

# Persistan Atrial Fibrillasyon: Klinik ve Elektrofizyolojik Özellikler

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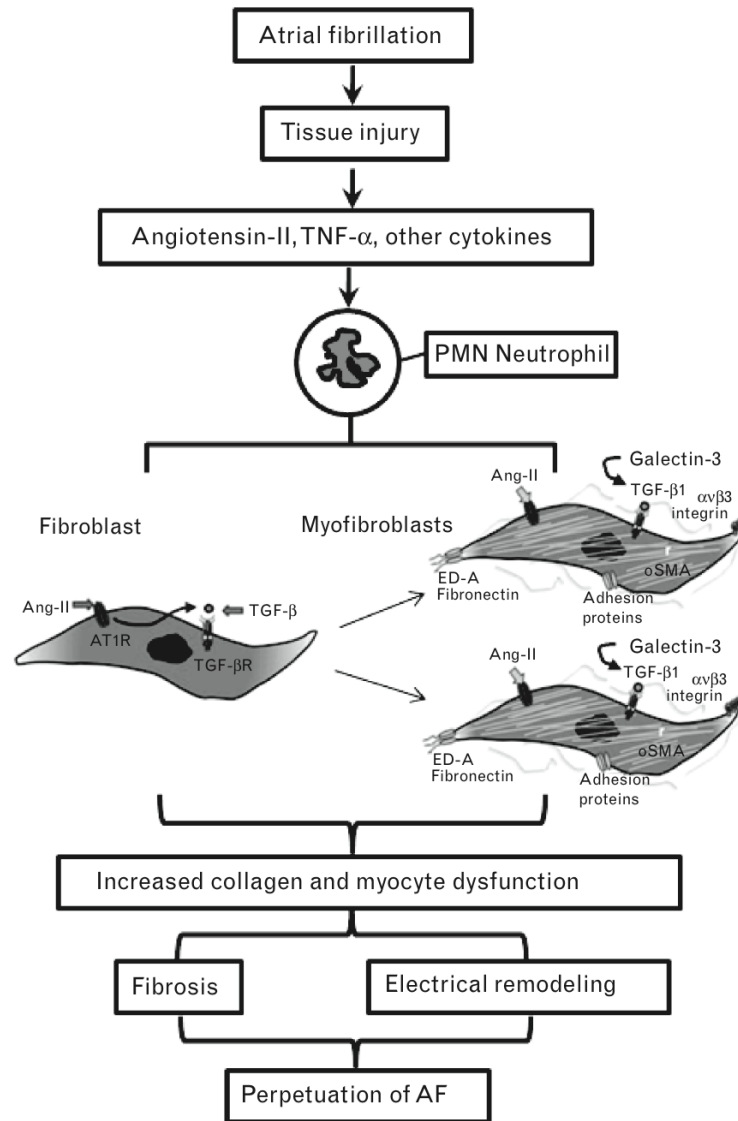
*5.Atrial Fibrillasyon Zirvesi, Antalya 2016*

# Önemli noktalar-1

- AF, klinik yaşamda en sık karşılaşılan devamlılık gösteren aritmi ve embolik inmenin ana sebebidir.
- Mekanizmalar net olarak anlaşılamamakla beraber, AF atriyumlarda elektriksel yeniden şekillenme ve fibroza yol açar.
- Fibroz ve elektriksel yeniden şekillenme yaygın intrasellüler sinyal yollarının sonucudur ve aritminin stabilizasyonuna ve devamına katkıda bulunur.

# Önemli noktalar-2

- AF'nun devamı fibroblastların miyofibroblastlara dönüşmesine ve iyon kanal disfonksiyonuna yol açar. Bununla birlikte miyositlerde apoptoz ve ekstrasellüler matriks üretimi ve yıkımı ile birlikte elektriksel ve yapısal yeniden şekillenmeye katkıda bulunur.
- Bütün bu yeniden şekillenmede ve AF devamını önlemede temel hedef profibrotik bir protein olan galektin-3'tür.



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**CLINICAL PRACTICE GUIDELINE: FULL TEXT**

# 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

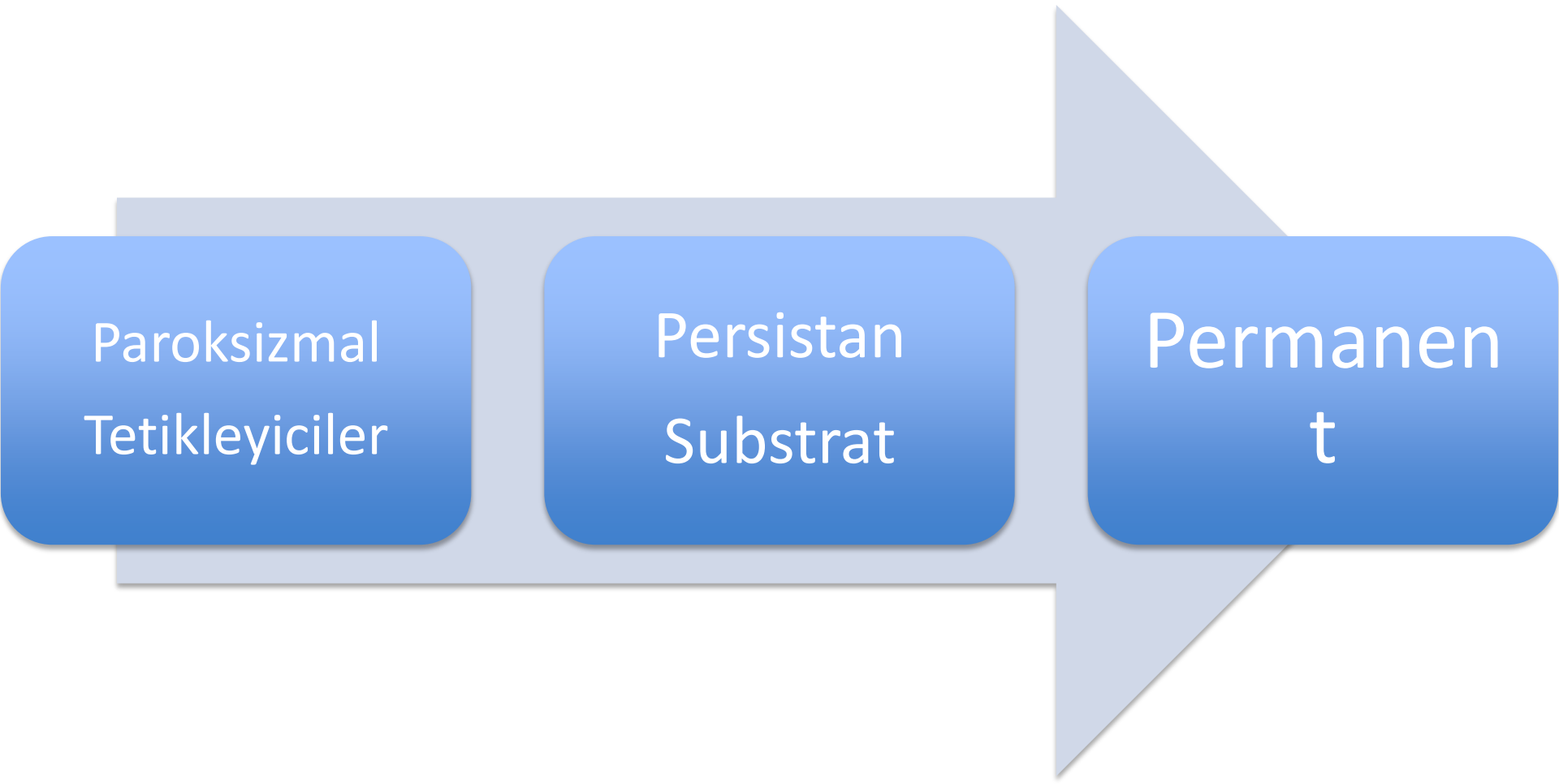


A Report of the American College of Cardiology/American Heart Association  
Task Force on Practice Guidelines and the Heart Rhythm Society

Developed in Collaboration With the Society of Thoracic Surgeons

# Sınıflama

- Paroksizmal AF
- **Persistan AF: 7 günden uzun süreli AF**
- Uzun persistan AF
- Permanent AF



Paroksizmal  
Tetikleyiciler

Persistan  
Substrat

Permanen  
t

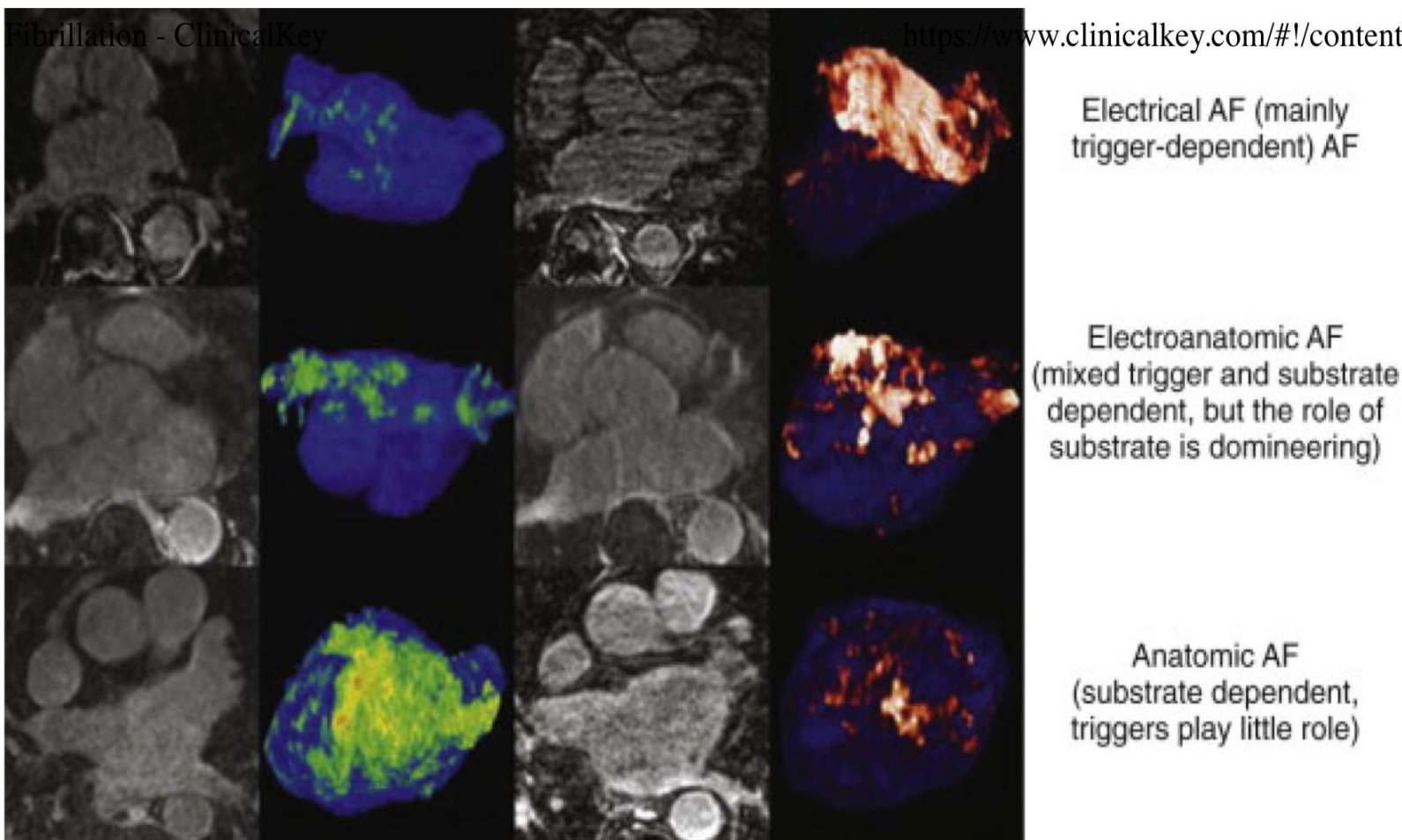


FIGURE 42-7

Stages of progression of atrial fibrillation assessed by delayed-enhancement magnetic resonance imaging.

(From Mahnkopf C, Badger TJ, Burgon NS, et al: *Evaluation of the left atrial substrate in patients with lone atrial fibrillation using delayed-enhanced MRI: Implications for disease progression and response to catheter ablation*, Heart Rhythm 7:1475–1481, 2010.)



# Prospective European Survey on Atrial Fibrillation Ablation: Clinical Characteristics of Patients and Ablation Strategies Used in Different Countries

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**Survey on Atrial Fibrillation Ablation. Background:** Atrial fibrillation (AF) ablation is widely adopted. Our aim was to conduct a prospective multicenter survey to verify patients' characteristics, approaches, and technologies adopted across Europe.

**Methods and Results:** A total of 35 centers in 12 countries actively participated in the study and 940 patients (median age 60 years) were enrolled. AF was paroxysmal, persistent, and long-lasting persistent in 52.4%, 36%, and 11.6% of patients, respectively; 95.5% of patients were symptomatic and 91.4% were refractory to antiarrhythmic therapy. Redo procedures were performed in 20.9%. Pulmonary vein isolation (PVI) emerged as the cornerstone of ablative therapy and has been performed in 98.7% of procedures, with confirmation of PVI in 92.9% of cases. The ablation of nonparoxysmal AF was not generally limited to isolating the PVs and several adjunctive approaches are adopted, particularly in the case of long-lasting persistent AF. Linear lesions or elimination of complex fractionated atrial electrograms were more frequently added. Circular mapping catheters and imaging techniques were seen to be used in about two-thirds of cases. Radiofrequency energy was delivered through open irrigated catheters in 68% of cases.

**Conclusions:** European centers are largely following the recommendations of the guidelines and the expert consensus documents for AF ablation. AF ablation is mainly performed in relatively young patients with symptomatic drug refractory AF and no or minimal heart disease. Patients with paroxysmal AF are the most frequently treated with a quite uniform ablative approach across Europe. A less standardized approach was observed in nonparoxysmal AF patients. (*J Cardiovasc Electrophysiol*, Vol. 25, pp. 1074-1081, October 2014)

*atrial fibrillation, catheter ablation, survey*

TABLE 4				
Comparison of Clinical and Procedural Variables Between Patients with Paroxysmal, Persistent, and Long-Lasting Persistent Atrial Fibrillation				
	Paroxysmal	Persistent	Long-Lasting	P Value
Age (years)	58 (51–64)	61 (54–67)	62 (52–67)	<0.001
AF history (years)	4 (2–7)	5 (3–8)	5 (3–7)	0.046
LA diameter (mm)	41 (38–44)	44 (41–47)	48 (44–51)	<0.001
LVEF (%)	60 (58–65)	58 (54–62)	55 (48–58)	<0.001
Duration of energy pulses delivered (minutes)	35 (25–50)	43 (28–60)	48 (28–69)	<0.001
Number of energy pulses delivered	43 (31–58)	45 (32–61)	48 (33–73)	<0.001
Total fluoroscopy time (minutes)	28 (17–44)	30 (18–49)	30 (20–55)	0.035
Total procedure duration (minutes)	150 (120–190)	180 (120–220)	190 (120–240)	<0.001

Data reported as medians (Q1–Q3). AF = atrial fibrillation; LA = left atrium; LVEF = left ventricular ejection fraction.

# Mekanizma

- Hızlı uyarı çıkaran fokal odak- fibrillatuar yayılım

Artmış otomatisite

Tetiklenmiş aktivite

- Çoklu reentri

Rastgele (random) reentri

Fonksiyonel reentri (rotor)

Mikro- ve makro-reentri

# Trigger-Based Mechanism of the Persistence of Atrial Fibrillation and Its Impact on the Efficacy of Catheter Ablation

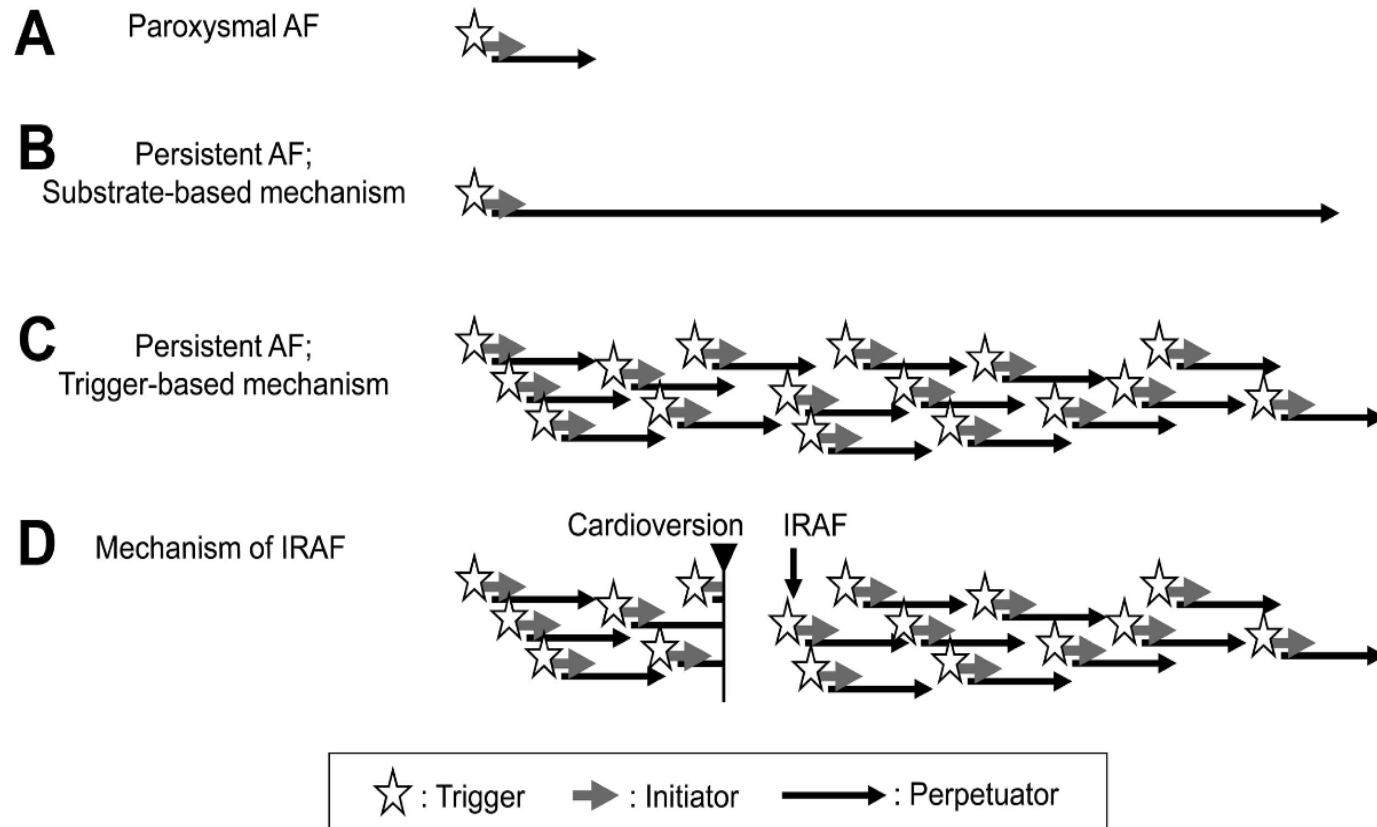
Koichi Inoue, MD, PhD; Toshiya Kurotobi, MD, PhD; Ryusuke Kimura, MD, PhD;  
Yuko Toyoshima, MD; Norihisa Itoh, MD, PhD; Masaharu Masuda, MD;  
Yoshiharu Higuchi, MD, PhD; Motoo Date, MD, PhD; Yasushi Koyama, MD, PhD;  
Atsunori Okamura, MD, PhD; Katsuomi Iwakura, MD, PhD; Kenshi Fujii, MD, PhD

**Background**—We investigated the possibility that a frequent trigger action might play a role in the development of persistent atrial fibrillation (PeAF) and the presence of a substrate.

**Methods and Results**—In 263 consecutive patients who underwent catheter ablation (CA) for PeAF, electric cardioversion was performed at the beginning of the procedure to determine the presence or absence of an immediate recurrence of AF (IRAF). We defined an IRAF as a reproducible AF recurrence within 90 s after restoration of sinus rhythm by electric cardioversion. We performed a mean $\pm$ SD of  $1.3\pm0.5$  sessions of CA, including pulmonary vein isolation and ablation of the premature atrial contractions that triggered the IRAF (IRAF triggers), and observed the patients for 17 (10–27) months. An IRAF was observed in 70 patients (27%), but we could not ablate the IRAF triggers in 16 (23%) of these IRAF patients. The recurrence rate of PeAF was higher in patients with an unsuccessful IRAF trigger ablation than in those with successful IRAF trigger ablation (63% versus 11%;  $P<0.001$ ). A multivariable analysis also revealed that an unsuccessful IRAF trigger ablation was 1 of the independent predictors of recurrent PeAF (odds ratio, 10.9; 95% CI, 3.4–36.7).

**Conclusions**—In the PeAF patients with an IRAF, successful elimination of the IRAF triggers, in addition to pulmonary vein isolation, resulted in a successful CA. These results imply that such triggers play a major role in the AF persistence in these PeAF patients. (*Circ Arrhythm Electrophysiol.* 2012;5:295-301.)

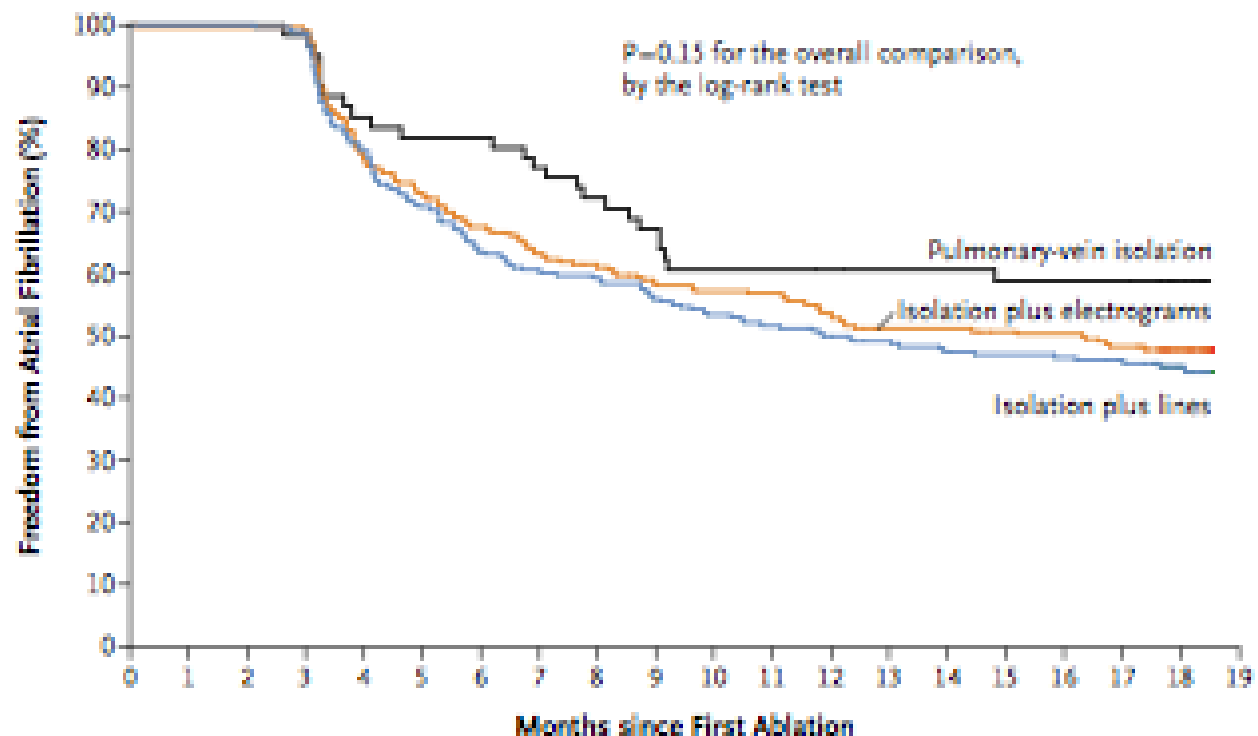
**Key Words:** atrial fibrillation ■ persistent atrial fibrillation ■ catheter ablation ■ persistence ■ triggers



ORIGINAL ARTICLE

## Approaches to Catheter Ablation for Persistent Atrial Fibrillation

Atul Verma, M.D., Chen-yang Jiang, M.D., Timothy R. Betts, M.D., M.B., Ch.B.,  
Jian Chen, M.D., Isabel Deisenhofer, M.D., Roberto Mantovan, M.D., Ph.D.,  
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Endrj Menardi, M.D., Paul Novak, M.D., and Prashanthan Sanders, M.B., B.S., Ph.D.,  
for the STAR AF II Investigators\*



#### No. at Risk

Pulmonary-vein isolation	61	60	50	41	36	23
Isolation plus electrograms	244	242	161	137	124	72
Isolation plus lines	244	240	152	133	115	57

**Figure 2. Freedom from Atrial Fibrillation.**

The graph shows Kaplan–Meier estimates of freedom from documented atrial fibrillation more than 30 seconds after a single procedure, with or without the use of antiarrhythmic medications. There were no significant differences between groups ( $P=0.15$ ). Isolation plus electrograms denotes ablation with pulmonary-vein isolation plus additional ablation of complex fractionated electrograms; Isolation plus lines refers to ablation with pulmonary-vein isolation plus additional linear ablation.

# Prevalence and distribution of focal triggers in persistent and long-standing persistent atrial fibrillation



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**BACKGROUND** The relevance of focal triggers in persistent atrial fibrillation (PerAF) and long-standing persistent atrial fibrillation (LSPAF) has not been previously investigated.

**OBJECTIVE** We prospectively evaluated the prevalence and distribution of AF triggers in patients referred for catheter ablation of PerAF and LSPAF.

**METHODS** We analyzed consecutive patients undergoing first time AF ablation who underwent a standardized trigger protocol including cardioversion of induced or spontaneous AF and infusion of up to 20 µg of isoproterenol for 15–20 minutes either before or after pulmonary vein (PV) isolation accomplished. Triggers were defined as AF/sustained atrial tachyarrhythmia or repetitive atrial premature depolarizations.

**RESULTS** A total of 2168 patients were included (mean age  $57 \pm 11$  years; 1636 [75%] men), with 1531 patients having paroxysmal AF (PAF) (71%), 496 having PerAF (23%), and 141 having LSPAF (7%). PV triggers were found in 1398 patients with PAF (91%), 449 patients with PerAF (91%), and 129 patients with LSPAF (91%) ( $P = .856$  for comparison across groups). Non-PV triggers were

elicited in a total of 234 patients (11%), and the prevalence was similar across the different types of AF (PAF, 165 [11%]; PerAF, 54 [11%]; LSPAF, 15 [11%];  $P = .996$  for comparison across groups).

**CONCLUSION** PVs are the main AF trigger site in patients with PerAF and LSPAF, with an overall prevalence similar to that found in patients with PAF. These results support the current recommendations for PV isolation as the cornerstone of catheter ablation to eliminate AF triggers in PerAF and LSPAF.

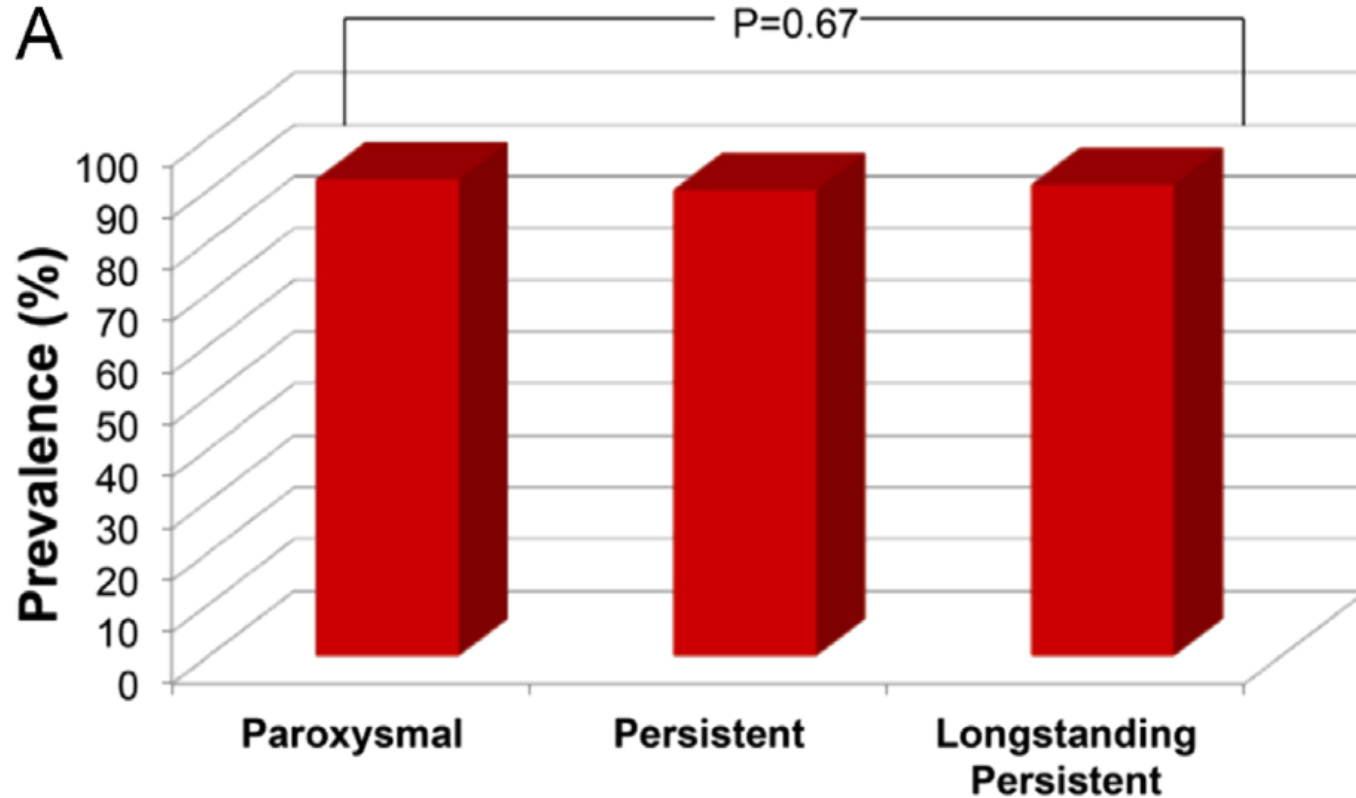
**KEYWORDS** Atrial fibrillation; Catheter ablation; Focal triggers

**ABBREVIATIONS** AF = atrial fibrillation; APD = atrial premature depolarization; AT = atrial tachyarrhythmia; AVNRT = atrioventricular nodal reentrant tachycardia; CS = coronary sinus; ECG = electrocardiogram; ICE = intracardiac echocardiography; LSPAF = long-standing persistent atrial fibrillation; PAF = paroxysmal atrial fibrillation; PerAF = persistent atrial fibrillation; PV = pulmonary vein

(Heart Rhythm 2016;13:374–382) © 2016 Heart Rhythm Society. All rights reserved.



# PV tetikleyicilerin sıklığı



# Primer persistan AF

1289

## Primary Persistent Atrial Fibrillation: A Distinct Arrhythmia Subentity of an Ablation Population

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**Primary Persistent AF.** *Introduction:* Persistent atrial fibrillation (persAF) can occur either as a sustained arrhythmia that has progressed from initially paroxysmal AF or as primary persAF without a history of any spontaneously terminated episode. There is a paucity of data differentiating between the 2 different persAF entities. Thus, we prospectively evaluated baseline characteristics, electrophysiological features, and ablation outcome in these 2 patient cohorts.

*Methods and results:* A total number of 154 consecutive persAF patients ( $63 \pm 10$  years,  $f = 42$ , long-standing persAF = 60) were characterized in terms of having primary persAF (P-persAF group) or persAF that secondarily progressed from paroxysmal AF (S-persAF group). All patients underwent de novo catheter ablation using the stepwise approach. PersAF entities were characterized by detailed patient history, sequential Holter monitoring, and reports of documented modes of AF conversion, respectively. The P-persAF group had a higher number of young patients ( $<50$  years), a shorter AF history, and a higher number of congestive heart failure. The HATCH score did not differ between the groups. Procedural AF termination rate was significantly higher in S-persAF than in P-persAF patients ( $n = 55$  [81%] vs.  $n = 58$  [68%],  $P = 0.043$ ). At 1-year follow-up, the arrhythmia-free survival after a single procedure was significantly lower in patients with P-persAF (26% vs. 43%,  $P = 0.016$ ). Categorization to P-persAF was the strongest independent predictor of arrhythmia recurrence.

*Conclusions:* P-persAF seems to be a specific arrhythmia entity that is associated with a lower AF-termination rate and a worse outcome after catheter ablation as compared to S-persAF. (*J Cardiovasc Electrophysiol*, Vol. 26, pp. 1289-1294, December 2015)

*atrial fibrillation, catheter ablation, left atrium, paroxysmal atrial fibrillation, persistent atrial fibrillation*

# Primer persistan AF

- Sol ventrikül yapısında ve fonksiyonlarında daha ciddi bozulmaya sahip
- AF-CL aynı ancak, ablasyon sırasında AF sonlanma oranı daha düşük
- Tek bir ablasyon sonrası aritmisiz yaşam oranı daha düşük.
- Bu gruptaki genç hastalarda kateter ablasyonun başarısı daha düşük.

# Human atrial fibrillation substrate: towards a specific fibrotic atrial cardiomyopathy

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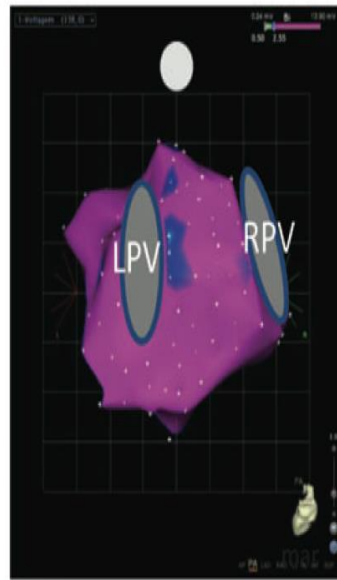
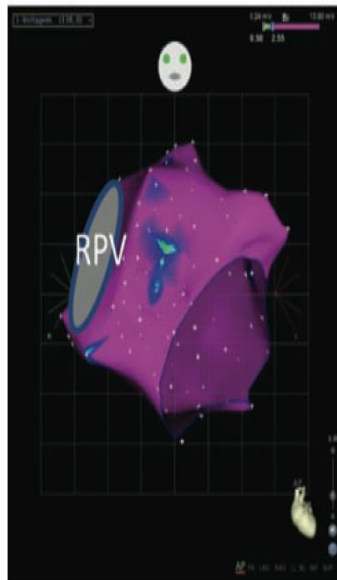
Received 11 March 2013; revised 11 April 2013; accepted 15 May 2013; online publish-ahead-of-print 11 June 2013

The atrial structure/substrate of patients with atrial fibrillation (AF) and clinically similar characteristics can present very differently, and also the 'phenotype' (i.e. paroxysmal, persistent, and long standing persistent) of the arrhythmia cannot comprehensively explain these differences. It was unclear why some patients stay in paroxysmal AF for decades, whereas other patients with the same characteristics progress to persistent AF within a few months. In this review, evidence is described that AF patients without apparent structural heart disease have a chronic fibrotic bi-atrial substrate. There is also evidence from intraoperatively obtained specimen analysis, post-mortem autopsy findings, electroanatomic mapping studies, and delayed enhancement-MRI investigations that a higher mean value of fibrosis is detected in patients with persistent vs. paroxysmal AF but that the variability in the extend of fibrosis is always very high with part of paroxysmal AF patients having massive fibrosis and part of persistent AF patients showing mild fibrosis. In addition, patients undergoing ablation very early after the first AF episodes show already significant fibrosis. These data do not support a causal relationship that AF (significantly) produces fibrosis in the sense of 'AF begets AF' instead of being a consequence of the fibrotic process. In patients with mitral stenosis, evidence for reverse atrial remodelling after commissurotomy was reported, however, in patients with 'lone' AF, the atrial substrate progressed after successful AF elimination indicating towards the independent/progressive disease process of an underlying structural atrial disease called fibrotic atrial cardiomyopathy. Other 'conventional wisdoms' also need to be re-considered including the aetiological role of age and arterial hypertension for human structural atrial remodelling.

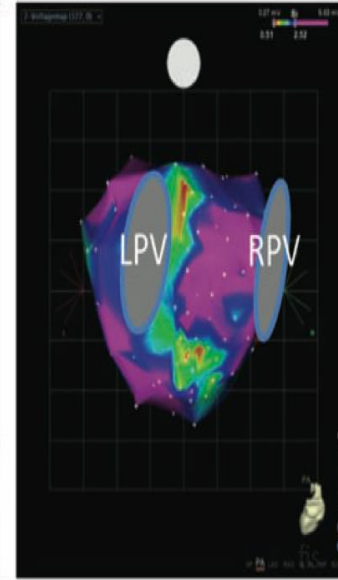
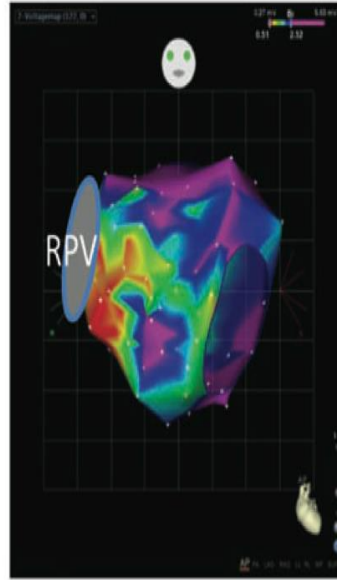
## **Keywords**

Atrial fibrillation • Fibrosis • Cardiomyopathy • Substrate • Pathophysiology

- A
- Patient with „focal AF“/no atrial fibrosis
  - Age, 47 years
  - No structural heart disease
  - Paroxysmal AF for 12 years  
(in the last 2 years almost daily episodes)
  - AF episode length minutes to maximal 2 h



- B
- Patient with moderate atrial fibrosis
  - Age, 49 years
  - No structural heart disease
  - Paroxysmal AF for only 7 months  
(estimated overall 10 – 12 AF episodes)
  - AF episode length directly 24 – 36 h



# Sonuç olarak;

- AF'nun paroksizmal, persistan ve uzamış persistan olarak sınıflaması altta yatan atriyumların substrat karakteristiğini ve patofizyolojik mekanizmaları tam olarak yansıtmamaktadır.
- AF'nun yapısal kalp hastalıklarına sekonder geliştiği hastalara ilaveten, AF'nun atriyumların primer fibrotik hastalığına bağlı geliştiği hastalarda vardır.
- Persistan AF hastalarının bir kısmında temel patofizyolojik mekanizma tetikleyiciler iken, hastaların önemli bir kısmında ise AF'nin devamından elektriksel ve yapısal olarak yeniden şekillenmiş olan atriyumlar sorumludur.

- Sabrınız için teşekkürler.....