10. Atriyal Fibrilasyon Zirvesi 2021

11–13 Kasım 2021 • Calista Kongre Merkezi Antalya

Atriyal Fibrilasyon Hastasında Eşlik Eden Hastalıkların Yönetimi

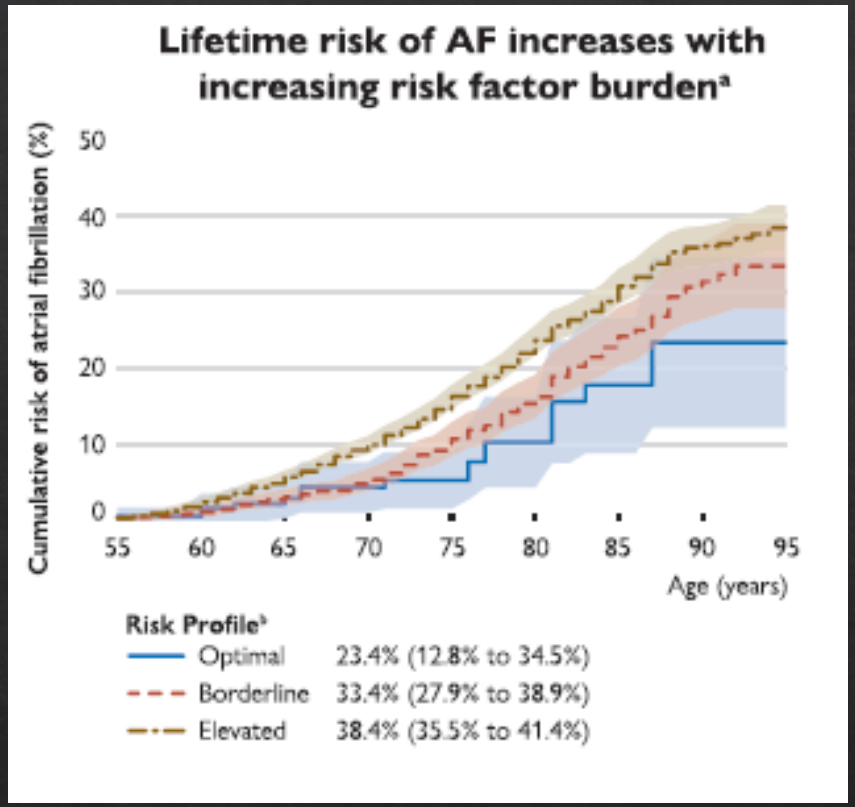
Dr. Burak Sezenöz

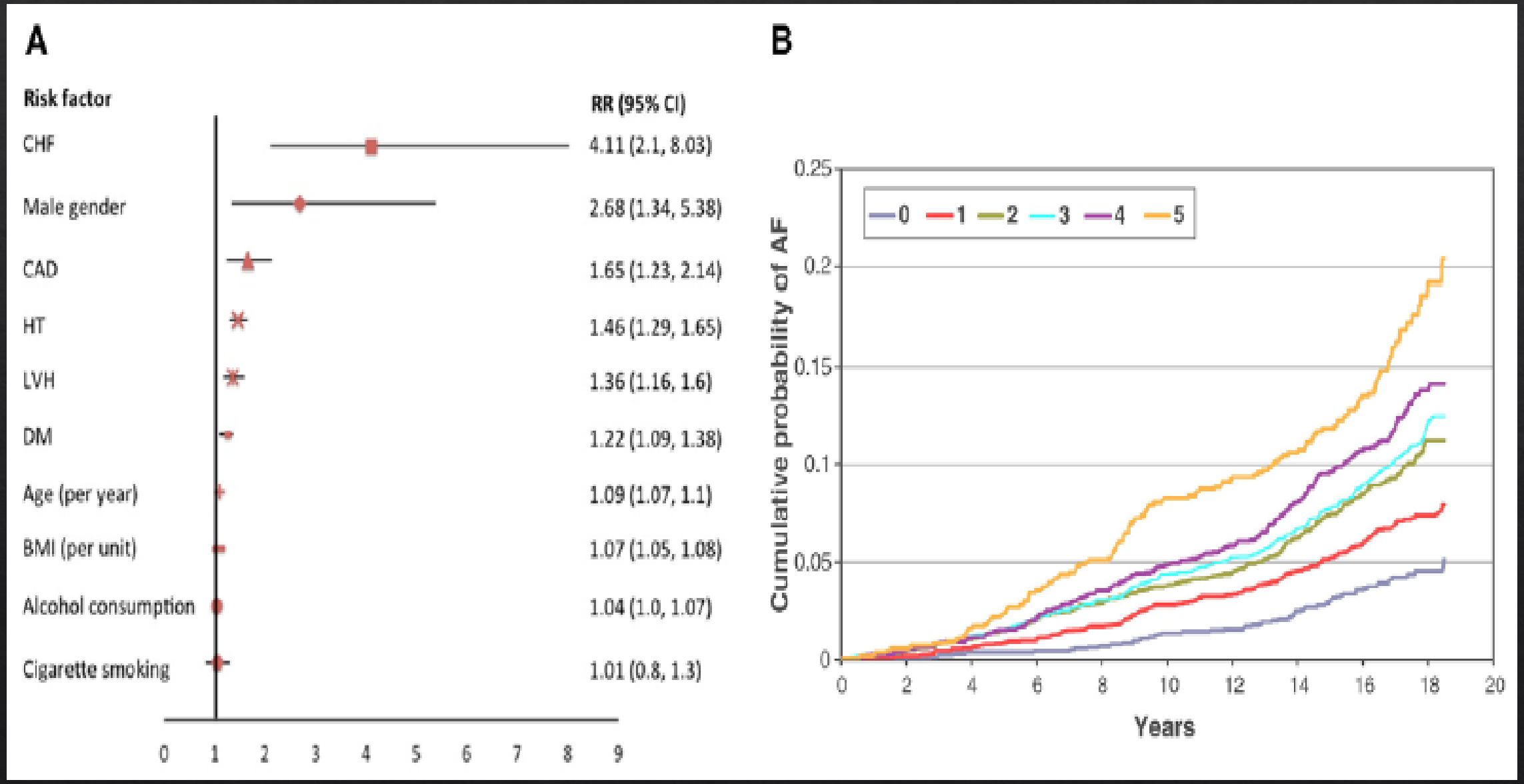
Gazi Üniversitesi

Kardiyoloji ABD

13.11.2021

- AF dünyada tüm nedenlere bağlı ölümlerin en başta gelen nedenlerinden biri
- Bir çok kardiyovasküler risk faktörünün AF gelişiminin bağımsız öngörücüleri olduğu bilinmektedir
- Son dönemde birincil ve ikincil korunmada değiştirilebilir risk faktörlerinin katkısı daha iyi anlaşılmış ve tedavinin odak noktası haline gelmiştir

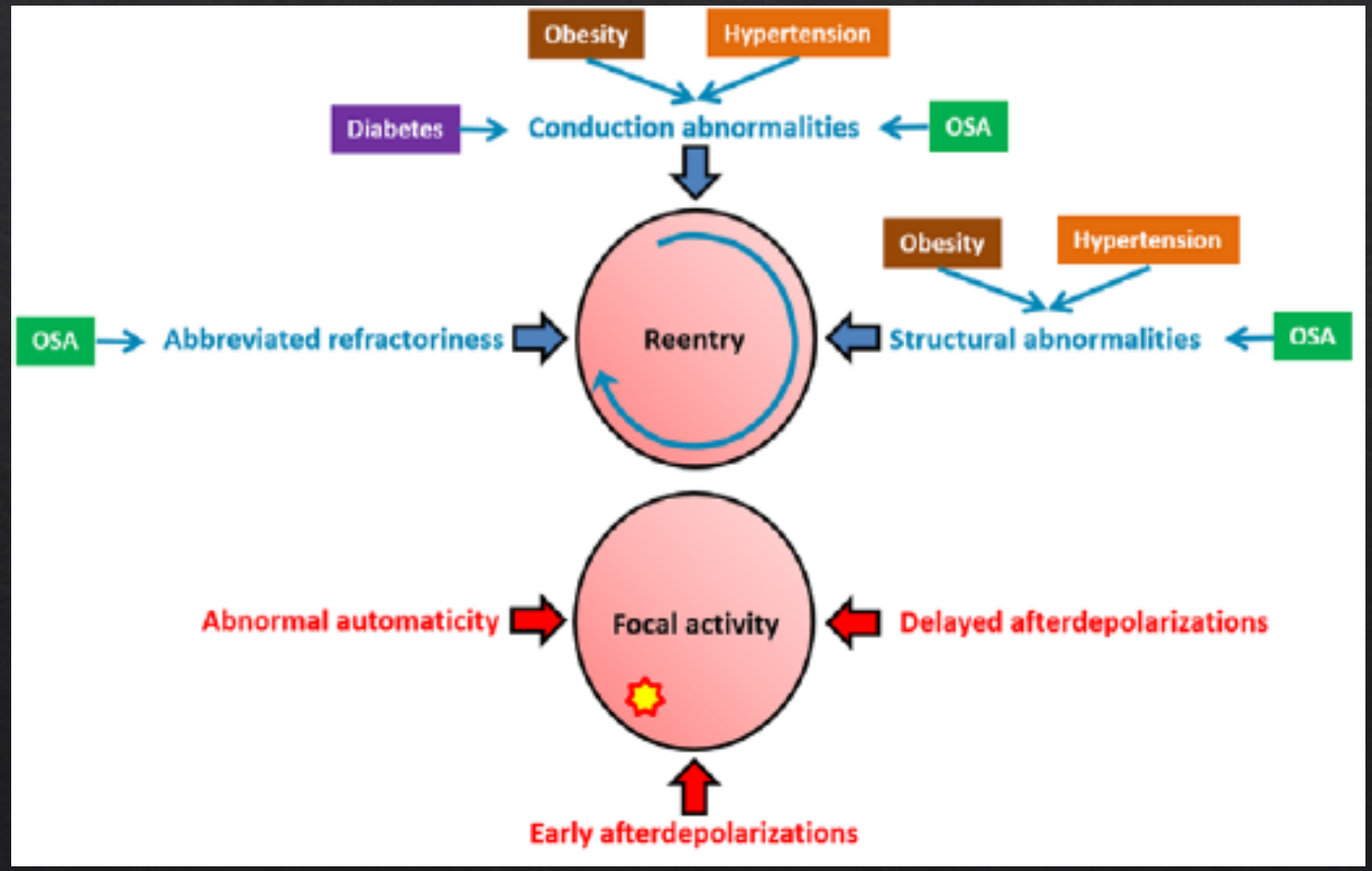




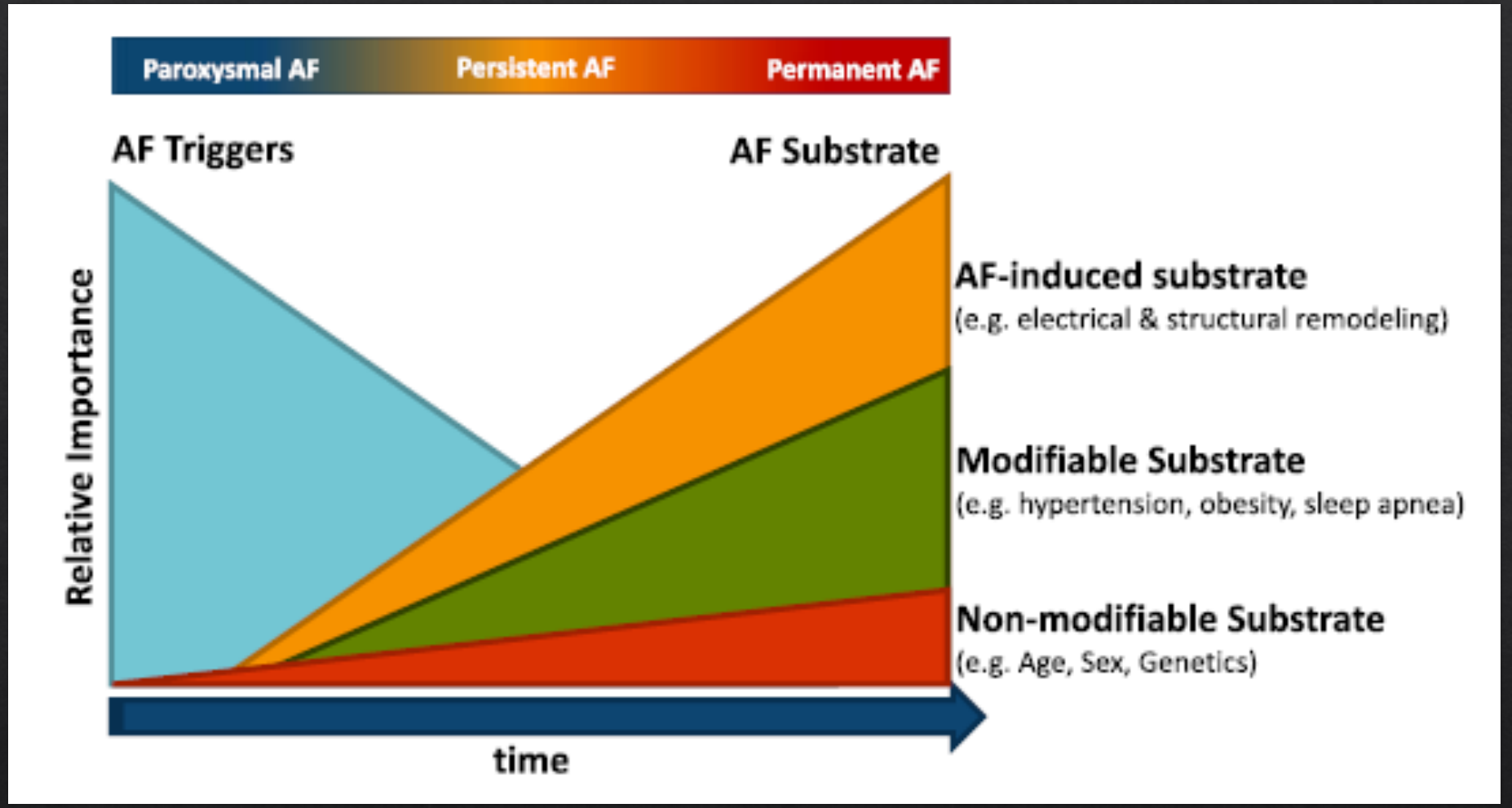
Circulation. 2017;136:583–596.

RF'lerinin AF patofizyolojisindeki yeri

- Nörohumoral aktivasyon
- Yapısal yeniden şekillenme
- Elektriksel yeniden şekillenme
- İnflamasyon ve oksidatif stres
- Otonomik disfonksiyon
- .....



Circulation. 2017;136:583–596.



TEDAVİ BAŞARISI

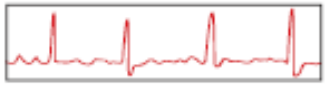
PROGNOZ

RACE (2002)

Atriyal substratta ilerleme

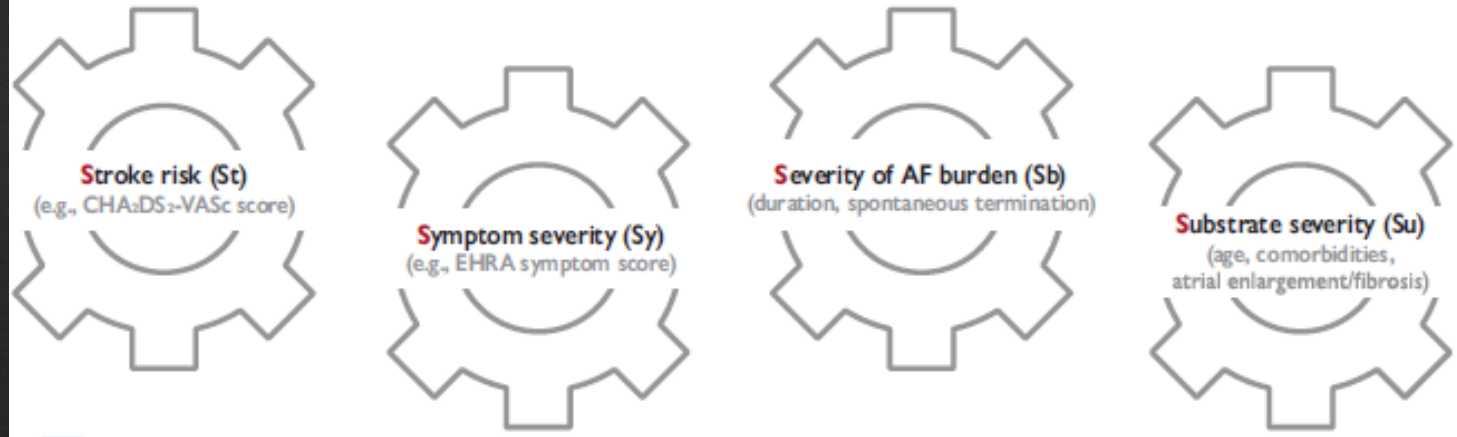
EAST-AF NET (2020)

Confirm AF

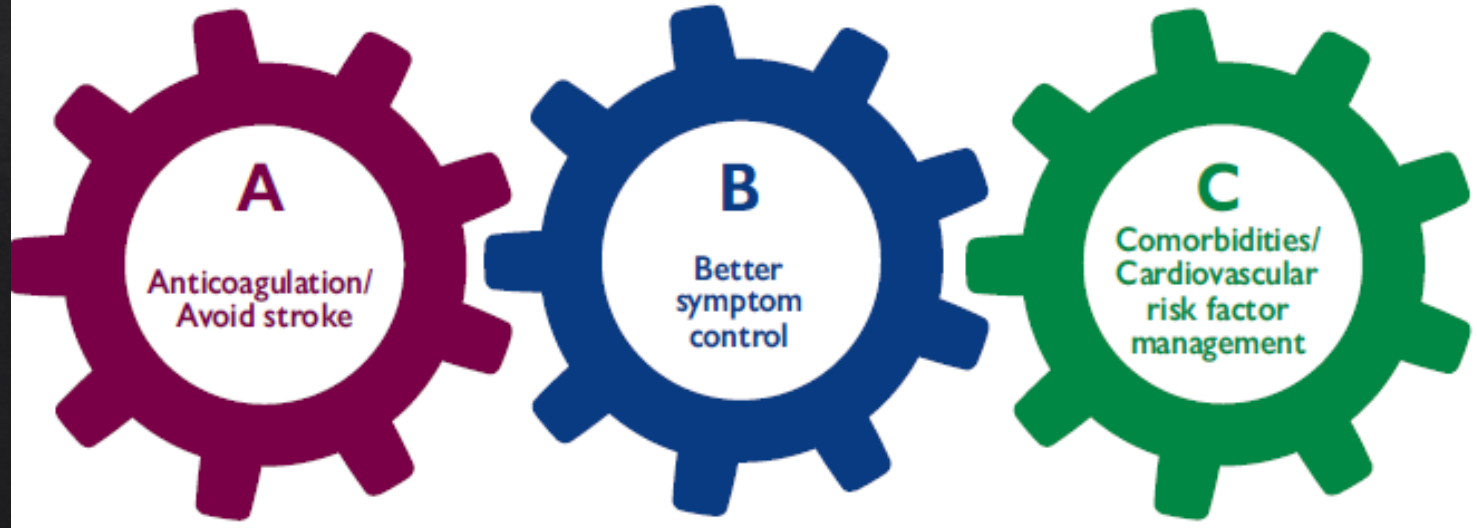


A 12-lead ECG or a rhythm strip showing AF pattern for ≥30 s

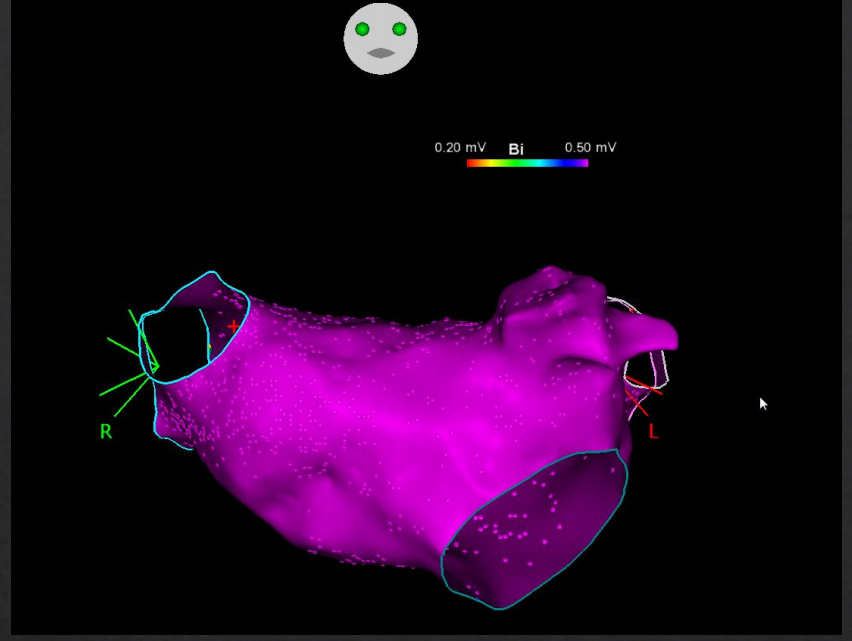
Characterise AF (the 4S-AF scheme)

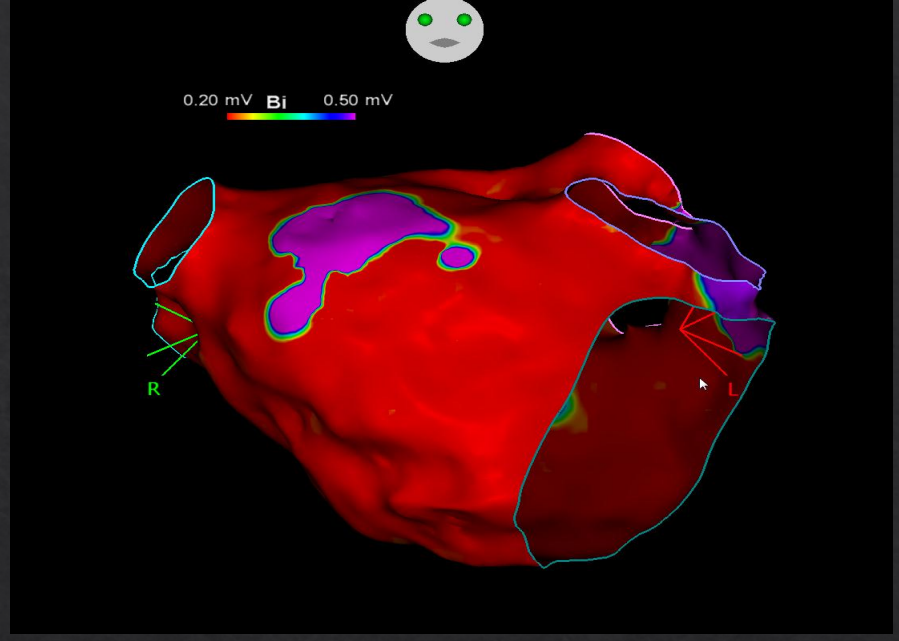


Treat AF: The ABC pathway

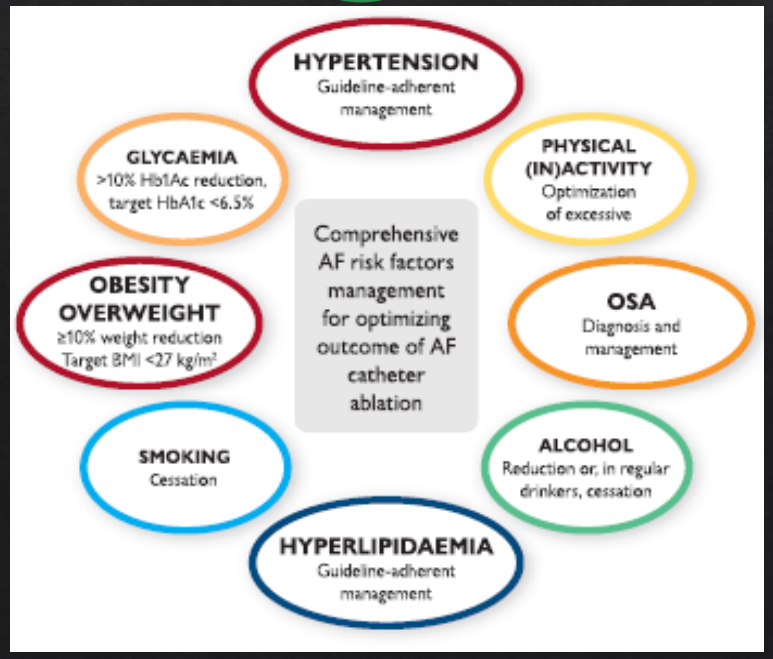


European Heart Journal (2020) 42, 373498





AF + Eşlik eden Hast ⛔ Atrial Kardiyomiyopati



AF risk faktörleri

Birincil ve İkincil korunma, Mortalitenin-mobiditenin azaltılması
- Yaşam tarzı değişiklikleri
- Risk faktör modifikasyonu
- Altta yatan hastalıkların tedavisi

Modifiye edilebilir
- **Hipertansiyon**
- **Dibetes Mellitus**
- **Obezite**
- **OSA**
- **Alkol**
- **Dislipidemi**
- **Fiziksel aktivite**
- **Sigara**

Kısmen modifiye edilebilir veya edilemez
- **Kalp yetmezliği**
- **KAH**
- **Valvuler KH**
- **KOAH**
- **Yaşlanma**
- **Genetik**

Sol atriyal yeniden şekillenme

AF gelişmesi ve progresyonu

Birincil ve İkincil korunma, Mortalitenin-mobiditenin azaltılması
- Antikoagülasyon
- Ritim Kontrolü
- Hız kontrolü

Recommendations	Class	Level
Identification and management of risk factors and concomitant diseases is recommended as an integral part of treatment in AF patients.	I	B
Modification of unhealthy lifestyle and targeted therapy of intercurrent conditions is recommended to reduce AF burden and symptom severity.	I	B

1. Yaşam tarzı değişiklikleri
2. Obezite
3. Hipertansiyon
4. Diabetes Mellitus
5. Kalp Yetersizliği
6. Obstrüktif Uyku Apne Sendromu(OSAS)

Yaşam Tarzı Değişiklikleri

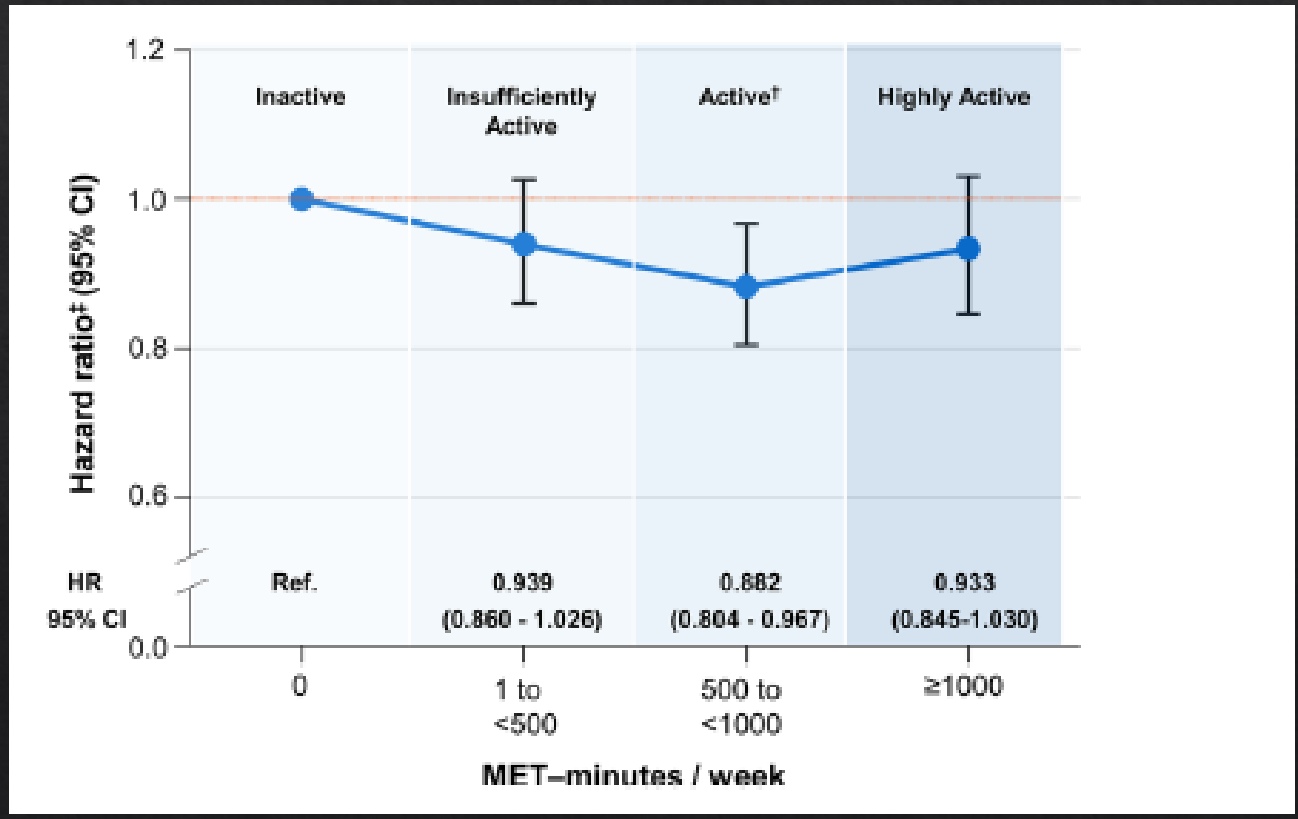
- Hasta eğitimi – Hasta odaklı tedavi
- Sigara bırakılmalı
- Kronik kafein(kahve) tüketiminin zaralı olduğunu gösteren çalışma yok*
- Alkol alımı kısıtlanmalı (< 30 g/hafta)

Advice and management to avoid alcohol excess should be considered for AF prevention and in AF patients considered for OAC therapy	IIa	B

*Can J Cardiol . 2014 Apr;30(4):448-54.

Egzersiz ve AF

- Egzersiz (aerobik) – 3-4/7 gün , 30 dk/gün → 250 dk/hafta hedeflenebilir
- U eğimi mevcut



Sci Rep . 2019 Sep 13;9(1):13270.

Obezite – AF ilişkisi

- Obezite neticesinde kalpte meydana gelen yapısal, fonksiyonel, nörohumoral, inflamatuvar, hemodinamik değişiklikler neticesinde AF gelişebilir
- Sol atriyal yeniden şekillenme ve fonksiyon bozukluğu zemin hazırlar
- Obezite paradoksu AF çalışmalarında gösterilmiştir (AFFIRM, ARISTOTLE, ORBIT-AF)
- Kontrollü kilo verme, fiziksel aktivitenin arttırılması, kardiyo-pulmoner sağlık !!!

Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort

A Long-Term Follow-Up Study (LEGACY)

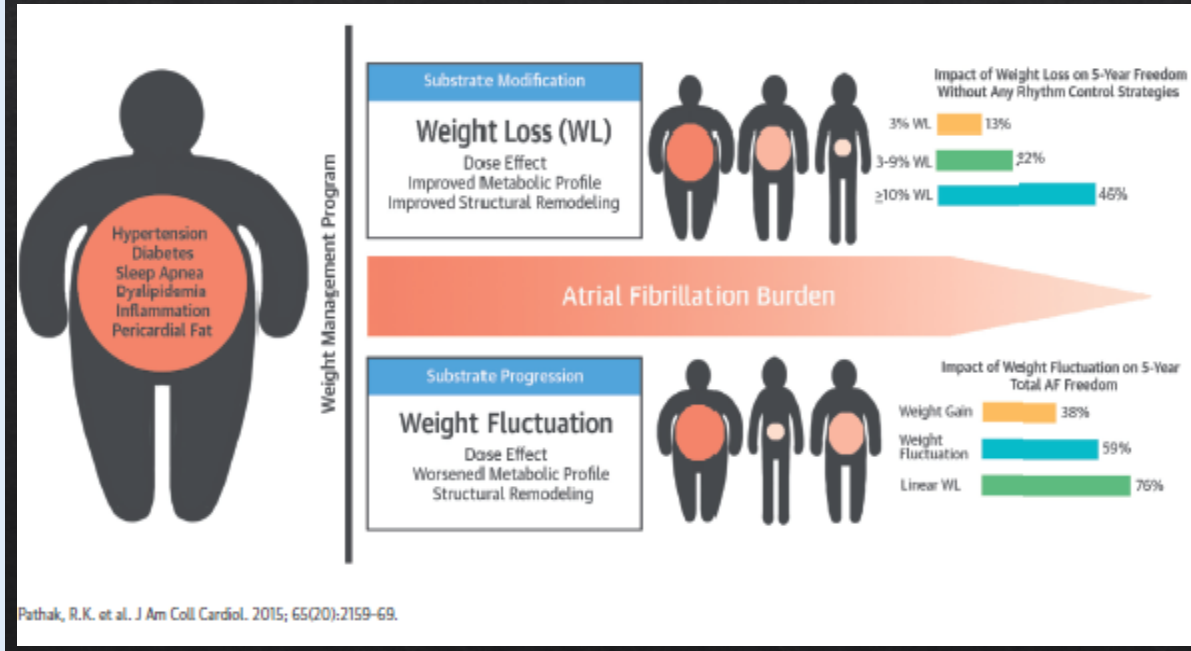
BACKGROUND Obesity and atrial fibrillation (AF) frequently coexist. Weight loss reduces the burden of AF, but whether this is sustained, has a dose effect, or is influenced by weight fluctuation is unknown.

OBJECTIVES This study sought to evaluate the long-term impact of weight loss and weight fluctuation on rhythm control in obese individuals with AF.

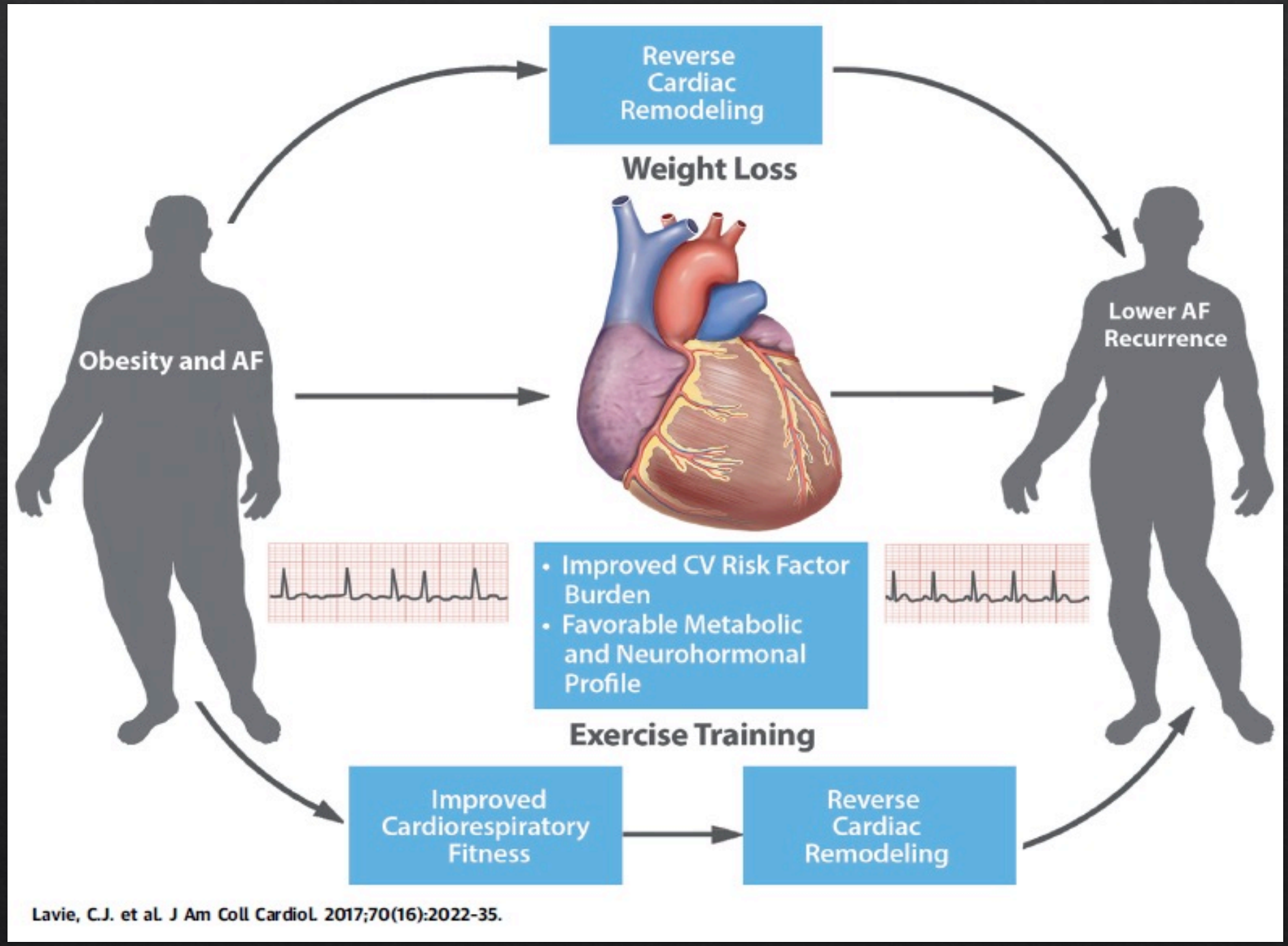
METHODS Of 1,415 consecutive patients with AF, 825 had a body mass index ≥27 kg/m^2 and were offered weight management. After screening for exclusion criteria, 355 were included in this analysis. Weight loss was categorized as group 1 (≥10%), group 2 (3% to 9%), and group 3 (<3%). Weight trend and/or fluctuation was determined by yearly follow-up. We determined the impact on the AF severity scale and 7-day ambulatory monitoring.

RESULTS There were no differences in baseline characteristics or follow-up among the groups. AF burden and symptom severity decreased more in group 1 compared with groups 2 and 3 ($p < 0.001$ for all). Arrhythmia-free survival with and without rhythm control strategies was greatest in group 1 compared with groups 2 and 3 ($p < 0.001$ for both). In multivariate analyses, weight loss and weight fluctuation were independent predictors of outcomes ($p < 0.001$ for both). Weight loss ≥10% resulted in a 6-fold (95% confidence interval: 3.4 to 10.3; $p < 0.001$) greater probability of arrhythmia-free survival compared with the other 2 groups. Weight fluctuation >5% partially offset this benefit, with a 2-fold (95% confidence interval: 1.0 to 4.3; $p = 0.02$) increased risk of arrhythmia recurrence.

CONCLUSIONS Long-term sustained weight loss is associated with significant reduction of AF burden and maintenance of sinus rhythm. (Long-Term Effect of Goal directed weight management on Atrial Fibrillation Cohort: A 5 Year follow-up study [LEGACY Study]; ACTRN12614001123639) (J Am Coll Cardiol 2015;65:2159–69) © 2015 by the American College of Cardiology Foundation.



Pathak, R.K. et al. J Am Coll Cardiol. 2015; 65(20):2159-69.

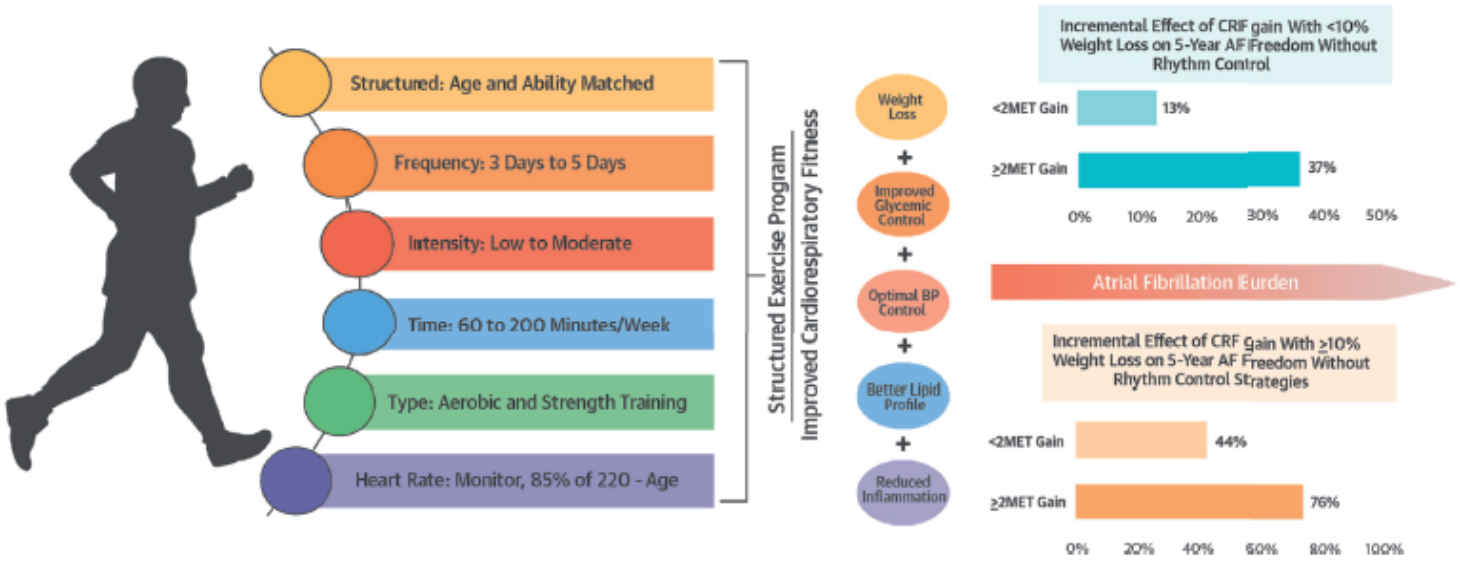


Lavie, C.J. et al. J Am Coll Cardiol. 2017;70(16):2022-35.

Impact of CARDIOrespiratory FITness on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation

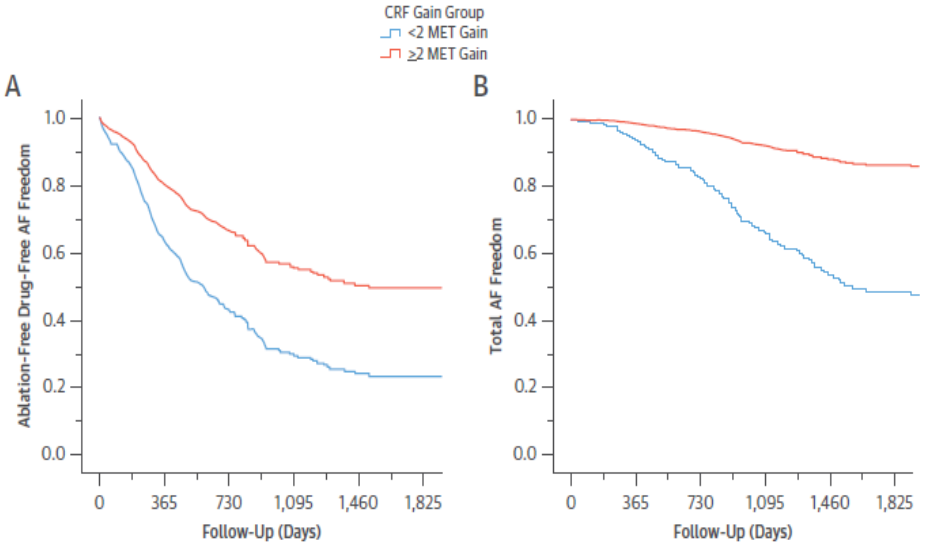
The CARDIO-FIT Study

CENTRAL ILLUSTRATION Cardiorespiratory Fitness and AF Recurrence: CARDIO-FIT trial



Pathak, R.K. et al. J Am Coll Cardiol. 2015; 66(9):985-96.

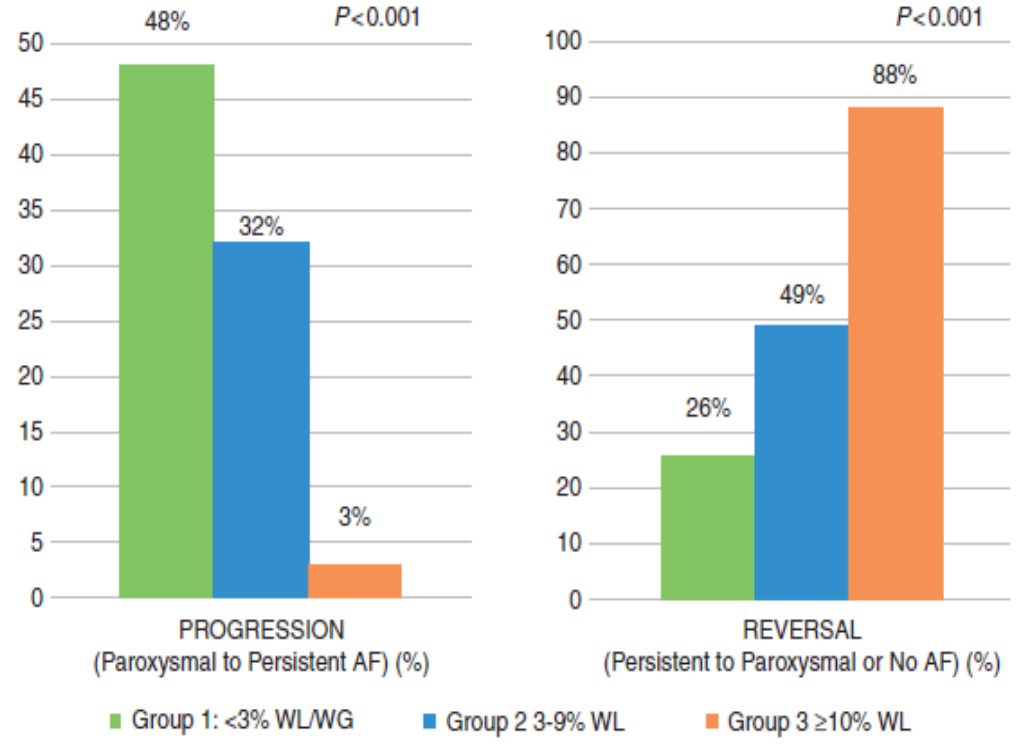
FIGURE 3 Outcomes of AF Freedom According to Cardiorespiratory Fitness Gain (<2 METs Gain vs. ≥2 METs Gain)



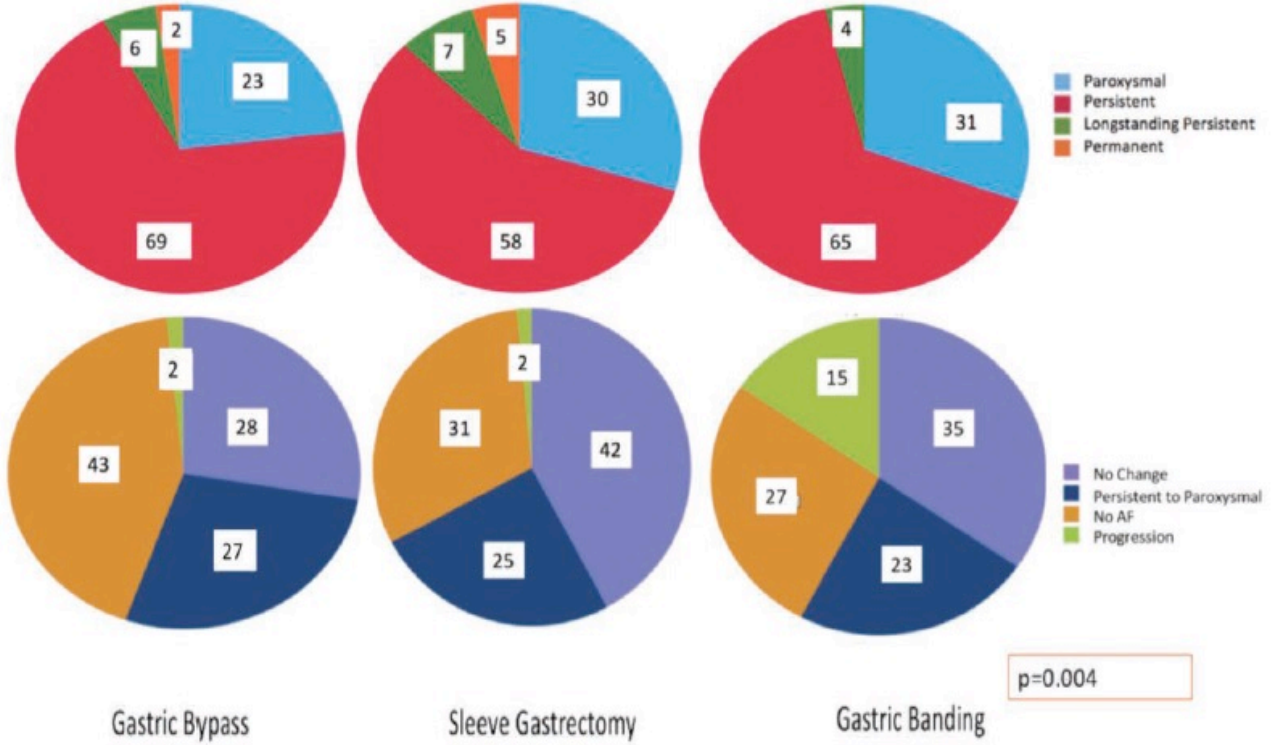
Time (Days)	0	365	730	1,095	1,460	1,825
≥2 MET Gain	127	105	78	52	38	19
<2 MET Gain	181	104	63	36	20	16

0	365	730	1,095	1,460	1,825
127	124	109	84	62	33
181	166	132	86	51	32

REVERSE-AF 2018-Europace



Bariatrik Operasyonun etkisi 2020 (CIRC-EP)



Hipertansiyon-AF

- Kümülatif olarak en sık birlikte görüldüğü kardiyovasküler hastalık
- AF taraması önemli (Sınıf I)
- Risk faktörü, tedavi hedefi, komplikasyon belirteci, vs.
- CHADSVASc ve HASBLED bileşeni
- HT tedavisi olmazsa olmaz (<130/80 mmHg)
- Dinamik olarak değerlendirilmeli

HT tedavisi

- Atriyal ve ventriküler gerilim
- Miyokardiyal fibroz
- Atriyal sertlik ve yapısal yeniden şekillenme

- Optimal tedavi sağkalımı

- RAAS blokajı birincil korunmada önemli özellikle LVH mevcut ise
- Hız kontrolü gerekli ise b-bloker veya KKB (Sınıf I)

DM ve AF ilişkisi

- DM hastalarında AF gelişme riski yüksek(~%40)
- AF gelişen hastalarda iskemik komplikasyon daha fazla (Hiperkoagübilite, endotel fonksiyon bozukluğu ve fibrinoliz)
- CHADSVASc skoru bileşeni (DM kontrolü ?)

- Diabetik hastalarda insidans yüksek, prognoz kötü

  AMA

- Glisemik kontrol kötüleştikçe (HBa1c > %7)
- DM süresi uzadıkça

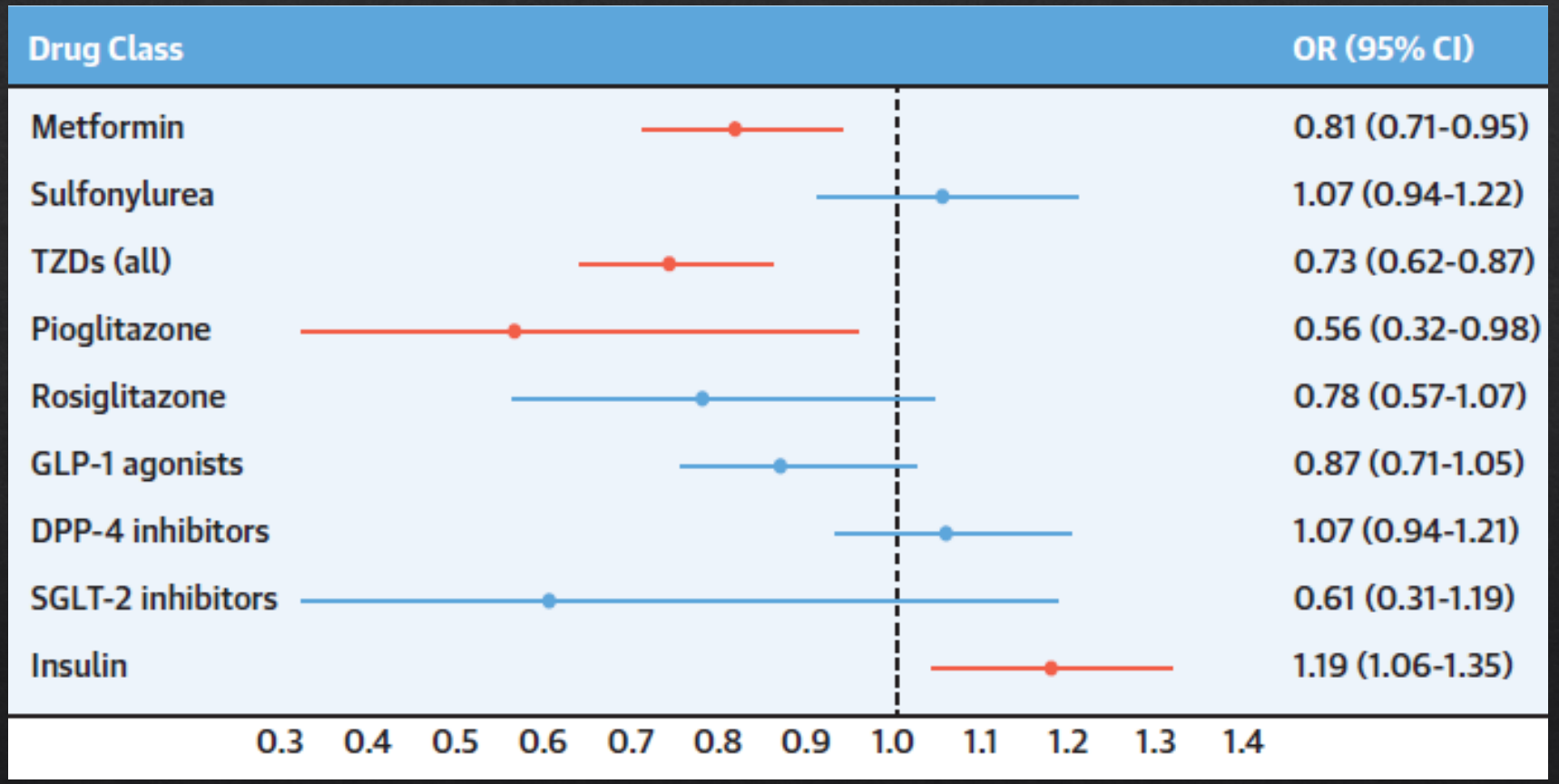
  PROGNOZ DAHA KÖTÜ !!!

- İyi glisemik kontrol AF ablasyon başarısını arttırıyor (RRR %30)*

*JACC Clin Electrophysiol . 2019 Aug;5(8):897-903.

DM tedavisi ve AF insidansı

- OAD ilaçlar atrial yeniden şekillenmeyi ve AF insidansını azaltabilir (Metformin)
- Yeni çalışmaya ihtiyaç var

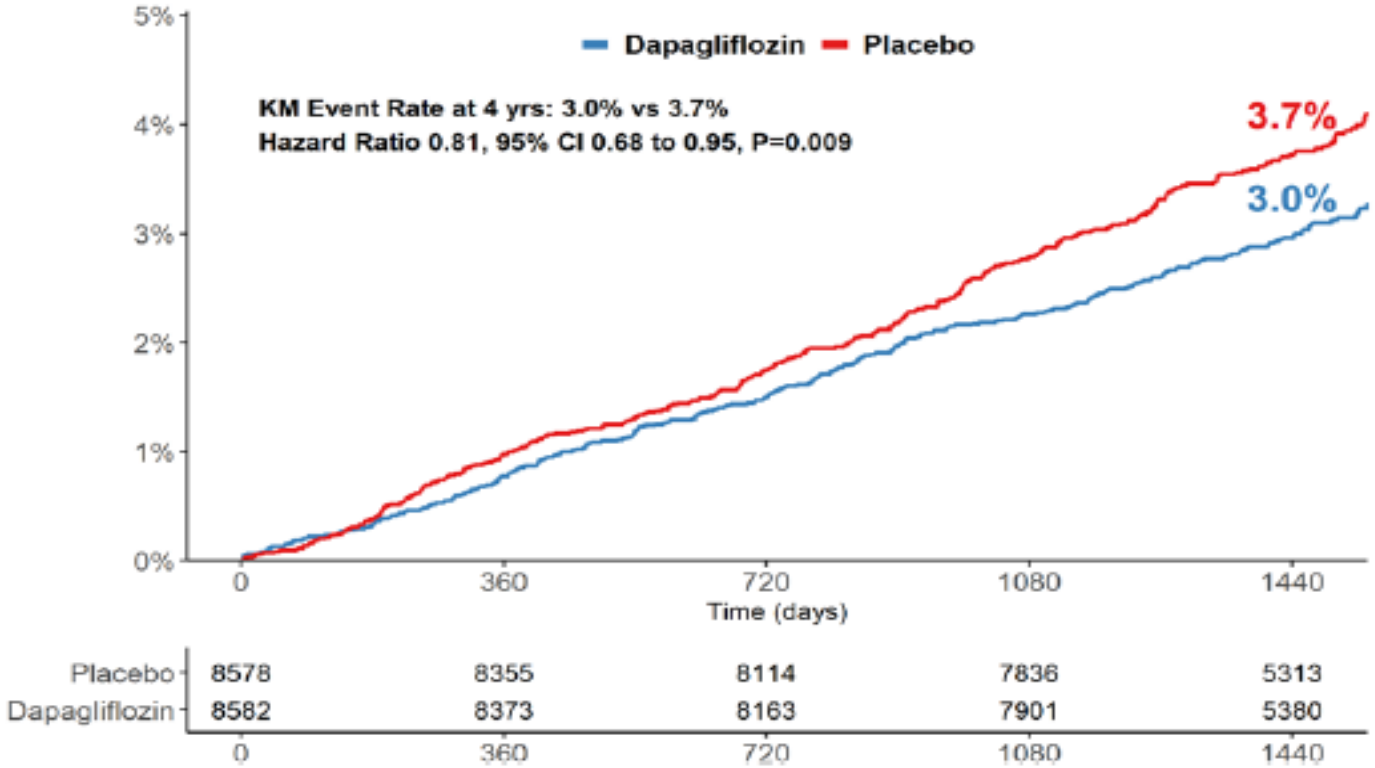


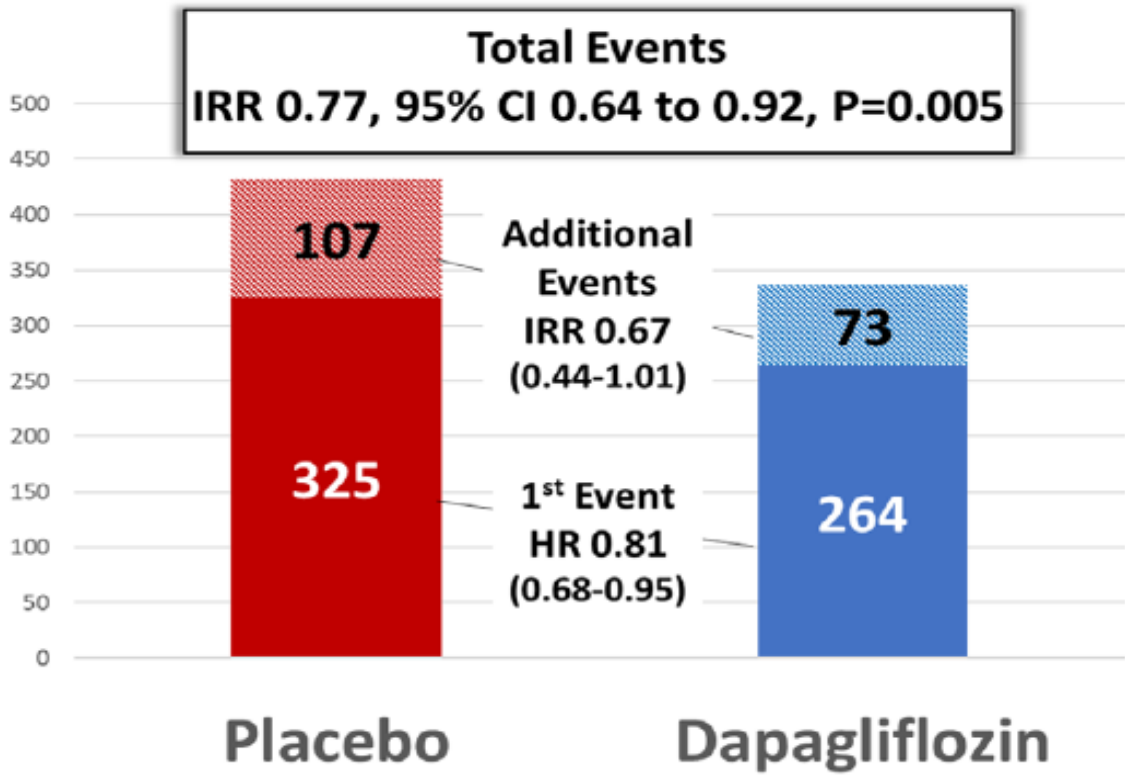
J Am Coll Cardiol . 2019 Aug 27;74(8):1107-1115.

ORIGINAL RESEARCH ARTICLE

Effect of Dapagliflozin on Atrial Fibrillation in Patients With Type 2 Diabetes Mellitus

Insights From the DECLARE-TIMI 58 Trial

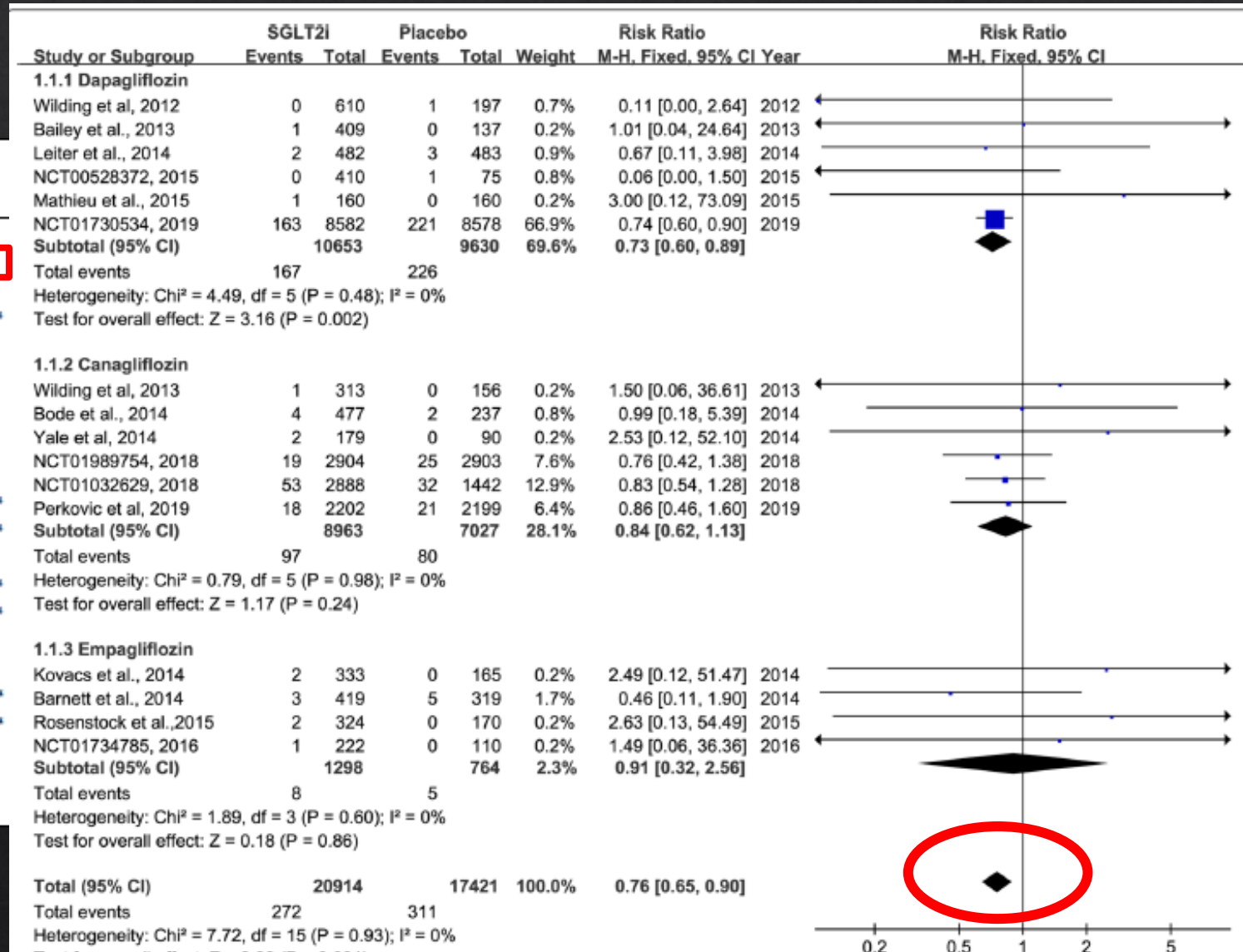




SGLT2 İnhibitörleri & AF

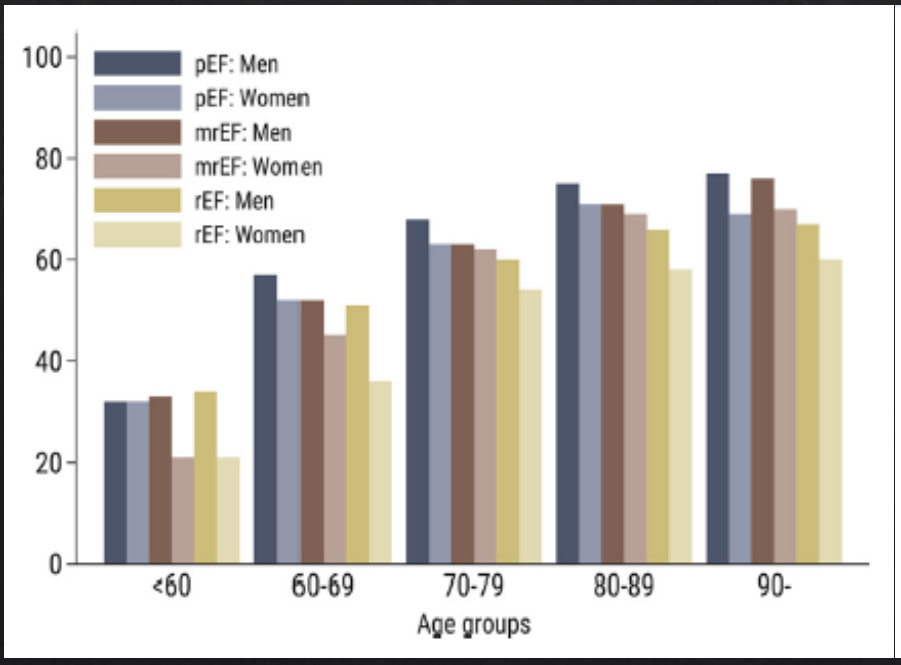
Outcomes of interest	Numbers of analyzed studies	SGLT2i patients	Placebo patients	RR (95% CI)	p value
Primary outcomes					
Incidence of AF/AFL	16	20,914	17,421	0.76 (0.65 to 0.90)	0.001*
All-cause mortality	12	19,809	16,920	0.91 (0.83 to 0.99)	0.03*
Heart failure	10	18,701	16,485	0.73 (0.64 to 0.84)	<0.00001*
Cerebrovascular events	13	20,199	16,986	1.06 (0.85 to 1.32)	0.19
Myocardial infarction	13	19,747	16,949	0.95 (0.78 to 1.16)	0.65
Secondary outcomes					
Urinary tract infection rate	15	12,332	8842	1.17 (1.03 to 1.32)	0.01*
Adjusted mean HbA1c (%) change from baseline					
Low dosage	9	2652	2601	−0.62 (−0.89 to −0.34)	<0.00001*
High dosage	11	3214	3230	−0.70 (−0.91 to −0.50)	<0.00001*
Adjusted mean body weight loss (kg) change from baseline					
Low dosage	5	778	776	−2.12 (−2.91 to −1.34)	<0.00001*
High dosage	7	1398	1405	−1.89 (−2.13 to −1.65)	<0.00001*
Adjusted mean blood pressure (mm Hg) change from baseline					
Systolic blood pressure					
Low dosage	6	2283	2257	−3.34 (−4.12 to −2.56)	<0.00001*
High dosage	7	2709	2736	−4.11 (−4.86 to −3.36)	<0.00001*
Diastolic blood pressure					
Low dosage	6	2283	2257	−1.11 (−1.62 to −0.6)	<0.0001*
High dosage	6	2236	2257	−1.69 (−2.17 to −1.12)	<0.0001*

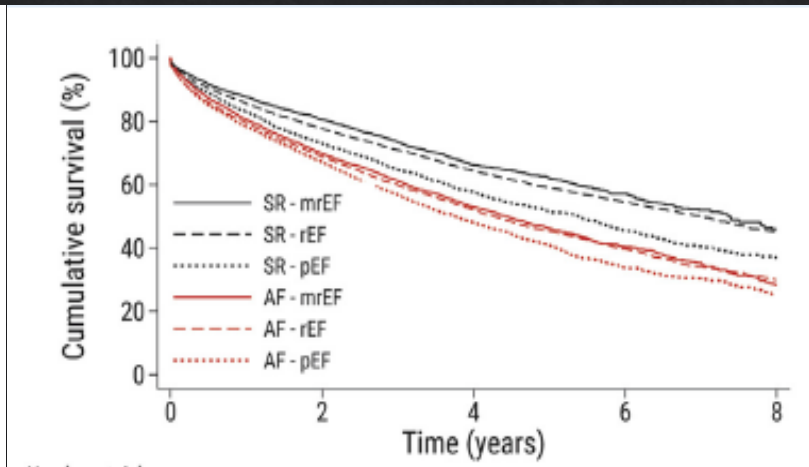
Cardiovasc Diabetol . 2020 Aug 26;19(1):130.



Kalp Yetersizliği ve AF

- Atriyal Fibrilasyon ⟺ Kalp Yetersizliği
- Prevelans % 17-65
- SR kıyasla daha fazla mortalite, hospitalizasyon ve inme ile ilişkili





Number at risk

SR - mrEF	3585	2129	1087	377	93
SR - rEF	10767	6210	3261	1236	312
SR - pEF	3345	1814	870	262	53
AF - mrEF	5312	2721	1262	396	82
AF - rEF	12187	6092	2932	1010	230
AF - pEF	6250	2992	1314	350	64

Association between atrial fibrillation and all-cause mortality according to ejection fraction

	Multivariable adjusted hazard ratio (95% CI)
HFpEF *(n=9595)*	1.11 (1.02-1.21)
HFmrEF *(n=8897)*	1.22 (1.12-1.33)
HFrEF *(n=22954)*	1.17 (1.11-1.23)

Reference category: Sinus rhythm.

J Am Coll Cardiol HF 2017;5:565–74.

Farmakolojik Tedavi

- ACEi ve ARB'ler öncelikle tercih edilmeli (tersine yeniden şekillenme, AF yükünde azalma)
- Aldosterone antagonsitleri olasılıkla etkili ancak kanıtlanmış değil (antifibrotik)*
- B-blokerler hız kontrolünde birinci basamak, ikincil koruma (sağkalıma faydası?)
- SGLT2 inhibitörleri faydalı olabilir (DAPAgliflozin)

*Europace (2016) 18, 672–678.

Sacubitril/Valsartan

- Antiaritmik olabilir mi?
- Kılavuzlarda bu konu ile ilgili öneri bulunmuyor
- Hayvan deneylerinde atriyal yeniden şekillenmeyi tersine çevirdiği gösterildi
- İnsanlarda eko çalışmalarında başarılı (atrial strain)

Sacubitril/valsartan reduces atrial fibrillation and supraventricular arrhythmias in patients with HFrEF and remote monitoring: preliminary data from the SAVE THE RHYTHM

F. Guerra[1], L. Pimpini[2], M. Flori[3], D. Contadini[4], G. Stronati[1], F. Gioacchini[1], M.F. Massara[1], F. Gennaro[5], R. Antonicelli[2], P. Busacca[3], M. Luzi[4], A. Dello Russo[1], P. Marchese[5]

[1]Marche Polytechnic University of Ancona, Cardiology and Arrhythmology Clinic, Ancona, Italy; [2]National Institute of Hospital and Care for Elderly (INRCA), Department of Cardiology, Ancona, Italy; [3]Ospedale della Misericordia, Department of Cardiology, Urbino, Italy; [4]General Hospital, Department of Cardiology, Macerata, Italy; [5]Cardiology ASUR-AV5 Mazzoni Hospital, Department of Cardiology, Ascoli Piceno, Italy

On behalf of SAVE THE RHYTHM

Funding Acknowledgement: Type of funding source: None

Background: Sacubitril/valsartan, the first combined angiotensin receptor-neprilysin inhibitor, has demonstrated a significant benefit compared to angiotensin inhibitor in decreasing ventricular arrhythmias and appropriate implantable cardioverter defibrillator (ICD) shocks in patients with heart failure with reduced ejection fraction (HFrEF). At present, there is no study which evaluates the effect of sacubitril/valsartan on the supraventricular arrhythmic burden in HFrEF patients with an ICD or cardiac resynchronisation therapy-defibrillator (CRT-D) and remote monitoring.

Purpose: To evaluate the effect of sacubitril/valsartan on the supraventricular arrhythmic burden in HFrEF patients with an ICD or CRTD and remote monitoring.

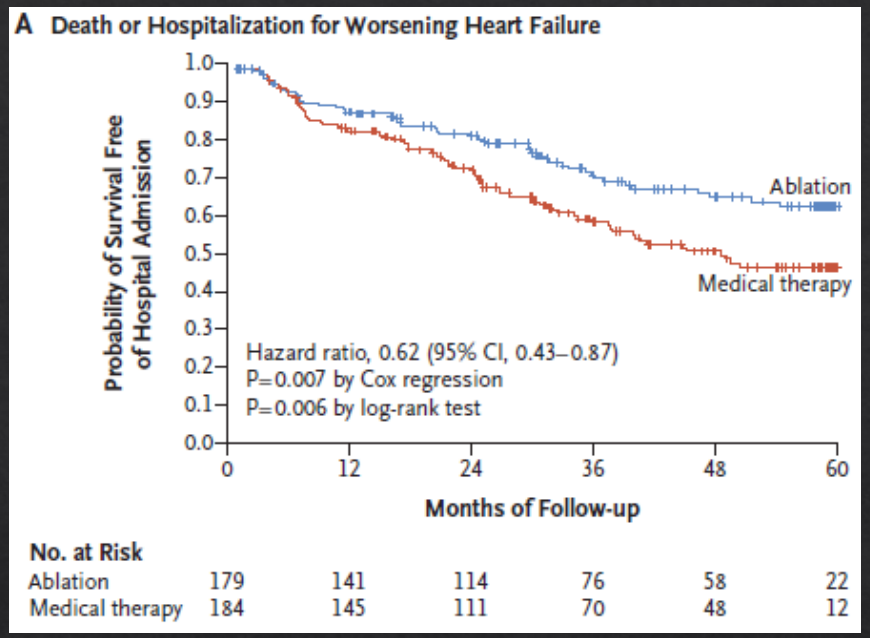
Methods: The SAVETHERHYTHM ((SAacubitril Valsartan rEal-world registry evaluating THE arRHYTHMia burden in HFrEF patients with implantable cardioverter defibrillator) is a multicentre, observational, prospective registry enrolling all patients with HFrEF, ICD or CRT-D actively followed through remote monitoring and starting treatment with sacubitril/valsartan. All patients are followed-up for at least one year after sacubitril/valsartan start. The primary endpoint is the mean number of sustained atrial tachycardia or atrial fibrillation (AT/AF) episodes per month. Secondary endpoints include the total burden of AT/AF (defined as the percentage of time in AT/AF per day), the mean number of premature ventricular contractions (PVC) per hour and the percentage of biventricular pacing per day (in patients with CRT-D). All primary and secondary endpoints are collected through remote monitoring.

Results: At the time of the first ad interim analysis, 60 patients (85.2% male, age 69±10 years) were consecutively enrolled. After treatment with sacubitril/valsartan, patients with at least one episode of AT/AF per month decreased from 32.8% to 21.3% ($p=0.015$). A significant decrease in number of AT/AF episodes (from 4.3 to 1.2 per year), in AT/AF burden (from 12% to 9%) and in number of PVC (from 83 to 74 per hour) were seen in patients with a previous diagnosis of paroxysmal or persistent AF (n=15; all $p<0.05$). Patients with permanent AF (n=7) experienced no benefits from sacubitril/valsartan therapy in terms of arrhythmic burden reduction. Patients with no previous history of AF (n=38) showed a decrease in number of AT/AF episodes (from 2.0 to 0.8 per year) and in number of PVC (from 77 to 49 per hour, all $p<0.05$). No new diagnosis of clinical AF was made after starting treatment with sacubitrl/valsartan, and patients with subclinical AT/AF episodes decreased from 8% to 3%.

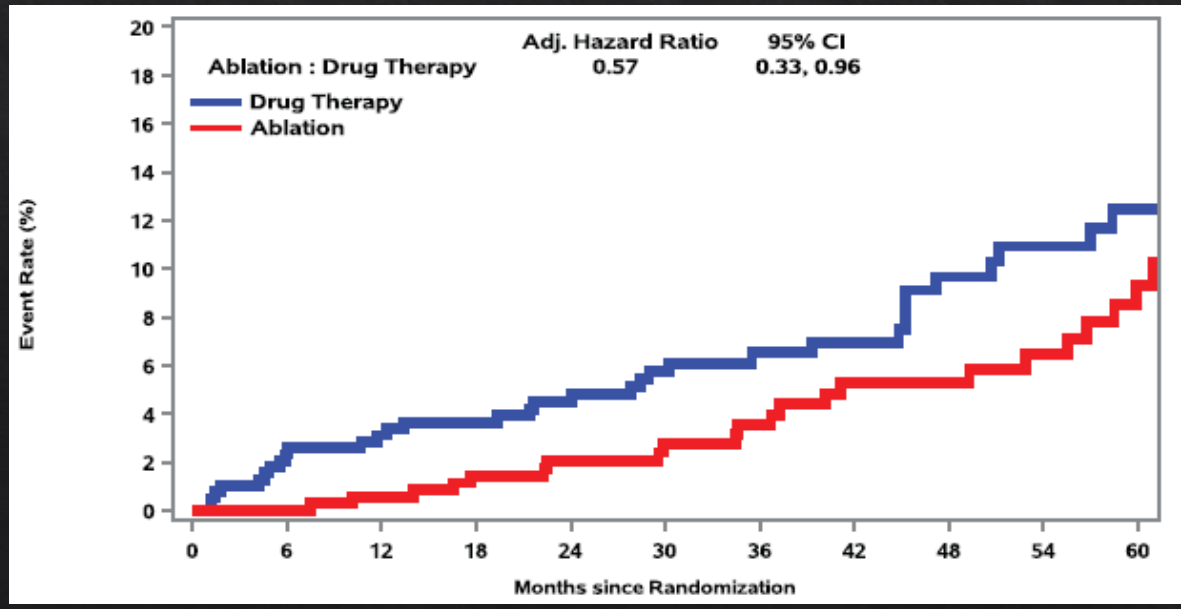
Conclusions: Preliminary data suggest that therapy with sacubitril/valsartan could decrease arrhythmic burden in patients with non-permanent AF and reduce subclinical AT/AF episodes in patients with no history of AF. No positive effect has been noted in patients with permanent AF.

Kateter ablasyon

- Ritim kontrolü ön planda düşünülmeli
- Mevcut çalışmalar KY hastalarında kateter ablasyonun EF'de artış, FK iyileşme ve sağkalım faydası olduğunu gösterdi!!!



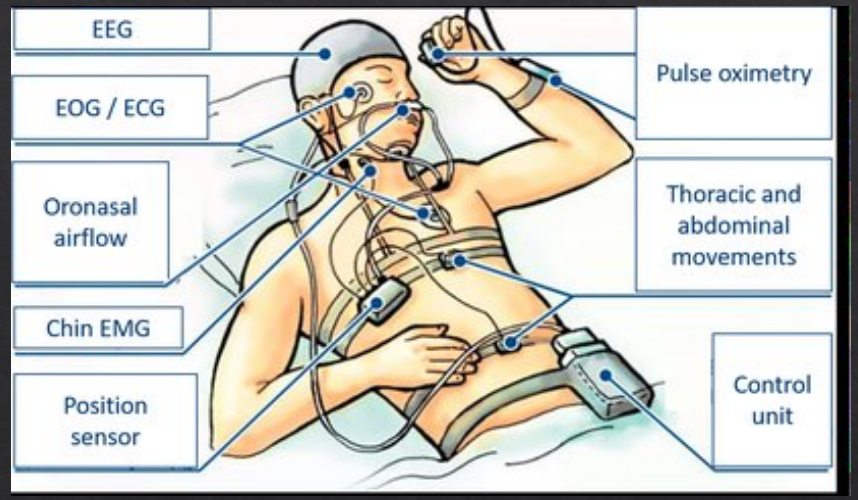
First-line therapy	
AF catheter ablation: • Is recommended to reverse LV dysfunction in AF patients when tachycardia-induced cardiomyopathy is highly probable, independent of their symptom status.	I
• Should be considered in selected AF patients with HFrEF to improve survival and reduce HF hospitalization.	IIa

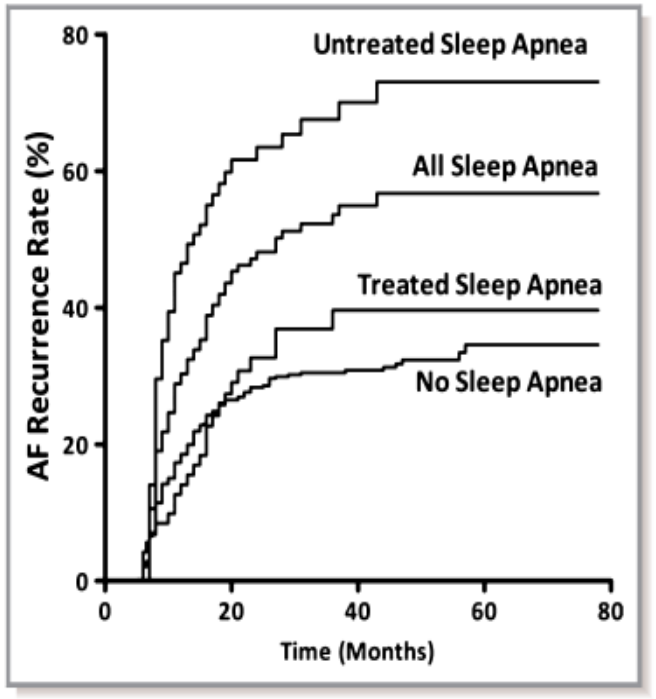


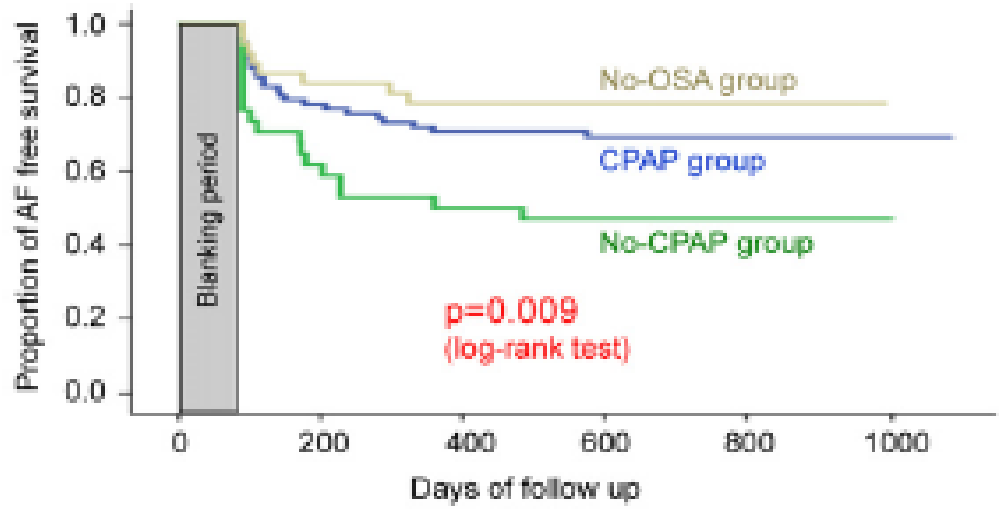
N Engl J Med 2018;378:417-27.
Circulation. 2021;143:1377–1390.

OSAS ve AF

- OSAS AF arasında pozitif korelasyon mevcut
- İnme için bağımsız öngördürücü
- AF tedavi etkinliğini azaltıyor (KV, ablasyon, vs.)
- Tarama önemli!!! (polisomnografi altın standart)



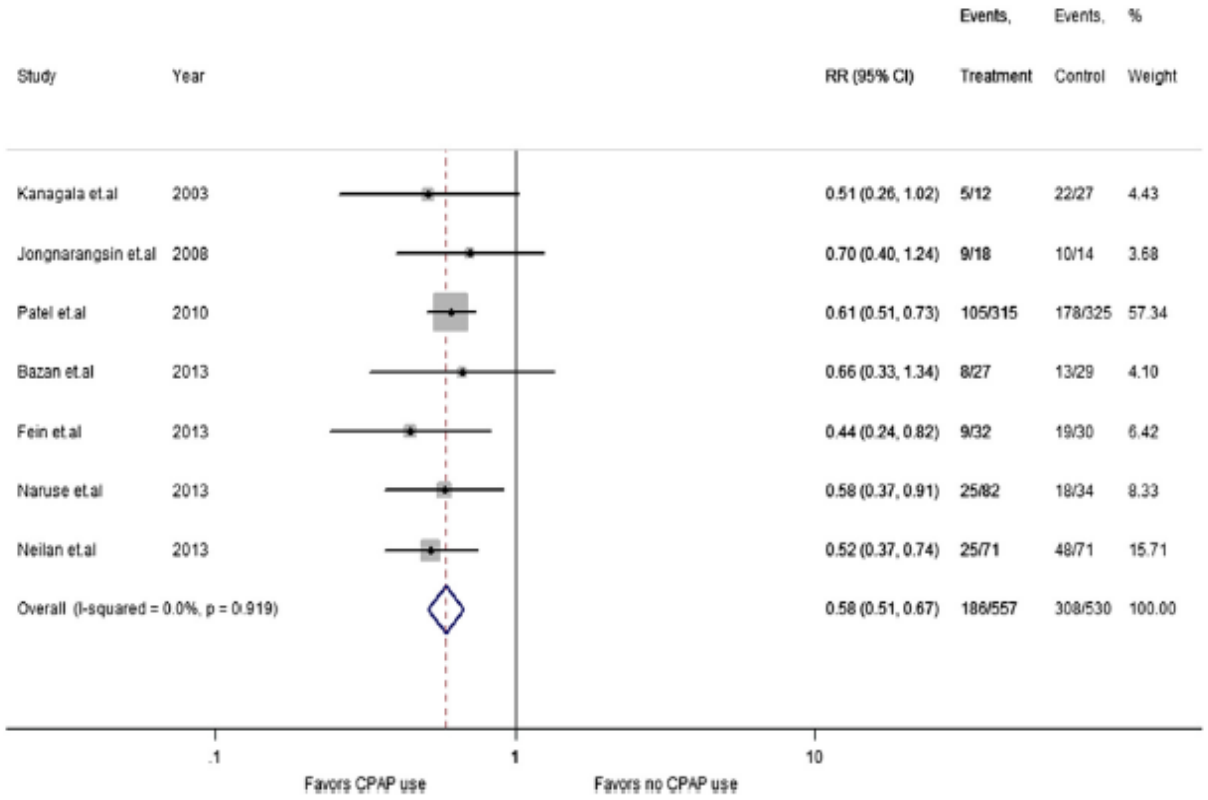




Patients at risk					
No-OSA	37	34	31	30	29
No-CPAP	34	26	21	18	17
CPAP	82	75	64	60	58

- *J Am Heart Assoc . 2013 Nov 25;2(6):e000421.*
- *Heart Rhythm . 2013 Mar;10(3):331-7.*
- *J Am Coll Cardiol EP 2015;1-2:41–51*

FIGURE 2 Forest Plot to Compare AF Recurrence in Users Versus Nonusers of CPAP In Patients With OSA



OSAS hastalarında CPAP tedavisi ablasyon başarısını arttırıyor
Mekanizma ???
Hedef???

AF Kılavuzlarında OSAS Tarama ve Tedavisi

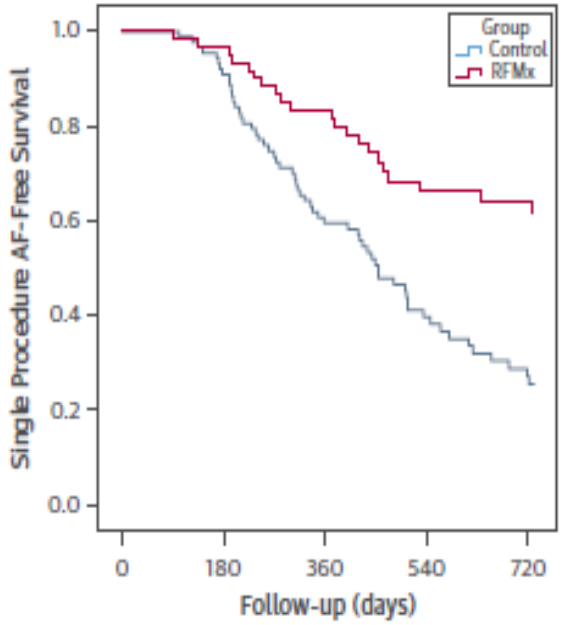
- CPAP faydalı ancak zamanlama, uzun dönem veriler yetersiz

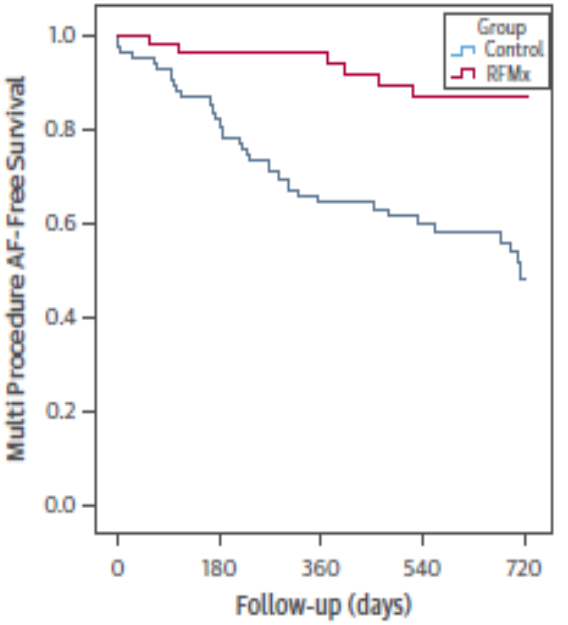
- 2014 ACC AF kılavuzu IIa
- 2016 ESC-AF kılavuzu Sınıf IIa
- 2017 AF ablasyon kılavuzu Sınıf IIa
- 2020 ESC AF kılavuzu II b
- 2020 CCS AF kılavuzu tarama ve tedavi öneriliyor

Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation

The ARREST-AF Cohort Study

	Control Group (n = 88)			RFM Group (n = 61)			
	Baseline	Follow-Up†	p Value*	Baseline	Follow-Up†	p Value*	p Value†
Risk factors							
Weight, kg	96.6 ± 16.8	95.8 ± 17.6	0.13	100.7 ± 17.6	87.5 ± 14.9	<0.001	0.002
BMI, kg/m^2	32.1 ± 4.7	31.8 ± 4.9	0.12	33.5 ± 4.6	29.1 ± 3.9	<0.001	<0.0011
Mean SBP, mm Hg	158.7 ± 21.3	138.2 ± 18.0	<0.001	160.8 ± 20.3	126.8 ± 12.8	<0.001	0.006
DM with HbA_{1c} ≥7%, n	17	5		9	0		0.001
No. with AHI >30	54	46		32	16		<0.001
Medication use							
No. of antiarrhythmic agents	1.0 ± 0.2	0.7 ± 0.7	<0.001	1.1 ± 0.3	0.3 ± 0.6	<0.001	<0.001
No. of antihypertensive agents	1.6 ± 1.2	1.9 ± 1.3	0.2	1.5 ± 1.1	1.2 ± 0.9	0.04	<0.001
Echocardiographic measures							
LA volume index, ml/m^2	42.4 ± 10.4	39.5 ± 12.1	0.07	42.5 ± 12	30.4 ± 8.3	<0.001	0.001
LV septum, mm	11.0 ± 2.0	10.9 ± 0.19	0.047	12.0 ± 2.0	9.6 ± 0.17	<0.001	<0.001
LVIDd, cm	5.1 ± 0.7	5.1 ± 0.6	0.204	5.3 ± 0.5	4.9 ± 0.6	<0.001	0.047
LVEF, %	60 ± 10.1	61.1 ± 8	0.538	61.3 ± 10	62.6 ± 5.5	0.524	0.971
Atrial Fibrillation Severity Score							
AF frequency (1-10)	6.6 ± 1.1	3.2 ± 1.1	<0.001	6.8 ± 1.2	2.0 ± 0.9	<0.001	<0.001
AF duration (1.25-10)	6.7 ± 1.3	3.3 ± 1.3	<0.001	6.4 ± 1.6	2.1 ± 0.9	<0.001	0.001
AF episode severity (1-10)	6.9 ± 1.3	5.2 ± 1.9	<0.001	6.6 ± 1.5	3.3 ± 1.5	<0.001	<0.001
AF symptom subscale (0-35)	23.1 ± 3.7	13.3 ± 6.2	<0.001	22 ± 5.2	7.1 ± 4.6	<0.001	<0.001
Global well-being (1-10)	2.5 ± 0.9	5.7 ± 2.0	<0.001	2.4 ± 0.9	7.6 ± 1.7	<0.001	<0.001





Time (days)	0	180	360	540	730
RFM	61	59	48	33	27
Control	88	79	51	28	16

0	180	360	540	730
61	55	46	32	25
88	72	51	36	23

Psikyatri

Fizyoterapist

Uyku bozuklukları

Kardiyolog

Hasta Yakınları

Endokrinolog

Diyetisyen

AileHekimi

Teşekkür ederim ….