

ORIGINAL RESEARCH

RHYTHM DISORDERS AND ELECTROPHYSIOLOGY

Impact of an Organized Treatment Pathway on Management of Atrial Fibrillation



The ER2EP Study

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ABSTRACT

BACKGROUND Atrial fibrillation (AF) is the most common arrhythmia reported worldwide. There is significant heterogeneity in AF care pathways for a patient seen in the emergency room, impacting access to guideline-driven therapies.

OBJECTIVES The purpose of this study was to compare the difference in AF outcomes between those treated with an organized treatment pathway vs routine-care approach.

METHODS The emergency room to electrophysiology service study (ER2EP) is a multicenter, prospective observational registry (NCT04476524) enrolling patients with AF from sites where a pathway for management of AF was put in place compared to sites where a pathway was not in place within the same health system and the same physicians providing services at all sites. Multivariable regression modeling was performed to identify predictors of clinical outcomes. Beta coefficient or odds ratio was reported as appropriate.

RESULTS A total of 500 patients (ER2EP group, n = 250; control group, n = 250) were included in the study. The mean age was 73.4 ± 12.9 years, and 52.2% were males. There was a statistically significant difference in primary endpoint [time to ablation (56 ± 50.9 days vs 183.3 ± 109.5 days; $P < 0.001$), time to anticoagulation initiation (2.1 ± 1.6 days vs 19.7 ± 35 days, $P < 0.001$), antiarrhythmic drug initiation (4.8 ± 7.1 days vs 24.7 ± 44.4 days, $P < 0.001$) compared to the control group, respectively. As such, this resulted in reduced length of stay in the ER2EP group compared to the control group (2.4 ± 1.4 days vs 3.23 ± 2.5 days, $P = 0.002$).

CONCLUSIONS This study provides evidence that having an organized pathway from the emergency department for AF patients involving electrophysiology services can improve early access to definitive therapies and clinical outcomes. (JACC Adv 2024;3:100905) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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**ABBREVIATIONS
AND ACRONYMS****AAD** = antiarrhythmic drugs**AF** = atrial fibrillation**EP** = electrophysiology**ER** = emergency room**LOS** = length of stay**OAC** = oral anticoagulation
drugs

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with a reported worldwide prevalence of 33.5 million, accounting for 0.5% of the world population.¹ AF is said to be an epidemic, and it is expected to triple by 2050 in the United States with a parallel surge worldwide.² With more than 454,000 hospitalizations, AF remains a significant cause of morbidity and mortality, contributing to 158,000 deaths per year in the USA.^{3,4} In addition, more recent studies have demonstrated its association with cognitive decline, independent of associated embolic stroke.⁵ Early catheter ablation for AF has been shown to improve patient outcomes compared to traditional medical management. Studies have shown that early catheter ablation results in better symptom control, improved quality of life, reduced hospitalizations, and lower risk of stroke and other complications compared to medical management alone.^{6,7} However, no study has been performed to evaluate the impact of early consultation with an electrophysiologist(s) on the outcome of patients with AF.

The annual volume of AF-related admissions has been steadily increasing with a substantial increase in the median hospital charge per patient, resulting in a huge economic burden on the health care system.⁸ The initial contact with health care systems for AF patients typically happens through the emergency room (ER) or a primary care physician office. There is significant heterogeneity in the course these patients take by the time they end up with definitive treatment options. The inherent delays in the referral process to get these patients to the appropriate health care providers could impact outcomes for these patients.

Many patients with AF end up in ERs for medical care, some with the new onset and others with known AF with related issues. ER physicians have a unique opportunity to triage and provide emergency medical care and potentially minimize the morbidity and mortality associated with AF by directing these patients to appropriate services for improved and more directed care. However, substantial variation exists in the ER practice patterns, such as selecting rate vs rhythm control, timing and need for initiating oral

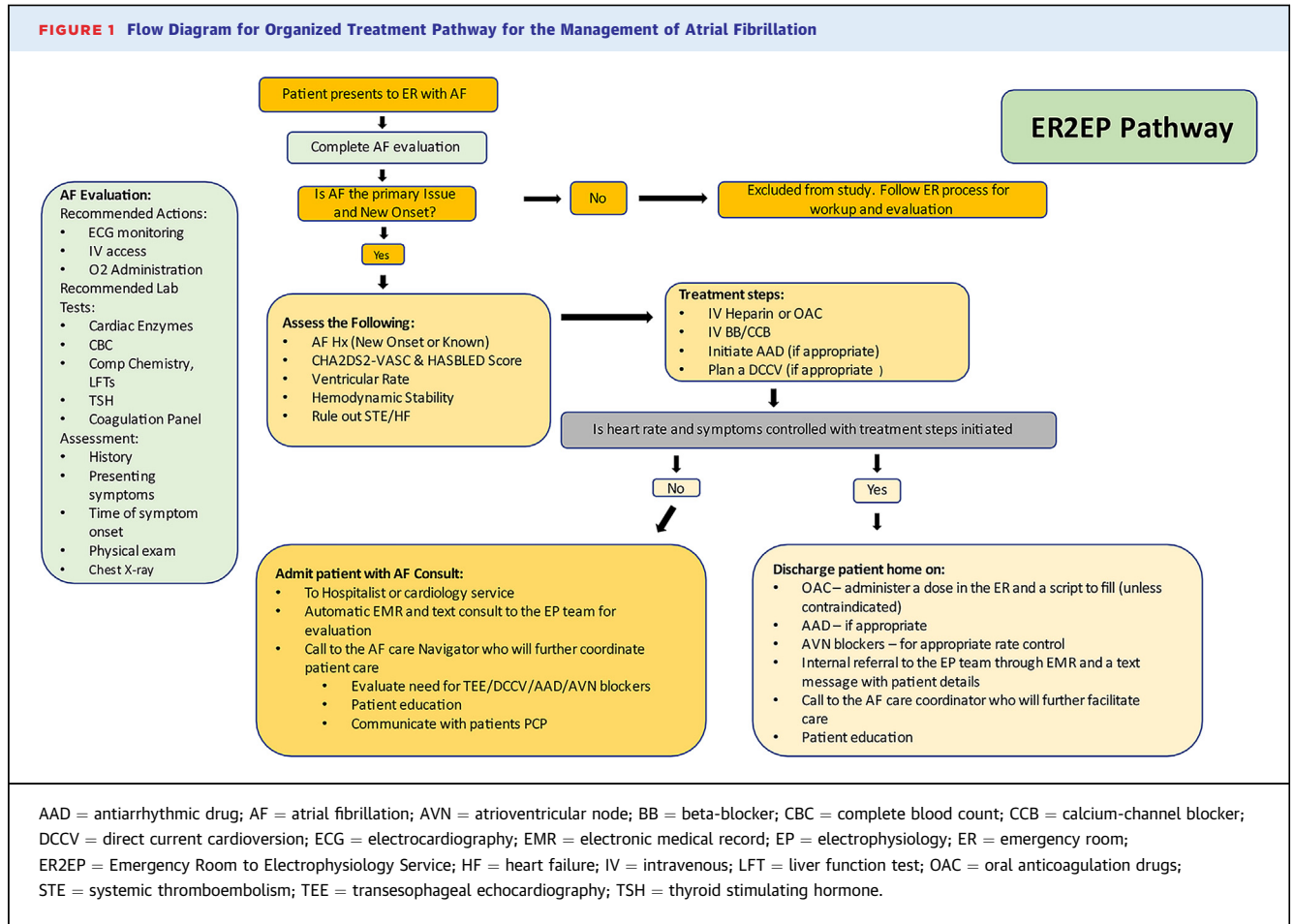
anticoagulation (OAC) for stroke prevention, ER vs inpatient treatment, and cardiology consultation, which could lead to disparate patient care.⁹ Therefore, there is a clear need to standardize practice starting from the ER, which can lead to improved treatment outcomes and, in turn, decrease the overall length of hospital stay, which might help and provide economic relief to the patients and health care systems.¹⁰ In this multicenter study, we hypothesized that implementing an appropriate, standardized referral protocol involving the electrophysiology (EP) service for management of AF could significantly improve access to care and, thereby, reduce AF-related complications and hospitalizations compared to the routine care pathway that currently exists.

METHODS

STUDY DESIGN AND POPULATION. The ER2EP (emergency Room to Electrophysiology Service) study is a multicenter, prospective observational registry (NCT04476524) enrolling patients with AF from sites where a pathway was put in place compared to sites where a pathway was not in place within the same health system and the same physicians providing services at all sites between 2019 and 2022. The participating sites included: 1) the Kansas City Heart Rhythm Research Institute, Overland Park, Kansas; and 2) the Texas Cardiac Arrhythmia Institute, Austin, Texas. Institutional review board approval was obtained for the conduct of the study. The study group consisted of patients who presented to the ER at the participating sites with new-onset AF as a primary diagnosis. Patients were admitted to the hospital if clinically indicated, and EP service was consulted simultaneously along with routine management strategy. On the contrary, an outpatient consultation with EP service was arranged if the patient was discharged home. The control group consisted of patients from 2 ER sites within the same health system where the ER2EP program was not implemented. These patients had their routine care without any directly organized EP referrals. Regardless of the group, EP services were managed by the same groups in all the facilities. The ER physicians managed the point of care in the ERs at their discretion. All patients

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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were followed for at least 12 months, and the relevant clinical data were collected.

INCLUSION AND EXCLUSION CRITERIA. ER2EP arm. All patients aged 18 years old who presented to the ER with new-onset AF as the primary diagnosis were included in the study. These patients were treated under the ER2EP treatment approach, as shown in Figure 1. They were subsequently compared to the contemporary comparator group who presented to the ER with AF as their primary diagnosis and were treated per the discretion of the attending physician with a routine standard of care. In addition, patients were excluded if they had previously established AF, cardiology, or EP care.

ENDPOINTS. The study’s primary endpoints were: 1) time to definitive therapy [EP evaluation, ablation, antiarrhythmic drug (AAD), and OAC drug initiation]; and 2) length of stay (LOS). The secondary endpoints included: 1) the number of clinic/ER visits due to heart-related issues [chest pain, recurrence of AF, acute coronary syndrome]; 2) a number of hospitalizations; 3) cardioversions; and 4) heart failure

syndrome, stroke/transient ischemic attacks, and major bleeding events (BARC-5 criteria).¹¹ All patients were followed up for 12 months, as appropriate.

STATISTICAL ANALYSIS. Due to a lack of precedent robust clinical data, we performed an investigative study to evaluate the impact of an organized treatment pathway on AF patients from the ER2EP study. Continuous variables were summarized using mean ± SD, while categorical variables were summarized as frequency and percentages of the total. Comparison analysis between groups was made using a paired t-test, Mann-Whitney U test or chi-square, or Fisher exact as appropriate. Multivariable regression modeling was performed to identify predictors of clinical outcomes. β coefficient or OR was reported as appropriate. Bonferroni correction was not performed due to prespecified outcomes in the trial. All tests were 2-tailed, and a P value <0.05 was considered statistically significant. The statistical analyses were performed using SPSS Statics version 28.0.0.0 (IBM Corp).

TABLE 1 Baseline Characteristics of the Study Population

	ER2EP Group (n = 250)	Control Group (n = 250)	P Value
Age, y	73.2 ± 14.1	73.6 ± 11.6	0.73
Male	134 (53.6%)	127 (50.8%)	0.53
Body mass index, kg/m ²	31.35 ± 10.5	31.63 ± 7.9	0.74
Race			
Caucasians	206 (84%)	219 (87.6%)	0.72
African American	31 (12.4%)	27 (10.8%)	0.56
Hispanic/Latino	6 (2.4%)	4 (2%)	0.63
Others	7 (2.8%)	-	-
Hypertension	210 (84%)	213 (85.2%)	0.91
Hyperlipidemia	122 (48.8%)	121 (48.4%)	0.93
Diabetes mellitus	64 (25.6%)	59 (23.6%)	0.60
Coronary artery disease	82 (32.8%)	79 (31.6%)	0.77
Stroke/TIA	31 (12.4%)	26 (10.4%)	0.48
Peripheral artery disease	6 (2.4%)	9 (3.6%)	0.43
Obstructive sleep apnea	38 (15.2%)	35 (14%)	0.70
Cardiomyopathy	18 (7.2%)	24 (9.6%)	0.33
Smoker	65 (26%)	71 (28.4%)	0.55
Atrial fibrillation			
Paroxysmal	112 (44.8%)	148 (59.2%)	0.001
Nonparoxysmal	138 (55.2%)	102 (40.8%)	0.001
CHA ₂ DS ₂ VASC score	3.09 ± 1.0	3.14 ± 0.9	0.56

Values are mean ± SD or n (%).
ER2EP = Emergency Room to Electrophysiology Service study; TIA = transient ischemic attack.

RESULTS

A total of 500 patients (ER2EP group, n = 250; control group, n = 250) were included in the study, of which 52.2% were men, and the mean age was 73.4 ± 12.9 years. The 2 groups were well balanced with respect to major baseline demographics. However, there was a lower prevalence of paroxysmal AF subtype in the ER2EP group compared to the control arm. **Table 1** highlights the baseline characteristics of the study population.

All patients in the ER2EP group had EP evaluation vs 52.8% (n = 132) in the control group (*P* < 0.001). There was a significant reduction in time to the first EP evaluation in the ER2EP group (3.78 ± 5.4 [median 1] days vs 90.5 ± 78.7 [median 128] days in the control group; *P* < 0.001). A total of 45.2% (n = 226) underwent AF ablation, of which 47.6% (n = 119) were in the ER2EP group vs 42.8% (n = 107) in the control group (*P* = 0.28). There was increased utilization of OAC (92.4% [n = 231] vs 81.2% [n = 203]; *P* < 0.001) and oral AADs (74.8% [n = 187] vs 45.2% [n = 113]; *P* < 0.001) in the ER2EP group compared to the control group, respectively. About 64.4% (n = 161) in the ER2EP group vs 63.6% (n = 169) of patients in the

control group required admission to the hospital at the time of index presentation (*P* = 0.45). The LOS during index hospitalization visits in the ER2EP group compared to the control group (2.4 ± 1.4 [median 2] days vs 3.23 ± 2.5 [median 3] days, *P* = 0.002).

PRIMARY OUTCOME. There was a significant reduction in time to ablation (56 ± 50.9 [median 36] days vs 183.3 ± 109.5 [median 197] days, *P* < 0.001; β -coefficient -127.21; 95% CI: -150.33 to -104.09; *P* < 0.001), time to AAD initiation (4.8 ± 7.1 [median 2] days vs 24.7 ± 44.4 [median 6] days, *P* < 0.001; β -coefficient -20.64; 95% CI: -27.30 to -13.99; *P* < 0.001) and time to OAC initiation (2.1 ± 1.6 [median 1] days vs 19.7 ± 35 [median 5.5] days, *P* < 0.001; β -coefficient -16.57; 95% CI: -21.51 to -11.63; *P* < 0.001) compared to control group, respectively in multivariable regression analysis (model adjusted for AF subtype and baseline characteristics) (**Tables 2 and 4, Figure 2**).

SECONDARY OUTCOMES. There was no mortality in either group. There was significantly lower ER visit for heart-related issues (5.2% [n = 13] vs 10.4% [n = 26], *P* = 0.03) and a lower number of hospitalizations after index presentation during the study period (19.6% [n = 49] vs 36% [n = 90], *P* < 0.001) in the ER2EP group compared to the control group, respectively. Heart failure syndrome (4% [n = 10] vs 9.2% [n = 23], *P* = 0.05), stroke (4.4% [n = 11] vs 7.2% [n = 18], *P* = 0.18), bleeding complications (6.8% [n = 17] vs 4% [n = 10], *P* = 0.17), and the number of cardioversions (6.4% [n = 16] vs 10.8% [n = 27], *P* = 0.25) were similar between the 2 groups (**Table 3**).

Multivariable regression analysis demonstrated reduced odds of ER visits for heart-related issues (OR: 0.38, 95% CI: 0.19-0.79; *P* = 0.01), heart failure syndrome episodes (OR: 0.37, 95% CI: 0.17-0.83; *P* = 0.02) without increased risk of stroke (OR: 0.60, 95% CI: 0.28-1.32; *P* = 0.21) and bleeding complications (OR: 1.74, 95% CI: 0.77-3.93; *P* = 0.18) in the ER2EP group compared to control, respectively. As such, this translated into a reduction in the number of ER visits for heart-related issues (OR: 0.38; 95% CI: 0.19-0.79; *P* = 0.01) and subsequent hospitalizations in the ER2EP group compared to the control group (OR: 0.43; 95% CI: 0.29-0.65; *P* = 0.001), respectively (**Table 4**).

DISCUSSION

Adapting an organized care pathway is a well-known method to standardize patient care. Having such pathways helps minimize the variation in the care

process and heterogeneity in delivery. Previous studies have shown that minimal adherence to guideline-based therapies leads to suboptimal patient care.¹² Our study highlights the importance of following an organized pathway for the management of AF, and involvement of EP services earlier in the care pathway minimizes the delay in the initiation of AAD, OAC, and referral for catheter ablation, leading to a decrease in the number of hospitalizations and ER visits for cardiac-related issues, with a nonsignificant decline in cardioversions, heart failure admissions, stroke/transient ischemic attack, and bleeding complications, which might help decrease LOS and reduce health care utilization. While the secondary endpoints did not reach statistical significance, but showed a positive trend in favor of the ER2EP pathway (Figure 2).

AF is known to be associated with increased stroke risk. OAC should be initiated sooner rather than later in patients with high stroke risk (based on CHA₂DS₂-VASc score) if there are no contraindications. Data suggest that approximately 50% of patients with an indication for OAC do not receive it.¹³ In a large retrospective study including 4,338 patients, the median time to initiation of OAC was 5 days (IQR: 1-43 days), and 2.2% of patients had strokes before OAC initiation. Clinical factors such as female sex, white race, previous falls, pulmonary disease, malignancy, and chronic kidney disease were associated with delayed OAC initiation.¹⁴ Similarly, in another study, 82% of patients with CHA₂DS₂-VASc score of ≥2 with no OAC contraindication were referred to start OAC, although only 69% were initiated, thereby highlighting a dramatic underutilization of OAC. They also observed higher failure rates in initiating outpatient OAC in up to 56% of cases. Potential reasons include (not limited to) a lack of discharge instructions, patient education, and communication with primary care physicians.¹⁵ Although no differences in serious harm, strokes, or mortality were seen between the 2 groups in our study, the clinical events were higher in the control group, which could be primarily driven by marked delays in referral to specialized services, ie, lack of specialist appointments, lack of early diagnostic testing, or delay in initiation of AAD/OAC. Our study highlights that early recognition, better patient education through multidisciplinary teams, and an organized pathway can decrease the delay in initiating oral OAC, thereby helping improve clinical outcomes (regardless of factors associated with delayed OAC, as noted in prior studies).

Early rhythm control strategy for the treatment of AF is associated with reduced mortality, stroke, and heart failure hospitalization.^{7,16,17} A pooled analysis

TABLE 2 Primary Outcomes

	ER2EP Group	Control Group	P Value
EP evaluation performed	250 (100.0)	132 (52.8)	<0.001
Time to EP evaluation (d)	3.78 ± 5.4 1 (1-36)	90.5 ± 78.7 128 (30-340)	<0.001
Ablation performed	119 (47.6)	107 (42.8)	0.28
Time to ablation (d)	56.0 ± 50.9 36 (22-244)	183.3 ± 109.5 197 (91-347)	<0.001
Antiarrhythmic drug started	187 (74.8)	113 (45.2)	<0.001
Time to antiarrhythmic drugs (d)	4.8 ± 7.1 2 (1-7)	24.7 ± 44.4 6 (2-30)	<0.001
Oral anticoagulation prescribed	231 (92.4)	203 (81.2)	<0.001
Time to oral anticoagulation (d)	2.1 ± 1.6 1 (1-3)	19.7 ± 35 5.5 (2-22)	<0.001
Hospitalization at index visit	161 (64.4)	169 (63.6)	0.45
Length of stay for index visit (d)	2.4 ± 1.4 2 (1-3)	3.23 ± 2.5 3 (2-4)	0.002

Values are n (%), mean ± SD, or median (IQR). EP = electrophysiology; ER2EP = emergency room to electrophysiology service study.

of 6 randomized controlled trials comparing AAD with catheter ablation reported that early catheter ablation was associated with reductions in recurrent atrial arrhythmia (53% vs 32.5%) and hospitalization (18.7% vs 5.6%).⁶ Our study's findings align with prior published studies demonstrating early rhythm control strategy, as the ER2EP arm was associated with reduced number of heart-related ER visits (5% vs 10%) and hospitalizations compared to the control group. Therefore, early assessment and institution of appropriate therapy (AAD, catheter ablation, and/or rate control as indicated) by the specialist is vital to improving clinical outcomes.

LOS is considered a marker of hospital resource utilization and, overall reflects on the efficiency of the health care system. Prolonged LOS poses a significant economic burden on patients and the health care system.^{18,19} Given that AF is on the rise globally, implementing guidelines that can improve overall LOS can potentially result in significant cost savings.

TABLE 3 Secondary Outcomes

	ER2EP Group	Control Group	P Value
ER visit for heart-related issues	13 (5.2%)	26 (10.4%)	0.03
Patients hospitalized after index presentation	49 (19.6%)	90 (36%)	<0.001
Cardioversion	16 (6.4%)	27 (10.8%)	0.25
Heart failure syndrome	10 (4%)	23 (9.2%)	0.05
Stroke	11 (4.4%)	18 (7.2%)	0.18
Bleeding complications	17 (6.8%)	10 (4%)	0.17

Values are n (%).
ER = emergency room; ER2EP = emergency Room to Electrophysiology Service study.

TABLE 4 Multivariable Predictors for Primary and Secondary Outcomes

	β -Coefficient or OR (As Appropriate)	95% CI	P Value
Primary outcome			
Time to ablate	-127.21 ^a	-150.33 to -104.09	<0.001
Time to antiarrhythmic drugs	-20.64 ^a	-27.30 to -13.99	<0.001
Time to oral anticoagulation	-16.57 ^a	-21.51 to -11.63	<0.001
Length of stay	-0.84 ^a	-1.3 to -0.38	<0.001
Secondary outcome			
ER visit for heart-related issues	0.38 ^b	0.19-0.79	0.01
Time to EP evaluation	-87.02 ^a	-97.21 to -76.83	<0.001
Antiarrhythmic drugs	3.65 ^b	2.46-5.40	<0.001
Oral anticoagulants	2.84 ^b	1.58-5.14	0.001
Hospitalization after index presentation	0.43 ^b	0.29-0.65	<0.001
Cardioversions	0.56 ^b	0.29-1.09	0.09
Heart failure syndrome	0.37 ^b	0.17-0.83	0.02
Stroke	0.60 ^b	0.28-1.32	0.21
Bleeding complications	1.74 ^b	0.77-3.93	0.18

Model adjusted for atrial fibrillation type and baseline demographics. ^a β -coefficient. ^bOR.
EP = electrophysiology; ER = emergency room.

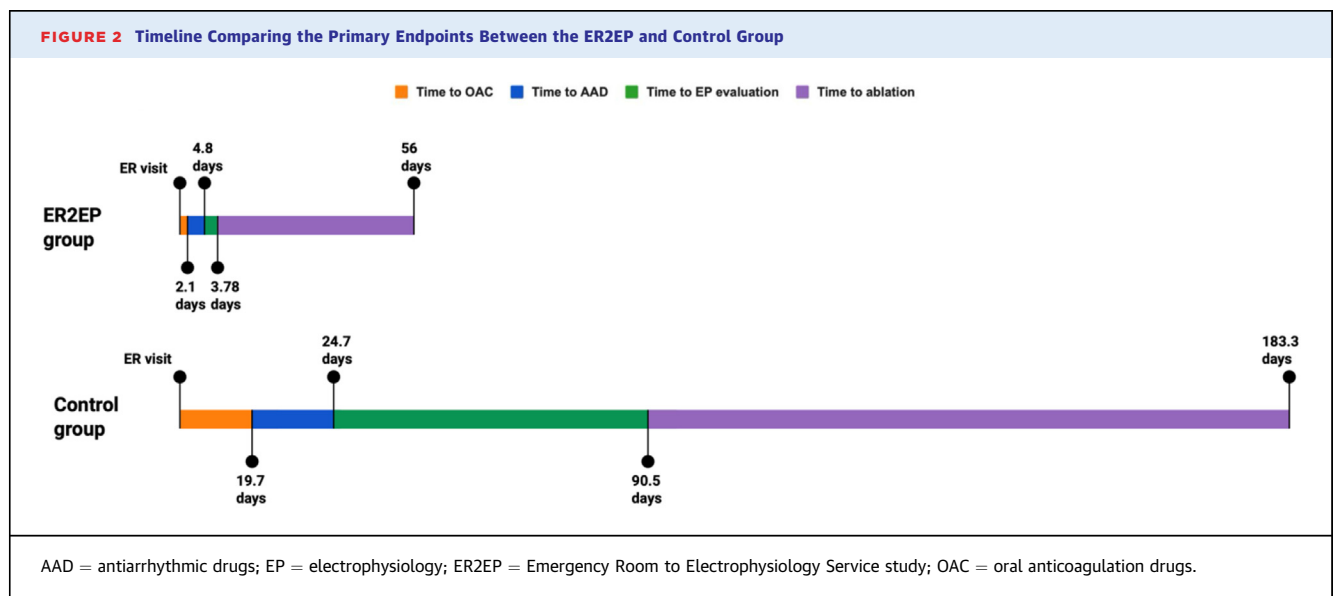
Our study is the first to report significant differences in LOS between the 2 groups (2.4 ± 1.4 days vs 3.2 ± 2.5 days, $P = 0.002$) at the time of index hospitalization finding, which is different from prior published studies.^{7,20,21} The probable explanation could be due to a predefined, organized pathway that might help physicians and health care teams with early decision-making in initiating OAC and AAD and timely referring them to EP for an ablation. Early involvement of cardiac electrophysiologists in the care team and sharing evidence-based literature with patients and families might help improve outcomes

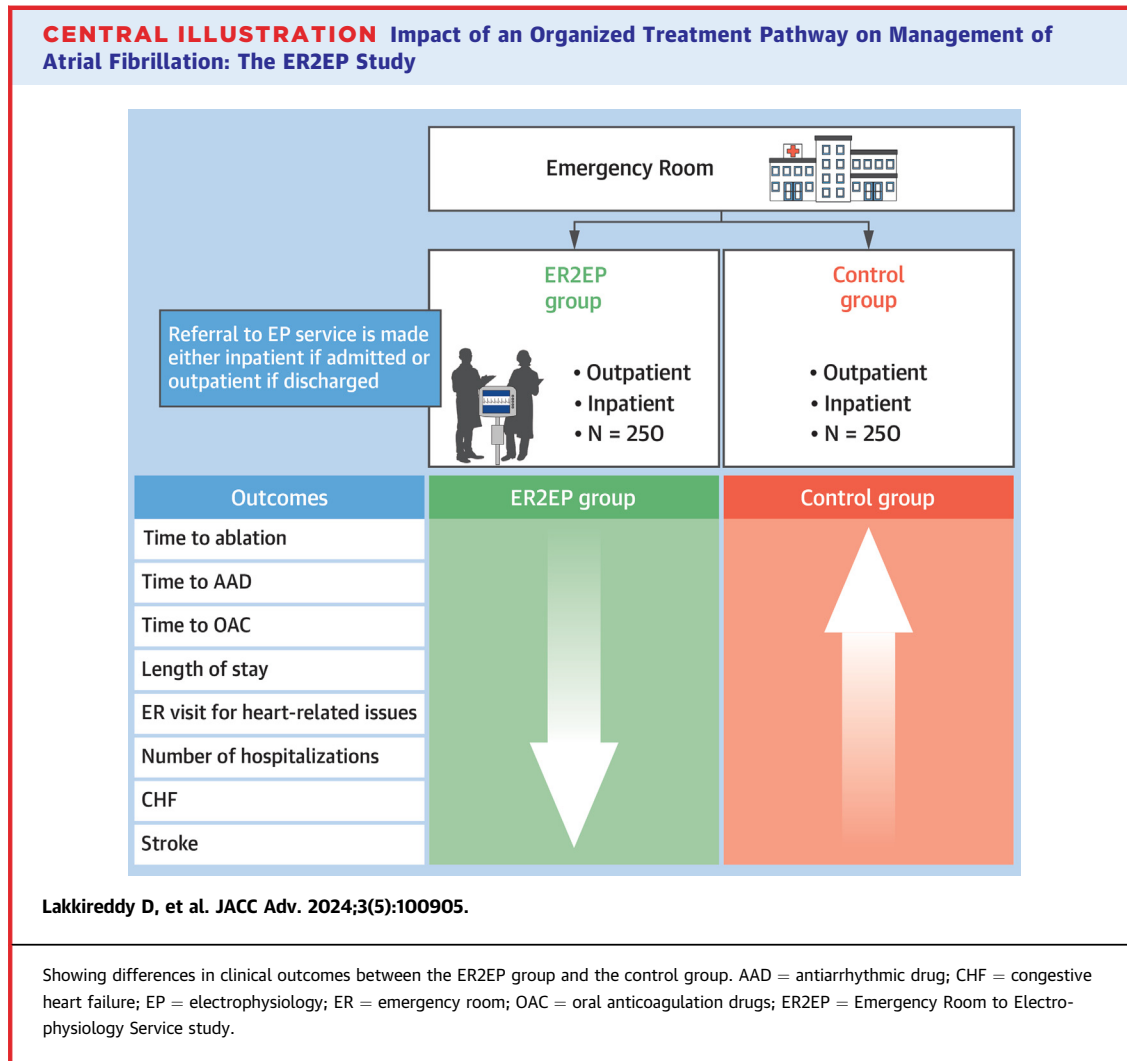
and reduce readmission and overall health care utilization.²²

Our study serves as a guiding tool in the management of AF patients, demonstrating that an evidence-based, systemic, organized pathway might lead to improved patient care and potentially serve as an economic relief to both patients and health care systems. By simply managing a single element in the entire workflow of introducing early referral to EP services from ER, there is potential for significant improvement in many of the therapy indices.

STUDY LIMITATIONS AND CLINICAL IMPLICATIONS

This study has several limitations. The most important limitation is the nonrandomized nature of the study. ER2EP is a prospective observational registry enrolling patients from sites where a pathway was implemented compared to sites where a pathway was not in place within the same system and with the same physicians providing services at all sites. Therefore, there remains a risk of bias among the participating sites, which are high-volume, busy cardiac electrophysiology centers and may have expedited the overall course in the management of AF even in the control group. The differences in outcomes between the 2 groups may be even more significant in less organized facilities where the emphasis on care pathways is less stressed. The control group comes from patients from different ERs where the specific protocol was not implemented, and there could have been individual differences in the attitudes of treating ER physicians on how they managed AF patients. This, to some degree, could





have impacted the poor performance of the control group. In addition, there was a significantly higher number of patients with nonparoxysmal AF in the ER2EP group compared to the control group, which could account for the aggressive treatment approach in the ER2EP group compared to the control group (more so from early referral to EP and initiating care in the ER); however, findings of the study remained consistent even after adjustment for AF type and baseline demographics in multivariable regression. Another crucial point to consider is the exclusion of patients with known AF. Even though patients with established care with cardiology or EP services are eliminated from the study, they still need proper direction for their care, and continued engagement of these services is important to improve outcomes. In addition, both groups were missing details on NYHA functional class, European Heart Rhythm Association

score, and dosing of AAD and OAC. Further, larger multicenter studies are needed to validate our findings. The economic data on the new pathway implementation is being collected and analyzed. It will be presented in future manuscripts.

CONCLUSIONS

This study provides evidence that an organized pathway for AF patients can improve outcomes for AF ablation, AAD, OAC, and LOS (**Central Illustration**). We hope such guidelines will boost the efficiency of ER and the health care system in managing AF.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE:

There remains significant heterogeneity in the management of AF patients during their index presentation in the ER. This impacts early access to guideline-driven therapies. ER2EP serves as a stepping-stone clinical registry that proposes the universal adoption of an organized treatment pathway for the management of AF.

TRANSLATIONAL OUTLOOK: The approach of an organized treatment pathway with early consultation with a cardiac electrophysiologist can significantly improve the timing of initiating AAD, OAC, and AF ablation. This leads to decreased hospital LOS as well as lower subsequent hospitalizations for heart failure syndrome and heart-related issues. Implementing such pathways will boost the efficiency of ER and the health care system in managing AF.

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