Atrial Fibrillation in the ARCADIA Trial

Hooman Kamel for the ARCADIA Investigators

Disclosures

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Atrial cardiopathy biomarkers and atrial fibrillation in the ARCADIA trial

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Table 1. Characteristics of patients screened for atrial cardiopathy in ARCADIA, stratified by subsequent detection of AF.

Characteristic[a]	Atrial fibrillation (*N* = 254)	No atrial fibrillation (*N* = 3491)
Age, mean (SD), years	71.7 (9.7)	65.8 (10.6)
Female, no. (%)	134 (52.8%)	1604 (45.9%)
Race, no. (%) [*N* = 3659][b]		
Asian	2 (0.8%)	68 (2.0%)
Black or African American	43 (17.1%)	649 (19.0%)
Other	205 (81.7%)	2645 (77.6%)
White	1 (0.4%)	46 (1.3%)
Ethnicity, no. (%) [*N* = 3724][b]		
Hispanic or Latino	15 (6.0%)	343 (9.9%)
Not Hispanic or Latino	237 (94.0%)	3129 (90.1%)
Medical comorbidities		
Hypertension	200 (78.7%)	2512 (72.0%)
Prior or current tobacco use	104 (40.9%)	1426 (40.8%)
Diabetes	76 (29.9%)	1052 (30.1%)
Coronary artery disease	26 (10.2%)	265 (7.6%)
Heart failure	18 (7.1%)	136 (3.9%)
Peripheral artery disease	5 (2.0%)	67 (1.9%)
Atrial cardiopathy biomarkers		
$PTFV_1$, mean (SD), μV*ms [*N* = 3673]	3798 (2,660)	3426 (2,259)
NT-proBNP, median (IQR), pg/mL [*N* = 3580]	416 (258–751)	96 (45–231)
LA diameter index, mean (SD), cm/m^2 [*N* = 3125]	2.1 (0.4)	1.8 (0.4)
Days from stroke to biomarker screening, mean (SD)	1.9 (4.3)	3.0 (25.3)

AF: atrial fibrillation; IQR: interquartile range; LA: left atrial; NT-proBNP: amino terminal pro-B-type natriuretic peptide; $PTFV_1$: P-wave terminal force in lead V_1; SD: standard deviation.

[a]Percentages may not total 100 because of rounding.

[b]Other race was defined as American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or more than one race. Site investigators and coordinators were instructed to directly ask participants to report their self-identified race and ethnicity, which were then categorized per NIH guidelines.

Table 2. Associations between baseline atrial cardiopathy biomarkers and subsequent detection of atrial fibrillation in ARCADIA.

Biomarker	Model 1	Model 2	Model 3
$PTFV_1$	1.15 (1.03–1.28)	1.03 (0.92–1.14)	-
NT-proBNP	1.99 (1.85–2.13)	1.83 (1.69–1.97)	1.88 (1.67–2.11)
LADI	1.34 (1.20–1.50)	1.25 (1.14–1.38)	1.25 (1.14–1.37)

LADI: left atrial diameter index; NT-proBNP: amino terminal pro-B-type natriuretic peptide; $PTFV_1$: P-wave terminal force in lead V_1.
Data are presented as risk ratios (95% confidence intervals) per standard-deviation increase in the atrial cardiopathy biomarker variables. Model 1 was unadjusted. Model 2 included all three biomarkers together. Model 3 additionally adjusted for age, sex, race, ethnicity, hypertension, diabetes, coronary artery disease, heart failure, peripheral artery disease, and tobacco use, with variables reduced using stepwise reverse selection with a *p*-value threshold of 0.2.

Table 3. Discrimination of baseline atrial cardiopathy biomarkers for predicting subsequent AF in ARCADIA.

Variables included in predictive model	C-statistic (95% CI)
$PTFV_1$, NT-proBNP, LADI	0.82 (0.79–0.85)
NT-proBNP, LADI	0.82 (0.79–0.85)
NT-proBNP, $LADI_{central}$	0.80 (0.77–0.83)
NT-proBNP, $LAVI_{central}$	0.81 (0.78–0.84)
NT-proBNP, LADI, age	0.82 (0.79–0.85)
NT-proBNP	0.80 (0.77–0.83)
LADI	0.67 (0.63–0.72)
$LADI_{central}$	0.67 (0.64–0.71)
$LAD_{central}$	0.66 (0.63–0.70)
$LAVI_{central}$	0.71 (0.67–0.74)
$PTFV_1$	0.54 (0.50–0.58)
Age	0.66 (0.63–0.70)

Figure 1. Calibration of atrial cardiopathy biomarkers for predicting AF in ARCADIA.

Each open circle represents 1 of 20 groups of ARCADIA trial participants. Patients were grouped by their predicted probability of atrial fibrillation (AF) based on a relative risk regression model comprised of NT-proBNP, left atrial dimension index, and P-wave terminal force in ECG lead V_1. The circle's position on the x-axis represents the group's predicted probability of atrial fibrillation. The circle's position on the y-axis represents the actual proportion of patients in the group who developed atrial fibrillation. The dashed blue line represents perfect calibration

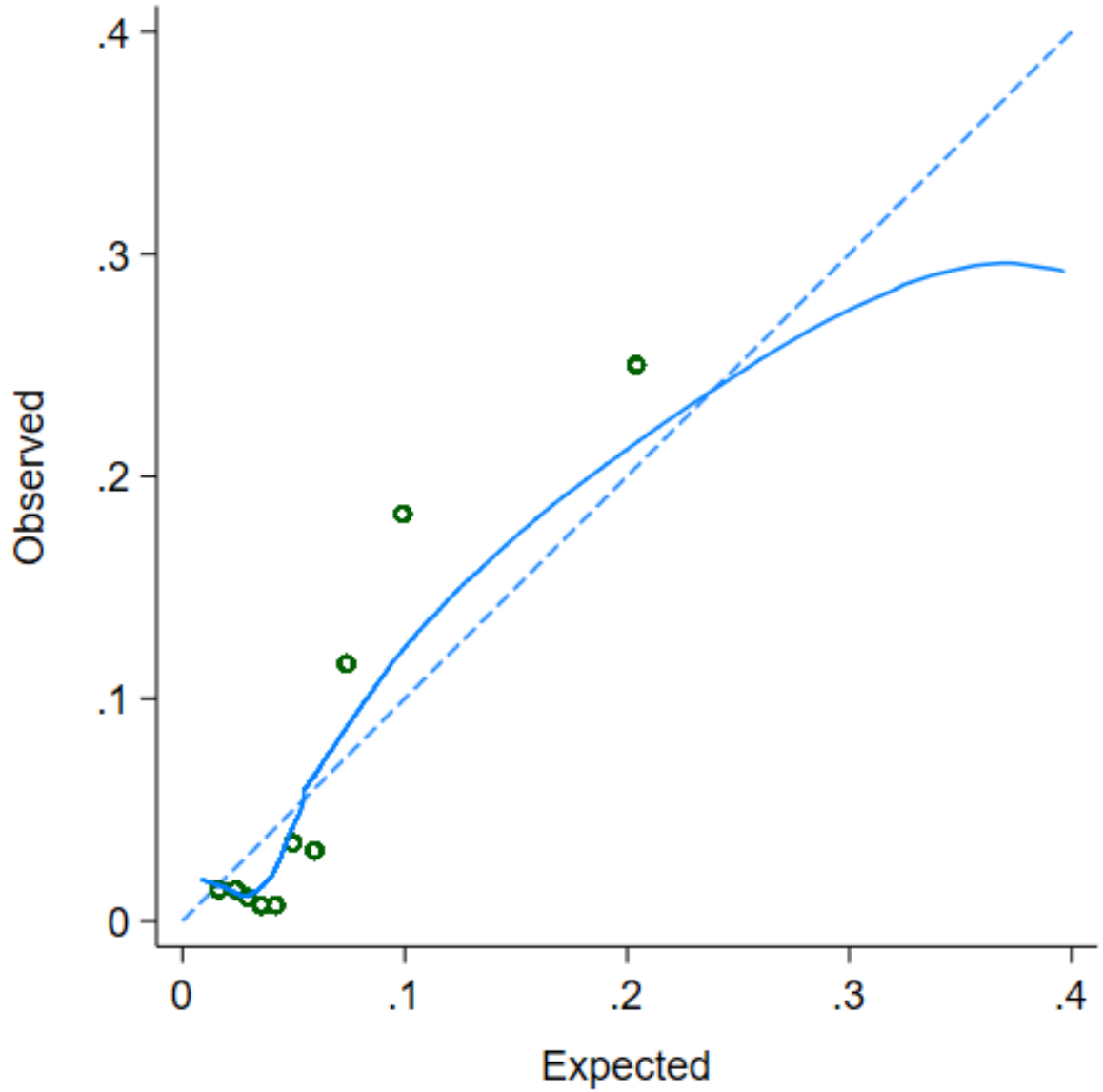

Table 4. Sensitivity analysis of associations between baseline atrial cardiopathy biomarkers and subsequent detection of atrial fibrillation in the ARCADIA trial.

Patient population	$PTFV_1$[a]	NT-proBNP[a]	LADI[a]	Discrimination[b]
Eligible	0.84 (0.74–0.95)	1.30 (1.15–1.47)	1.18 (1.10–1.26)	0.67
Randomized	0.81 (0.68–0.95)	1.38 (1.15–1.66)	1.25 (1.11–1.41)	0.69

LADI: left atrial diameter index; NT-proBNP: amino terminal pro-B-type natriuretic peptide; $PTFV_1$: P-wave terminal force in lead V_1.
[a]Data are presented as risk ratios (95% confidence intervals) or hazard ratios (95% confidence intervals) per standard-deviation increase in the atrial cardiopathy biomarker variables in a model that included all three biomarkers together.
[b]Data are presented as c-statistics or Harrell's C.

Limitations

- Differential ascertainment of AF based on eligibility for randomization
- Heterogeneity in AF monitoring and ascertainment

Conclusions

Biomarkers used to identify atrial cardiopathy in ARCADIA were associated with and predictive of subsequent AF detection, suggesting neutral results of trial not entirely due to suboptimal biomarkers of atrial cardiopathy

Predictive performance of biomarkers was modest, supporting further research to identify other measures that can identify a more severe form of atrial cardiopathy with a high risk of AF

Heart-Rhythm Monitoring Practices, Detection of Atrial Fibrillation, and Effect of Anticoagulation in the ARCADIA Trial

Figure 1. Flow Diagram of Patients Included in Analysis of Heart-Rhythm Monitoring Practices in the ARCADIA Trial.

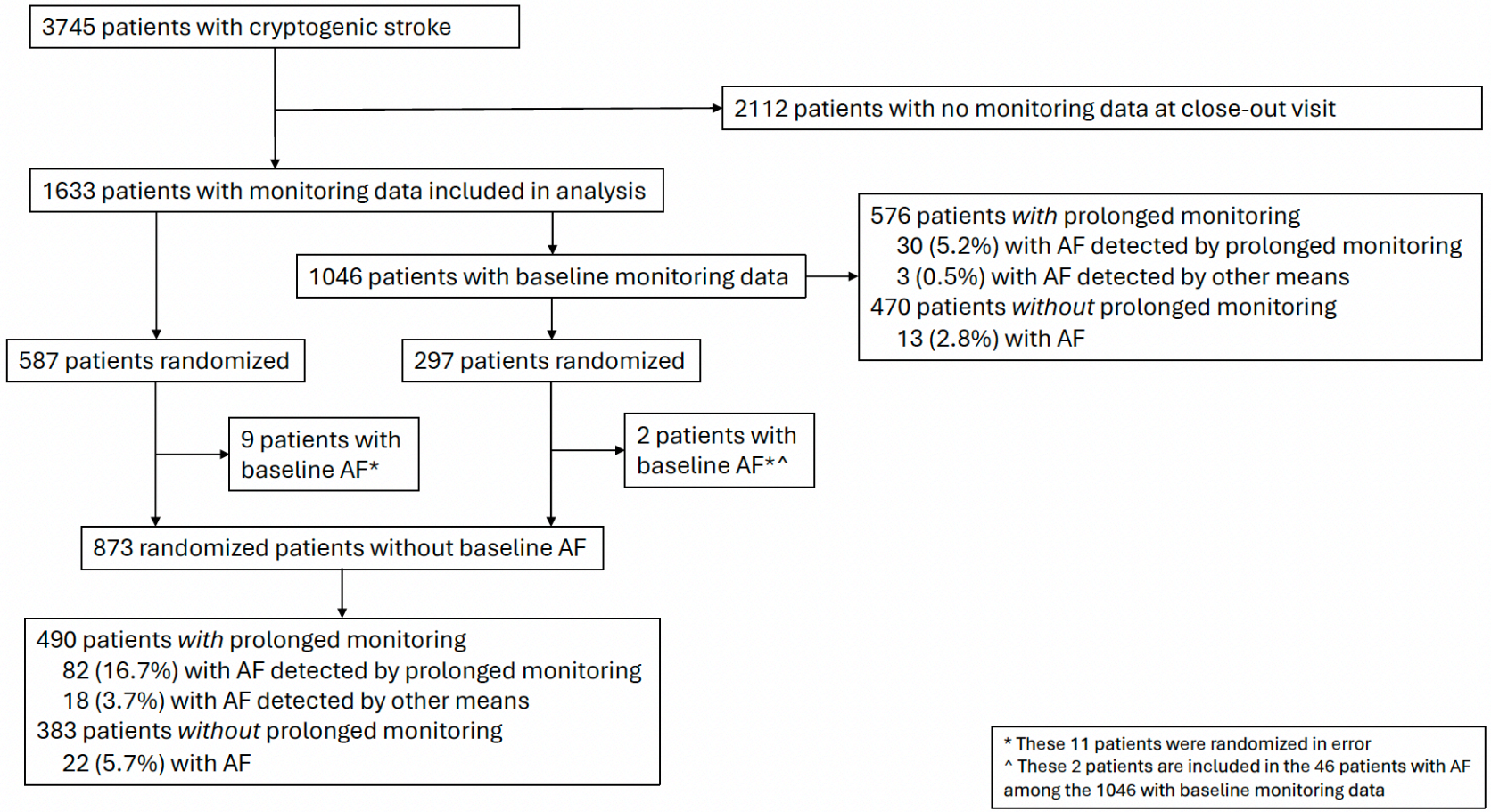

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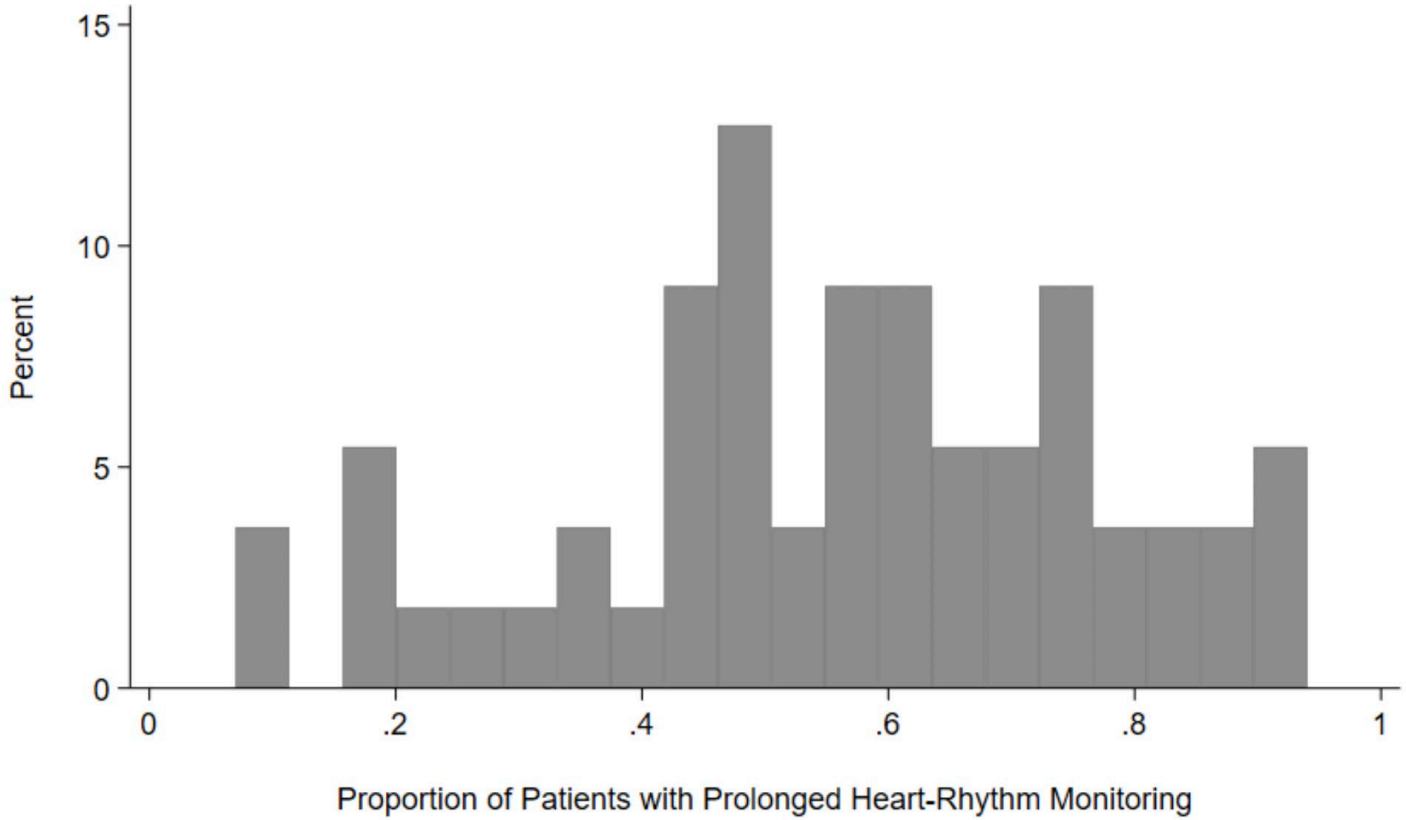
Table 2. Proportions of ARCADIA Patients Undergoing Prolonged Heart-Rhythm Monitoring.[a]

	Any Prolonged Monitoring	External Ambulatory Monitor	Implantable Loop Recorder	Both[b]
Overall (n = 1,633)	58.6%	34.7%	29.3%	5.5%
Before randomization (n = 1,046)	55.1%	39.0%	18.6%	2.6%
After randomization (n = 873)	56.2%	21.7%	39.4%	4.9%

Table 3. Factors Associated with Prolonged Heart-Rhythm Monitoring in the ARCADIA Trial.[a]

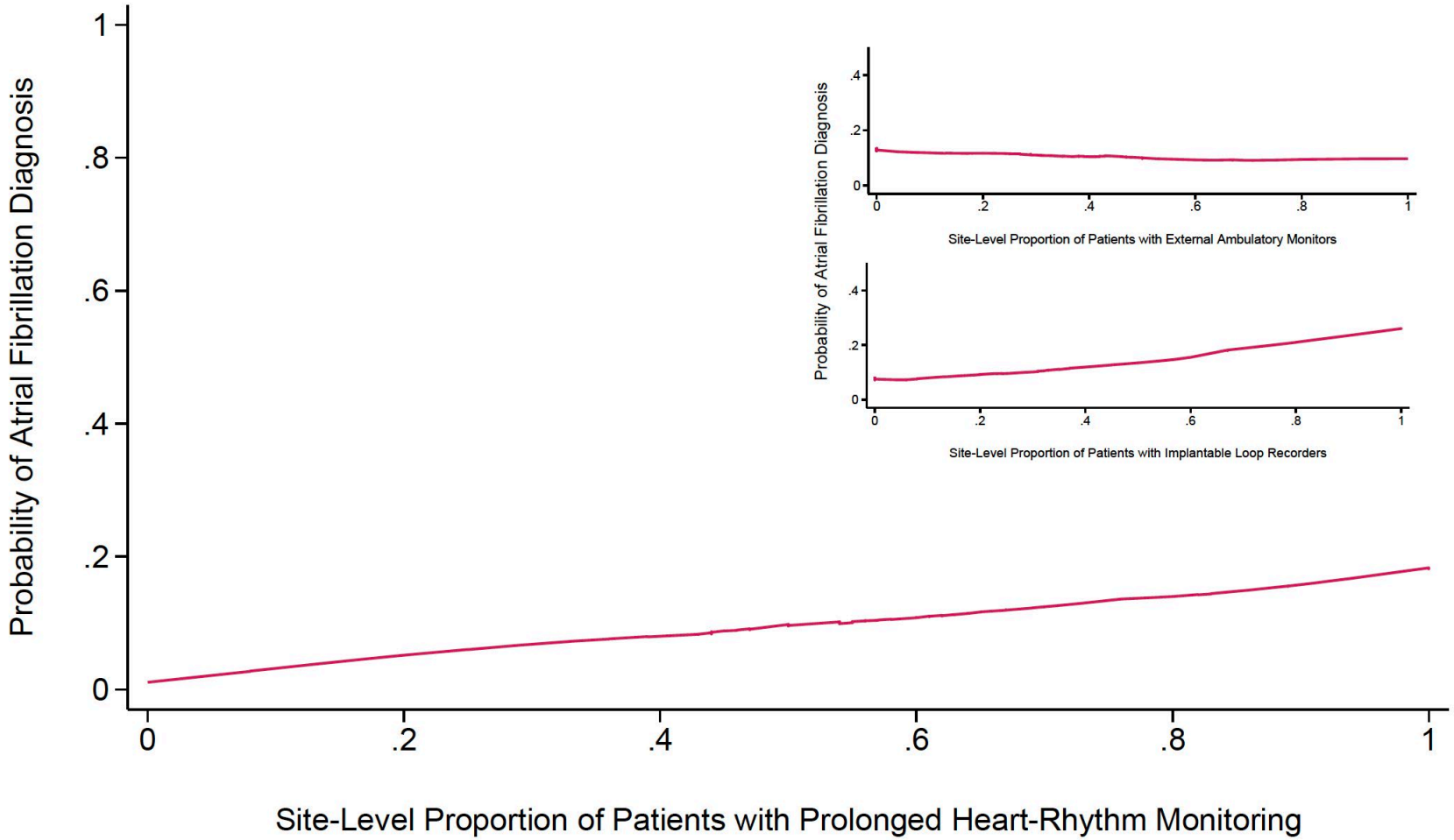
Characteristic	Risk Ratio (95% CI)	*P* value
Age (per decade)	1.04 (1.00-1.08)	0.047
Female sex	1.07 (0.98-1.17)	0.14
Asian, Black, Hispanic, or other race-ethnicity	0.84 (0.74-0.95)	0.006
Modified Rankin Scale (per point)	0.97 (0.93-1.01)	0.12
National Institutes of Health Stroke Scale (per point)	0.98 (0.96-1.00)	0.037
Peripheral artery disease	0.71 (0.49-1.05)	0.09

Figure 2. Distribution Across Sites of the Proportion of Patients Undergoing Prolonged Heart-Rhythm Monitoring.



Only sites with >10 patients in this sample are shown (96 sites had ≤10 patients and 55 had >10 patients).

Figure 3. Relationship between Site-Level Proportion of Patients Undergoing Prolonged Heart-Rhythm Monitoring and Detection of Atrial Fibrillation.



Limitations

- Lacked detail on precise type and duration of monitoring
- Data available for only a subset of trial participants
- Potential confounding in association between monitoring and AF

Conclusions

- Prolonged heart-rhythm monitoring appears fairly widespread at North American stroke centers participating in stroke trials
- More monitoring at site level associated with greater risk of AF detection
- Substantial practice variation and sociodemographic disparities
- Future studies needed to identify optimal and equitable strategies for assessing risk of cardioembolic stroke after cryptogenic stroke

Other Secondary Analyses of the ARCADIA Trial

Hooman Kamel for the ARCADIA Investigators

Pending paper topics

- Cancer
- LV injury
- Brain infarction in multiple arterial territories
- Vascular risk factors and effect of anticoagulation

JAMA Neurology | Original Investigation

Apixaban vs Aspirin in Patients With Cancer and Cryptogenic Stroke
A Post Hoc Analysis of the ARCADIA Randomized Clinical Trial

Babak B. Navi, MD, MS; Cenai Zhang, MS; Benjamin Miller, MD; Mary Cushman, MD, MSc; Scott E. Kasner, MD, MSCE; Mitchell S. V. Elkind, MD, MS; David L. Tirschwell, MD, MSc; W. T. Longstreth Jr, MD, MPH; Richard A. Kronmal, PhD; Morin Beyeler, MD; Jordan Elm, PhD; Richard M. Zweifler, MD; Joseph Tarsia, MD; Carlo W. Cereda, MD; Giovanni Bianco, MD; Gianluca Costamagna, MD; Patrik Michel, MD; Joseph P. Broderick, MD; David J. Gladstone, MD; Hooman Kamel, MD, MS; Christopher Streib, MD, MS

Table 3. Outcomes Among Participants With History of Cancer at Enrollment Stratified by Treatment Group

	Aspirin (n = 76)		Apixaban (n = 61)		
Outcome	No. (%)	Incidence rate, No./100 person-years (95% CI)	No. (%)	Incidence rate, No./100 person-years (95% CI)	HR (95% CI)
Primary outcome					
Major ischemic or major hemorrhagic event	16 (21.1)	12.8 (7.8-20.9)	8 (13.1)	7.8 (3.9-15.7)	0.61 (0.26-1.43)
Secondary efficacy outcome					
Recurrent ischemic stroke	7 (9.2)	5.3 (2.5-11.2)	5 (8.2)	4.7 (1.9-11.2)	0.87 (0.28-2.76)
Ischemic or hemorrhagic stroke	9 (11.8)	6.8 (3.6-13.2)	5 (8.2)	4.7 (1.9-11.2)	0.68 (0.23-2.03)
Major arterial ischemic event	9 (11.8)	7.0 (3.7-13.5)	6 (9.8)	5.6 (2.5-12.5)	0.79 (0.28-2.23)
Symptomatic DVT or PE	6 (7.9)	4.7 (2.1-10.4)	1 (1.6)	0.9 (0.1-6.7)	0.21 (0.02-1.71)
Major ischemic event	14 (18.4)	11.2 (6.6-18.9)	7 (11.5)	6.6 (3.1-13.9)	0.59 (0.24-1.47)
Secondary safety outcome					
All-cause mortality	4 (5.3)	3.0 (1.1-8.1)	3 (4.9)	2.8 (0.9-8.7)	0.94 (0.21-4.19)
Symptomatic ICH	2 (2.6)	1.5 (0.4-6.1)	0	NA	NA
Major hemorrhagic event	2 (2.6)	1.5 (0.4-6.1)	1 (1.6)	1.0 (0.1-6.9)	0.61 (0.06-6.73)

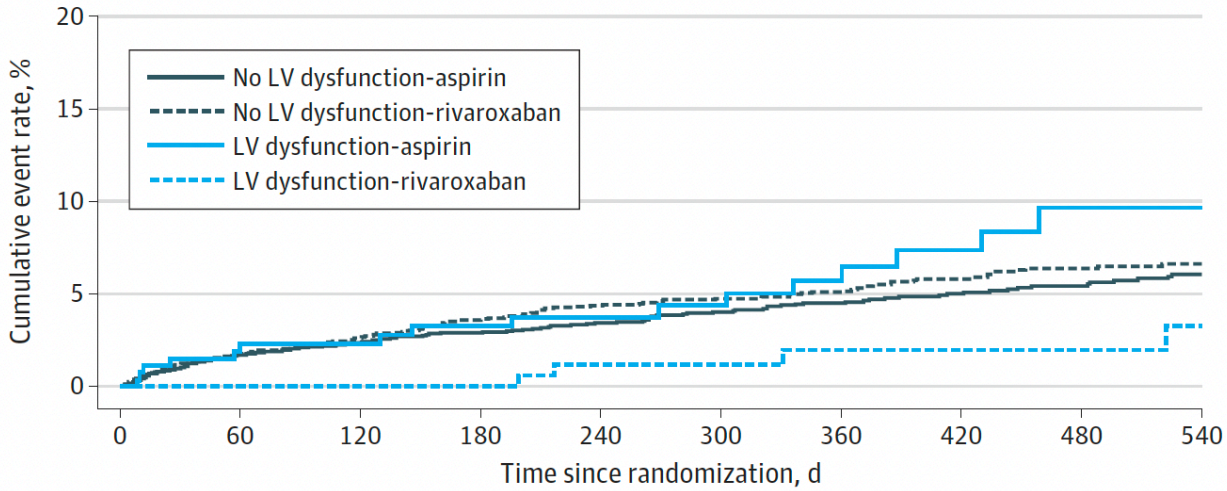
JAMA Neurology | Original Investigation

Left Ventricular Dysfunction Among Patients With Embolic Stroke of Undetermined Source and the Effect of Rivaroxaban vs Aspirin

A Subgroup Analysis of the NAVIGATE ESUS Randomized Clinical Trial

Alexander E. Merkler, MD, MS; Lesly A. Pearce, MS; Scott E. Kasner, MD; Ashkan Shoamanesh, MD; Lee A. Birnbaum, MD; Hooman Kamel, MD, MS; Kevin N. Sheth, MD; Richa Sharma, MD, MPH

Figure 2. Kaplan-Meier Curves for Time to Primary Outcome Event by Left Ventricular Dysfunction and Assigned Treatment



No. at risk

No LV dysfunction-aspirin	3282	2910	2594	2302	1972	1709	1426	1201	958	721
No LV dysfunction-rivaroxaban	3323	2935	2600	2311	1967	1708	1430	1181	941	697
LV dysfunction-aspirin	273	242	220	195	166	149	120	96	63	47
LV dysfunction-rivaroxaban	229	213	197	178	156	141	121	102	85	70

LV injury and anticoagulation in ARCADIA

- EF, fractional shortening, and WMA from echo lab
- Analysis led by Alex Merkler, Richa Sharma, Fadi Nahab, and others
- Directly informed RESOLVE trial proposal
- Results submitted for ISC 2025

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ECG, Echo, and Laboratory Cores

Outcome Adjudication Core and Medical Safety Monitor

NIH/NINDS

The BMS-Pfizer Alliance

Roche Diagnostics