Atriyal Fibrozis ve Klinik Yansıması

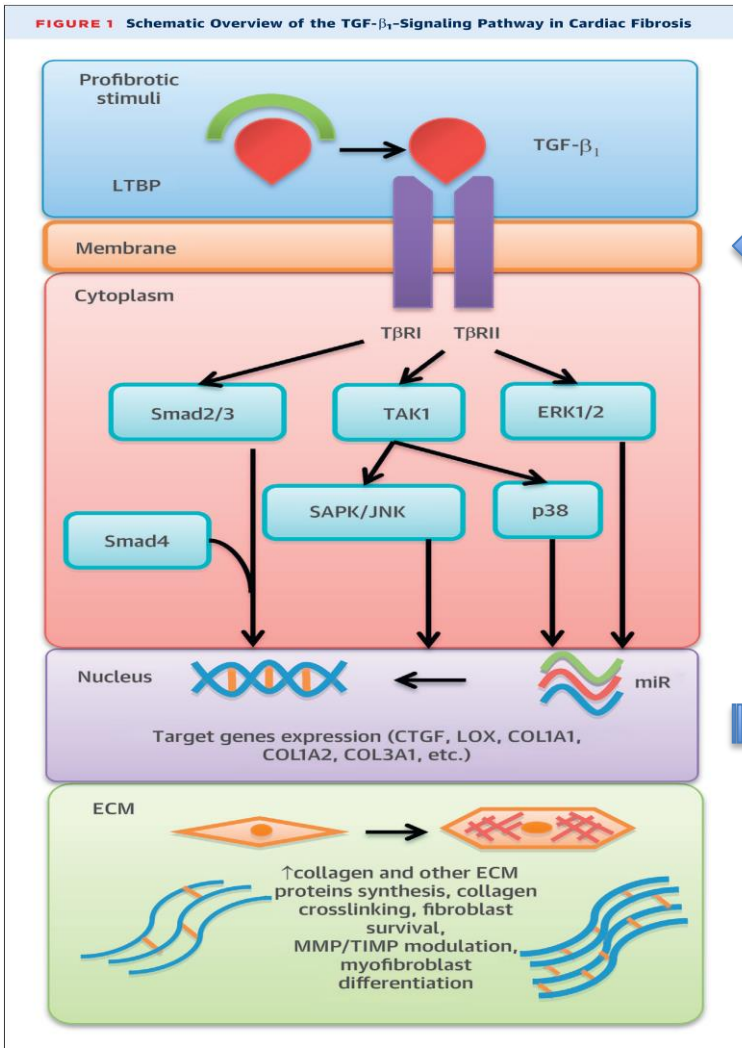
Mehmet Kanadaşı

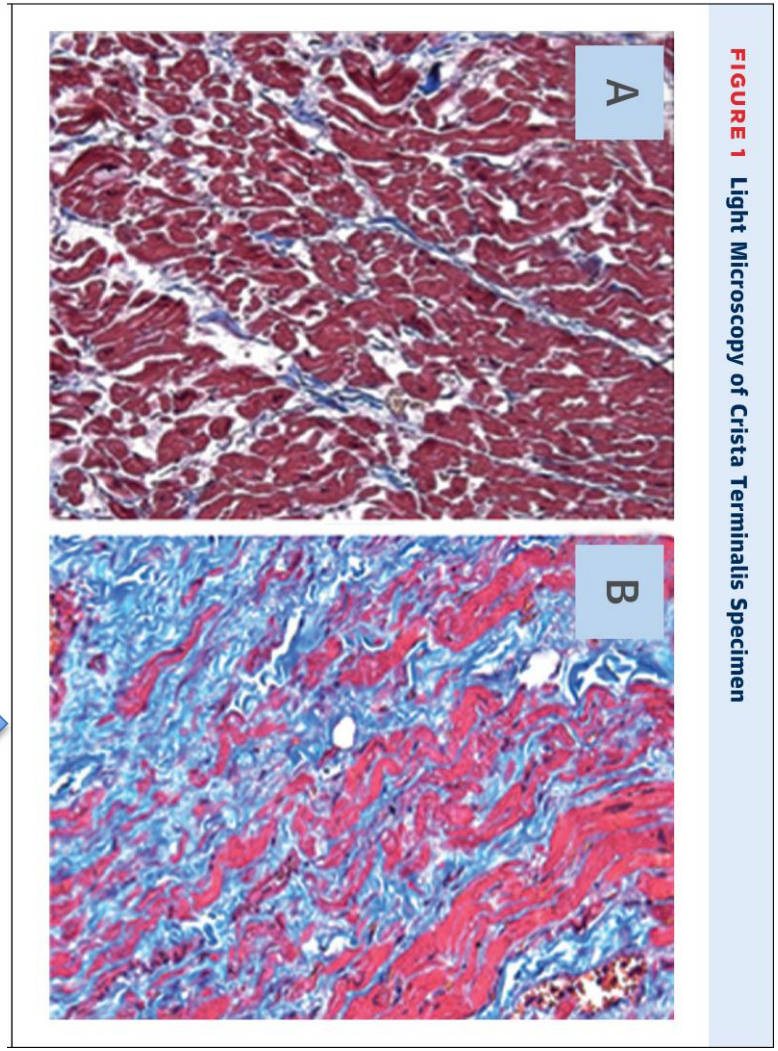
Çukurova Üniversitesi Tıp Fakültesi

Kardiyoloji

5. AF Zirvesi, 12 Şubat 2016, Antalya

Atriyal fibrozis ?

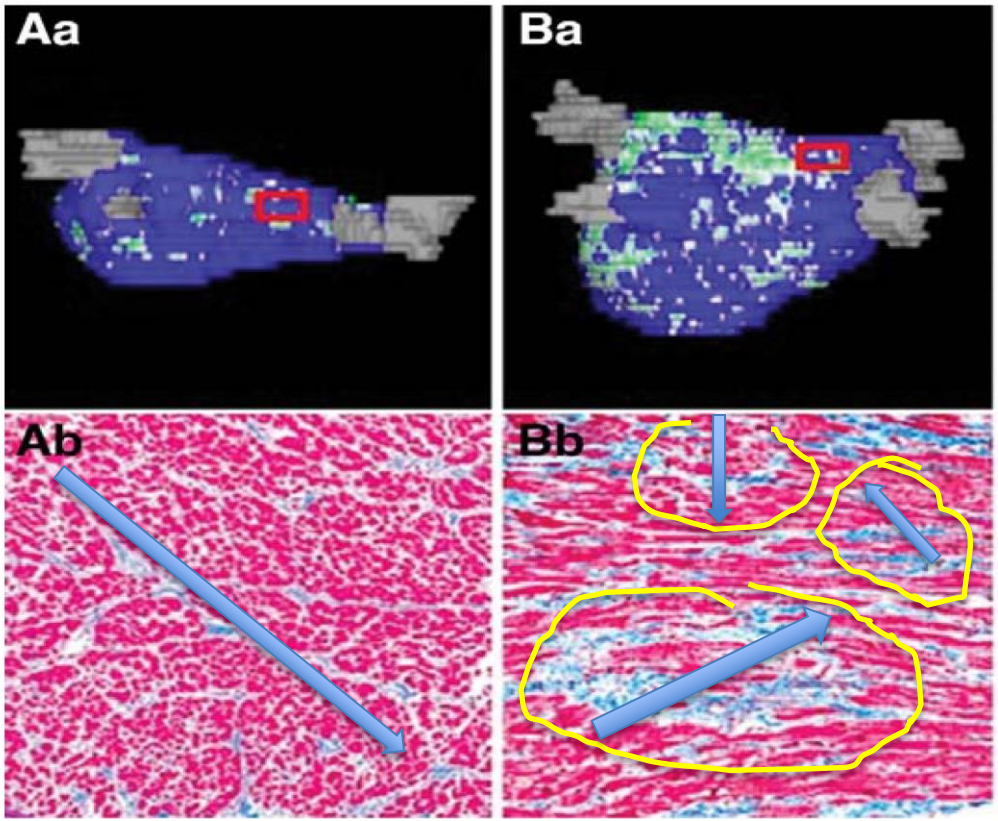




KY
Kapak hast.
HT
KAH
Persistan AF

Fibrozis ve impuls iletimi

Normal Atriyum **Fibrozis içeren atriyum**

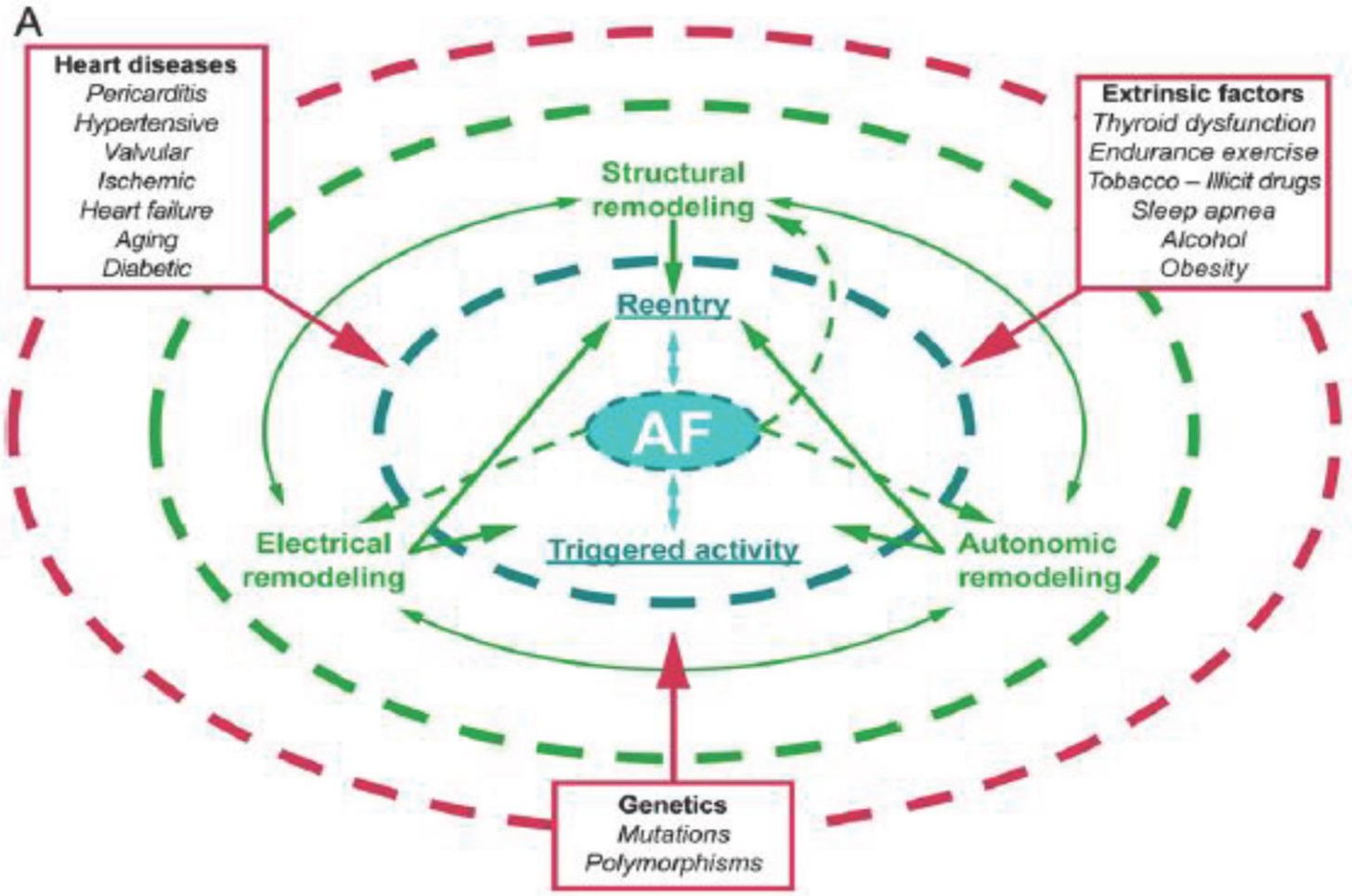


Hızlı ve İzotopik iletim **Yavaş ve anizotopik iletim**

(*Circ Arrhythm Electrophysiol*. 2014;7:23-30.)

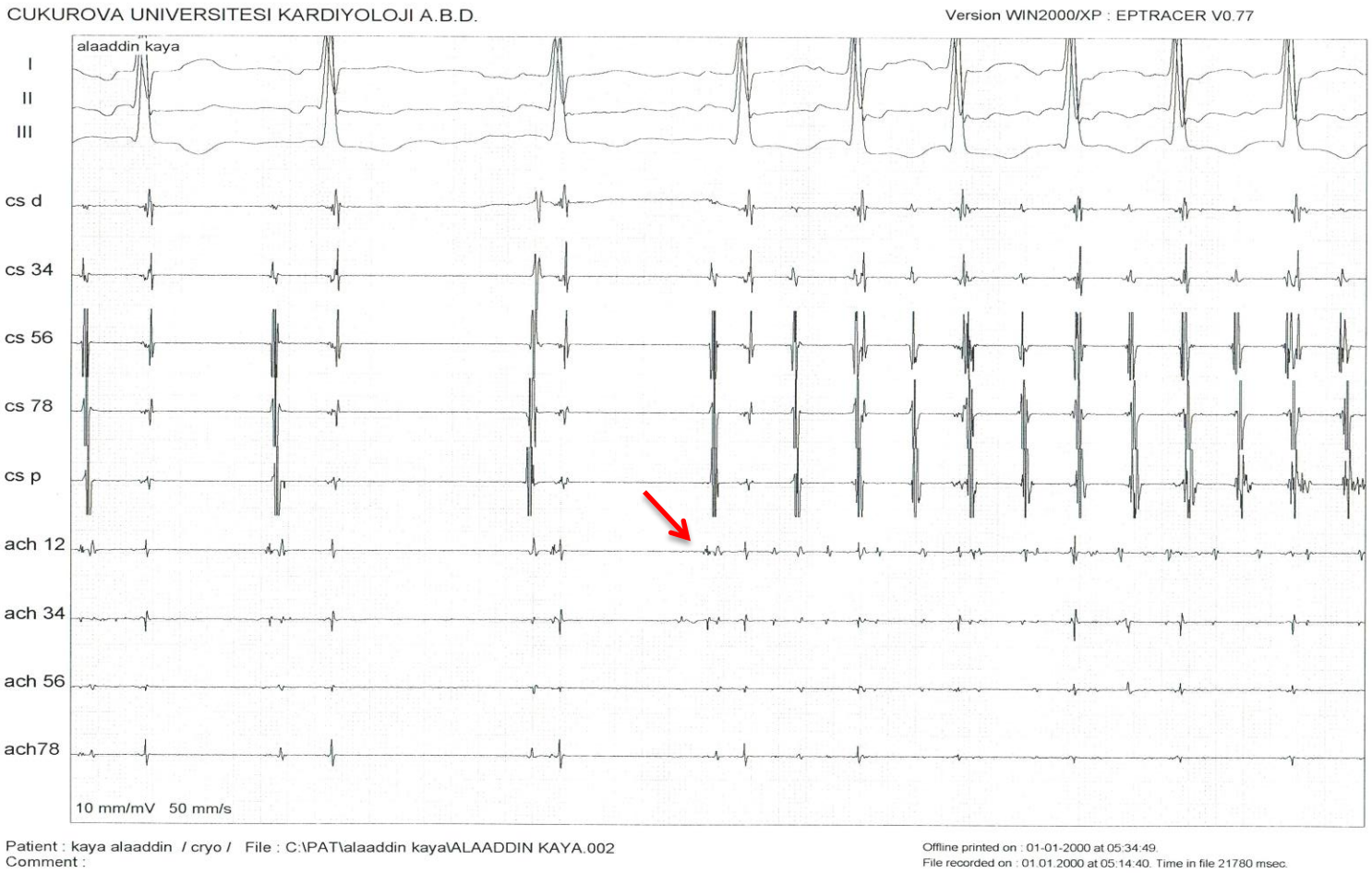
Y. Xu et al./Medical Hypotheses 80 (2013) 53–56

AF mekanizması

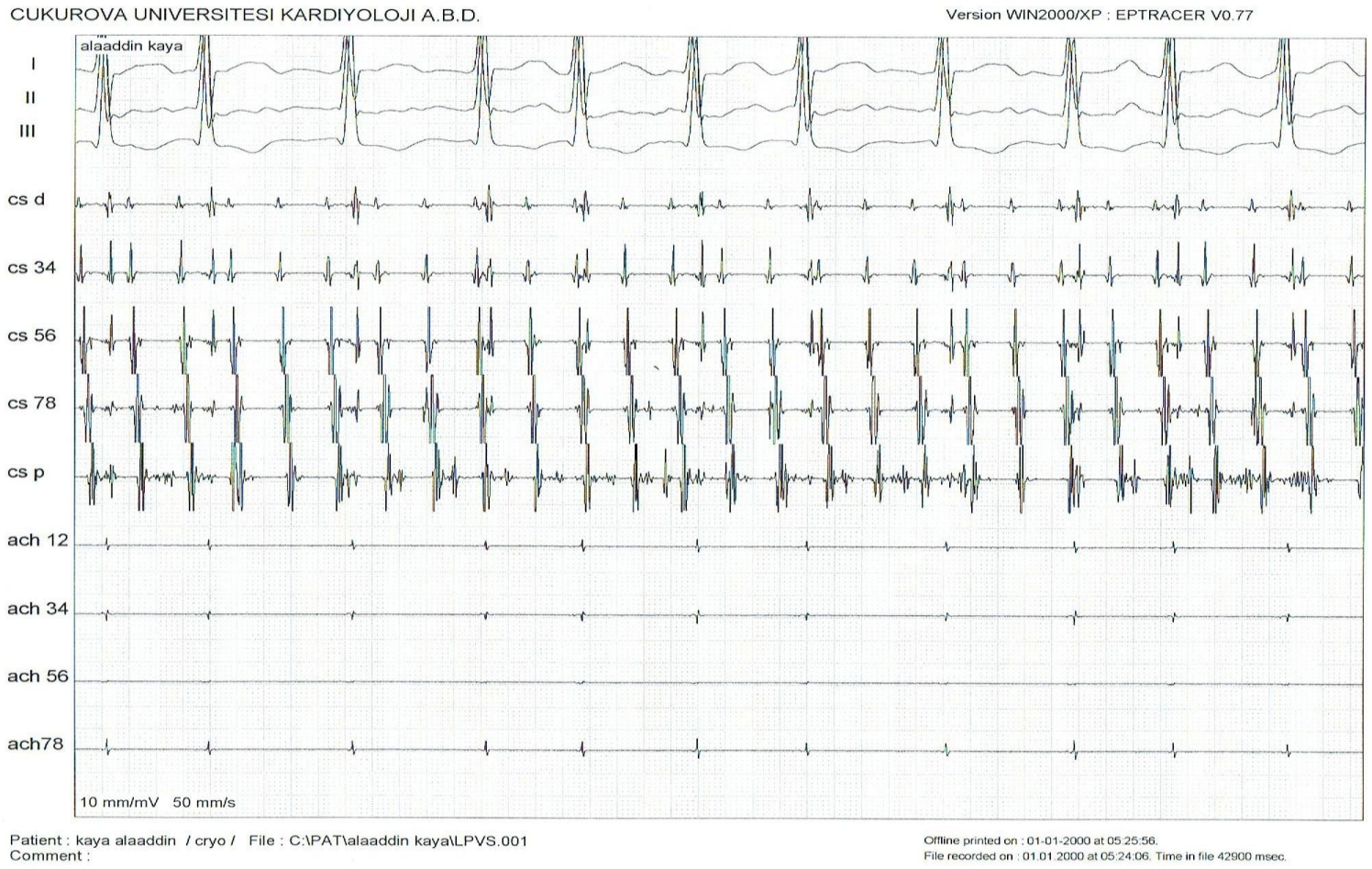


Camm, J; Am Heart J 2012

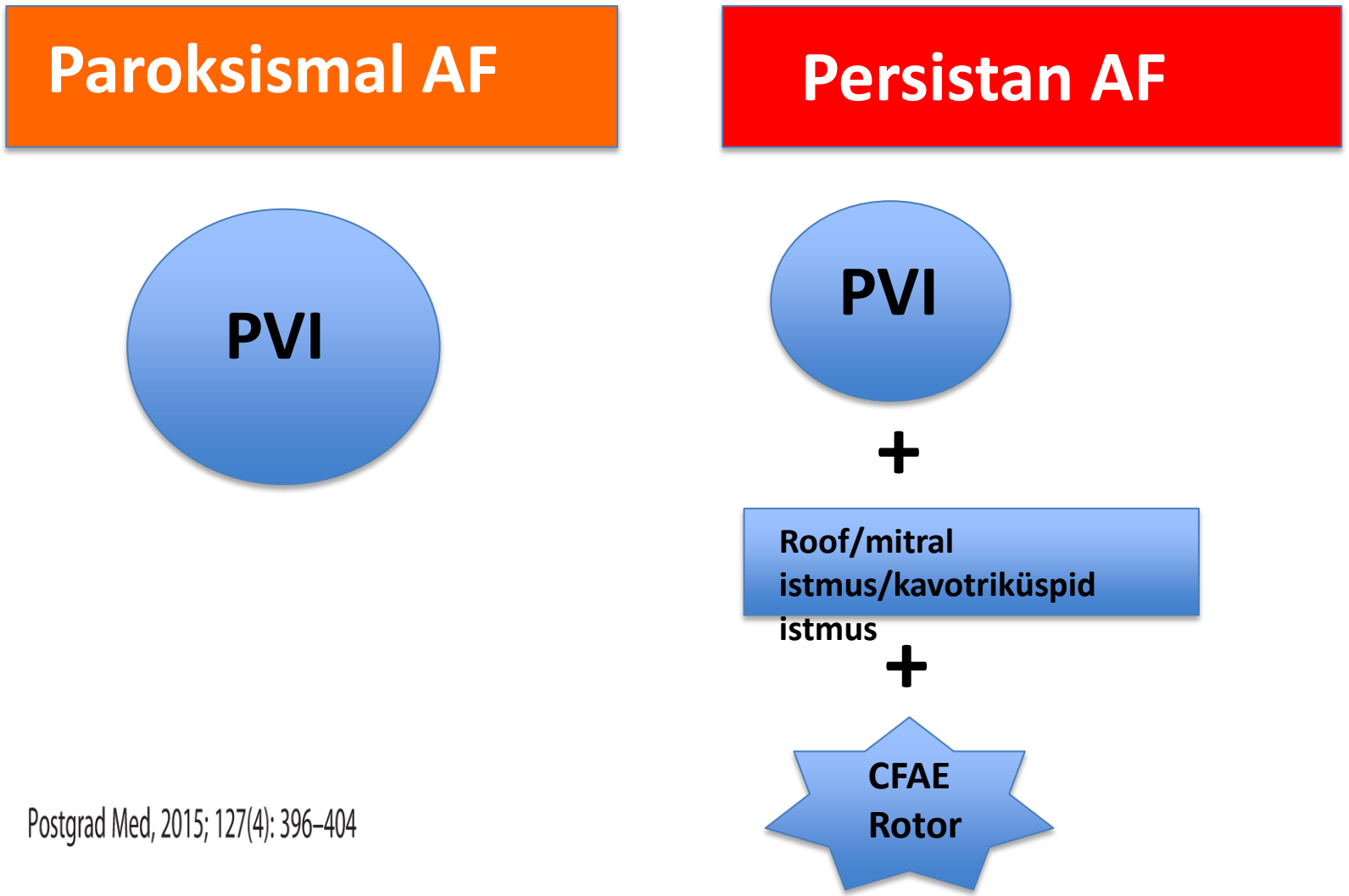
Tetikçi: Sol üst pulmoner ven



Tetikleyici yok ama AF devam ediyor



AF’de ablasyon önerileri



Postgrad Med, 2015; 127(4): 396–404

AF'de işlem sırasındaki ablasyon başarısı uzun dönem sonuçları desteklemiyor!

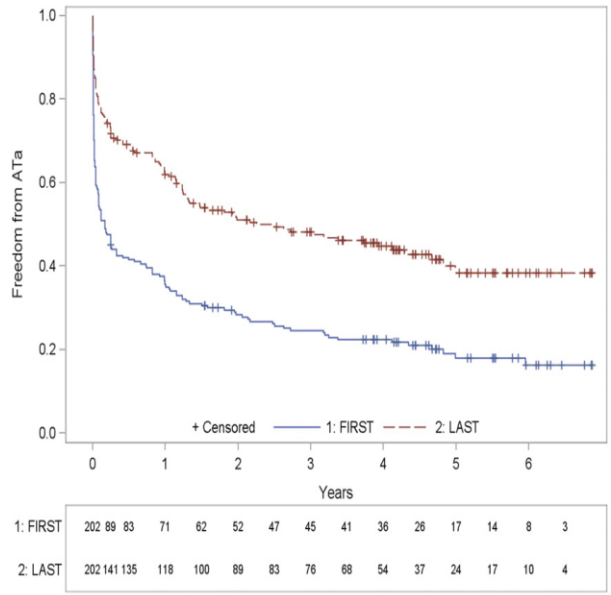
Heart Rhythm Disorders

Catheter Ablation of Long-Standing Persistent Atrial Fibrillation

5-Year Outcomes of the Hamburg Sequential Ablation Strategy

Roland Richard Tilz, MD, Andreas Rillig, MD, Anna-Maria Thum, Anita Arya, MD, Peter Wohlmuth, Andreas Metzner, MD, Shibu Mathew, MD, Yasuhiro Yoshiga, MD, Erik Wissner, MD, Karl-Heinz Kuck, MD, Feifan Ouyang, MD

Hamburg, Germany



%45

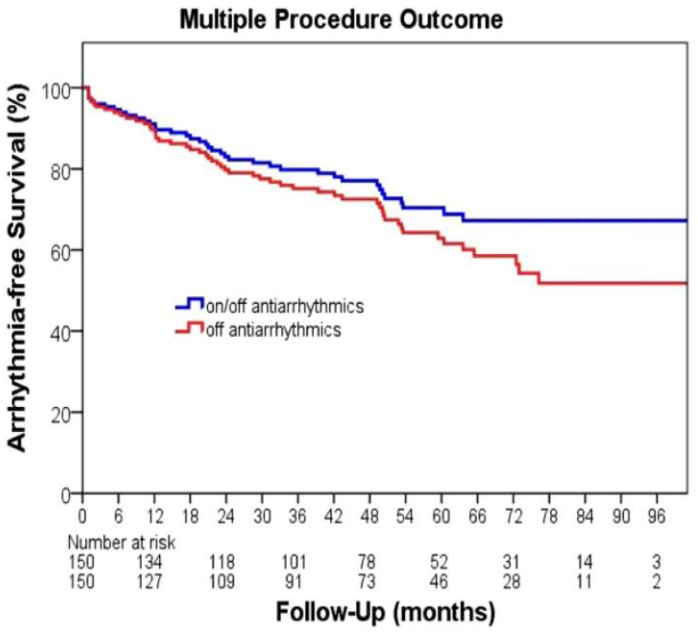
%20

Figure 3 Single and Multiple Procedure Outcomes

Kaplan-Meier event-free survival curve after the first procedure **(blue line)** and after the last procedure **(red line)**. Plus sign **(+)** indicates censored. **Numbers at bottom** indicate patients at risk. ATa = atrial tachyarrhythmia.

Five-Year Outcome of Catheter Ablation of Persistent Atrial Fibrillation Using Termination of Atrial Fibrillation as a Procedural Endpoint

Daniel Scherr, MD; Paul Khairy, MD, PhD; Shinsuke Miyazaki, MD; Valerie Aurillac-Lavignolle, BSc; Patrizio Pascale, MD; Stephen B. Wilton, MD; Khaled Ramoul, MD; Yuki Komatsu, MD; Laurent Roten, MD; Amir Jadidi, MD; Nick Linton, MD, PhD; Michala Pedersen, MD; Matthew Daly, MD; Mark O'Neill, MD; Sebastien Knecht, MD, PhD; Rukshen Weerasooriya, MD; Thomas Rostock, MD; Martin Manninger, MD; Hubert Cochet, MD; Ashok J. Shah, MD; Sunthareth Yeim, MD; Arnaud Denis, MD; Nicolas Derval, MD; Meleze Hocini, MD; Frederic Sacher, MD; Michel Haissaguerre, MD; Pierre Jais, MD

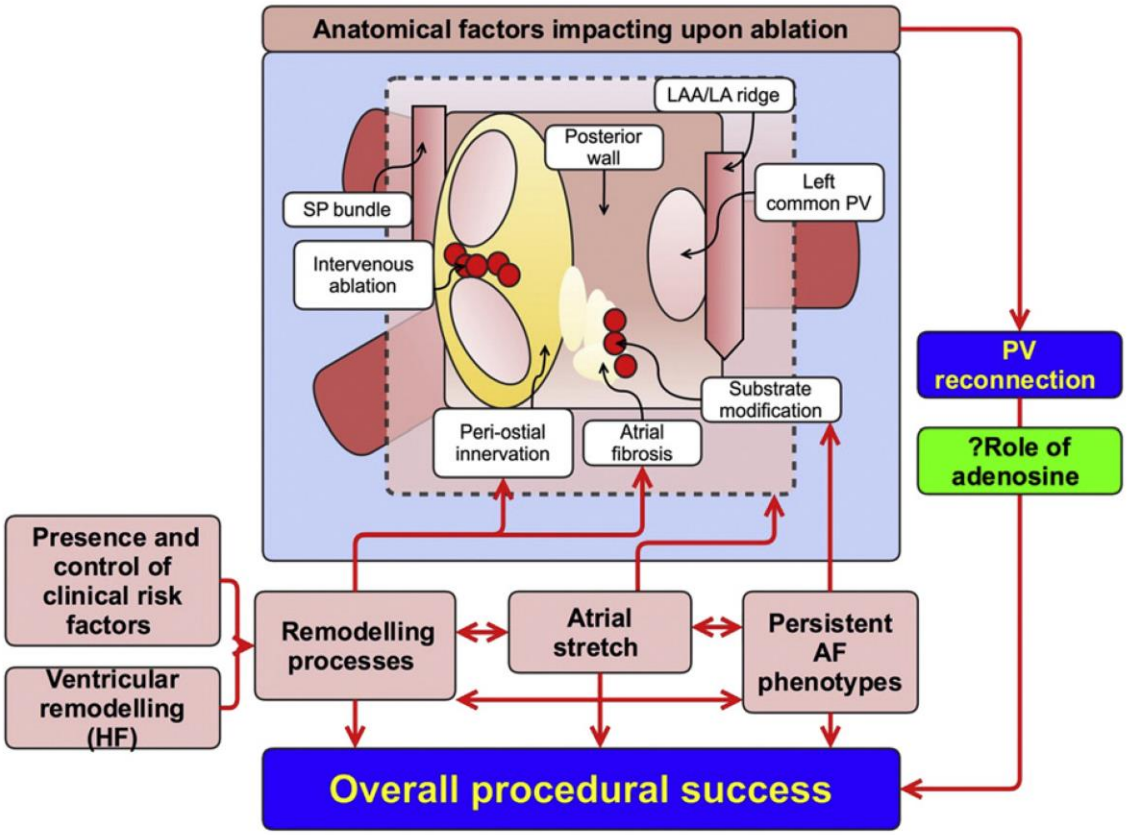


%74

%65

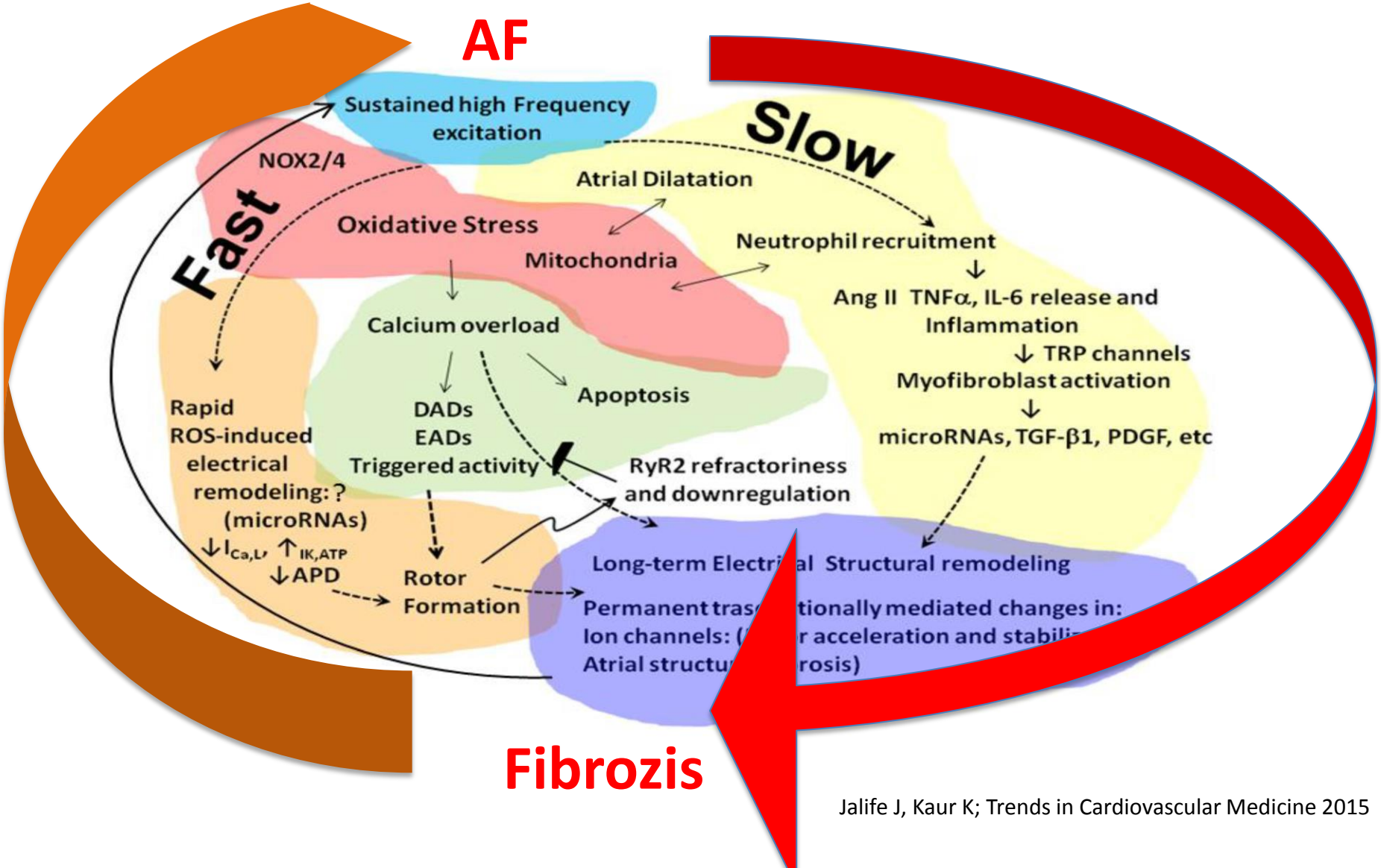
Circ Arrhythm Electrophysiol. **2015;8:18-24.**

Af ablasyonu sonrası nüksün sebepleri



PROGRESS IN CARDIOVASCULAR DISEASES 58 (2015) 152–167

AF fibrozisi, fibrozis AF'yi besler



Jalife J, Kaur K; Trends in Cardiovascular Medicine 2015

Atriyal fibrozisi hedefleyen klinik yaklaşımlar

- Atriyal fibrozisin gösterilmesi
  - Biyobelirteçler
  - Görüntüleme yöntemleri
    - Late Gadolinum Enhancement Magnetic Resonance Imaging (LGE-MRI)
    - Electro-Anatomic Voltage Mapping Imaging (EAVMI)
- Atriyal fibrozisi hedefleyen tedavi yaklaşımları
  - LGE-MRI kılavuzlu ablasyon yaklaşımı
  - EAVMI ile substrat ablasyonu (Box Isolation of Fibrosis Area –BIFA)
  - Antifibrotik tedavi stratejileri

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Novel fibro-inflammation markers in assessing left atrial remodeling in non-valvular atrial fibrillation

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Source of support: The abstract of this manuscript has been accepted and presented as an oral presentation in The 29th National Cardiology Congress, October 26-29/2013, Antalya, Turkey

Background: Structural remodeling is associated with the fibroinflammatory process in the atrial extracellular matrix. In the present study we aimed to investigate whether serum levels of new circulating remodeling markers differ in patients with atrial fibrillation (AF) compared to patients with sinus rhythm.

Material/Methods: The study population included 52 patients diagnosed with non-valvular AF and 33 age-matched patients with sinus rhythm. Serum levels of Galectin-3, matrix metalloproteinase-9 (MMP-9), lipocalin-2 (Lcn2/NGAL), N-terminal propeptide of type III procollagen (PIIINP), Hs-Crp, and neutrophil-to-lymphocyte ratio (NLR) were measured. The left atrial volume (LAV) was calculated by echocardiographic method and LAV index was calculated.

Results: Galectin-3, MMP-9, and PIIINP levels were significantly higher in AF patients except NGAL levels (1166 pg/ml (1126–1204) and 1204 pg/ml (1166–1362) p=0.001, 104 (81–179) pg/ml and 404 (162–564) pg/ml p<0.0001, and 1101 (500–1960) pg/ml and 6710 (2370–9950) pg/ml p<0.0001, respectively). The NLR and Hs-CRP levels were also higher in AF (2.1±1.0 and 2.7±1.1 p=0.02 and 4.2±1.9 mg/L and 6.0±4.7 mg/L p=0.04, respectively). In correlation analyses, NLR showed a strongly significant correlation with LAVi, but Hs-CRP did not (p=0.007 r=0.247, Pearson test and p=0.808 r=0.025, Pearson test, respectively). Moreover, Galectin-3, MMP-9, and PIIINP had a strong positive correlation with LAVi (p=0.021 r=640, Spearman test and p=0.004 r=0.319 Pearson test, and p=0.004 r=0.325 Pearson test, respectively).

Conclusions: Novel fibrosis and inflammation markers in AF are correlated with atrial remodeling. Several unexplained mechanisms of atrial remodeling remain, but the present study has taken the first step in elucidating the mechanisms involving fibrosis and inflammation markers.

Galectin 3 and incident atrial fibrillation in the community

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Background Galectin 3 (Gal-3) is a potential mediator of cardiac fibrosis, and Gal-3 concentrations predict incident heart failure. The same mechanisms that lead to cardiac fibrosis in heart failure may influence development of atrial fibrosis and atrial fibrillation (AF). We examined the association of Gal-3 and incident AF in the community.

Methods Plasma Gal-3 concentrations were measured in 3,306 participants of the Framingham Offspring cohort who attended the sixth examination cycle (1995-1998, mean age 58 years, 54% women). Cox proportional hazards regression models were used to assess the association of baseline Gal-3 concentrations and incident AF.

Results Over a median follow-up period of 10 years, 250 participants developed incident AF. Crude incidence rates of AF by increasing sex-specific Gal-3 quartiles were 3.7%, 5.9%, 9.1%, and 11.5% (log-rank test $P < .0001$). In age- and sex-adjusted analyses, each 1-SD increase in $\log_e$-Gal-3 was associated with a 19% increased hazard of incident AF (hazard ratio 1.19, 95% CI 1.05-1.36, $P = .009$). This association was not significant after adjustment for traditional clinical AF risk factors (hazard ratio 1.12, 95% CI 0.98-1.28, $P = .10$).

Conclusion Higher circulating Gal-3 concentrations were associated with increased risk of developing AF over the subsequent 10 years in age- and sex-adjusted analyses but not after accounting for other traditional clinical AF risk factors. Our results do not support a role for Gal-3 in AF risk prediction. Further studies are needed to evaluate whether Gal-3 plays a role in the development of AF substrate similar to HF. (Am Heart J 2014;167:729-734.e1.)

Electrophysiology

Circulating fibrosis biomarkers and risk of atrial fibrillation: The Cardiovascular Health Study (CHS)

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Background Cardiac fibrosis is thought to play a central role in the pathogenesis of atrial fibrillation (AF). Retrospective studies have suggested that circulating fibrosis biomarkers are associated with AF, but prospective studies are limited.

Methods We measured circulating levels of 2 fibrosis biomarkers, procollagen type III, N-terminal propeptide (PIIINP) and transforming growth factor β1 among participants of the CHS, a population-based study of older Americans. We used Cox proportional hazards and competing risks models to examine adjusted risk of incident AF over a median follow-up of 8.8 years.

Results Levels of PIIINP were assessed in 2,935 participants, of whom 767 developed AF. Compared with the median PIIINP level (4.45 μg/L), adjusted hazard ratios (95% CIs) were 0.85 (0.72-1.00) at the 10th percentile, 0.93 (0.88-0.99) at the 25th percentile, 1.04 (0.95-1.04) at the 75th percentile, and 1.07 (0.90-1.26) at the 90th. Transforming growth factor β1 levels, assessed in 1,538 participants with 408 cases of incident AF, were not associated with AF risk.

Conclusion In older adults, PIIINP levels were associated with risk of incident AF in a complex manner, with an association that appeared to be positive up to median levels but with little relationship beyond that. Further studies are required to confirm and possibly delineate the mechanism for this relationship. (Am Heart J 2014;167:723-728.e2.)

Biyobelirteçlerin klinik rutinde kullanımı ?

TABLE 1 Studies on Mechanisms of Atrial Fibrosis in AF in Humans

First Author, Year (Ref. #)	n (AF/SR)	Sample Tested	LVEF, % (AF/Controls)	Results (AF vs. Controls)	Observed Associations
Adam et al., 2010 (105)	5/5	LAA	61 ± 6/59 ± 6	↑collagen, CTGF, NADPHox, Rac1, N-cadherin, connexin 43, Ang II	NA
Adam et al., 2012 (106)	5/5	LAA	61 ± 6/59 ± 6	↑miR-21	miR-21 with collagen, CTGF, Rac1, LOX, Ang II
Cao et al., 2013 (107)	48/24	RAA	63 ± 5 (paroxysmal), 64 ± 5 (persistent)/ 64 ± 3	↑OPG, RANKL, RANK, RANKL/OPG ratio	(In AF) OPG, RANKL, RANK, RANKL/OPG ratio with collagen types I and III
Dawson et al., 2013 (108)	17/30* 17/19	Plasma RAA	60 ± 2/69 ± 1	↓miR-29b ↓miR-29b in chronic AF	NA
Gramley et al., 2007 (109)	42/104	RAA	48 ± 12	↑collagen content, activity ↔MMP2, MMP9 (mRNA and protein levels), ↓PAI, TIMP1 and 2 (mRNA) with ↑ duration of AF	NA
Gramley et al., 2010 (68)	42/116	RAA	50 ± 11/47 ± 12	↑collagen content, HIF-1α, HIF-2α, VEGF, KDR, pKDR, and microvessel density	NA
Gramley et al., 2010 (110)	61/102	RAA	48 ± 11	↑collagen content, early ↑ and later ↓ responsiveness to TGF-β1 with ↑ duration of AF: initially ↑TGF-β1 (mRNA and protein), TβRII, phSmad2, Smad4 (protein) followed by a ↓TβRI phSmad2 (protein) and ↑Smad7 (protein)	NA
Kallergis et al., 2008 (111)	70/20	Serum	60 ± 4 (paroxysmal), 56 ± 9 (persistent)/ 60 ± 5	↑CITP, CICP, TIMP1	NA
Ko et al., 2011 (112)	10/10	RAA	53 ± 15/44 ± 17	↑collagen content, CTGF (protein and mRNA)	NA
Li et al., 2013 (113)	28/12	RA	NA	↑collagen content, TGF-β1, Smad3, and CTGF	TGF-β_1, CTGF (mRNA and protein) with collagen content, TGF-β_1, CTGF
Mayyas et al., 2010 (114)	32/21	LAA	51 ± 2/53 ± 3	↑ET-1 ↔ET_AR or ET_BR	ET-1 with LA size, AF persistence
Nishi et al., 2013 (115)	16/13	RA	70 ± 8 (unsuccessful Maze), 53 ± 15 (successful Maze)/ 62.0 ± 9	↑miR-21, miR-23b, miR-199b, miR-208b	miR-21 with collagen content
Okumura et al., 2011 (116)	50/0	Serum	NA	↓hsCRP, IL-6, ANP, BNP ↑MMP2, TIMP2, CITP during follow-up	MMP2 with AF recurrence
Polyakova et al., 2008 (117)	24/24	RA, RAA	46 ± 10/46 ± 13	↑collagen content, MMP2, MMP9, TIMP1, TIMP2, RECK, TGF-β1, Smad2 and phSmad2	NA
Qu et al., 2009 (118)	20/20	RA	51 ± 15/63 ± 14.63	↑collagen content, TNFα, IL-6 and NFκB activity	NFκB activity with TNFα, IL-6, and collagen content
Rahmutula et al., 2013 (59)	17/NA	RA	NA	↑TGβ1 and TGF-β_1 signaling-related proteins (e.g., phSmad2, Smad6, Ang II)	NA
Richter et al., 2011 (119)	30/0	Serum	62 ± 2	↑MMP9, TGF-β1, PIIINP after ablation	PIIINP with AF recurrence; MMP9, TGF-β_1 with ablation-induced LA volume reduction; MMP9 with RF energy on ablation
Rudolph et al., 2010 (120)	34/35	Plasma, RAA	49 ± 89/52 ± 9	↑MPO	NA
Swartz et al., 2012 (121)	18/36	LAA, RAA, serum	49 ± 12/51 ± 8	↑collagen content, collagen type I, III, TGF-β_1, Ang II (mRNA) ↑PICP, PIIINP	Collagen content with PICP
Wang et al., 2015 (122)	30/17	LAA	63 ± 7/70 ± 4	↑miR-146b-5p, MMP9, collagen content; ↓TIMP4	miR-146b-5p with TIMP4 and collagen content
Wilhelm et al., 2006 (123)	30/20	RAA	NA	↔collagen content	NA
Wu et al., 2013 (124)	200/0	Plasma	53 ± 10/57 ± 6†	NA	TGF-β_1 with AF recurrence

Biyobelirteçler fibrozisi değil fibrozisin neden olduğu klinik sonuçları işaret etmekte…
Cut off değer yok…

Fibrozisin görüntülenmesi

Late Gadolinum Enhancement-MRI

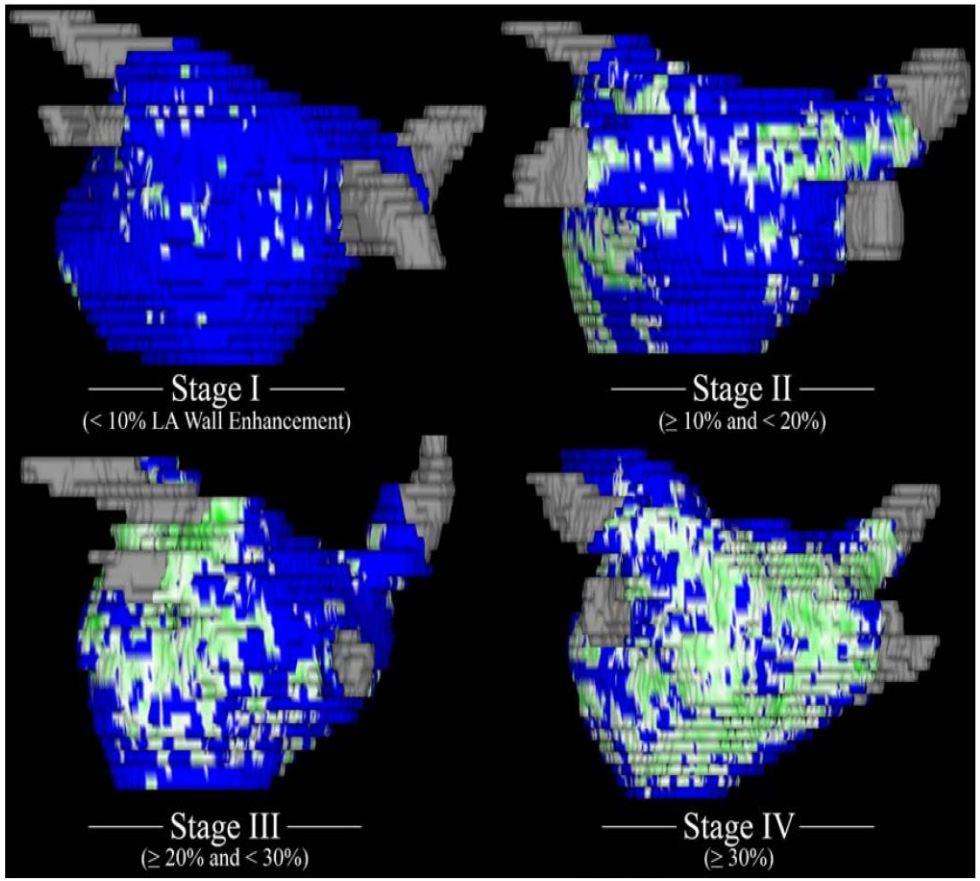


Figure 2. Four stages of left atrial (LA) structural remodeling (SRM) based on 3-dimensional late gadolinium enhancement MRI scans. Representative examples from patients in each stage of LA remodeling in posterior–anterior views (above examples of stages I–IV are 3%, 13%, 26%, and 56%, respectively). Normal LA wall is displayed in blue with SRM changes in green. The pulmonary veins are shown in gray.

(*Circ Arrhythm Electrophysiol*. 2014;7:23-30.)

Atrial Fibrillation Ablation Outcome Is Predicted by Left Atrial Remodeling on MRI

Table 1. Comparison of Baseline Characteristics Across Structural Remodeling Stages in the AF Group

	Stage I (n=133)	Stage II (n=140)	Stage III (n=71)	Stage IV (n=42)	*P* Value
Age, y	63±13	65±11	66±13	67±12	0.17
Women, %	33.8	30.7	42.3	47.6	0.06
Hypertension, %	62.9	61.4	57.8	66.7	0.81
Diabetes mellitus, %	11.4	12.9	21.1	21.4	0.08
Coronary disease, %	13.6	12.5	24.4	14.3	0.10
Congestive heart failure, %	6.1	13.0	12.7	7.1	0.41
LV ejection fraction, %	58±12	59±10	57±12	56±13	0.16
CVA/TIA, %	6.1	7.9	11.3	16.7	0.03
Paroxysmal AF, %	61.7	46.4	49.3	26.2	0.002
Persistent AF, %	38.4	53.6	50.7	73.8	0.002
Previous AAD use (%)	22.6	12.9	18.5	15.0	0.11
Atrial volume/BSA, mL/m^2	48±18	51±18	52±21	64±24	<0.0001
LA fibrosis, %	6.7±2.0	15.2±2.9	23.3±2.8	40.9±10.4	<0.0001

AAD indicates anti-arrhythmic drug; AF, atrial fibrillation; BSA, body surface area; CVA, cerebrovascular accident; LA, left atrial; LV, left ventricular; and TIA, transient ischemic attack.

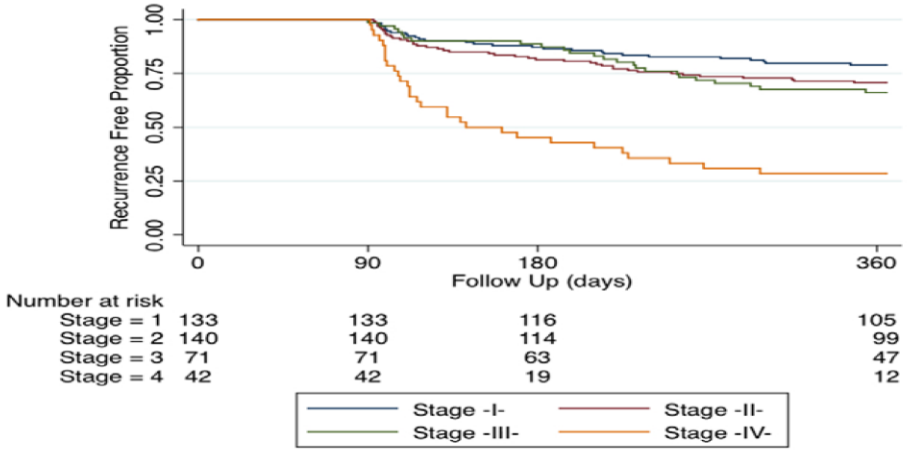


Figure 3. Kaplan–Meier rates of atrial fibrillation (AF) recurrence. Post-AF ablation recurrences according to 4 stages of atrial structural remodeling during 1-year follow-up period.

Table 3. Univariate and Multivariate Predictors of Arrhythmia Recurrence After Catheter Ablation: 1-Year Follow-Up

	Univariate Analysis			Multivariate Analysis		
	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value
Age (per 10-y increase)	1.22	1.05–1.43	0.011	1.12	0.94–1.34	0.192
Women	1.09	0.75–1.57	0.636	0.84	0.56–1.25	0.393
Hypertension	1.61	1.09–2.38	0.016	1.33	0.86–2.04	0.195
Diabetes mellitus	1.80	1.18–2.75	0.006	1.64	1.03–2.61	0.036
Coronary disease	1.19	0.75–1.88	0.465	0.75	0.45–1.24	0.260
Congestive heart failure	1.19	0.68–2.07	0.543	1.17	0.65–2.09	0.607
Persistent AF	1.47	1.08–1.99	0.014	1.09	0.76–1.55	0.648
SRM stage						
Stage I	Referent			Referent		
Stage II	1.47	0.91–2.38	0.116	1.29	0.81–1.82	0.303
Stage III	1.65	0.96–2.86	0.069	1.49	0.92–2.32	0.166
Stage IV	5.47	3.26–9.2	<0.0001	4.89	2.37–6.28	<0.0001
LA volume index (10 mL/m^2)	1.16	1.07–1.26	<0.0001	1.05	0.96–1.17	0.279

AF indicates atrial fibrillation; CI, confidence interval; LA, left atrial; and SRM, structural remodeling.

(*Circ Arrhythm Electrophysiol*. 2014;7:23-30.)

MR kılavuzlu AF tedavisi

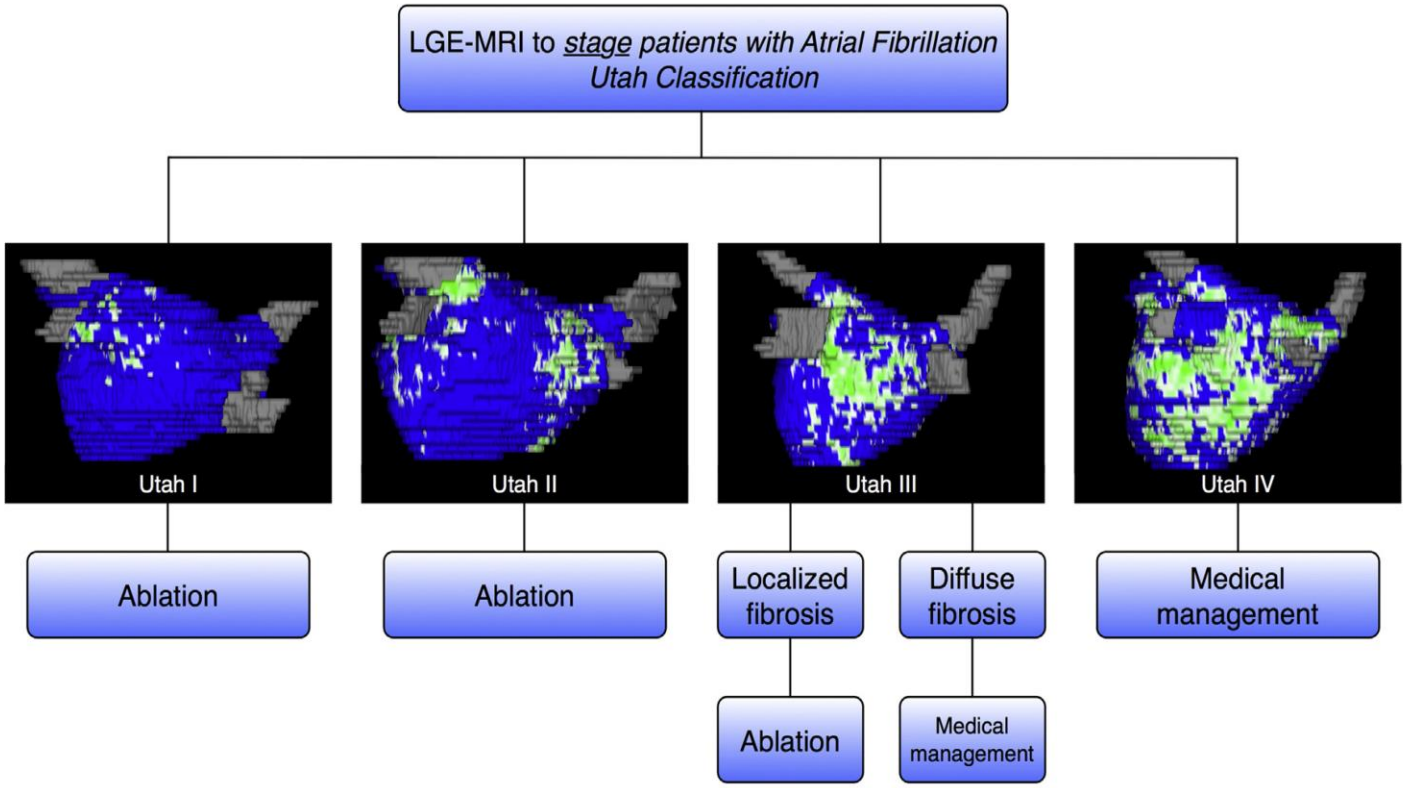


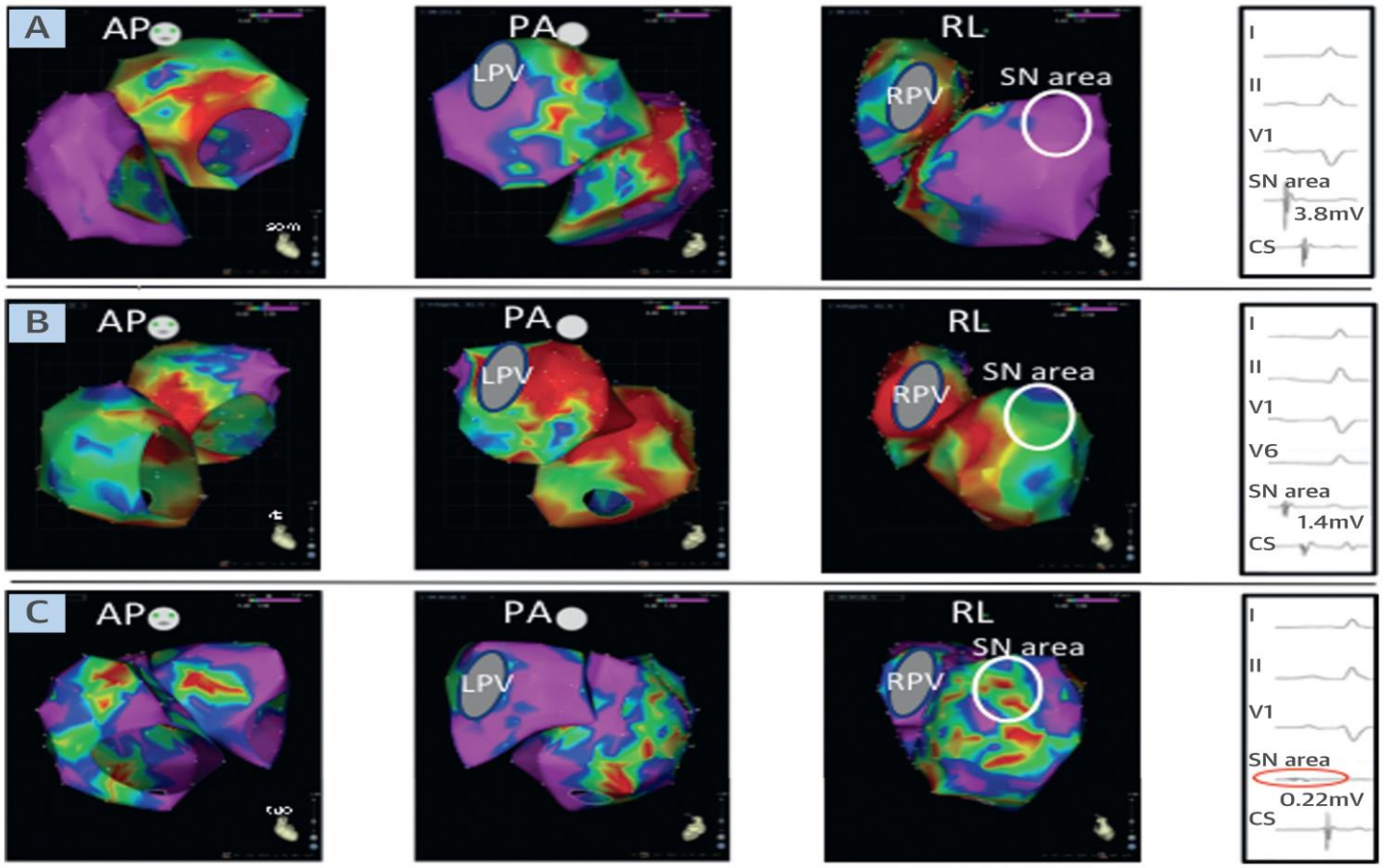
Figure 6. Personalized treatment of atrial fibrillation. LGE-MRI, late gadolinium enhancement magnetic resonance imaging.

Pim G, Marrouche N; Eur Heart J. 2015 Sep 25.

Fibrozisin görüntülenmesi

Elektro-anatomik voltaj mapping

FIGURE 2 Bi-Atrial Voltage Mapping



These 3 patients had atrial fibrillation (AF) and different right and/or left atrial low-voltage distribution. The patients had **(A)** normal voltages in the anatomic region of the sinus node (SN) area and clinically normal sinus rhythm, **(B)** moderately reduced voltages in the SN area and clinically mild sinus bradycardia, and **(C)** significantly reduced voltages (0.22 mV) in the SN area and clinically severe sinus bradycardia. The projections were anterior (AP), posterior (PA), and right lateral (RL). Color coding: **red** for voltages <0.5 mV and **purple** for voltages >1.5 mV. CS = coronary sinus; LPV = left pulmonary veins; RPV = right pulmonary veins.

(J Cardiovasc Electrophysiol, Vol. 27, pp. 22-30, January 2016)

Box Isolation of Fibrotic Areas (BIFA): A Patient-Tailored Substrate Modification Approach for Ablation of Atrial Fibrillation

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ANDREAS RIEGER, M.D., and DOREEN SCHREIBER, M.D.

TABLE 1

Patients Characteristics

	Nonparoxysmal Patients n = 31		P-Value BIFA vs. Solely PVI	Paroxysmal Patients (Nondurable PVI) n = 10
	BIFA n = 18	Solely PVI n = 13		
Men, n (%)	11 (61.1)	13 (100)	0.025	5 (50)
Age (years)	66 ± 10	59 ± 10	0.074	62 ± 11
LVEF (%)	58 ± 8	56 ± 11	0.671	59 ± 12
LA (mm)	45 ± 7	43 ± 3	0.538	42 ± 5
Persistent AF duration (months)	16.92	14.73	0.05	n.a.
median [min–max]	[2–56]	[1–72]		
CHA2DS2-Vasc score	1.3 ± 0.9	0.9 ± 0.9	0.215	2.0 ± 0.9
Heart failure, n (%)	1 (5.6)	2 (15.4)	1.000	1 (10)
Hypertension, n (%)	14 (77.8)	5 (38.5)	0.060	5 (50)
Age >65 years, n (%)	12 (66.7)	5 (38.5)	0.157	5 (50)
Age >75 years, n (%)	3 (16.7)	0 (0)	0.255	1 (10)
Diabetes mellitus, n (%)	1 (5.6)	2 (15.4)	0.588	2 (20)
Stroke, n (%)	2 (11.1)	1 (7.7)	1.000	1 (10)
Vascular disease, n (%)	2 (11.1)	0 (0)	0.457	2 (20)
Obesity, n (%)	5 (27.8)	5 (38.5)	0.701	2 (20)
OSA, n (%)	0 (0)	0 (0)	1.000	1 (10)

LVEF = left ventricular ejection fraction; LA = left atrial diameter; OSA = obstructive sleep apnea.

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Figure 1. Left atrial voltage mapping in four patients with recurrences of paroxysmal atrial fibrillation despite durable pulmonary vein isolation (PVI) showing the variable severity and localization of left atrial fibrosis. Box isolation of the fibrotic areas (BIFA) is done in all cases with connection to the previous PVI lines. Color coding: red for substantially reduced voltages <0.5 mV and purple >1.5 mV. LPV and RPV = left and right pulmonary veins.

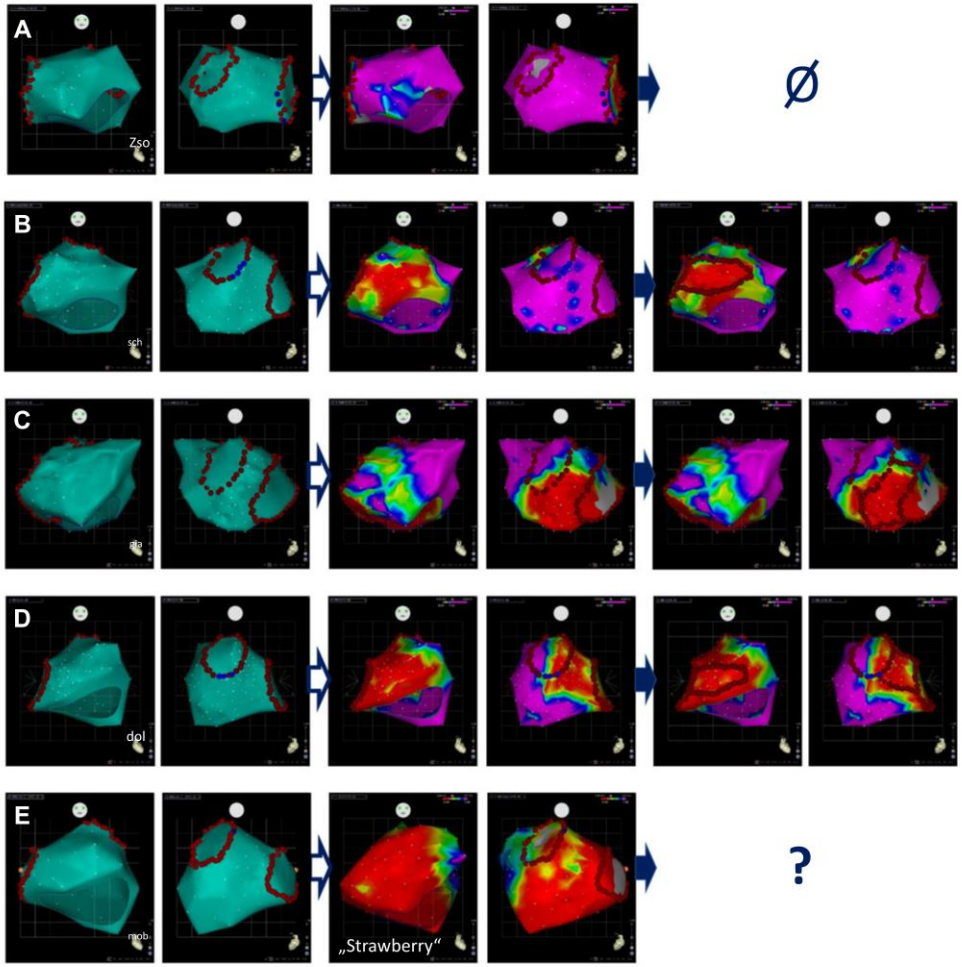

Figure 4. *Individually tailored substrate modification strategy in patients with non-paroxysmal atrial fibrillation (AF). After circumferential pulmonary vein isolation (PVI) during ongoing AF, the patients are electrically cardioverted and electroanatomic voltage mapping is performed during sinus rhythm. A: In patients without substantial low-voltage areas, the procedure is done with PVI. B–D: In patients with areas of low voltage, box isolation of fibrotic areas (BIFA) is performed according to the individual localization of the substrate. E: In patients with massive and diffuse fibrosis, no clear BIFA concept is available and additional ablation procedures are discouraged after failure of PVI. Abbreviations as in Figures 1 and 2.*

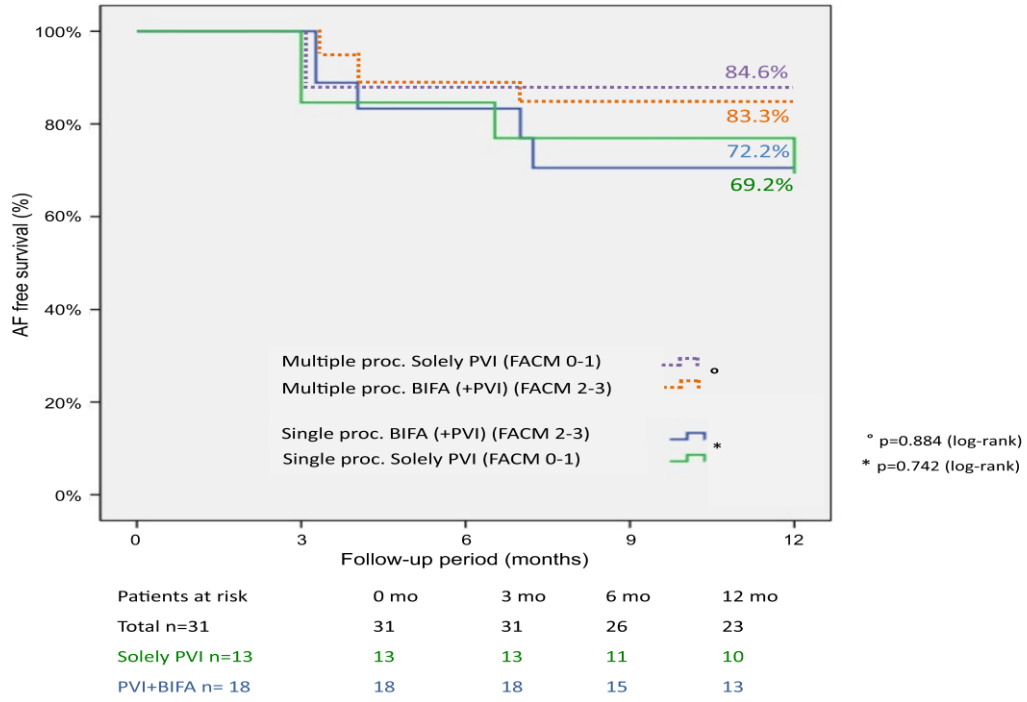

Figure 5. *Kaplan–Meier curves demonstrating 1-year arrhythmia-free survival after catheter ablation of nonparoxysmal atrial fibrillation patients. The blue and orange curves represent the results after BIFA ablation (+PVI) in FACM 2–3 patients showing single and multiple procedure (proc.) success rates. The results of the solely PVI approach in FACM 0–1 patients are shown in green and purple, accordingly. Dashed lines demonstrate multiple procedure result. Other abbreviations as in Figures 1 and 2.*

Results: **First, EAVM during sinus rhythm was done in redo cases of 10 pts with paroxysmal AF despite durable PVI. Confluent low-voltage areas (LVA) were found in all pts and were targeted with circumferential isolation, so-called box isolation of fibrotic areas (BIFA). This strategy led to stable sinus rhythm in 9/10 pts and was transferred prospectively to first procedures of 31 pts with nonparoxysmal AF. In 13 pts (42%), no LVA (<0.5 mV) were identified, and only PVI was performed. In 18 pts (58%), additional BIFA strategies were applied (posterior box in 5, anterior box in 7, posterior plus anterior box in 5, no box in 1 due to diffuse fibrosis). Mean follow-up was 12.5 ± 2.4 months. Single-procedure freedom from AF/atrial tachycardia was achieved in 72.2% of pts and in 83.3% of pts with 1.17 procedures/patient.**

Conclusions: **In approximately 40% of pts with nonparoxysmal AF, no substantial LVA were identified, and PVI alone showed high success rate. In pts with paroxysmal AF despite durable PVI and in approximately 60% of pts with nonparoxysmal AF, individually localized LVA were identified and could be targeted successfully with the BIFA strategy.** *(J Cardiovasc Electrophysiol, Vol. 27, pp. 22-30, January 2016)*

Fibrozisi önleme yaklaşımları (Antifibrotik tedavi)

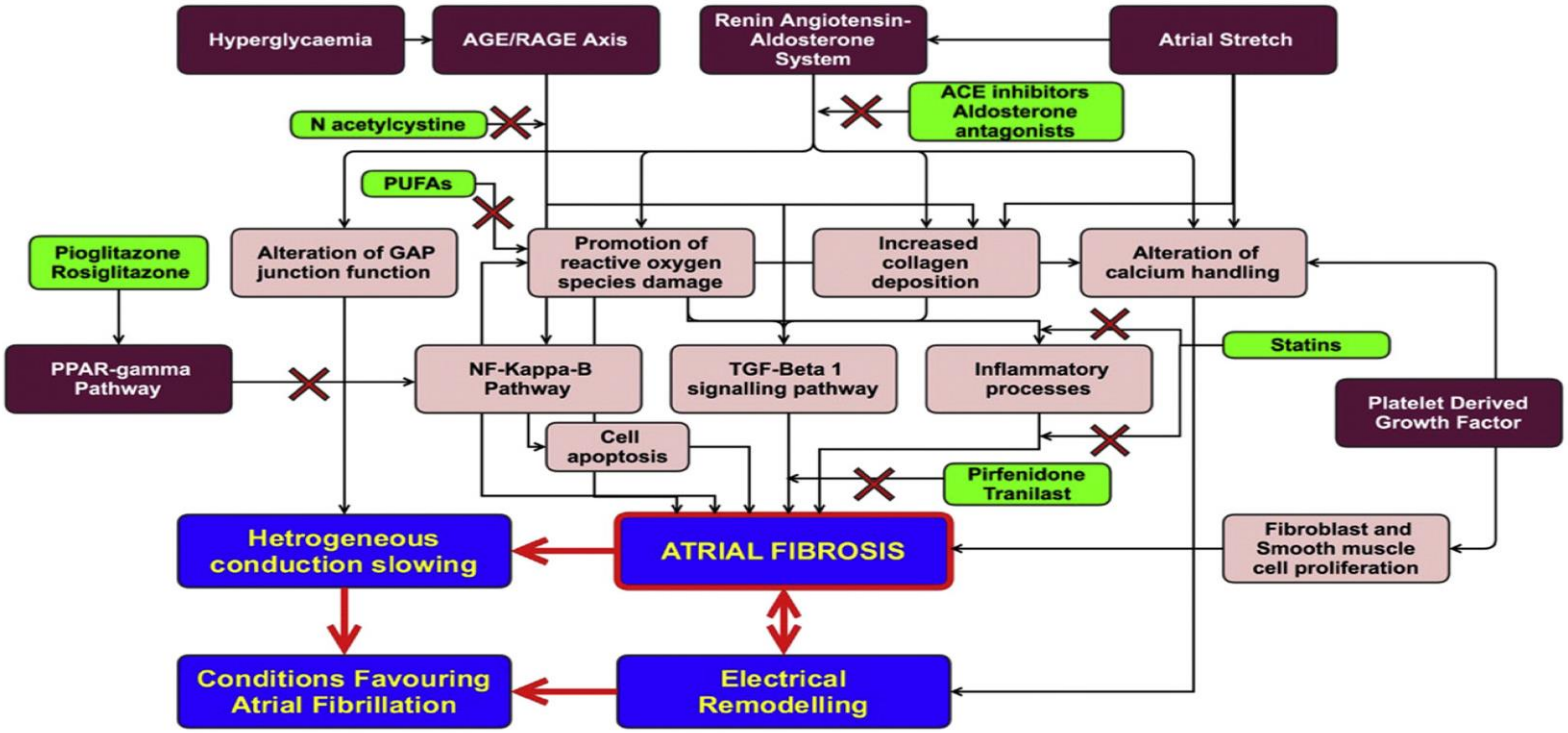

Fig 3 – The complex interplay of physiological processed involved in structural remodelling in AF. *Abbreviations*: ACE = angiotensin converting enzyme, PUFA = poly-unsaturated fatty acids, (R)AGE = (Receptor) for advanced glycalation end-products, PPAR = peroxisome proliferator-activated receptor, TGF = transforming growth factor, NF-Kappa-B = nuclear factor kappa light-chain-enhancer of activated B cells.

AF tedavisine mekanizma bazlı yaklaşım (bireysel tedavi)

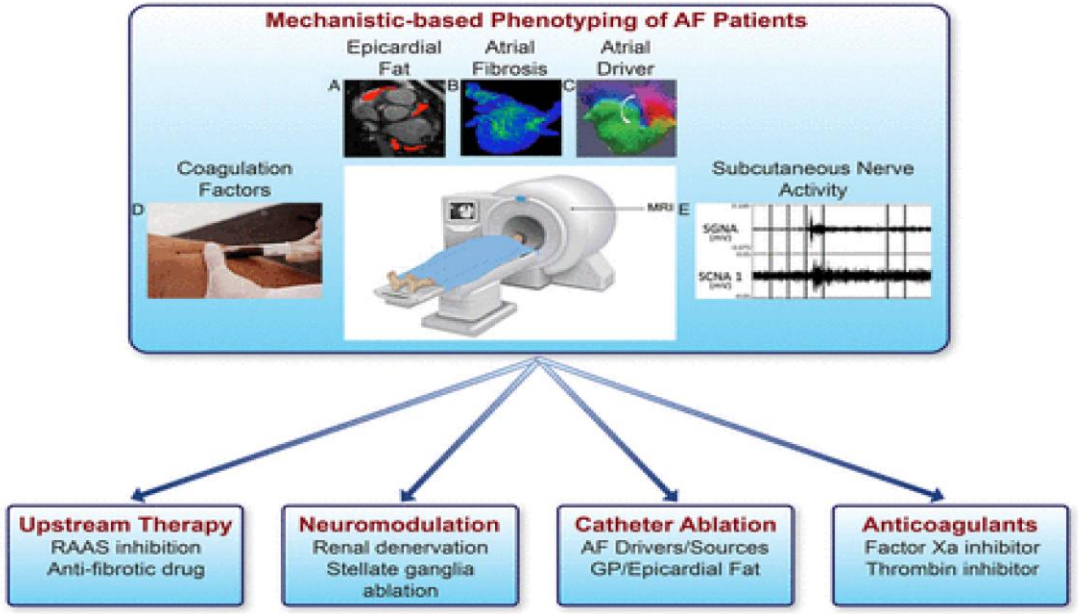

Figure 3
Individualized mechanistic-based atrial fibrillation management. Various non-invasive substrate based atrial mapping can help to improve phenotyping of AF patients. These may include: (*A*) atrial pericardial adipose tissue assessment using CMR from Mahajan *et al.*[60]; (*B*) atrial fibrosis detection using LGE-CMR from Daccarett *et al.*[46]; (*C*) non-invasive mapping of AF rotors from Haissaguerre *et al.*[130]; (*D*) assessment of pro-coagulation state; (*E*) assessment of sympathetic tone from measurement of subcutaneous nerve activity from Robinson *et al.*[123]

Lau DH; Eur Heart J. 2015 Nov 17