex, diabetes mellitus, onset of AF, and the type or aetiology of HF (Table 4).

Cerebrovascular events during follow-up

Cerebrovascular accident rates at the 3-year follow-up were 3.1% when SR was restored and 2.3% when AF persisted (HR [95% CI] = 1.28 [0.50–3.28], p = 0.614) in the crude study population. After propensity score matching, cerebrovascular event rates were 3.3% and 3.1% (HR [95% CI] = 1.28 [0.44–3.67], p = 0.652), respectively.

DISCUSSION

The benefit of rhythm control over rate control strategies in patients with AF has been controversial thus far in terms of mortality [4, 5, 8, 9]. Therefore, the current guidelines recommend restoration and maintenance of SR mainly in patients with symptomatic AF [10]. However, very high-risk patients with AF, such as the patients with AHF in the present study, have not been adequately evaluated. The data showed a significantly lower in-hospital mortality rate when initial AF was successfully converted to SR either by drugs or electrical cardioversion in patients with AHF after adjustments for various covariates. And interestingly, this beneficial effect on mortality persisted during the long-term follow-up. The HF readmission rate was also lower in the SR conversion group in the matched population. There was no significant difference in terms of cerebrovascular events, both in-hospital and during follow-up.

Atrial fibrillation and HF are two very prevalent cardiovascular diseases, often

considered to be epidemic [1, 11]. These two cardiovascular diseases share many risk factors, such as ageing, hypertension, diabetes mellitus, and underlying ischemic/valvular heart disease. Moreover, AF and HF can aggravate each other. There are several suggested mechanisms by which AF facilitates the development of HF. First, AF decreases cardiac output not only because of the consequences of poor ventricular rate control but also those of irregular ventricular filling and loss of atrial contraction. Decreased cardiac output augments neuro-hormonal activation observed in HF. Functional mitral annular enlargement is another possible explanation for HF development in patients with AF. On the other hand, HF can also cause AF development through atrial enlargement, vasoconstrictive neuro-hormonal milieu, and atrial fibrosis [1, 12]. These interconnections between AF and HF lead to a high prevalence of AF in patients with HF [13], which was 27% in this KorAHF registry.

Beyond its high prevalence, there is evidence that AF involves increased adverse events in patients with congestive HF. In participants of the Framingham Heart Study, AF and HF showed a temporal association, and concomitant AF and HF resulted in a lower survival rate [14]. Retrospective post-hoc analysis of the SOLVD (Studies of Left Ventricular Dysfunction) Prevention and Treatment trials demonstrated that the presence of AF increased the risk of all-cause mortality in patients with left ventricular systolic dysfunction [15]. A recent meta-analysis of randomised trials concluded that AF increased adverse events in patients with chronic HF after adjusting for other clinical risk factors (adjusted OR 1.40) [16]. Regarding the timing of AF and HF diagnosis, a community-based study suggested that the negative effect of AF on patients with HF was greater with incident AF than with prevalent AF [17]. The Framingham cohort [14] and MADIT II (Multicenter Automatic Defibrillator Trial II) trial demonstrated supporting results [18].

On the other hand, the impact of concomitant AF in patients presenting with AHF syndrome appears less clear. In contrast to the results from patients with chronic HF, data from the ATTEND registry showed no difference in 30-day all-cause mortality between patients with (3.04%) or without AF (3.88%) [13]. Additionally, in the KorAHF registry, the in-hospital all-cause mortality of the AF population (4.2%) was not different from that of the overall population (5.3%). These results might suggest that AF is not a worse etiology or more aggravating factor for AHF syndrome than other etiologic factors, although AF is a

significant risk factor for adverse outcomes in patients with chronic HF.

Despite the increase in adverse events by the presence of AF in patients with congestive HF, large randomized trials such as the AF-CHF (Atrial Fibrillation and Congestive Heart Failure) study [5] and DIAMOND-CHF trial (Danish Investigations of Arrhythmia and Mortality on Dofetilide in Congestive Heart Failure) [19] demonstrated no benefit of a rhythm control strategy in those patients. However, this result was often accounted for by the adverse effects of anti-arrhythmic drugs, especially in AF patients with left ventricular dysfunction, and the benefit of maintaining sinus rhythm itself was not completely denied. Maintaining sinus rhythm using catheter ablation has been reported to improve functional capacity and LVEF compared with the rate control strategy [20–22], and more recent trials demonstrated a survival benefit of catheter ablation in patients with AF and chronic HF, emphasising the importance of maintaining sinus rhythm itself [23–25]. Data herein, also suggest the importance of attempts to maintain SR in AF patients with an acute setting of HF.

In the setting of AHF with AF, benefits of the restoration of SR have not been adequately evaluated, perhaps because of difficulties in conducting large randomized clinical trials in this population. In the KorAHF registry, all-cause mortality was significantly lower when initial AF was converted to SR either by drug (amiodarone) or electrical cardioversion in patients with AHF. Despite emerging evidence for the benefit of catheter ablation in patients with AF and congestive HF, performing catheter ablation is not widely accepted in the setting of AHF syndrome. Therefore, the present study data may reflect the clinical outcomes of rhythm control strategies in a daily practice setting. In this study, there was no difference in in-hospital mortality irrespective of whether AF persisted or successful conversion to SR was acquired in the overall population. However, after adjustments for various clinical predictors for mortality, in-hospital mortality was significantly better in the SR conversion group. Interestingly, the beneficial effect of conversion to SR in patients with AHF and AF was still significant after discharge from the index HF admission, suggesting the importance of adequate treatment of the index HF admission. Restoring SR and maintaining it during index HF admission appeared to affect not only the in-hospital outcomes but also the long-term outcomes over several years.

Limitations of the study

There were several limitations to this study. This was a non-randomised, registry-based study and might have been affected by unmeasured confounding factors. Since the attending physician's intension regarding AF treatment strategy (rhythm control vs. rate control) was not collected in this registry, the definition of the present study groups is different from that of the rhythm and rate control strategy groups in previous randomized trials. The KorAHF registry did not collect data on the rhythm status during follow-up, thus further analysis according to the recurrence of AF during follow-up was not available. Further studies are warranted to confirm the effect of rhythm control strategies for AF in these high-risk patients with AHF.

CONCLUSIONS

In this large multicenter KorAHF registry, patients with AHF and AF had significantly lower future mortality rates when rhythm treatments for AF were successfully applied. These results underscore the importance of restoring SR in patients presenting with AHF.

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Conflict of interest: None declared

References

1. Verma A, Kalman JM, Callans DJ. Treatment of patients with atrial fibrillation and heart failure with reduced ejection fraction. Circulation. 2017; 135(16): 1547–1563, doi: 10.1161/CIRCULATIONAHA.116.026054, indexed in Pubmed: 28416525.

2. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. J Am Coll Cardiol. 2019; 74(1): 104–32.
3. January CT, Wann LS, Alpert JS, et al. Jr., 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014; 64(21): e1–76.
4. Wyse DG, Waldo AL, DiMarco JP, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med. 2002; 347(23): 1825–1833, doi: 10.1056/NEJMoa021328, indexed in Pubmed: 12466506.
5. Roy D, Talajic M, Nattel S, et al. Rhythm control versus rate control for atrial fibrillation and heart failure. N Engl J Med. 2008; 358(25): 2667–2677, doi: 10.1056/NEJMoa0708789, indexed in Pubmed: 18565859.
6. Lee SE, Cho HJ, Lee HY, et al. A multicentre cohort study of acute heart failure syndromes in Korea: rationale, design, and interim observations of the Korean Acute Heart Failure (KorAHF) registry. Eur J Heart Fail. 2014; 16(6): 700–708, doi: 10.1002/ejhf.91, indexed in Pubmed: 24797348.
7. Lim NK, Lee SE, Lee HY, et al. Clinical Characteristics and Outcome of Acute Heart Failure in Korea: Results from the Korean Acute Heart Failure Registry (KorAHF). Korean Circ J. 2017; 47(3): 341–353, doi: 10.4070/kcj.2016.0419, indexed in Pubmed: 28567084.
8. Van Gelder IC, Hagens VE, Bosker HA, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. N Engl J Med. 2002; 347(23): 1834–1840, doi: 10.1056/NEJMoa021375, indexed in Pubmed: 12466507.
9. Flaker GC, Blackshear JL, McBride R, et al. Antiarrhythmic drug therapy and cardiac mortality in atrial fibrillation. The Stroke Prevention in Atrial Fibrillation Investigators. J Am Coll Cardiol. 1992; 20(3): 527–532, doi: 10.1016/0735-1097(92)90003-6, indexed in Pubmed: 1512329.
10. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline) A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology. 2011; 57(2): 223–42.
11. Braunwald E. Cardiovascular Medicine at the Turn of the Millennium: Triumphs, Concerns, and Opportunities. N Engl J Med. 1997; 337(19): 1360–1369, doi: 10.1056/nejm199711063371906.
12. Anter E, Jessup M, Callans DJ. Atrial fibrillation and heart failure: treatment considerations for a dual epidemic. Circulation. 2009; 119(18): 2516–2525, doi: 10.1161/CIRCULATIONAHA.108.821306, indexed in Pubmed: 19433768.
13. Kajimoto K, Sato N, Takano T, et al. investigators of the Acute Decompensated Heart Failure Syndromes (ATTEND) registry. Relationship of renal insufficiency and clinical features or comorbidities with clinical outcome in patients hospitalised for acute heart failure syndromes. Eur Heart J Acute Cardiovasc Care. 2016; 6(8): 697–708, doi: 10.1177/2048872616658586, indexed in Pubmed: 27363422.

14. Santhanakrishnan R, Wang Na, Larson MG, et al. Atrial fibrillation begets heart failure and vice versa: temporal associations and differences in preserved versus reduced ejection fraction. Circulation. 2016; 133(5): 484–492, doi: 10.1161/CIRCULATIONAHA.115.018614, indexed in Pubmed: 26746177.
15. Dries D, Exner D, Gersh B, et al. Atrial fibrillation is associated with an increased risk for mortality and heart failure progression in patients with asymptomatic and symptomatic left ventricular systolic dysfunction: a retrospective analysis of the SOLVD trials. J Am Coll Cardiol. 1998; 32(3): 695–703, doi: 10.1016/s0735-1097(98)00297-6.
16. Mamas MA, Caldwell JC, Chacko S, et al. A meta-analysis of the prognostic significance of atrial fibrillation in chronic heart failure. Eur J Heart Fail. 2009; 11(7): 676–683, doi: 10.1093/eurjhf/hfp085, indexed in Pubmed: 19553398.
17. Chamberlain AM, Redfield MM, Alonso A, et al. Atrial fibrillation and mortality in heart failure: a community study. Circ Heart Fail. 2011; 4(6): 740–746, doi: 10.1161/CIRCHEARTFAILURE.111.962688, indexed in Pubmed: 21920917.
18. Zareba W, Steinberg J, McNitt S, et al. Implantable cardioverter-defibrillator therapy and risk of congestive heart failure or death in MADIT II patients with atrial fibrillation. Heart Rhythm. 2006; 3(6): 631–637, doi: 10.1016/j.hrthm.2006.02.012.
19. Torp-Pedersen C, Møller M, Bloch-Thomsen P, et al. Dofetilide in Patients with Congestive Heart Failure and Left Ventricular Dysfunction. N Engl J Med. 1999; 341(12): 857–865, doi: 10.1056/nejm199909163411201.
20. Anselmino M, Matta M, Castagno D, et al. Catheter ablation of atrial fibrillation in chronic heart failure: state-of-the-art and future perspectives. Europace. 2016; 18(5): 638–647, doi: 10.1093/europace/euv368, indexed in Pubmed: 26857188.
21. Hunter RJ, Berriman TJ, Diab I, et al. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). Circ Arrhythm Electrophysiol. 2014; 7(1): 31–38, doi: 10.1161/CIRCEP.113.000806, indexed in Pubmed: 24382410.
22. Jones DG, Haldar SK, Hussain W, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in heart failure. J Am Coll Cardiol. 2013; 61(18): 1894–1903, doi: 10.1016/j.jacc.2013.01.069, indexed in Pubmed: 23500267.
23. Di Biase L, Mohanty P, Mohanty S, et al. Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device: Results From the AATAC Multicenter Randomized Trial. Circulation. 2016; 133(17): 1637–1644, doi: 10.1161/CIRCULATIONAHA.115.019406, indexed in Pubmed: 27029350.
24. Ullah W, Ling LH, Prabhu S, et al. Catheter ablation of atrial fibrillation in patients with heart failure: impact of maintaining sinus rhythm on heart failure status and long-term rates of stroke and death. Europace. 2016; 18(5): 679–686, doi: 10.1093/europace/euv440, indexed in Pubmed: 26843584.
25. Marrouche N, Brachmann J, Andresen D, et al. Catheter ablation for atrial fibrillation with heart failure. N Engl J Med. 2018; 378(5): 417–427, doi: 10.1056/nejmoa1707855.

Table 1. Baseline characteristics.

	Overall AF patients			**Matched population**		
	SR restored (n = 212)	**AF (n = 1,662)**	**P**	**SR restored (n = 167)**	**AF (n = 501)**	**P**
Age [years]	67 ± 14	71 ± 12	< 0.001	68 ± 13	68 ± 14	0.840
Male	104 (49.1)	866 (52.1)	0.403	83 (49.7)	274 (54.7)	0.303
Hypertension	114 (53.8)	999 (60.1)	0.077	91 (57.7)	226 (54.5)	0.528
Diabetes mellitus	57 (26.9)	483 (29.1)	0.510	46 (27.5)	147 (29.3)	0.730
CAD	37 (17.5)	346 (20.8)	0.262	32 (19.2)	116 (23.2)	0.333
Valvular heart disease	41 (19.3)	393 (23.6)	0.162	32 (19.2)	77 (15.4)	0.304
Cerebrovascular disease	32 (15.1)	325 (19.6)	0.119	22 (13.2)	62 (12.4)	0.893
CKD	17 (8.0)	197 (11.9)	0.098	14 (8.4)	43 (8.6)	1.00
De novo heart failure	115 (54.2)	705 (42.4)	0.001	90 (53.9)	271 (54.1)	1.00
Lung congestion	164 (77.4)	1303 (78.4)	0.729	112 (76.6)	410 (81.8)	0.176
Previous HF admission	65 (30.7)	652 (39.3)	0.019	52 (31.1)	147 (29.3)	0.732
New onset AF	108 (51.9)	499 (30.4)	< 0.001	85 (50.9)	261 (52.1)	0.858
Tachycardia induced HF	105 (49.5)	729 (43.9)	0.118	88 (52.7)	251 (50.1)	0.623
CHA_2DS_2-VASc score	4.4 ± 1.7	4.8 ± 1.7	0.001	4.4 ± 1.7	4.4 ± 1.5	0.766
Malignancy	21 (9.9)	132 (7.9)	0.326	16 (9.6)	39 (7.8)	0.569
ICU admission	134 (63.2)	642 (38.6)	< 0.001	99 (59.3)	297 (59.3)	1.00
Mechanical ventilation	54 (25.5)	172 (10.3)	< 0.001	33 (19.8)	98 (19.6)	1.00
Hemoglobin [g/dL]	12.7 ± 2.2	12.7 ± 2.2	0.903	12.8 ± 2.2	12.8 ± 2.1	0.693
Creatinine [mg/dL]	1.3 ± 1.4	1.3 ± 1.0	0.939	1.2 ± 0.9	1.3 ± 0.8	0.604
High BNP or NT-proBNP	162 (88.0)	1220 (81.4)	0.034	128 (88.9)	424 (91.0)	0.557
LVEF [%]	37 ± 16	41 ± 16	< 0.001	37 ± 17	36 ± 16	0.550
LA dimension [mm]	49 ± 10	54 ± 10	< 0.001	50 ± 10	50 ± 8	0.882
Discharge medication						
ACEI or ARB	123 (58.0)	1062 (63.9)	0.110	102 (61.1)	323 (64.5)	0.486
Beta-blocker	99 (46.7)	802 (48.3)	0.723	78 (46.7)	270 (53.9)	0.128

Data are expressed as number (%) or mean ± standard deviation. ACEI — angiotensin-converting enzyme inhibitor; AF — atrial fibrillation; ARB — angiotensin receptor blocker; BNP — B-type natriuretic peptide; CAD — coronary artery disease; CKD — chronic kidney disease; HF — heart failure; ICU — intensive care unit; LA — left atrium; LVEF — left ventricular ejection fraction; NT-proBNP — N-terminal-pro B-type natriuretic peptide; SR — sinus rhythm

Table 2. In-hospital outcomes.

	Overall population						Matched population			
	SR (n = 212)	**AF (n = 1,662)**	**Unadjusted OR (95% CI)**	**P**	**Adjusted OR (95% CI)**	**P**	**SR (n = 167)**	**AF (n = 501)**	**Unadjusted OR (95% CI)**	**P**
All-cause mortality	9 (4.2%)	70 (4.2%)	1.01 (0.44–2.07)	0.982	0.26 (0.08–0.88)	0.031	5 (3.0%)	37 (7.4%)	0.39 (0.15–1.00)	0.050
Cardiovascular death	8 (3.8%)	50 (3.0%)	1.26 (0.51–2.74)	0.545	0.40 (0.11–1.40)	0.151	5 (3.0%)	27 (5.4%)	0.54 (0.21–1.43)	0.216
Cerebral vascular accident	2 (0.9%)	27 (1.6%)	0.58 (0.07–2.32)	0.449	0.56 (0.12–2.65)	0.465	2 (1.2%)	7 (1.4%)	0.86 (0.18–4.16)	0.847

Odds ratios (OR) for in-hospital clinical outcomes of the sinus rhythm (SR) conversion group compared to the atrial fibrillation (AF) persistent group; CI — confidence interval

Table 3. Predictors for all-cause mortality at follow-up in an overall population.

	Unadjusted HR (95% CI)	**P**
Conversion to sinus rhythm	0.70 (0.54–0.91)	0.007
Age (per 1 year)	1.05 (1.04–1.05)	< 0.001
Male	1.05 (0.91–1.22)	0.481
Hypertension	1.36 (1.17–1.59)	< 0.001
Diabetes	1.52 (1.31–1.77)	< 0.001
Ischemic heart disease	1.51 (1.28–1.79)	< 0.001
Valvular heart disease	1.34 (1.14–1.58)	< 0.001
Cerebrovascular disease	1.48 (1.25–1.76)	< 0.001
Chronic kidney disease	2.36 (1.96–2.85)	< 0.001
ADHF (vs. de novo)	1.77 (1.51–2.06)	< 0.001
Lung congestion	1.27 (1.06–1.54)	0.011
Previous HF admission	1.80 (1.55–2.10)	< 0.001
New onset AF	0.80 (0.68–0.94)	0.007
Tachycardia-induced HF	0.61 (0.52–0.71)	< 0.001
Malignancy	1.36 (1.07–1.73)	0.013
ICU admission	1.27 (1.10–1.48)	0.001
Mechanical ventilation	1.75 (1.43–2.14)	< 0.001
Hemoglobin (per 1 g/dL)	0.81 (0.79–0.84)	< 0.001
Creatinine (per 1 mg/dL)	1.17 (1.13–1.21)	< 0.001
High BNP or NT-proBNP	1.36 (1.09–1.68)	0.006
LVEF > 40%	1.03 (0.88–1.20)	0.745
LA (per 1 mm)	1.01 (1.00–1.01)	0.134
ACEI or ARB at discharge	0.57 (0.49–0.65)	< 0.001
Beta-blocker at discharge	0.59 (0.51–0.68)	< 0.001

ADHF — acute decompensated heart failure; CI — confidence interval; HR — hazard ratio; other abbreviations as for Table 1

Table 4. Subgroup analysis for mortality in a matched population.

	No. of patients	Adjusted HR (95% CI)	P	Interaction *P*
Age				
≥ 65 years	429	0.43 (0.28–0.64)	< 0.001	0. 283
< 65 years	239	0.78 (0.35–1.73)	0.549	
Gender				
Male	357	0.38 (0.23–0.65)	< 0.001	0. 139
Female	311	0.63 (0.39–1.04)	0.068	
Diabetes mellitus				
Yes	193	0.64 (0.33–1.24)	0.184	0.511
No	475	0.48 (0.31–0.74)	0.001	
Hypertension				
Yes	380	0.34 (0.21–0.54)	<0.001	0.021
No	288	0.89 (0.51–1.57)	0.703	
New-onset AF				
Yes	346	0.34 (0.19–0.60)	< 0.001	0. 216
No	322	0.56 (0.34–0.91)	0.019	
Type of HF				
De novo	361	0.35 (0.19–0.65)	< 0.001	0.101
ADHF	307	0.62 (0.39–0.99)	0.043	
Etiology of HF				
Ischemic	148	0.40 (0.18–0.86)	0.019	0.229
Non-ischemic	520	0.55 (0.36–0.83)	0.005	

Abbreviations as for Tables 1 and 3.

Figure 1. Flowchart of the study population; AAD — anti-arrhythmic drug; AF — atrial fibrillation; AHF — acute heart failure; DCC — direct current cardioversion; KorAHF — The Korean Acute Heart Failure registry.

Figure 2. Clinical outcomes in overall study population; **A.** Mortality, **B.** Heart failure (HF) rehospitalization; (**C**) Composite of mortality and HF rehospitalization; AF — atrial fibrillation; CI — confidence interval; HR — hazard ratio; SR — sinus rhythm.

Figure 3. Clinical outcomes in a propensity-score matched population; **A** Mortality; **B.** Heart failure (HF) rehospitalization; **C.** Composite of mortality and HF rehospitalization; abbreviations as for Figure 2.

Figure 1

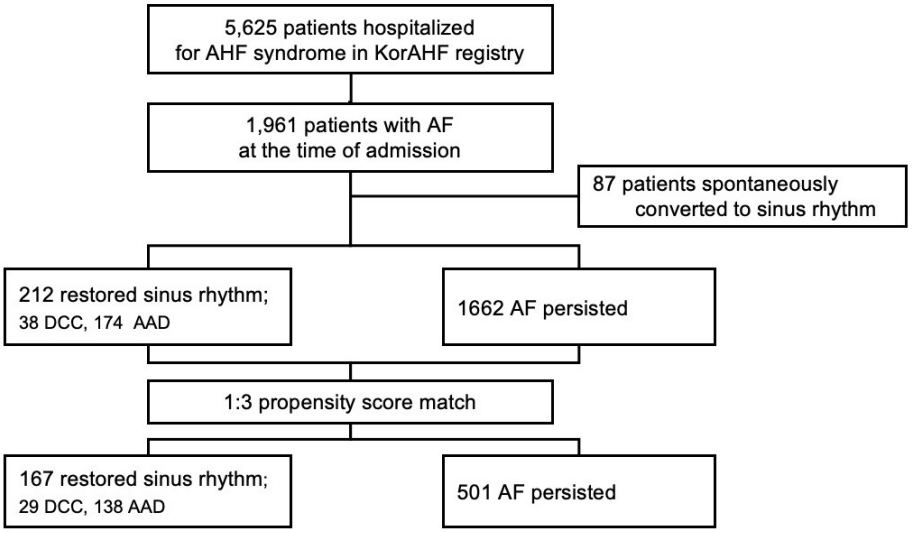
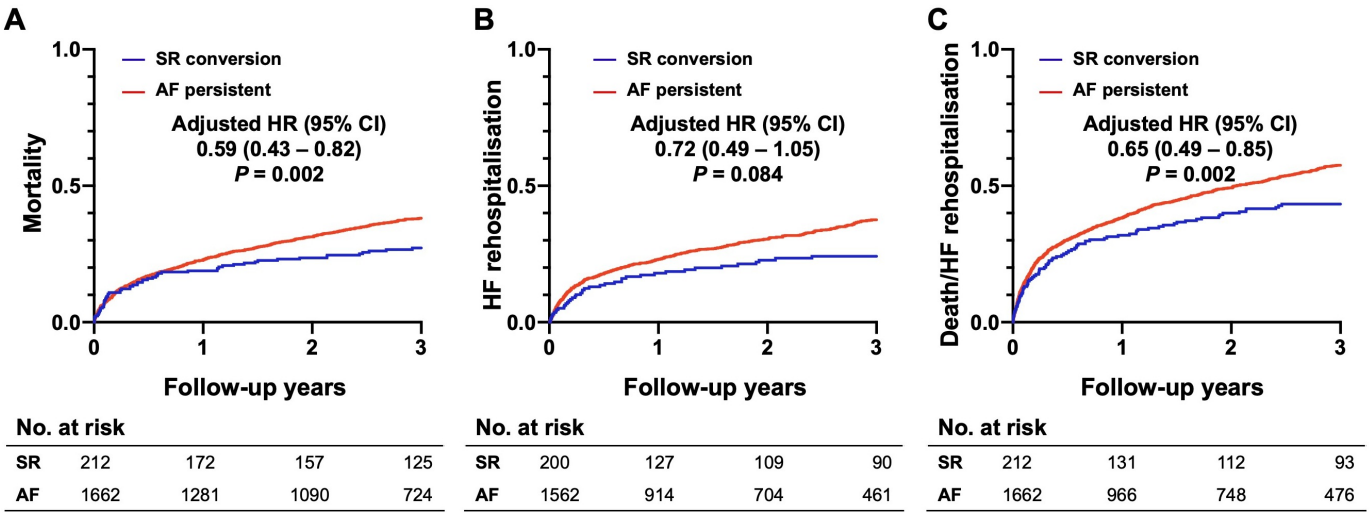

5,625 patients hospitalized for AHF syndrome in KorAHF registry
1,961 patients with AF at the time of admission
87 patients spontaneously converted to sinus rhythm
212 restored sinus rhythm; 38 DCC, 174 AAD
1662 AF persisted
1:3 propensity score match
167 restored sinus rhythm; 29 DCC, 138 AAD
501 AF persisted

Figure 2

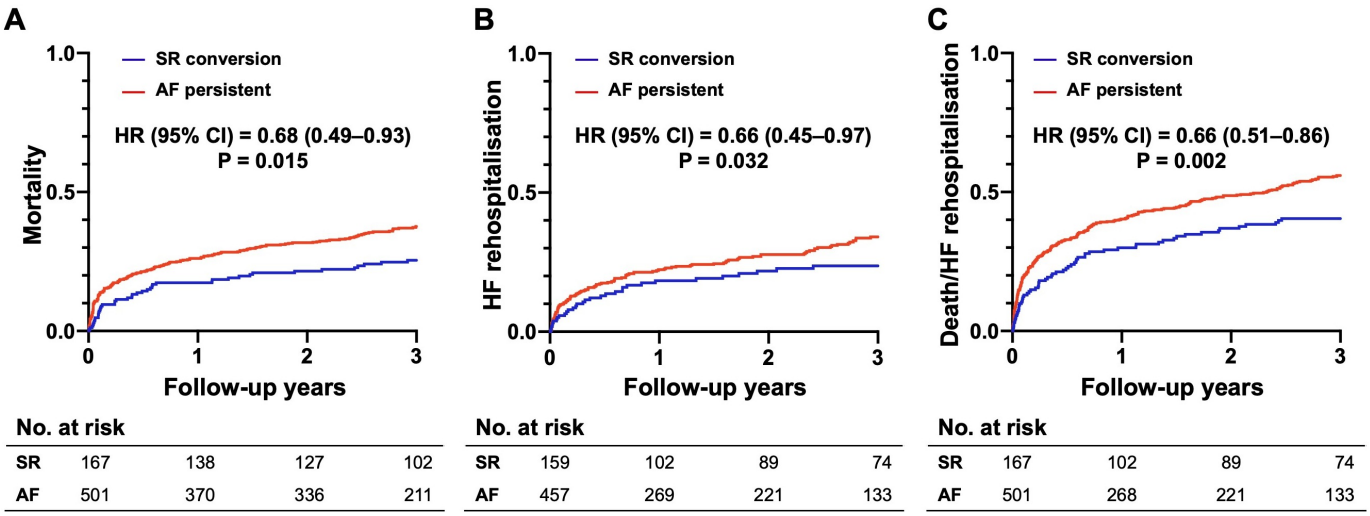


No. at risk				
SR	212	172	157	125
AF	1662	1281	1090	724

No. at risk				
SR	200	127	109	90
AF	1562	914	704	461

No. at risk				
SR	212	131	112	93
AF	1662	966	748	476

Figure 3



No. at risk				
SR	167	138	127	102
AF	501	370	336	211

No. at risk				
SR	159	102	89	74
AF	457	269	221	133

No. at risk				
SR	167	102	89	74
AF	501	268	221	133