

ORIGINAL RESEARCH

Understanding Transient Left Ventricular Ejection Fraction Reduction During Atrial Fibrillation With Artificial Intelligence

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BACKGROUND: Atrial fibrillation (AF) can cause a reduction in left ventricular ejection fraction (LVEF) that resolves rapidly upon restoration of sinus rhythm. We used artificial intelligence to understand (1) how often transient LVEF reduction during AF is from mismeasurement due to AF's beat-to-beat variability and (2) whether true transient AF-LVEF reduction has prognostic significance.

METHODS: In this observational study, we analyzed all patients at a large academic center with a transthoracic echocardiogram in AF and subsequent transthoracic echocardiogram in sinus rhythm within 90 days. We classified patients by their clinically reported LVEFs: no AF-LVEF reduction, transient AF-LVEF reduction that recovered after conversion to sinus rhythm, or persistent AF-LVEF reduction that did not recover. We evaluated how automated multicycle AF-LVEF measurement using a validated artificial intelligence algorithm affected AF-LVEF and reclassified patients. We used Fine-Gray hazard modeling to analyze 1-year heart failure hospitalization risk.

RESULTS: In 810 patients (mean age 74.1 years, 34.3% female), 459 (56.7%) had no reduced AF-LVEF, 71 (8.8%) had transient AF-LVEF reduction, and 280 (34.6%) had persistent AF-LVEF reduction. In the group with transient AF-LVEF reduction, LVEF increased by 19.5% (95% CI, 12.0%–22.1%) upon conversion to sinus rhythm. AI reassessment increased AF-LVEF by 8.2% (95% CI, 6.0%–10.4%), reclassifying 20 (28.2%) patients as no longer having reduced AF-LVEF. The group with transient AF-LVEF reduction, as determined by AI, had significantly higher 1-year heart failure hospitalization risk (hazard ratio, 2.28 [95% CI, 1.23–4.21], $P=0.003$).

CONCLUSION: Artificial intelligence may decrease misdiagnosis of reduced LVEF during AF and more accurately identify true transient AF-LVEF reduction, a potentially high-risk phenotype.

Key Words: atrial fibrillation ■ deep learning ■ echocardiography ■ heart failure

Atrial fibrillation (AF) is the most common arrhythmia worldwide and continues to increase in incidence due to population aging, increased detection, and higher risk factor prevalence.^{1,2} In addition to carrying a heightened risk of stroke, AF is also associated with the development of cardiomyopathy.^{3,4} However, it remains unclear why some individuals with AF develop cardiomyopathies whereas others do not.^{5,6} The durability of this dysfunction is also unpredictable,

as some reductions in left ventricular (LV) systolic function during AF may normalize quickly upon reversion to sinus rhythm.^{7–12} It is also known that AF causes significant beat-to-beat variations in diastolic filling time, which can lead to imprecision in the assessment of LV ejection fraction (LVEF) and potentially the misidentification of reduced EF cardiomyopathy.^{13–15}

The accurate assessment of LVEF during AF is especially relevant given recent trials showing

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CLINICAL PERSPECTIVE

What Is New?

- Patients can experience a reduction in left ventricular ejection fraction (LVEF) that normalizes quickly after converting from atrial fibrillation (AF) to sinus rhythm, a phenotype whose implications remain unclear.
- We used an artificial intelligence LVEF quantification algorithm to show that (1) such transient LVEF reductions during AF are often actually pseudo-reductions due to LVEF mismeasurement during AF and (2) true transient AF-LVEF reduction may confer a higher 1-year heart failure hospitalization risk than for patients with no AF-LVEF reduction.

What Are the Clinical Implications?

- The use of automated multibeam LVEF assessment should be considered in patients with AF to help reduce false diagnoses of reduced LVEF and increase identification of true transient AF-LVEF reduction, a potentially high-risk phenotype. Further research is needed to better understand how to manage patients with transient AF-LVEF reduction.

Nonstandard Abbreviations and Acronyms

HFmrEF	heart failure with mildly reduced ejection fraction
HFrEF	heart failure with reduced ejection fraction
TTE	transthoracic echocardiogram

potential benefits for early antiarrhythmics and ablation in patients with AF and heart failure with reduced EF (HFrEF) as well as possibly HF with mildly reduced EF (HFmrEF).^{6,16–20} It also has important implications for appropriate downstream workup and treatment, because systolic dysfunction often prompts ischemic testing and the aggressive initiation of guideline-directed medical therapies.^{21,22} Notably, studies have not shown benefit with these same interventions in patients with HF with preserved EF (HFpEF), meaning that clarifying the presence of true LVEF reduction is critical for choosing effective therapies.²²

Prior studies and guidelines have focused on patients with AF who have persistent reductions in LVEF and chronic HF.^{6,17,20} From our clinical experience, we hypothesized that there is another distinct group of individuals who develop transient reductions in LVEF only during AF that resolve upon reversion to sinus

rhythm and may not have HF symptoms. We further conjecture that some of these patients are misdiagnosed as having a reduced LVEF due to measurement imprecision and that those who truly have transient LVEF reductions may have a less severe phenotype than patients with chronic HFrEF/HFmrEF.

To clarify the significance of transient LVEF reduction during AF, we investigated (1) how often artificial intelligence (AI) LVEF assessment distinguished pseudo-reductions in LVEF during AF due to human measurement imprecision as opposed to true LVEF reduction and (2) whether transient LVEF reduction during AF has prognostic implications with regard to risk of future HF hospitalization (Figure 1).

METHODS

Data Availability

Given that the echocardiogram studies used in this paper have sensitive embedded patient information, raw video files are not available for sharing. However, the deep learning algorithm used for LVEF quantification is openly available online at <https://echonet.github.io/dynamic/>. The results of our deep learning analysis and anonymized patient data are available by reasonable request if appropriate approvals are obtained.

Patient Selection

We studied all patients in the echocardiogram database of a large urban, academic medical system from January 2014 to June 2021 who had a transthoracic echocardiogram (TTE) in AF followed by another TTE in sinus rhythm within 90 days. We used a 90-day window given that arrhythmia-induced cardiomyopathies are known to recover within this time period.²³ Both the AF and sinus rhythm TTEs were required to have an LVEF calculated by Simpson's biplane method of discs. All TTEs were previously read by cardiologists with level 2 or 3 certification by the American Society of Echocardiography as part of routine clinical care. Using manual chart review, we excluded patients who had intervening events or procedures that could have affected the LVEF. This included episodes of cardiac arrest, cardiac tamponade, cardiac surgery, or interventional procedures such as percutaneous coronary intervention, transcatheter aortic valve replacement, and transcatheter mitral valve edge-to-edge valve repair.

Patient demographics and comorbidities were derived from the electronic health records system using *International Classification of Diseases, Ninth Revision (ICD-9)* and *Tenth Revision (ICD-10)* diagnostic coding.^{24,25} These patient characteristics describe the patient at the time of the patient's AF TTE. We stratified our final cohort into 3 groups (no AF-LVEF reduction,

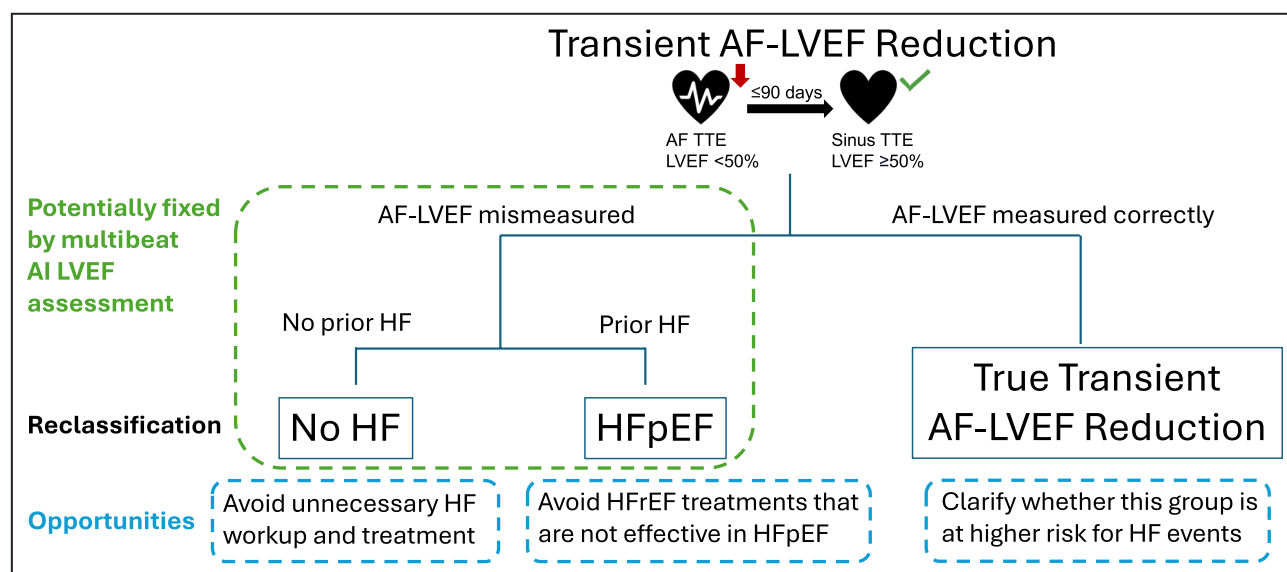


Figure 1. Conceptual model for better differentiating and understanding transient AF-LVEF reduction.

AF indicates atrial fibrillation; AI, artificial intelligence; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; and TTE, transthoracic echocardiogram.

transient AF-LVEF reduction, and persistent AF-LVEF reduction) based on whether the AF TTE was clinically interpreted as having a reduced LVEF <50% and whether the follow-up sinus rhythm TTE had a reduced LVEF <50%.

This study was approved by the Institutional Review Board at Cedars-Sinai Medical Center. This study complied with all institutional review board ethical regulations and was granted a waiver for informed consent because of the deidentified nature of the data.

Deep Learning LVEF Assessment

We investigated the implication of reassessing the AF-LVEF of all patients in our cohort using AI. For each AF TTE study in our cohort, apical 4-chamber video clips were extracted and isolated from the raw Digital Imaging and Communications in Medicine file. An automated preprocessing workflow was employed to strip identifying information, crop and mask videos to remove all labels and information outside of the scanning sector, and downsample clips by cubic interpolation to 112×112 pixels.

We applied a previously published deep learning algorithm EchoNet-Dynamic with pretrained weights to our cohort of processed videos to produce AI-based AF-LVEFs.²⁶ These AF-LVEFs are calculated from entire echo video clips that had a minimum of 64 frames and included multiple heart beats.

Outcome Measures

We sought to understand the relative hazards of HF hospitalization within 1 year of the follow-up sinus

rhythm TTE across our 3 patient groups (no AF-LVEF reduction, transient AF-LVEF reduction, and persistent AF-LVEF reduction) and whether this was affected by AI-based AF-LVEF reassessment. HF hospitalizations were identified using electronic health records admission and discharge information. A hospitalization was considered an HF hospitalization only if the first associated diagnosis was an HF ICD-9 or ICD-10 code as specified (Table S1). This method was used to maximize specificity for HF as the primary reason for hospitalization as opposed to as an accompanying secondary diagnosis. A subsample of patients was chart reviewed, and we verified the accuracy of this method. Deaths were also determined from the electronic health records.

Statistical Analysis

We compared the patient characteristics between the transient, persistent, and no AF-LVEF reduction groups using the *t* test for continuous variables and chi-square test for categorical variables. We ensured that continuous data were normally distributed before the use of *t* testing. Among patients in the group with transient AF-LVEF reduction, we quantified and compared the change in LVEF between the AF and sinus rhythm TTEs using the paired *t* test.

We compared AI-based AF-LVEF measurements to the original clinical/cardiologist AF-LVEF readings using the paired *t* test and assessed how the AI-based AF-LVEF measurements reclassified patients as having an AF-LVEF reduction or not.

We graphed the cumulative incidence of heart failure hospitalization over 1 year across the 3 patient

groups (no AF-LVEF reduction, transient AF-LVEF reduction, and persistent AF-LVEF reduction), first as determined by clinical LVEF assessment and then again for the 3 groups as redefined by AI LVEF assessment.

In order to compare between the patient groups, we used the Fine–Gray subdistribution hazard model to analyze the risk of hospitalization due to HF while accounting for the competing risk of death. The Fine–Gray model extends the Cox proportional hazards model to handle competing risks by modeling the subdistribution hazard function, which allows for the direct estimation of the effect of covariates on the cumulative incidence function of the primary event. Covariates included age, sex, race, ethnicity, as well as history of HF, hypertension, diabetes, prior myocardial infarction, thromboembolic events (stroke/transient ischemic attack/thromboembolism), and chronic kidney disease.

Clinical Practice Patterns

Given the uncertainty in management approach to transient LVEF reduction during AF, we conducted an exploratory analysis to describe current real-world clinical practice patterns for this patient group. We conducted a chart review to follow the clinical course of all patients who had a transient LVEF reduction during AF as determined by the original clinical assessment. Specifically, we tracked instances when patients were subsequently given a new diagnosis of HFrEF/HFmrEF, underwent ischemic workup, or were prescribed new medications

for HFrEF/HFmrEF. We did not consider beta blockers a medication specific for HFrEF/HFmrEF given that they are commonly prescribed for AF rate control.

Software

Deep learning model inference was performed using the Python library PyTorch.

All statistical analyses were performed using R software (Version 4.1.0; R Foundation for Statistical Computing, Vienna, Austria). The Fine–Gray model was implemented using the *cmprsk* package.²⁷

RESULTS

Cohort Description

There were 872 patients who had an AF TTE followed by a sinus rhythm TTE within 90 days (Figure 2). After excluding patients in whom there had been an intervening event or procedure between their AF TTE and sinus rhythm TTE, the resultant cohort contained 810 patients. Of these patients, 459 (56.7%) did not have a reduced LVEF <50% while in AF (no AF-LVEF reduction), 71 (8.8%) had a reduced LVEF while in AF that subsequently recovered to ≥50% on the follow-up sinus rhythm TTE (transient AF-LVEF reduction), and 280 (34.6%) had a reduced LVEF while in AF that persisted on the follow-up sinus rhythm TTE (persistent AF-LVEF reduction). The most frequent indications for the follow-up sinus rhythm TTE included valvular

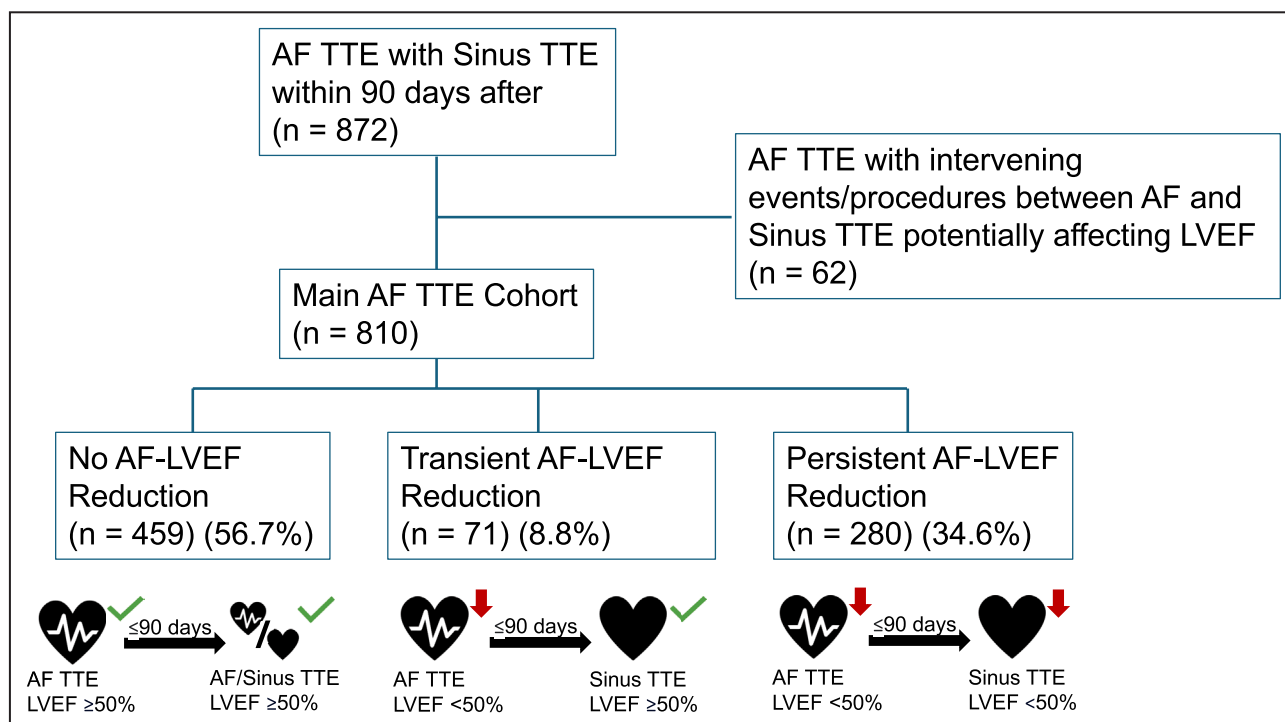


Figure 2. Cohort flow diagram.

AF indicates atrial fibrillation; LVEF, left ventricular ejection fraction; and TTE, transthoracic echocardiogram.

Table Patient Characteristics and Echo Measurements

	All patients	AF-LVEF reduction			P value	P value
		None	Transient	Persistent	Transient vs none	Transient vs persistent
n	810	459	71	280		
Age, y (mean±SD)	74.1±13.1	76.0±12.3	73.1±15.6	71.3±13.3	0.07	0.33
Female sex (%)	278 (34.3)	182 (39.7)	29 (40.8)	67 (23.9)	0.95	0.01
Race or ethnicity					0.73	0.08
American Indian	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)		
Asian	55 (6.8)	36 (7.9)	5 (7.0)	14 (5.0)		
Black	84 (10.4)	33 (7.2)	3 (4.2)	48 (17.3)		
Hispanic	63 (7.8)	32 (7.0)	8 (11.3)	23 (8.3)		
Non-Hispanic White	534 (66.2)	32 (7.0)	52 (73.2)	167 (60.1)		
Pacific Islander	4 (0.5)	1 (0.2)	0 (0.0)	3 (1.1)		
Other	45 (5.6)	29 (6.3)	2 (2.8)	14 (5.0)		
Unknown	21 (2.6)	11 (2.4)	1 (1.4)	9 (3.2)		
Heart failure	393 (48.5)	167 (36.4)	30 (42.3)	196 (70.0)	0.41	<0.001
Hypertension	495 (61.1)	276 (60.1)	42 (59.2)	177 (63.2)	0.98	0.62
Prior myocardial infarction	94 (11.6)	38 (8.3)	7 (9.9)	49 (17.5)	0.83	0.17
Peripheral arterial disease	127 (15.7)	77 (16.8)	9 (12.7)	41 (14.6)	0.49	0.82
Diabetes	200 (24.7)	109 (23.7)	11 (15.5)	80 (28.6)	0.16	0.04
Chronic kidney disease	203 (25.1)	108 (23.5)	12 (16.9)	83 (29.6)	0.28	0.05
AF LVEF by human	47.7 (18.9)	62.2 (7.6)	38.1 (7.7)	26.5 (10.3)	<0.001	<0.001
AF LVEF by artificial intelligence	49.6 (13.4)	58.6 (6.5)	46.3 (8.5)	35.8 (10.1)	<0.001	<0.001
AF heart rate	91.9 (24.8)	86.2 (24.0)	104.9 (26.3)	92.0 (21.4)	<0.001	<0.001
Sinus rhythm LVEF	49.8 (17.9)	61.0 (9.6)	57.6 (6.9)	29.3 (10.9)	<0.01	<0.001
Sinus rhythm heart rate	78.3 (19.0)	77.1 (19.1)	79.8 (24.1)	79.8 (16.8)	0.47	0.98
Days between AF and sinus transthoracic echocardiograms	26.7 (24.4)	28.0 (24.4)	27.8 (26.0)	24.4 (24.1)	0.94	0.3

AF indicates atrial fibrillation; and LVEF, left ventricular ejection fraction.

disease (39%), HF or cardiomyopathy (34.8%), and non-AF arrhythmias (10.5%) (Table S2).

In the analytic cohort, the average age was 74.1 years old, 34.3% were female, 33.8% were non-White (Table). There was a relatively high prevalence of comorbidities including preexisting HF (48.5%), hypertension (61.1%), diabetes (24.7%), and chronic kidney disease (25.1%). When comparing patients who had a transient LVEF reduction during AF to those with no LVEF reduction during AF, patients had a higher heart rate but otherwise no significant differences in demographics or comorbidities. When comparing patients who had a transient LVEF reduction during AF to those with persistent LVEF reduction, patients in the former group were more likely to be female, less likely to have a previous history of HF and diabetes, and had a higher LVEF and higher heart rate while in AF.

Reassessment of LVEF During AF Using AI

Among patients with a transient LVEF reduction while in AF that subsequently recovered, there was a mean

absolute increase in LVEF of 19.5% (95% CI, 12.0–22.1%, $P<0.001$) after an average of 27.8 days (SD 26.0 days) (Figure 3). Of these patients, 17 (24.0%) had a prior sinus rhythm TTE an average of 349.2 days (SD 380.1 days) earlier with a mean absolute LVEF decrease of 23.9% (95% CI, 17.6%–30.1%, $P<0.001$) when comparing the AF TTE to the prior sinus rhythm TTE. In the group with transient LVEF reduction, 27 (38.0%) patients were electrically cardioverted from AF to sinus rhythm, 43 (60.6%) received rhythm control medications, and 5 (7.0%) had an intervening AF ablation. After reassessing the LVEF of patients in AF using AI in this group, there was an absolute LVEF improvement of 8.2% (95% CI, 6.0%–10.4%, $P<0.001$) when comparing the AI-based AF-LVEF to the original clinical AF-LVEF assessment (Figure 3). The AI-based AF-LVEF reassessment resulted in 20 (28.2%) patients no longer having a reduced LVEF while in AF. We confirmed the safety of this reclassification; only 1 of the 20 patients who were reclassified to the lower risk group by AI experienced an HF hospitalization within the next year.

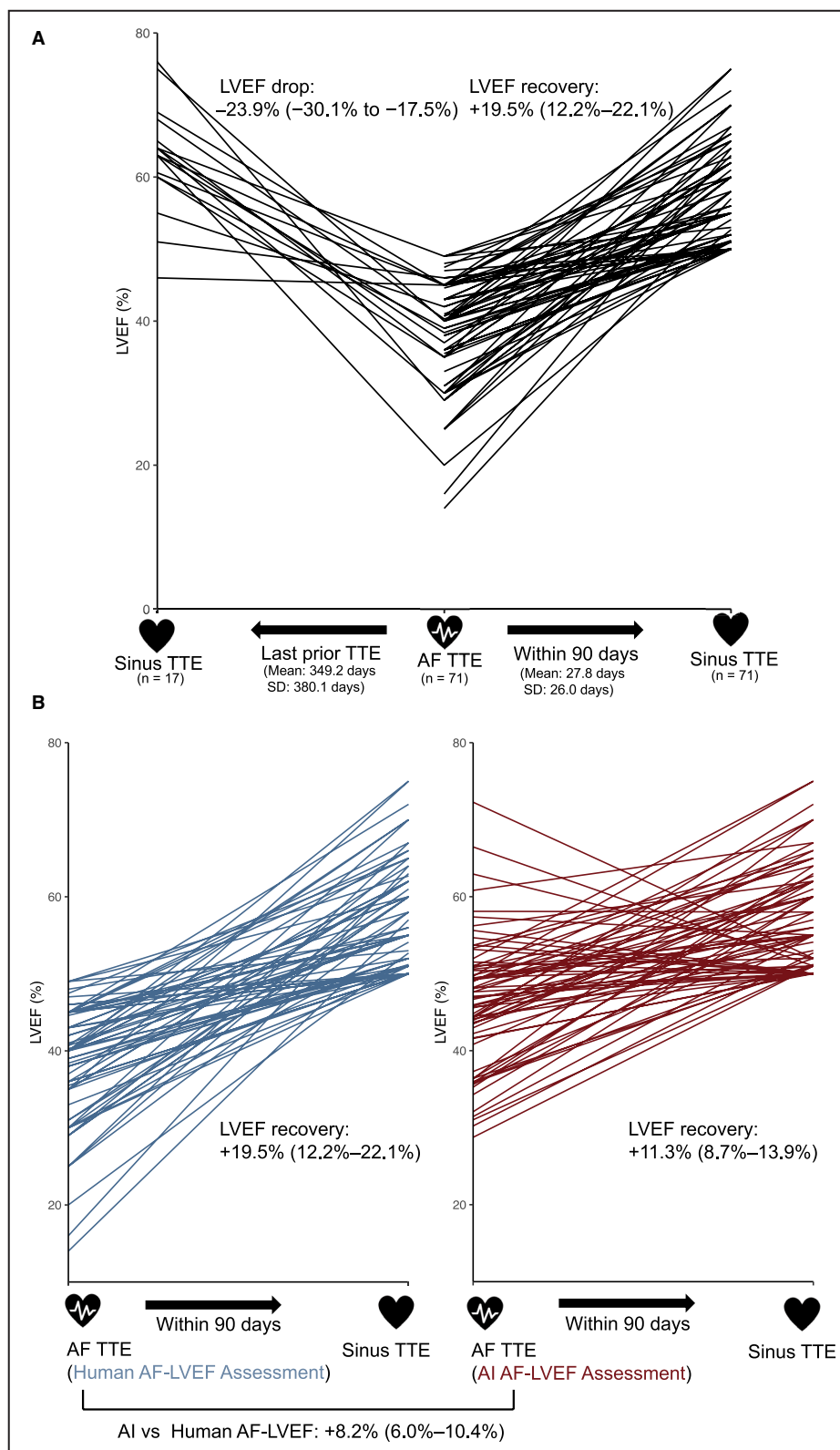


Figure 3. A, Changes in LVEF between AF and sinus rhythm among patients with a transient LVEF reduction while in AF based on clinical (human) AF-LVEF assessments. B, Changes in LVEF between AF and sinus rhythm comparing human to artificial intelligence AF-LVEF assessment.

AF indicates atrial fibrillation; AI, artificial intelligence; LVEF, left ventricular ejection fraction; and TTE, transthoracic echocardiogram.

Outcomes Based on LVEF Classification by Clinical Versus AI Assessment

When stratifying patients by their AF-LVEF as assessed by cardiologists, there was a significantly higher adjusted hazard of HF hospitalization within 1 year among patients with a persistent LVEF reduction compared with those with no LVEF reduction after adjusting for clinical risk factors and accounting for the competing risk of death (hazard ratio [HR], 2.06 [95% CI, 1.36–3.12], $P<0.001$) (Figure 4A). However, there was no statistically significant difference in HF hospitalization among patients with a transient LVEF reduction during AF compared with those with no LVEF reduction (HR, 1.73 [95% CI, 0.90–3.31], $P=0.10$).

When stratifying patients by AF-LVEF as assessed by AI, again there was a significantly higher hazard for HF hospitalization among patients with a persistent LVEF reduction compared with those with no LVEF reduction (HR, 2.04 [95% CI, 1.36–3.05], $P<0.001$) (Figure 4B). Additionally, there was also a significantly higher hazard for HF hospitalization for patients with a transient LVEF reduction compared with those with no LVEF reduction (HR, 2.28 [95% CI, 1.23–4.21], $P=0.003$).

To further confirm these findings, we conducted an additional analysis studying patients in the group with persistent AF-LVEF reduction by AI who had another sinus rhythm TTE within 90 days of their follow-up sinus rhythm TTE. We found that after expanding the window for LVEF recovery, there were 20 additional patients from

the group with persistent AF-LVEF reduction who had later recovered their LVEF. We reclassified these patients as having a transient AF-LVEF reduction phenotype and repeated the Fine–Gray analyses. Results were similar. Again, both the groups with persistent and transient LVEF reduction had a higher hazard for HF hospitalization compared with patients with no LVEF reduction (HR, 2.09 [95% CI, 1.39–3.15], $P<0.001$; HR, 2.96 [95% CI, 1.08–3.55], $P=0.03$, respectively) (Figure S1).

In an exploratory analysis to understand the current real-world implications of AF-LVEF assessments, we described the clinical management for patients in the group with transient LVEF reduction based on clinical AF-LVEF assessment. We found that following the reduced AF-LVEF assessment, 22 (31.0%) patients were given a new diagnosis of HFrEF/HFmrEF, 14 (19.7%) were considered to have worsened HFrEF/HFmrEF, and 35 (49.3%) patients were given no new diagnosis of HFrEF/HFmrEF (Figure S2). We also observed that 13 (18.3%) patients underwent an ischemic evaluation (6 diagnostic left heart catheterizations, 4 coronary computed tomography angiograms, and 3 stress tests) and 16 (19.7%) were started on new non-beta blocker HFrEF/HFmrEF medications.

DISCUSSION

In this study, we observed that a substantial portion of patients in AF will have a transient reduction in LVEF

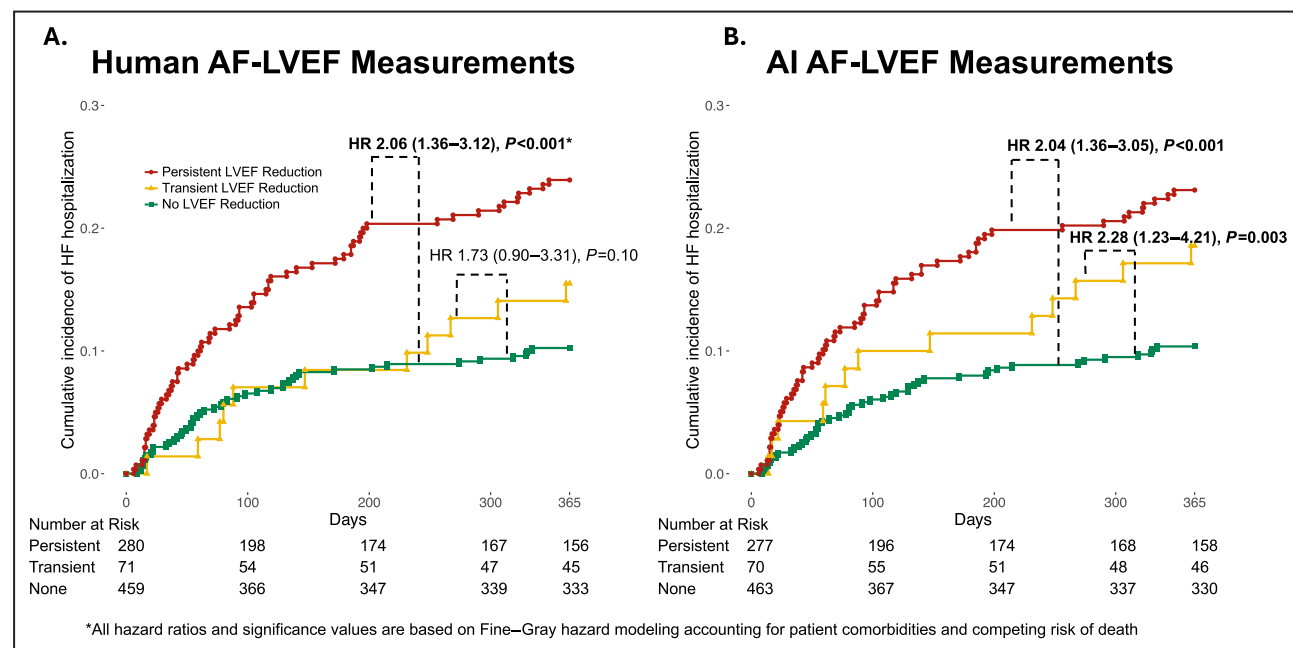


Figure 4. Cumulative incidence of heart failure hospitalization among patients with persistent, transient, and no LVEF reduction during AF, with groupings based on either (A) human or (B) artificial intelligence AF-LVEF measurements.

Hazard ratios comparing cumulative incidence curves are calculated from Fine–Gray hazard modeling accounting for patient comorbidities and competing risk of death. AF indicates atrial fibrillation; AI, artificial intelligence; HF, heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; and TTE, transthoracic echocardiogram.

that recovers quickly upon returning to sinus rhythm within 90 days. Reassessing the LVEF of these patients using AI reclassified more than a quarter of them as no longer having AF-LVEF reductions; these patients had a low future risk of HF hospitalization. Patients confirmed by AI to have a transient LVEF reduction while in AF had a more than 2-fold higher risk of HF hospitalization compared with those with no LVEF reduction during AF. AI assessment of LVEF during AF may therefore be an important tool for (1) decreasing misdiagnosis of reduced EF cardiomyopathy and (2) increasing the accurate diagnosis of true transient AF-LVEF reduction, a potentially high-risk phenotype.

Whereas previous research has primarily focused on individuals with AF and established HFrEF/HFmrEF, we explored an earlier at-risk population: patients who have transient reductions in LVEF during AF, many of whom do not carry a previous diagnosis of HF.^{16,17} To date, this patient group has not been well characterized. Our findings suggest that identification of this group has likely been hindered by imprecision from clinical measurements.

When using clinical LVEF measurements, we observed a prominent pattern in the group with transient AF-LVEF: the LVEF fell an average of 23.9 percentage points when going from sinus rhythm to AF with a subsequent recovery of an average of 19.5 percentage points after reverting back from AF to sinus rhythm. When reassessing the AF-LVEF using AI, the AF-LVEF increased on average by >8 percentage points, which attenuated this observed LVEF fall and recovery pattern. AI reassessment reclassified more than a quarter of the group with transient AF-LVEF as no longer having a reduced AF-LVEF.

The difference between the AI and clinical LVEF measurements likely stems from challenges in measuring AF-LVEF accurately. To reduce errors introduced by AF's beat-to-beat variability, guidelines recommend calculating AF-LVEF by averaging measurements over 5 beats.²⁸ However, this entails at least 20 separate endocardial tracings for a biplane LVEF assessment (end systole and end diastole for apical 4-chamber and apical 2-chamber views across 5 beats), which requires considerable time and effort and may not be routinely undertaken in clinical practice. AI LVEF assessment is therefore particularly useful during AF, because an AI algorithm provides an automated estimate of LVEF across multiple beats, which can reduce the variability in LVEF measurements.²⁶

Human AF-LVEF assessment, in misidentifying reduced AF-LVEF, may result in adverse downstream consequences. The reduced AF-LVEF label is at risk for leading to a misdiagnosis of HFrEF when the reduced AF-LVEF is considered alongside common AF symptoms such as dyspnea and fatigue that can be mistaken for HF symptoms.⁵ This, in turn, may result

in diagnosis-related patient anxiety and unnecessary further HFrEF workup and treatment. In our exploratory analysis, we found that in a fifth of patients with transiently reduced AF-LVEF, the diagnosis led to an ischemic evaluation or the start of new HFrEF medications. Even if a subsequent TTE in sinus rhythm shows LVEF recovery, unnecessary HFrEF guideline-directed medical therapies may be continued if clinicians attribute the LVEF recovery to the positive effects of the guideline-directed medical therapies rather than due to AF-LVEF mismeasurement.²⁹ Similarly, in patients with preexisting HFpEF, a reduced AF-LVEF label can result in the inappropriate use of HFrEF treatments that are ineffective in HFpEF. At least 1 previous meta-analysis, for example, intriguingly showed a lack of clinical benefit for beta blockers in patients with HFrEF and AF, raising the question of whether some of the patients in the included studies were mismeasured and in fact had HFpEF.³⁰

Interestingly, only when the patients with potentially misidentified transient AF-LVEF reduction were reclassified by AI and separated out did the group with transient AF-LVEF reduction clarify itself as having a potentially higher risk phenotype. This could reflect the misidentified patients being low risk and washing out the higher risk signal when included in the group. Those with true transient LVEF reduction during AF had a more than 2-fold risk of experiencing a HF hospitalization within 1 year compared with patients who did not experience LVEF reductions during AF.

These results are consistent with prior theories that transient LVEF-reductions during arrhythmias such as AF may represent early underlying myocardial disease that is exposed or caused by the arrhythmia.³¹ For example, 1 prior study of 24 patients demonstrated that patients with a prior tachycardia-induced cardiomyopathy who recovered were at higher risk for rapid decline in ventricular function upon tachyarrhythmia recurrence.³² It has also been shown that when AF becomes persistent, a substantial portion of patients will demonstrate ventricular scarring on imaging and that the amount of this scarring may be predictive of LVEF recovery after AF ablation.⁶ Proposed mechanisms for AF-induced cardiomyopathy include tachycardia-induced dysfunction, neurohormonal effects, and long-term myocardial structural changes.^{31,33} A transient reduction in LVEF during AF may therefore be a premonitory sign of a developing cardiomyopathy that could potentially benefit from early treatment. Future prospective studies are needed to further clarify whether early AF rhythm control and standard HFrEF/HFmrEF guideline-directed medical therapy have a role in prevention in this high-risk population. Indeed, we found that currently, at our large quaternary medical center, real-world practice patterns varied widely in

how to treat individuals with transient LVEF reductions during AF.

In summarizing our results, we revisit our initial conceptual model for transient AF LVEF reduction (Figure 1). Among patients who have been misdiagnosed because of AF LVEF clinical mismeasurement, accurate AI LVEF reassessment can be helpful in 2 ways: (1) in mislabeled patients who have never had a prior HF event and therefore most likely do not have true heart failure, AI LVEF reassessment helps avoid unnecessary HF diagnostic testing and treatments; and (2) in mislabeled patients who have had a prior HF event and therefore most likely have HFpEF instead of HFrEF, AI LVEF reassessment ensures that patients are not started on HFrEF treatments that are not effective in HFpEF. In the group of true transient AF LVEF reduction, our results support the idea that transient AF LVEF reduction may be an early HF phenotype with an increased risk of HF hospitalization. Future larger prospective studies will help clarify whether HFrEF treatments are effective in this patient population.

Several study limitations warrant consideration. This study used retrospective data from a single large academic medical center. Although TTE interpretation was performed by a large group of certified academic echocardiography readers, it is possible that site-specific biases could influence clinical LVEF interpretations. Although readers at our site are encouraged to follow echocardiography society guidelines, they are not audited or strictly required to calculate LVEFs from average measurements across multiple beats. We believe it is more informative that our results reflect real world clinical practice. Further validation in other sites would be helpful. This study included only patients who had a TTE in AF followed by a repeat TTE in sinus rhythm within 90 days. This could potentially select for a sicker patient population that may not generalize to all patients with AF. However, these same selection criteria were used for all 3 patient groups: patients with persistent, transient, and no AF-LVEF reduction, so the comparisons between the 3 groups should remain valid. We additionally used Fine-Gray analyses, which helped control for both patient risk factors as well as the competing risk of death. Nevertheless, prospective studies that systematically document LVEF after AF conversion to sinus rhythm in a broad population would be helpful for confirming our findings. This study included 810 patients, of whom 125 experienced a heart failure admission within 1 year. The group with transient AF-LVEF reduction as assessed by AI was small and contained 70 patients with 13 of them experiencing events. A larger study with longer follow-up would add additional statistical power in helping differentiate the relative risks of the AF-LVEF reduction subgroups. In this retrospective study we did not know the exact timing of the conversion to sinus rhythm for

many patients, meaning that some patients may have had a shorter window to realize LVEF recovery after cardioversion. This could have resulted in the misclassification of some patients in the group with persistent AF-LVEF reduction who really had a transient AF-LVEF reduction phenotype. We reported an additional analysis that helped ensure an expanded LVEF recovery window, which confirmed similar results. Nevertheless, a prospective study with continuous monitoring could help specify an amount of time in sinus rhythm for LVEF recovery, potentially improving the accuracy of the risk group classifications and enhancing the outcome differences observed between the groups. We chose to study an LVEF recovery threshold of 50% because it is the point at which most clinicians decide on starting HF guideline-directed medical therapies. However, larger studies in the future should also consider studying the outcome trajectories for patients who have partial LVEF recovery but may have not reach an LVEF >50%, as these patients may also have a different phenotype than patients whose LVEF does not change upon cardioversion. This research used the Echo-Dynamic AI LVEF quantification model, because it has been validated and shown to be accurate in large multicenter studies that included patients in both sinus rhythm and AF.^{26,34} However, this model used only apical 4-chamber TTE views and was not specifically tuned for AF; future AI models that include other TTE views and are specifically validated in AF subgroups could conceivably increase LVEF assessment accuracy and may be considered for future analyses. Lastly, it was difficult to know for sure whether the studied AF-LVEF reductions were necessarily caused by AF itself or potentially other concurrent disease processes that may have then improved between the AF and follow-up sinus rhythm TTE. We attempted to control for this effect as much as possible by manual chart review and excluding patients who had potentially confounding intervening medical events and procedures. Nevertheless, undetected residual confounding conditions remain possible.

Conclusions

In conclusion, AI-based measurement of LVEF improved the risk assessment of patients in AF, potentially preventing misdiagnosis of reduced ejection fraction cardiomyopathy in some while uniquely identifying others who experienced a transient reduction in LVEF that translated to a higher risk for HF hospitalization.

ARTICLE INFORMATION

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Disclosures

All other authors report no relevant disclosures.

Supplemental Material

Tables S1-S2

Figures S1-S2

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