

Supplemental material

Supplemental tables with references

Supplemental table 1. Reported risk factors of arrhythmia recurrence after AF ablation; classified by relative level of evidence

Established risk factors (meta-analysis and/or extensive consistent literature)
AF type(1–6)
Hypertension(4, 5, 7–12)
Obesity(13–15)
Metabolic syndrome(11, 16–18)
Chronic kidney disease(16, 17, 19–26)
Obstructive sleep apnea(27–31)
Probable risk factors (Extensive evidence with little conflicting data)
Age(3, 5, 19, 32–35)
Female gender(3, 6, 33, 34, 36–41)
Duration of AF history(42–46)
Duration of current AF episode/of persistent AF(34, 47–51)
Valvular heart disease(50, 52–55)
Cardiomyopathy(16, 17, 56–59)
Structural heart disease*(15, 37)
Chronic hemodialysis(24, 60–62)
Alcohol consumption(33, 63–66)
Possible risk factors (significantly conflicting results or limited body of evidence)
Male gender (very late recurrence)(67)
Diabetes mellitus(5, 11, 33, 68, 69)
Coronary artery disease(3, 68, 70)

Congestive heart failure(38, 71)
Dyslipidemia(7, 11, 68)
AF burden(72)
Primary persistent AF(73)
Chronic pulmonary disease(33)
History of hyperthyroidism(74) including amiodarone-induced(75)
Anxiety and depression(76, 77)
Smoking(42, 78)
Number of failed antiarrhythmic drugs(3, 46)
Prior stroke(22)
Permanent pacemaker for sick sinus syndrome(79)
Permanent pacemaker for atrioventricular block(80)

*Structural heart disease defined as various combinations of: coronary artery disease, valvular heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, hypertensive heart disease and grown-up congenital heart disease.

Supplemental table 2. Clinical prediction scores for arrhythmia recurrence after AF ablation

<u>AF recurrence prediction score</u>	<u>Area under the ROC curve</u>	<u>References</u>
APPLE	0.62	(19, 81)
ALARMEc	0.66	(16, 17)
MB-LATER	0.62-0.78	(67, 82)
BASE-AF2	0.94	(42)
CAAP-AF	0.65	(3)
DR-FLASH	Not reported	(36)
HATCH	Not predictive for AF recurrence	(83)
CHADS ₂	0.64	(68, 84)
CHA ₂ DS ₂ -VASc	0.55-0.63	(68, 84)
R ₂ CHADS ₂	0.54-0.55	(84)

ROC, receiver operating characteristic.

Supplemental table 3. Imaging predictors of arrhythmia recurrence after AF ablation
Structural atrial remodeling
LA volume (MRI/CT/US)(6, 85–88), area(44) and diameter(4, 5, 9, 39, 46, 89)
LA sphericity (MRI)(90, 91)
LA asymmetry index (US)(92) and LA vertical asymmetry (MRI, computational)(93)
Extent of LA fibrosis (delayed-enhancement MRI)(94–96)
Atrial T1 relaxation time (MRI, T1 mapping)(97, 98)
Large LAA volume (TEE(99) and CT(100))
Right atrial diameter (US(51, 101), CT(102)) and surface (US)(103)
LAVI to RAVI ratio (CT(104))
Mechanical atrial remodeling
Low global LA strain (US(105–111) and MRI(112))
Low LA function index (US)(113)
Low LA emptying fraction (LA angiography(30), US(52, 114) and CT(115))
Low LA passive emptying fraction (MRI)(116)
Low LA reservoir function (intracardiac US(117) and LA angiography(30))
LA stiffness index (diastolic compliance, MRI)(118)
High LA mechanical dispersion (US)(119)
Intra-atrial dyssynchrony (MRI)(120)
Total atrial conduction time (US)(121–125), inter- and intra-atrial electromechanical delay (US)(35)
Decreased LAA mechanical function (TEE)(99, 114, 122, 126–130)
LV dysfunction
LV ejection fraction (US)(12, 16, 131)
LV diastolic dysfunction (diastolic function grade(132), E/e' ratio(133–137), E/A ratio(138))
Ventricular fibrosis(139)
Left ventricular hypertrophy(140)

Others
Epicardial adipose tissue volume (CT(141–144) and TEE(145))
Larger PV size (MRI(146), CT(147, 148))
PV anatomy (4 discrete PVs, large ridges; MRI and CT)(149)

CT, computed tomography; LA, left atrium; LAA, left atrial appendage; LAVI, left atrial volume index; LV, left ventricle ; RAVI, right atrial volume index; TEE, transesophageal echocardiography; US, ultrasound.

Supplemental table 4. Examples of circulating biomarkers predicting arrhythmia recurrence after AF ablation
Inflammation and oxidative stress
CRP and hsCRP(12, 103, 150–154)
Erythrocyte sedimentation rate(155)
Elevated white blood cell count(12, 98)
IL-6(156, 157)
TNF-alpha(157)
Myeloperoxidase(158)
Monocyte to HDL ratio(43)
Neutrophil to lymphocyte ratio(159)
Uric acid(16, 160, 161)
Gamma-glutamyl transferase(162)
Post-procedural AGEs and TBARs(163)
Myocardial stretch and injury
NT-proBNP(127, 164)
BNP(150, 165–168)

ANP(154)
High-sensitive troponin T(86)
Fibrosis and extracellular matrix remodeling
Galectin-3(169)
sST2(170)
TGF-beta1 (conflicting results)(154, 155, 171–173)
cTGF(174)
TIMP-2(154)
MicroRNA-21(175)
Relaxin(98)
sRANKL and sRANKL/OPG ratio(176)
Comorbidity-associated biomarkers
Homocysteine (early recurrence)(177)
LDL cholesterol(154)
eGFR(21, 150)
Free T3 and free T4(178)
HbA1c in patients with type 2 diabetes(179)
Others
Anti-M2-R antibodies(180)
Endothelin-1(181)

Supplemental table 5. Electrocardiographic predictors of arrhythmia recurrence after AF ablation

Markers of atrial cardiomyopathy and underlying heart disease
Interatrial block/prolonged P wave duration(72, 182–184) and P wave duration index(185)
Decreased P wave morphology variability(186)
Prolonged PR interval(187) and first-degree AV block(78)
Bundle branch block (very late recurrence)(67)
Electrocardiographic signs of LV hypertrophy(188)
Longer QTc interval(189, 190)
LA voltage/Low-voltage areas(21, 191–193)
Longer sinus node recovery time(194, 195)
Characteristics of AF activity
AF cycle length(38, 49, 126)
Dominant frequency(48, 196)
F wave amplitude(48, 197, 198)
Organization index(48) and related spectral features(199)
Recurrence plot indices of AF waveform(200)
Distal to proximal CS frequency gradient(201)
High RA dominant frequency(202)
Low CS to RA dominant frequency gradient(202)
Non-PV triggers(22, 131, 203–206)
Acute PV reconnection at index procedure(192, 207)
Number of DC shocks and energy required to terminate AF pre-ablation(208)

AV, atrio-ventricular; CS, coronary sinus; DC, direct current; PV, pulmonary vein; RA, right atrium.

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