Cryobalon ile AF Ablasyonu: Klinik Sonuçlar

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Kateter Ablasyon: Klinik sonuçlar

- Prosedürel ve Klinik başarı
  - İşlemsel başarı (PVI)
  - Nüksler
  - İzlemde başarı
    - AF'suz sağkalım
  - QoL

- Komplikasyonlar
- Mortalite
- önemli AE
  - Stroke / TİA /sessiz ?
  - Pulmoner stenoz
  - PNP
  - Tamponad / Pk efüzyon
  - Perforasyon / PV çevresi hematom/hemoptizi
  - Gastroparezi
- Vasküler hasarlar
  - Hematom
  - Retroperitoneal kanama
  - Psödoanevrizma
  - AV fistül

Neden Cryobalon Ablasyon: RFA etkinlik

- 63 RFA çalışması / toplam 8789 hasta
- Başarı oranları işlem sayısı ve AAD kullanımına göre değişmekte

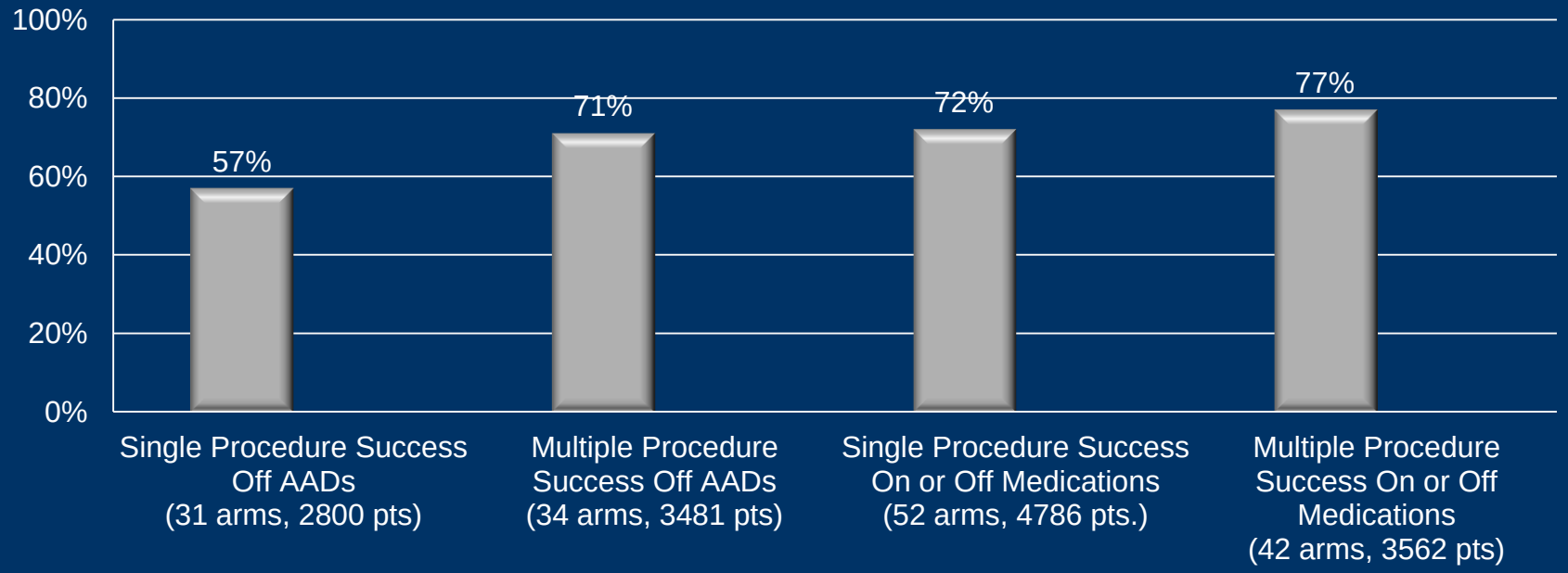
Ablasyon başarı oranları heterojen hasta grubuna göre değişmekte (PAF en başarılı):

PAF (69.8%), perAF (14.9%), long standing per AF (13.9%)

• Başarı oranları RFA ile AAD'lardan yüksek

• Adverse olaylar Ablasyonda daha AZ ama daha CİDDİ: 5% vs. 30% (RFA vs AAD)

RFA etkinliği (uzun dönem başarı)



Mean follow-up period was 14 mos. (2 -30 mos.) and blanking period ranged from 2 to 12 weeks.

Calkins H, et al. *Circ Arrhythmia Electrophysiol*. 2009; 2(4):349-61

Neden Cryobalon Ablasyon : RFA güvenlik

- 63 RFA çalışması / toplam 8789 hasta
- RFA bağlı majör komplikasyon: % 4,9
- En sık görülen komplikasyonlar:
  - PV stenozu (1.6%),
  - Kalp tamponadı (0.7%),
  - Perikardiyal efüzyon (0.6%),
  - Periprosedürel stroke (0.3%),
  - Periprosedürel GİA (0.2%)

Table 5. Safety Outcomes for Patients With AF Undergoing Catheter Ablation

Outcomes	t	n/N	%
Mortality			
Death overall	65	42/5781	0.7
Procedure-related	64	0/5192	0.0
Vascular access complications			
Arteriovenous fistula	32	1/2885	0.0
Bleeding	33	1/2960	0.0
Hematoma	38	17/3719	0.5
Pneumothorax	34	0/2974	0.0
Femoral artery pseudoaneurysm	34	15/3032	0.5
Periprocedure events			
Stroke, ischemic	62	17/5665	0.3
TIA	60	13/5467	0.2
Cardiac tamponade	63	45/5723	0.8
PE	60	3/5496	0.1
DVT	56	1/4758	0.0
Other embolism	57	10/5347	0.2
LA-esophageal fistula	60	0/5496	0.0
Other fistula	58	3/5407	0.1
Pericardial effusion	64	36/5719	0.6
PV stenosis*	65	91/5831	1.6
AV block	60	1/5496	0.0
CHF exacerbation	60	0/5496	0.0
Need for a pacemaker	46	4/3902	0.1
Total No. of patients with events	28	97/1964	4.9

t indicates No. of treatment groups; n, No. of patients with this adverse event; N, No. of patients evaluated in studies reporting this adverse event; %, percent of patients with adverse event of interest; TIA, transient ischemic accident; PE, pulmonary embolism; DVT, deep vein thrombosis; LA, left atrial; PV, pulmonary vein; AV, atrioventricular; CHF, congestive heart failure.

*>70% Stenosis (early, <7 days after ablation; late, >7 days after ablation).

Calkins H, et al. *Circ Arrhythmia Electrophysiol*. 2009; 2(4):349-61

AF kateter ablasyonu: RFA (referans)

Journal of the American Heart Association
OPEN ACCESS
American Heart Association | American Stroke Association

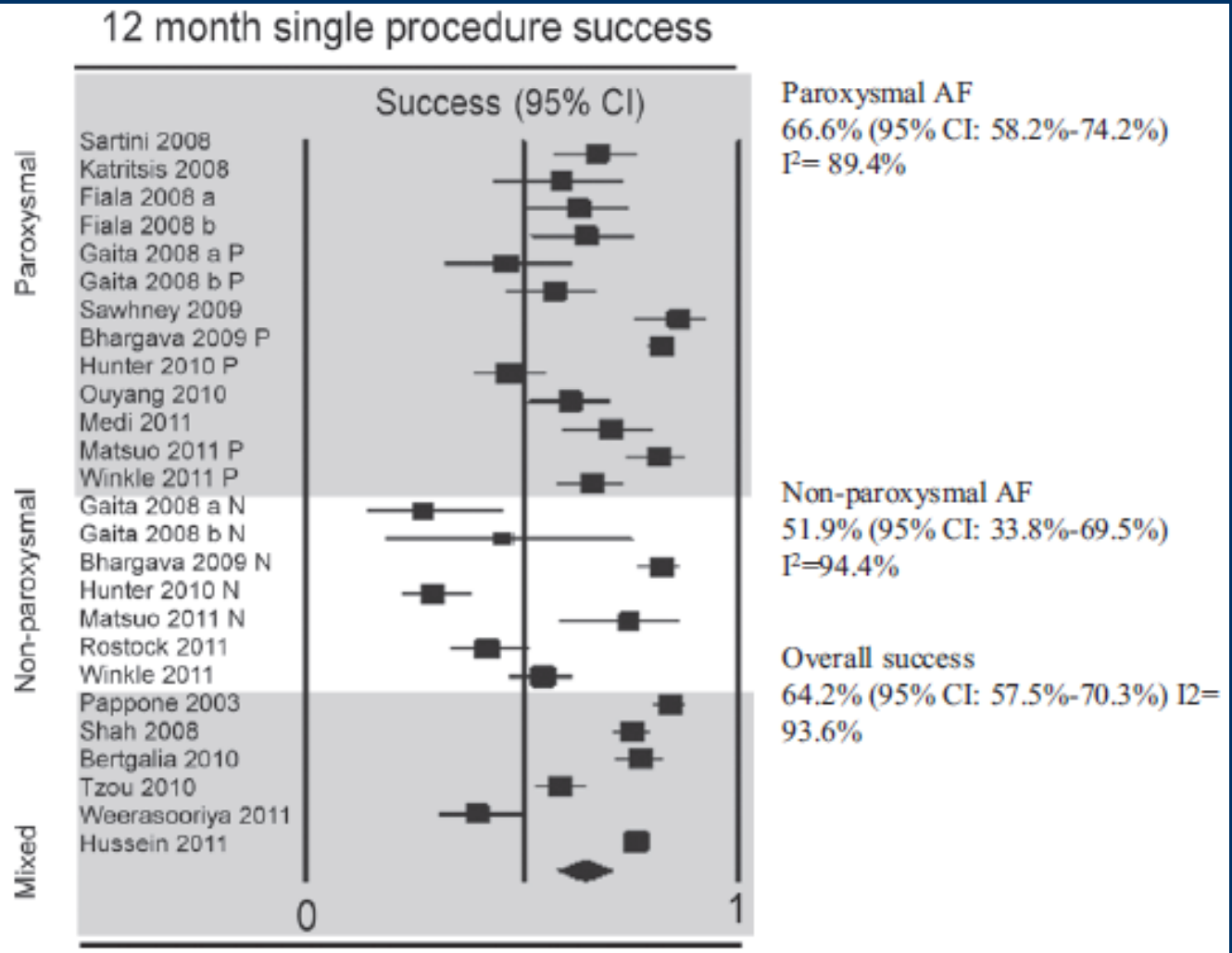
Long–term Outcomes of Catheter Ablation of Atrial Fibrillation: A Systematic Review and Meta –analysis

Anand N. Ganesan, Nicholas J. Shipp, Anthony G. Brooks, Pawel Kuklik, Dennis H. Lau, Han S. Lim, Thomas Sullivan, Kurt C. Roberts-Thomson and Prashanthan Sanders

J Am Heart Assoc 2013, 2:
doi: 10.1161/JAHA.112.004549
JAHA: Journal of the American Heart Association is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
Online ISSN: 2047-9980

19 çalışma; toplam 6167 hasta, ≥3 yıl takip

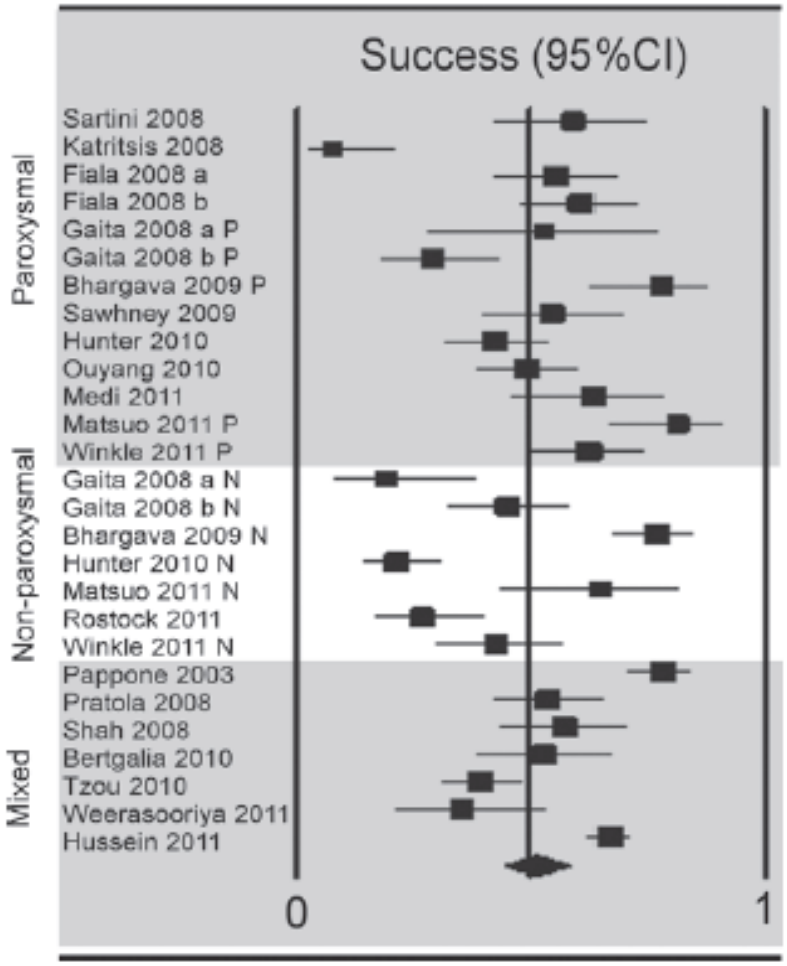
A



Fiala 2008 a – segmental pulmonary vein isolation arm; Fiala 2008 b Electroanatomic map guided ablation; Gaita 2009 a pulmonary vein isolation; Gaita 2009 b pulmonary vein isolation plus linear ablation.P = paroxysmal AF results for study. N= nonparoxysmal AF results for study. Single procedure success data for Shah et al., Bertaglia et al, and Tzou et al., were recalculated against original cohort size.

B

Late single procedure success



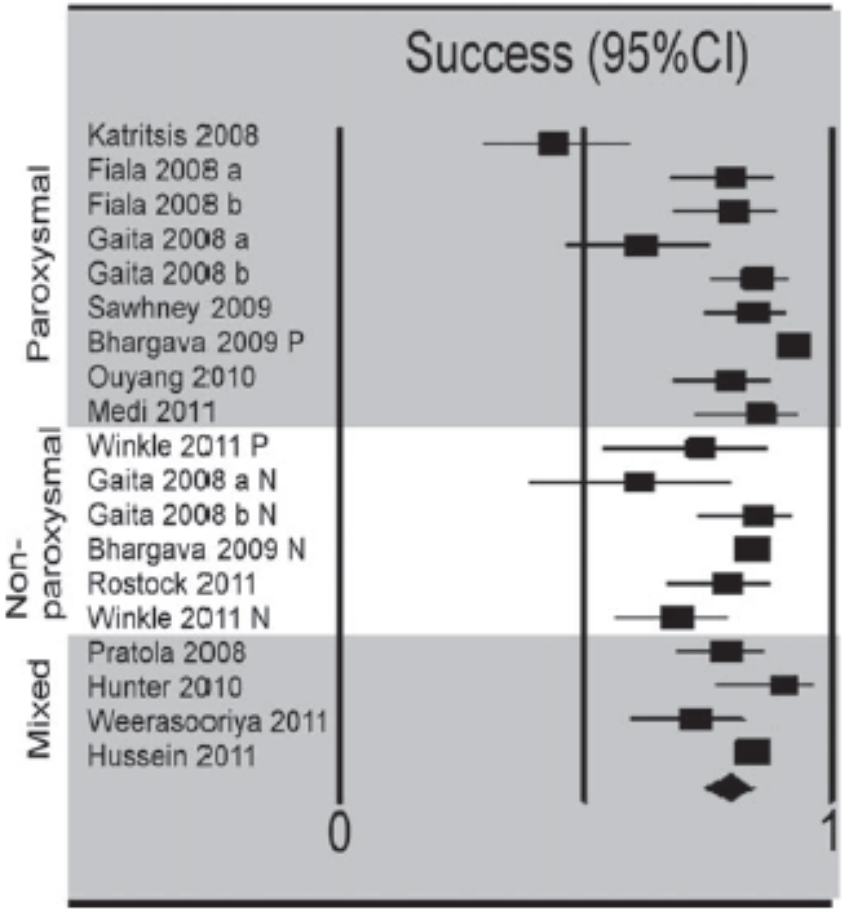
Paroxysmal AF
54.1% (95% CI:44.463.4%)
I^2= 79.1%

Non-paroxysmal AF
41.8% (95% CI: 25.2-60.5%)
I^2= 83.7%

Overall success
53.1% (95% CI: 46.2-60.0%)
I^2= 87.6%

Fiala 2008 a – segmental pulmonary vein isolation arm; Fiala 2008 b Electroanatomic map guided ablation; Gaita 2009 a pulmonary vein isolation; Gaita 2009 b pulmonary vein isolation plus linear ablation. P = paroxysmal AF results for study. N= nonparoxysmal AF results for study. Single procedure success data for Shah et al., Bertaglia et al, and Tzou et al., were recalculated against original cohort size.

Late multi-procedure success



Paroxysmal AF
79.0% (95% CI: 67.6%-87.1%)
I^2= 89.8%

Non-paroxysmal AF
77.8% (95% CI: 68.7-84.9%)
I^2= 71.9%

Overall success
79.8% (95% CI: 75.0-83.8%)
I^2= 83.9%

Fiala 2008 a – segmental pulmonary vein isolation arm; Fiala 2008 b Electroanatomic map guided ablation; Gaita 2009 a pulmonary vein isolation; Gaita 2009 b pulmonary vein isolation plus linear ablation.P = paroxysmal AF results for study. N= nonparoxysmal AF results for study

Neden Cryobalon Ablasyon

Hipotez: potansiyel avantajlar

- Endotel hasarlanması düşük → Düşük trombojenisite
  - Düşük serebral embolik olay riski
- Güvenlik → (antral ablasyon > segmental) Sadece circumferantial değil, geniş alan antral izolasyon sağlar (WACA)
  - Düşük PV stenozu riski
  - Düşük perforasyon riski
- PV antral ablasyon → Sade iyi-demarke olmuş yoğun ve homojen fibrozis gelişmesine yol açar. Bu lezyonlar aritmojenik olmadığı gibi altta yatan ekstrasellüler matriksi ve gerilim kuvvetini de korunur
  - Düşük AFLAT riski
- CryoAdherence → dokuya tutunma kateter stabilitesi sağlar ve istenmeyen komşu doku hasarlanmasını minimalize eder
  - Daha az floroskopi gereksinimi

Neden Cryobalon: Hipotez?

CBA teknolojisi işlem süresini azaltabilir ve özellikle;
lezyon bölgesinde trombüs oluşumu ile kateter travması ya da kateter/doku temas noktasında aşırı ısınmaya bağlı kardiyak perforasyon gibi RF kaynaklı komplikasyonları azaltabilir…

2001

First **percutaneous cryoablation** products in Europe. (Freezor® Focal Catheters)

2005

First Cryoballoon **in Europe** for the treatment of PAF (Arctic Front®)

2010

RCT: STOP-AF

US approval for Arctic Front

2011

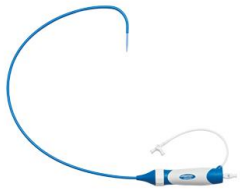
First EP catheter designed to be used with Arctic Front®: the Achieve® Mapping Catheter

2012

Arctic Front Advance™ Approval

Still the only **Cryoballoon** indicated for PAF

2013



FlexCath Advance™ Steerable Sheath

Cryobalon Ablasyon: Arctic Front (1.kuşak)

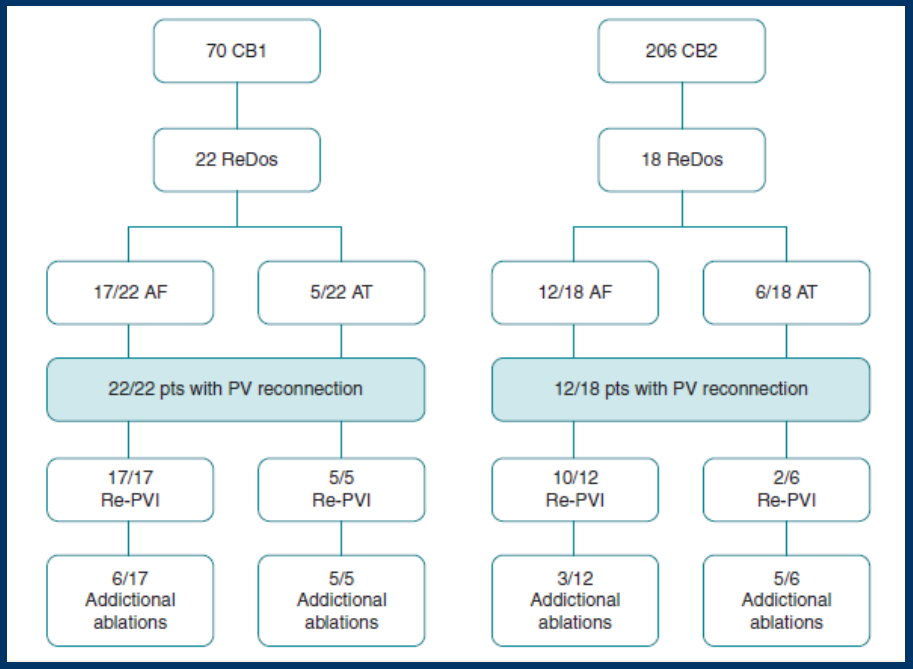
					Fu-time	N & hasta grubu	CBA PVI success	CBA Time (sn)	Touch-Up (%hasta)	Prcd time (dk)	Floro time (dk)	AF freedom w/o AAD (single)	2nd prcd. (% hasta)
Yves Van Belle	NL	2008	Europace	nonRCT - tek merkez	38 m	141 - PAF	**99,00%**	NA	Cryo- %39	207	50	**49,00%**	17,00%
Thomas Neumann	DE	2008	JACC	nonRCT - multicenter	12 m	346 - PAF	**97,00%**	240-360	Cryo- %16	170	40	**74,00%**	10,00%
Julian Chun	DE	2009	EHJ	nonRCT - tek merkez	9 m	27 - PAF	**98,00%**	300	NO	220	50	**70,00%**	NA
Kojodjojo	UK	2010	Heart	nonRCT- tek merkez	13 m	124 - PAF+perAF	**83,00%**	300	Cryo- %60	110	28	**77,00%**	14,00%
Pascal Defaye	FR	2011	Europace	nonRCT- tek merkez	9 m	117- PAF+perAF	**87,00%**	240	irgRF- %16	NA	NA	**68,00%**	NA
Jürgen Vogt	DE	2013	JACC	nonRCT - tek merkez	24 m	605 - PAF+perAF	**91,10%**	300-360	Cryo- NA	156	25,2	**74,90%**	38,40%
STOP-AF	NA	2013	JACC	RCT- multicenter	12 m	163 - PAF (163:82=245)	**83,00%**	240	Cryo- %16	371	63	**69,90%**	19,00%
Thomas Neumann	DE	2013	Europace	nonRCT- multicenter	**60 m**	163- PAF	**92,00%**	240-360	Cryo- %8	222	50,2	**53,00%**	NA
Maciej Woijcik	DE	2014	Rev Esp Cardiol	nonRCT- tek merkez	**60 m**	103- Lone PAF	**82,00%**	240-300	Cryo- %3,9	210	33	**77,00%**	NA

Cryobalon Ablasyon: Arctic Front (1.kuşak)

		Prc compl	Ölüm	Stroke	TİA	PV stenoz	PNP	Tampon ad	PK efüzyon	Hemo-PnöTx	Perfrsy.	Tx/kanama	hematom	psdAnvz AV fistül	Atr-Özf fistül
Yves Van Belle	2008	**NA**	0,00%	0,00%	NA	0,00%	**2,00%**	0,00%	5,00%	0,70%	0,00%	1,00%	0,07%	0,01%	0,00%
Thomas Neumann	2008	**NA**	0,00%	0,00%	NA	0,00%	**7,00%**	0,50%	NA	NA	NA	NA	1,40%	0,80%	0,00%
Julian Chun	2009	**11,00%**	0,00%	0,00%	NA	0,00%	**11,00%**	0,00%	NA	NA	0,00%	NA	NA	0,00%	0,00%
Kojodjojo	2010	**4,00%**	0,00%	0,00%	NA	0,00%	**0,16%**	0,00%	0,08%	NA	0,00%	NA	NA	0,00%	0,00%
Pascal Defaye	2011	**NA**	0,00%	0,00%	NA	0,00%	**3,00%**	0,01%	0,02%	0,01%	0,00%	NA	0,10%	0,00%	0,00%
Jürgen Vogt	2013	**NA**	0,00%	0,30%	0,0%	0,30%	**2,50%**	0,20%	0,20%	NA	0,00%	NA	NA	0,00%	0,00%
STOP-AF	2013	**3,10%**	0,00%	2,50%	1,8%	3,10%	**11,20%**	0,60%	NA	NA	0,00%	1,80%	NA	2,80%	0,00%
Thomas Neumann	2013	**NA**	0,00%	0,00%	0,6%	0,00%	**11,00%**	1,00%	2,00%	NA	0,00%	NA	2,50%	1,50%	0,00%
Maciej Woijcik	2014	**5,00%**	0,00%	0,00%	0,0%	0,00%	**4,80%**	0,90%	0,90%	0,00%	0,00%	0,00%	0,00%	0,00%	0,00%

CBA: 2. kuşak sonuçlar:

"Durability: nüks olguların incelemesi"



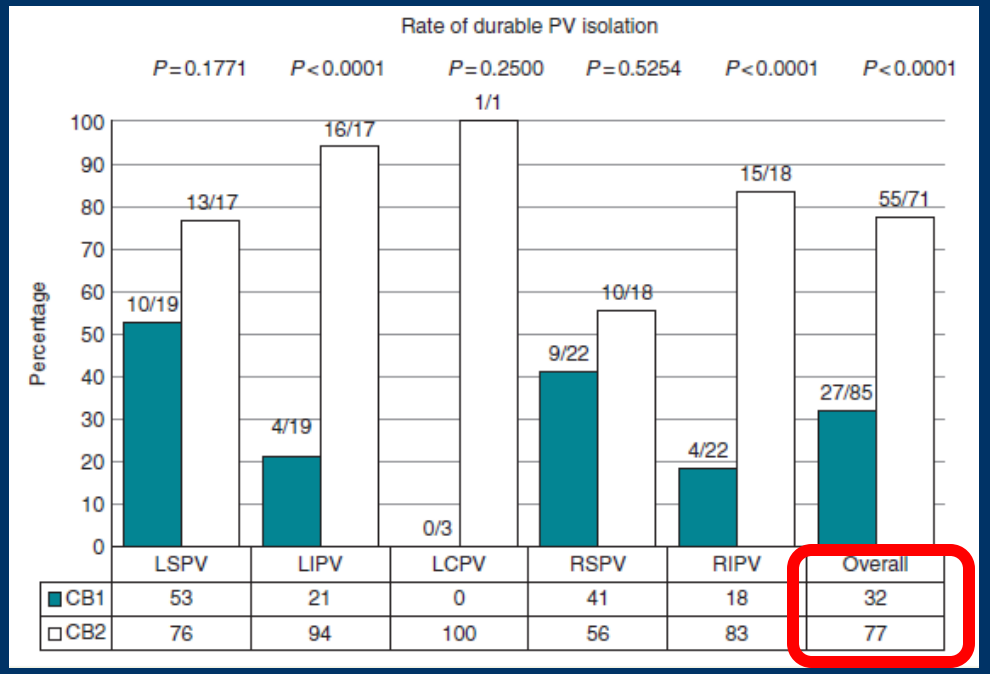


Table 2 Number of PVs reconnected per patient

	CB1 ($n = 22$)	CB2 ($n = 18$)	*P*-value
PVs reconnected per patient			
0	0/22	6/18	0.048
1	4/22	9/18	0.046
2	6/22	2/18	0.257
3	6/22	1/18	0.104
4	6/22	0/18	0.02
At least one PV reconduction	22/22	12/18	0.048

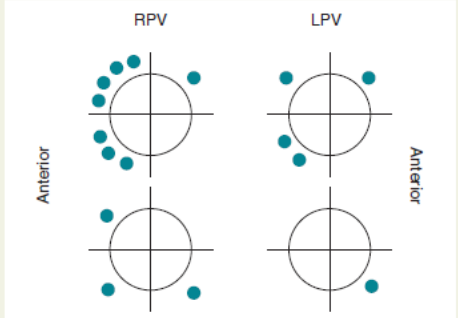
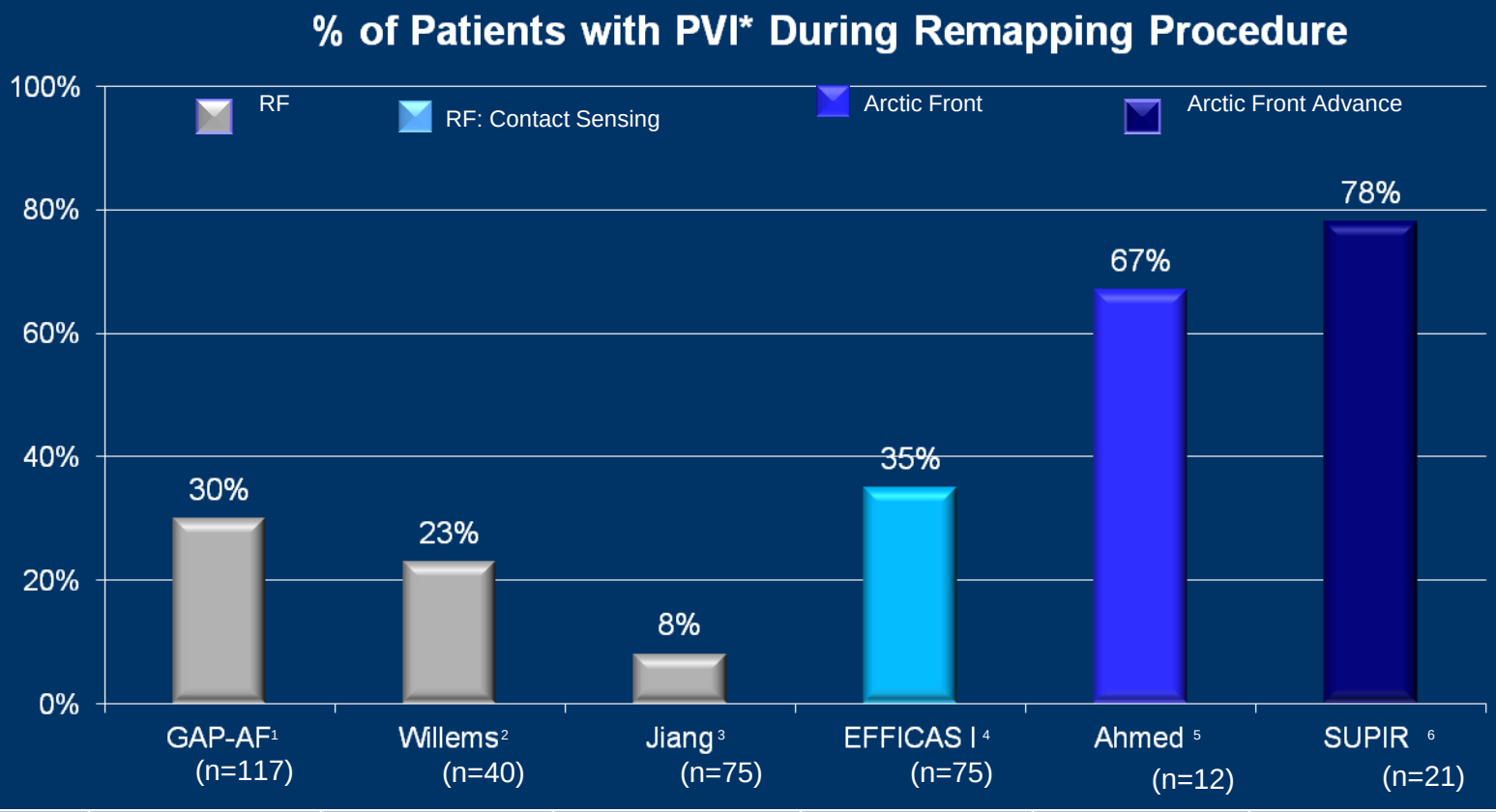


Figure 4 Spatial distribution of PV reconduction gaps in group CB2.

S. Bordignon, et al. Europace. 2014. doi:10.1093/europace/euu331

CBA vs RFA: PVI lezyon durability

Studies evaluating PV re-conduction using repeat electrophysiology and mapping after the index procedure



Follow-up**	3 Months	3 Months	12 months	3 months	3 months	3 months

**All 4 veins were isolated in invasive remapping procedure

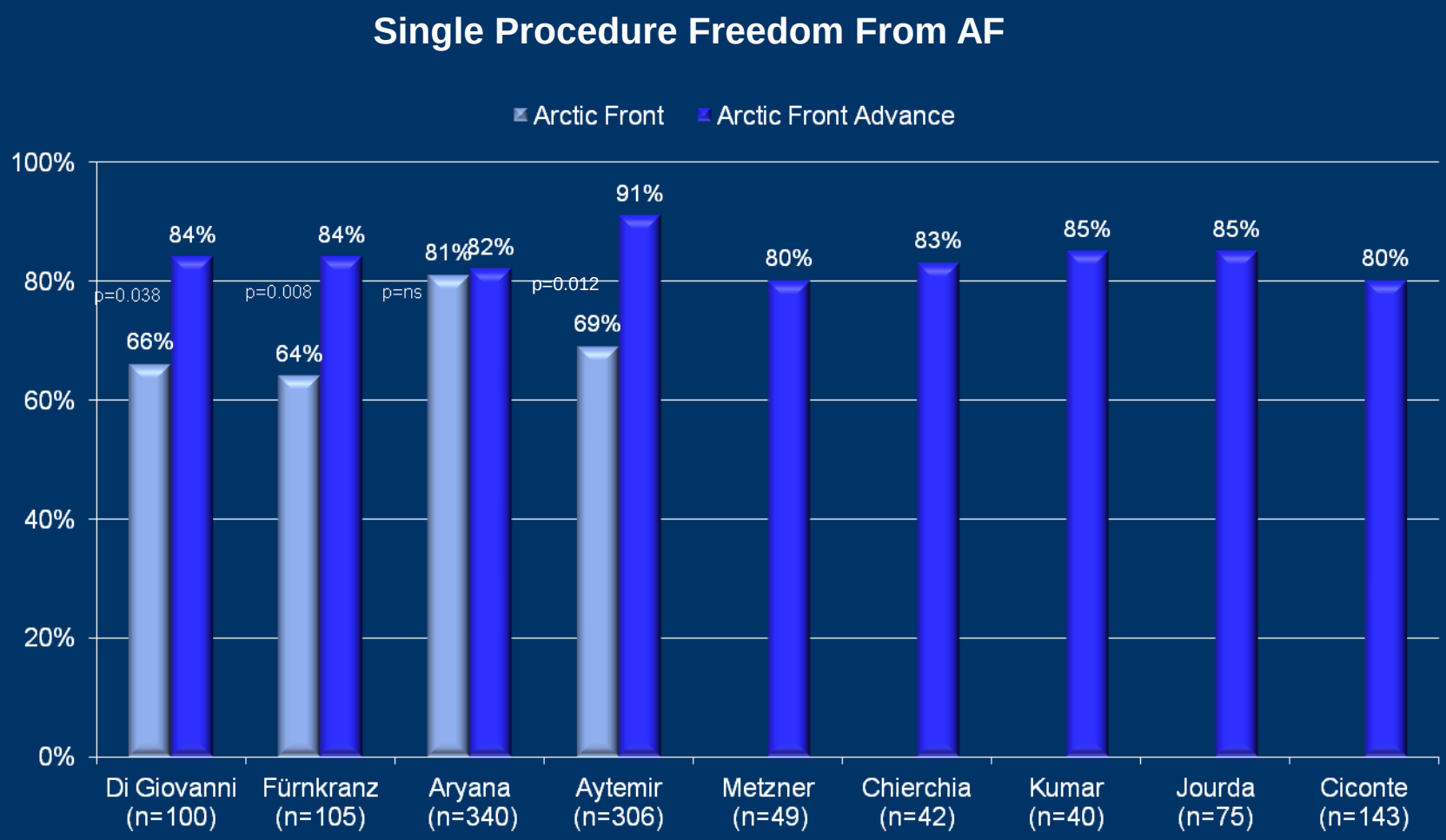
*Time between index procedure and re-mapping procedure. All patients were evaluated regardless of clinical symptoms

[1]Late Breaking Clinical Trials session I at the EHRA EUROPACE 2013 meeting in Athens, Greece [2] Williems, et al. J Cardiovasc Electrophysiol 2010; 21(10):1079-84. [3] Jiang, et al. Heart Rhythm. 2014;11(6):969-76 [4] Neuzil et al. Circ Arrhythm Electrophysiol.(2):327-33 [5] Ahmed, et al. J Cardiovasc Electrophysiol, 2010;21(7):731-7, [6] Petru, et al. International Symposium on Progress in Clinical Pacing 2014

CBA: 1. vs 2. kuşak sonuçlar:

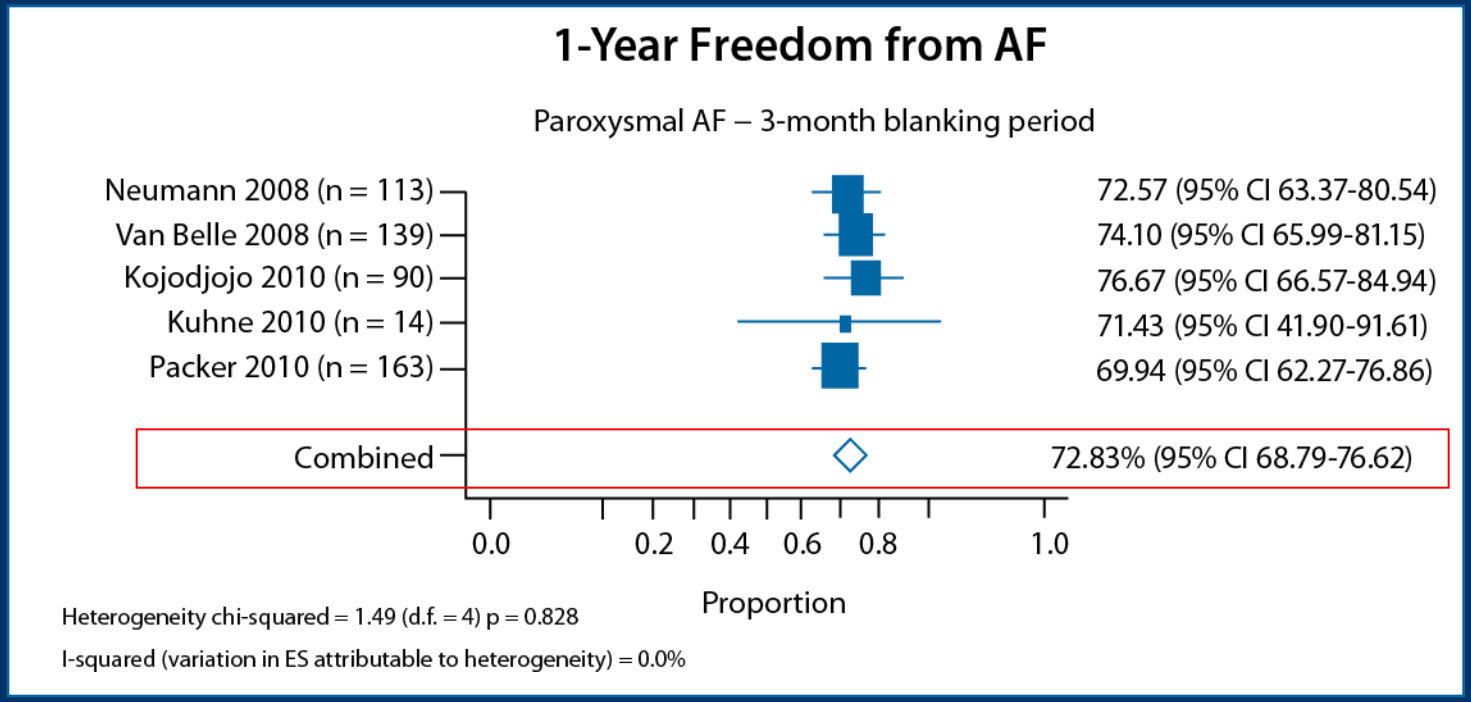
Achieve !			N	Fu-time	CBA time (sn)	Single CBA success		Erken Nüks		AF freedom w/o AAD (single)		komplikasyon	
						1.kuşak CB	2.kuşak CB-A	1.kuşak CB	2.kuşak CB-A	**1.kuşak CB**	**2.kuşak CB-A**	1.kuşak CB	2.kuşak CB-A
A. Metzner	2014	JCE	50	36 m	240 +bonus	NA	**99 %**	NA	20 %	**NA**	**80 %**	NA	**2 %**
G.Chierchia	2014	EP	42	11 m	240 +bonus	NA	**100 %**	NA	22 %	**NA**	**78 %**	NA	**7 %**
A. Fürnkranz	2013	JCE	60	3 m	300 vs 240	100 %	**100 %**	37 %	13 %	**NA**	**NA**	6,6 %	**3,3 %**
G.Di Giovanni	2014	JCE	100	12 m	240	98 %	**100 %**	18 %	6 %	**66 %**	**84 %**	10 %	**18 %**
F. Straube	2014	CAE	484	NO	300 vs 240	99 %	**100 %**	NA	NA	**NA**	**NA**	3,3 %	**3,3 %**
J. Liu	2015	Pace	125	12 m	NA	87,7 %	**92,7 %**	NA	NA	**59,7 %**	**89,7 %**	0 %	**8,8 %**
K. Aytemir	2015	EP	306	22 m	240 vs 300	99,5 %	**99,5 %**	18,2 %	11,0 %	68,5 %	**90,8 %**	**2,5 %**	**8,2 %**
A.Aryana	2014	JICE	340	16 m	NA	92,0 %	**98,0 %**	NA	NA	81 %	**82,0 %**	**12,1 %**	**18,0 %**

CB-A: Tek merkezli çalışmalarda orta-uzun dönem başarı



Di Giovanni, et al. *J Cardiovasc Electrophysiol.* 2014; 25(8):834-9 , Fürnkranz, et al. *Journal of Cardiovascular Electrophysiology 2014 ;*25(8):840-4, Aryana, et al. *J Interv Card Electrophysiol* 2014; In Press, Aytemir, et al. 2014; *Europace*; In Press, Metzner, et al. *Circ Arrhythm Electrophysiol.* 2014; 7(2):288-292 , Chierchia, et al. *Europace* 2014; 16(5):639-644, Kumar et al. *J Interv Card Electrophysiol* 2014; In Press, Jourda, et al. *Europace* 2014; In Press, Ciconte, et al. *Heart Rhythm*, In Press

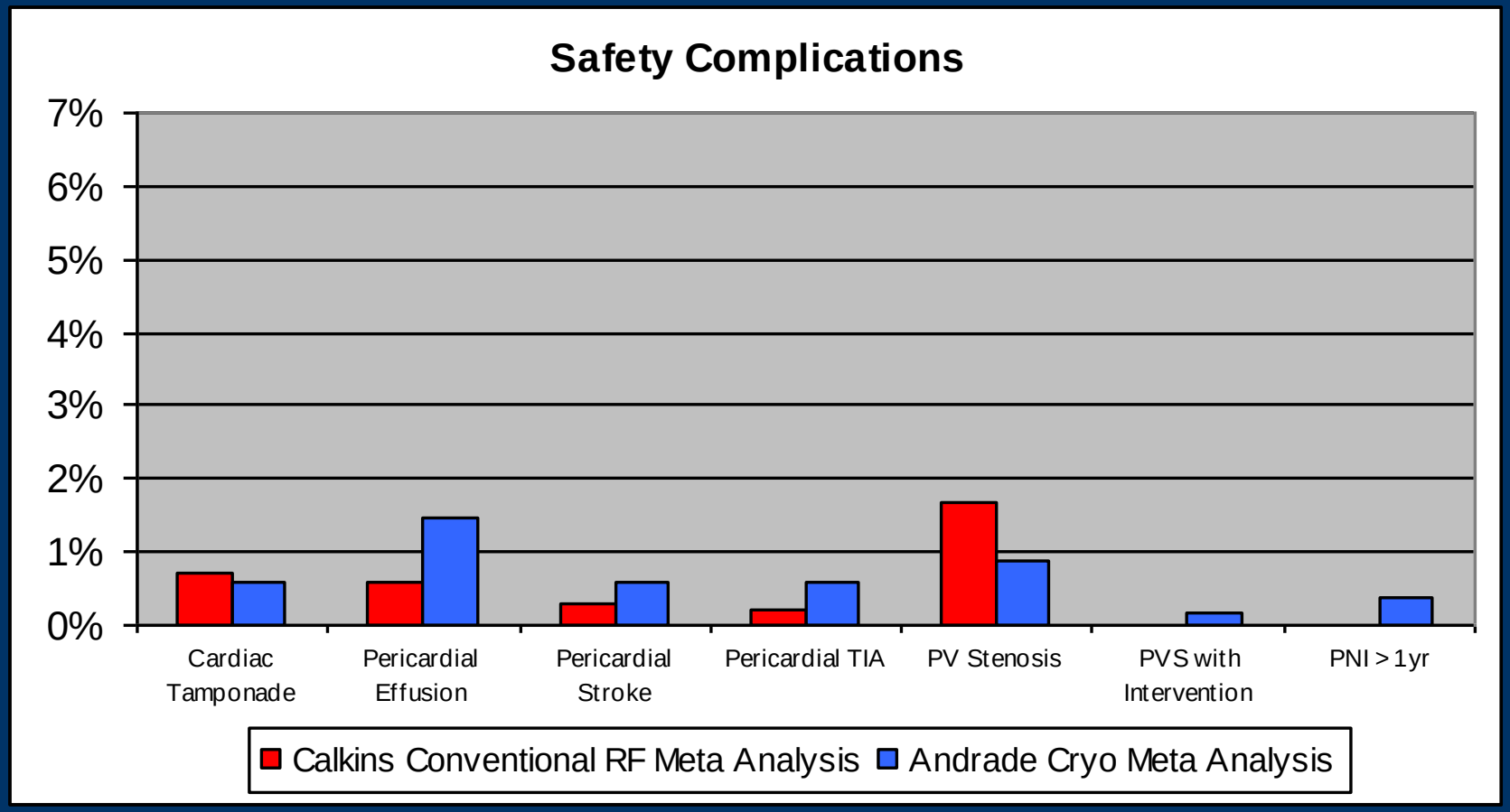
CBA vs RFA: meta-analizler



- Andrade, et al: 23 makale analizi
- Etkinlik:
  - Akut işlem başarısı: % 98
  - 12 aylık AFsiz hayat: % 72,8 (blanking+)
  - PAF nedeniyle RFA/CBA yapılanlarda 6-12 ay nüks oranları benzer

Andrade JG, Khairy P, Guerra PG, et al. Efficacy and Safety of Cryoballoon Ablation for Atrial Fibrillation – A Systematic Review of Published Studies. *Heart Rhythm*. 2011.

CBA vs RFA: meta-analizler



- Güvenlik:
  - RFA ile kıyaslanabilir ölçüde

[1] Andrade JG, et al. *Heart Rhythm*. Published online March 30, 2011.

[4] Calkins H, et al. *Circ Arrhythm Electrophysiol*. August 2009;2(4):349-361.

CBA vs RFA: meta-analizler

	n/N	%
Phrenic Nerve Palsy (PNP)		
Any reported PNP	86/1,349	6.38%
PNP persisting post-procedure	67/1,349	4.73%
PNP persisting > 1 year	5/1,349	0.37%
Pulmonary Vein Stenosis (PVS)		
Any PVS (per patient)	7/773	0.90%*
PVS requiring intervention	2/1,163	0.17%
Periprocedure events		
Stroke or TIA	4/1,241	0.32%
Myocardial infarction	3/1,231	0.24%†
LA-esophageal fistula	0/1,298	0.00%
Esophageal ulceration	6/116	5.17%‡
Pericardial effusion or tamponade	18/1,231	1.46%
Cardiac tamponade	7/1,231	0.57%
Pulmonary rupture	1/1,231	0.08%

* Studies reporting systematic screening for PVS with non-invasive imaging
† Two were transient due to air embolism and resolved without sequelae
‡ Outcome reported in three studies of systematic endoscopy post Cryoballoon ablation

Andrade JG, Khairy P, Guerra PG, et al. Efficacy and Safety of Cryoballoon Ablation for Atrial Fibrillation – A Systematic Review of Published Studies. *Heart Rhythm*. 2011.

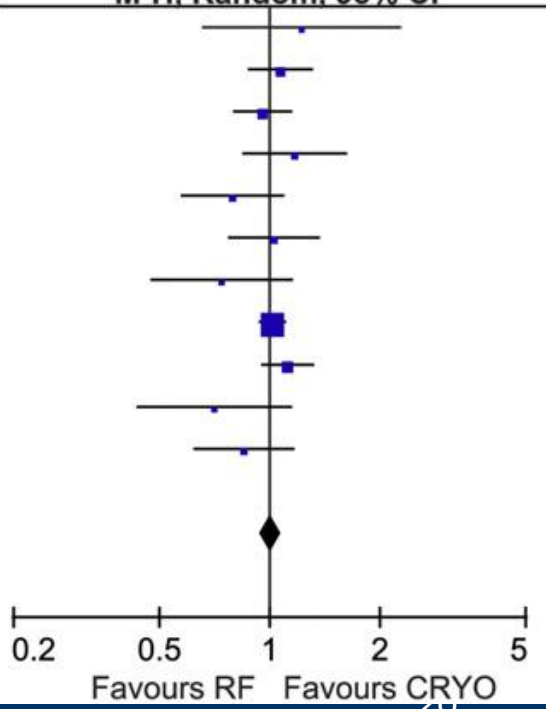
CBA vs RFA: meta-analizler

- The long-term efficacy of cryoballoon vs irrigated radiofrequency ablation for the treatment of atrial fibrillation: A meta-analysis
  - 11 makale, 1216 hasta,
  - **ort 16,5 ay izlemde AFsiz hayat: %66,9 vs & %65,1**

Study or Subgroup	CRYO Events	CRYO Total	RF Events	RF Total	Weight	Risk Ratio M-H, Random, 95% CI
Linhart 2009	11	20	9	20	1.1%	1.22 [0.65, 2.29]
Kojodjojo 2010	69	90	38	53	9.7%	1.07 [0.87, 1.31]
Kühne 2010	22	25	23	25	11.6%	0.96 [0.79, 1.15]
Sorgente 2010	23	30	19	29	3.9%	1.17 [0.84, 1.63]
Herrera 2012	19	30	24	30	4.0%	0.79 [0.57, 1.10]
Maagh 2013	22	30	30	42	5.0%	1.03 [0.77, 1.37]
Pokushalov 2013	17	40	23	40	2.1%	0.74 [0.47, 1.16]
Mandell 2013	59	62	58	62	42.5%	1.02 [0.93, 1.11]
Mugnai 2014	86	136	147	260	14.1%	1.12 [0.95, 1.32]
Pérez-Castellano 2014	12	25	17	25	1.8%	0.71 [0.43, 1.15]
Knecht 2014	34	71	40	71	4.2%	0.85 [0.62, 1.17]
Total (95% CI)		**559**		**657**	**100.0%**	**1.01 [0.94, 1.07]**
Total events	374		428			

Heterogeneity: Tau² = 0.00; Chi² = 10.54, df = 10 (P = 0.39); I² = 5%

Test for overall effect: Z = 0.16 (P = 0.87)



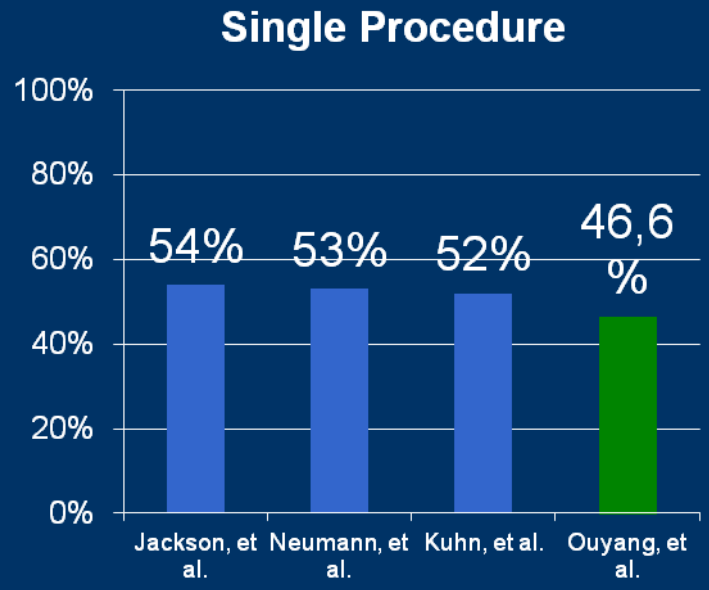
X. Cheng,et al. 2015. International Journal of Cardiology 181 (2015) 297–302

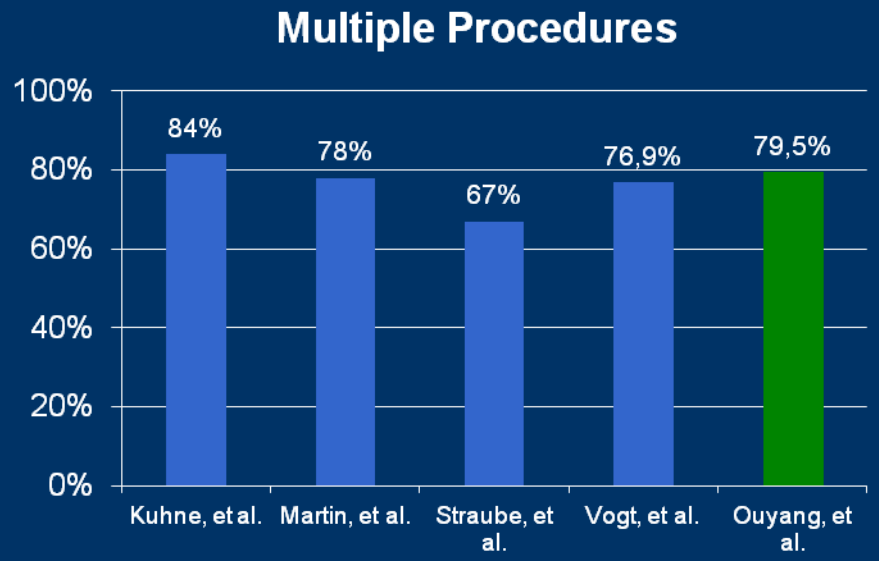
CBA vs Diğer Ablasyon Yöntemleri

					Fu-time	PVI		Komplikasyon		nüks		AFsiz Hayat	
						CBA	Comp.	CBA	Comp.	CBA	Comp.	CBA	Comp.
H.Malmbörg	2013	EP	110-PAF	CBA vs PVAC	12 m	**98 %**	93 %	**8 %**	2 %	NA	NA	46 %-60	34 %-54
L. Koch	2012	EP	32-PAF	CBA vs Mesh	inHo.	**76,5 %**	0 %	**5,9 %**	6,7 %	11,8 %	46,7 %	NA	NA
P. Maagh	2013	IJMS	119-AF	CBA vs Mesh	24 m	**92,3 %**	94,8 %	**NA**	NA	NA	NA	45 %	42,9 %
G. Mugnai	2014	AJC	396-PAF	CBA vs RFA	23 m	**96 5**	100 %	**8,1 %**	10 %	NA	NA	63,2 %	57,3 %
G. Ciconte	2015	EP	**100-perAF**	CBA vs RFA	12 m	100 %	100 %	3 %	4 %	47 %	52 %	60 %	56 %

CBA:

multiple prosedür ve uzun dönem AFsiz hayat





Measure	Vogt[1]	Neumann[2]	Straube[3]	Martin[4]	Jackson[5]	Kuhne[6]	Ouyang[7]
Median Follow-up	33 months	60 months	23 months	23 months	27 months	48 months	55 months
Freedom from AF	76.9%[a]	53%[b]	67%[a]	78%[a]	54%[b]	52%[b], 84%[a]	46.6%[b],79.5%[a]
Energy Source	Cryo	Cryo	Cryo	Cryo	Cryo	Cryo	RF

All referenced studies show long-term outcomes of paroxysmal AF patient population (references on next slide)

[a] Freedom from AF post multiple ablation procedures [b] Freedom from AF post single ablation procedure

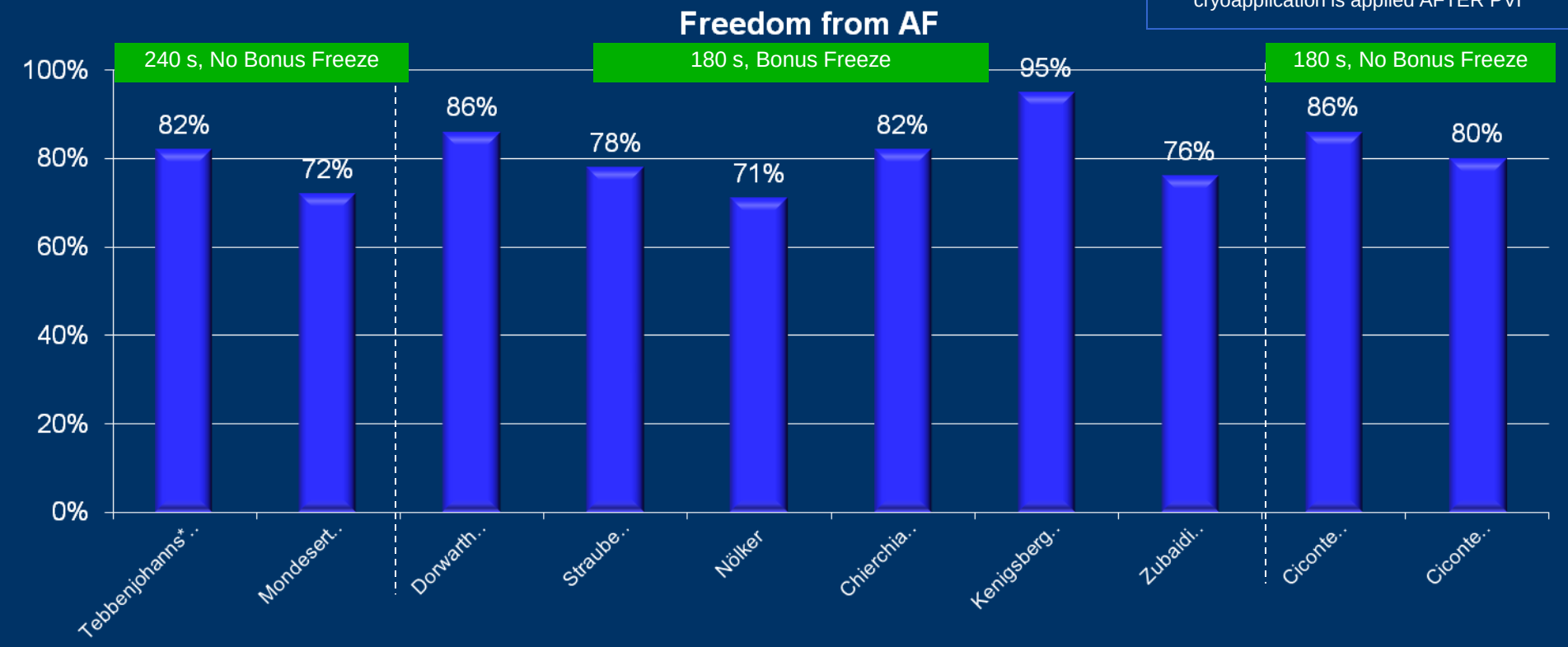
1. Vogt et al. Long-Term Outcomes After Cryoballoon Pulmonary Vein Isolation: Results From a Prospective Study in 605 Patients. JACC Volume 61, Issue 16, 23 April 2013, Pages 1707–1712
2. Neumann et al. Cryoballoon ablation of paroxysmal atrial fibrillation: 5-year outcome after single procedure and predictors of success. Europace, February 2013, doi:10.1093/europace/eut021
3. Straube, et al. Long-Term Results for Cryo Balloon Ablation: Single Center Large Experience From the Initial Cohort 2007 to 2010. PO01-134.
4. Martin, et al. Long-Term Outcome After Cryoballoon Pulmonary Vein Isolation: Retrospective Analysis in 239 Patients. HRS Poster Presentation PO03-54.
5. Jackson, et al. Freedom From Atrial Fibrillation Four Years After Cryoballoon Ablation. HRS Poster Presentation PO05-127
6. Kuhne, et al. 4-Year Follow-up After Ablation of Paroxysmal Atrial Fibrillation: Cryoballoon Versus Radiofrequency Catheter Ablation. HRS Poster Presentation PO04-62.
7. Ouyang, et al. Long-Term Results of Catheter Ablation in Paroxysmal Atrial Fibrillation: Lessons From a 5-Year Follow-up. Circulation, 2010; 122:2368-2377.

CBA: özel durumlar

2. Kuşak CB-A ile Dondurma süreleri:

Treatment Times Less than 240s or No Bonus Freeze with

Bonus Freeze= An additional cryoapplication is applied AFTER PVI



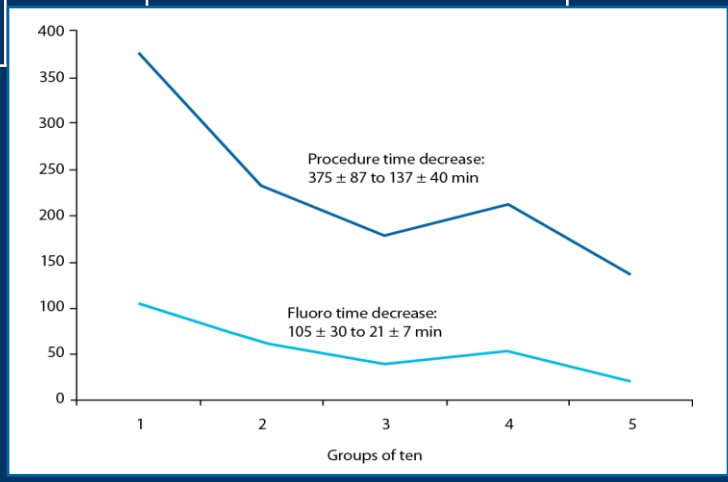
Application	240s No Bonus* Freeze	240s No Bonus Freeze	180s Bonus Freeze	180s Bonus Freeze	180s Bonus Freeze	180s Bonus Freeze	180 Bonus Freeze	TTE+ 2 Min Bonus Freeze 120s	180s No Bonus Freeze*	180s No Bonus Freeze
Follow-up	6 Months	4 months	6 months	6 months	6.4 months	5.7 months	6 months	12 months	7 months	12 months

*In patients where adenosine administration did not reveal dormant muscular sleeves

[1] Tebbenjohanns, J. et al Cardiostim 2014 Abstract, [2] Mondesert, et al. Cardiostim 2014 Abstract, [3] Dorwarth, et al. AF Symposium poster. BAF2014-30156, [4] Straube, et al. PO05-90. Heart Rhythm Society Meeting 2014, [5] Nölker [et] et al. Circulation 2014, [6] Chierchia GB, *J Interv Card Electrophysiol*. 2014;39(2):145-51, [7] Kenigsberg, et al. Heart Rhythm 2014; In press [8] Zubaidi, et al. *Circulation*. 2013;128:A17085, [9] Ciconte G, *J Cardiovasc Electrophysiol* 2014; In Press, Ciconte, G, *Heart Rhythm*,In Press

CBA: Learning Curve

Study	Procedure Time (minutes) Early	Late	p	Fluoroscopy Time (minutes) Early	Late	p	Balloon Applications Early	Late	p
Van Belle 2007[1]	375 ± 87	137 ± 40	< 0.10	105 ± 30	21 ± 7	< 0.01	145	60	< 0.01
Kühne 2010[2]	199 ± 56	152 ± 18	0.047	73 ± 30	42 ± 12	< 0.01			
Tang 2010[3]	191.4 ± 51.5	132.1 ± 23.1	< 0.01	44.4 ± 11.3	26.21 ± 10.9	0.17			



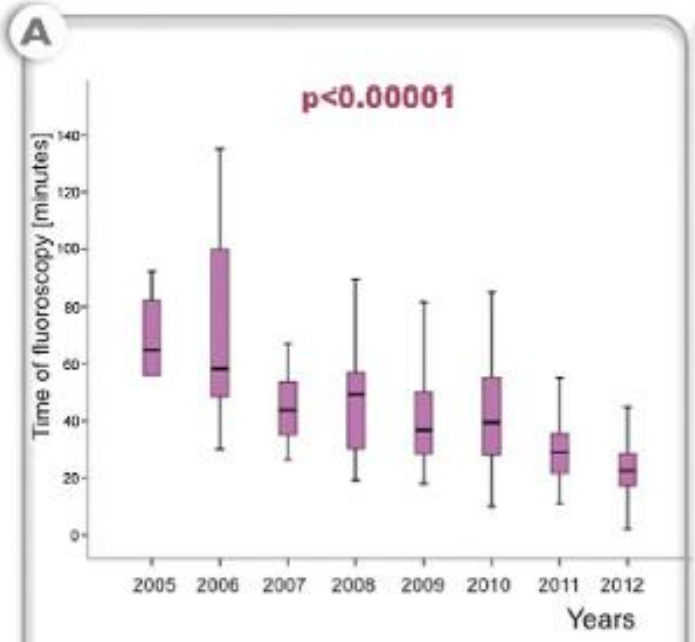
Andrade JG. *Heart Rhythm*. 2011.

[1] Van Belle Y, et al. *Eur Heart J*. 2007;28:2231-2237.

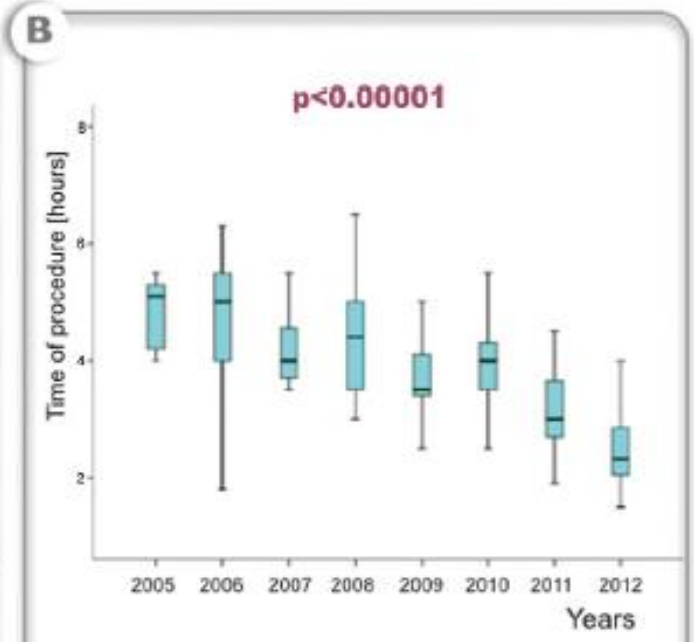
[2] Kühne M, et al. *Swiss Med Wkly*. 2010;140:214-221.

[3] Tang M, et al. *J Cardiovasc Electrophysiol*. 2010;21:626-631.

CBA: Learning Curve



Year	Fluoroscopy Time in minutes		
	25%	50%	75%
2005	55.90	64.70	82.00
2006	48.50	58.20	100.00
2007	35.15	43.80	53.60
2008	30.30	49.30	57.00
2009	28.50	36.80	50.00
2010	28.00	39.50	55.00
2011	21.77	29.00	35.50
2012	17.27	22.58	28.53



Year	Procedure time in hours		
	25%	50%	75%
2005	4.20	5.10	5.30
2006	4.00	5.00	5.50
2007	3.70	4.00	4.55
2008	3.50	4.40	5.00
2009	3.40	3.50	4.10
2010	3.50	4.00	4.30
2011	2.70	3.00	3.65
2012	2.05	2.32	2.85

M. Wojcik, et al. Circ Journal. 2014;78:1612

CBA: Learning Curve

Table 2. Incidence of Complications

Complications per year	Vascular complications n (%)	Cardiac tamponade n (%)	Pericardial effusion n (%)	PNP n (%)	All complications n (%)
2005, n=14	0	0	1 (7.14)	1 (7.14)	2 (14.28)
2006, n=52	1 (1.92)	1 (1.92)	2 (3.84)	3 (5.77)	7 (13.46)
2007, n=24	1 (4.17)	0	0	0	1 (4.17)
2008, n=25	0	0	0	2 (8.00)	2 (8.00)
2009, n=69	0	1 (1.45)	0	3 (4.35)	4 (5.80)
2010, n=53	0	1 (1.89)	1 (1.89)	2 (3.77)	4 (7.55)
2011, n=70	0	0	0	4 (5.71)	4 (5.71)
2012, n=117	0	0	0	11 (9.40)	11 (9.40)
CB, n=42	0	0	0	2 (4.76)	2 (4.76)
CBA, n=75	0	0	0	9 (12.00)	9 (12.00)
All, n=424	2 (0.47)	3 (0.71)	4 (0.94)	26 (6.13)	35 (8.25)

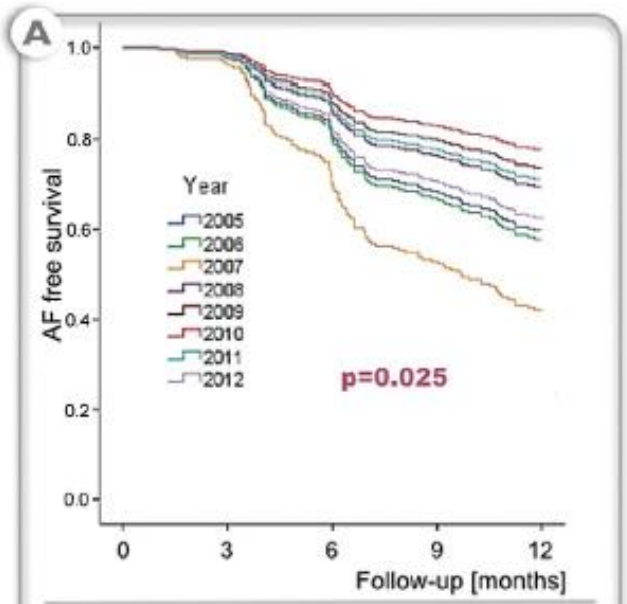
CB, cryoballoon; CBA, cryoballoon ablation; PNP, phrenic nerve palsy.

T. Neuman nekibi. 8 yıllık CBA tecrübesi

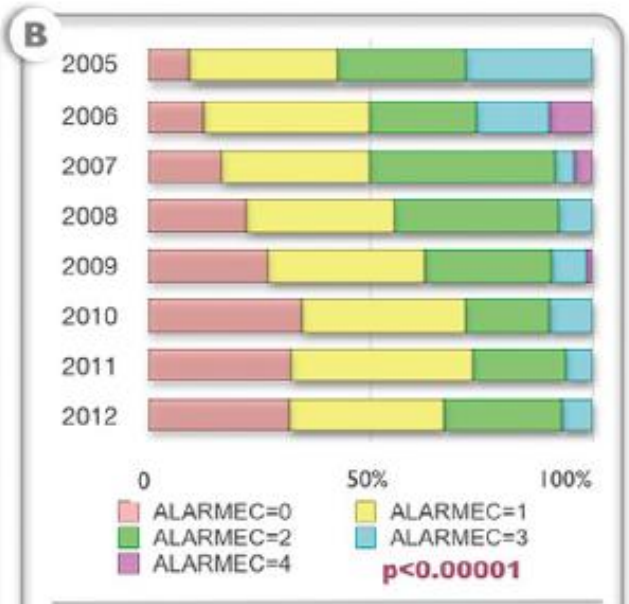
M. Wojcik, et al. Circ Journal. 2014;78:1612

CBA: Learning Curve

Hangi hastayı seçelim ?



Year	Outcome at 12 months FU: AF-recurrence	SR	Total
2005	6 (43%)	8 (57%)	14
2006	22 (42%)	30 (58%)	52
2007	14 (58%)	10 (42%)	24
2008	8 (32%)	17 (68%)	25
2009	19 (28%)	50 (72%)	69
2010	11 (21%)	42 (79%)	53
2011	19 (27%)	51 (73%)	70
2012	16 (14%)	101 (86%)	117
Total	**115 (27%)**	**309 (73%)**	**424**

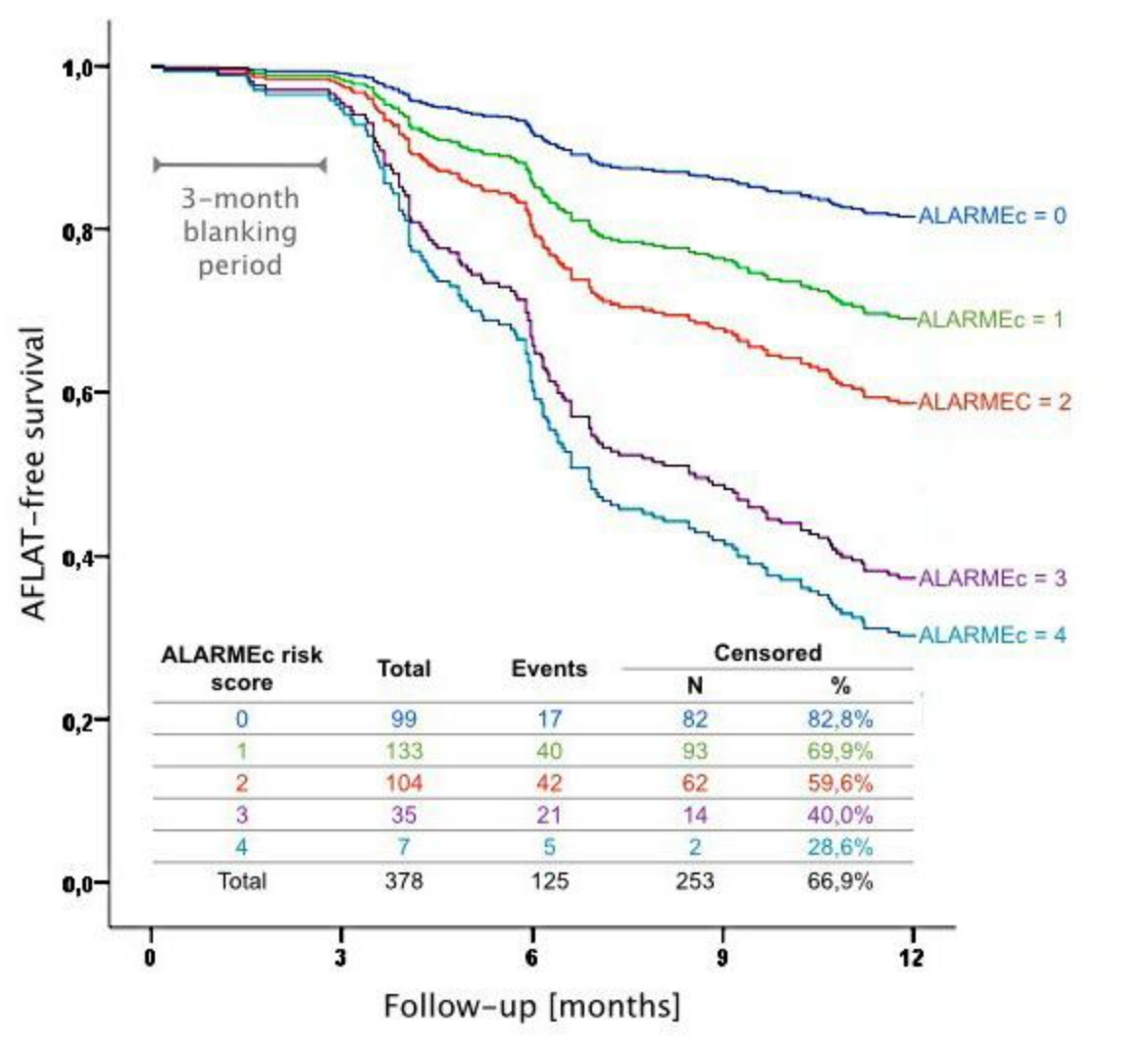


Year	ALARMEC risk score: 0	1	2	3	4	Total
2005	2 (14%)	5 (36%)	4 (29%)	3 (21%)	0	14
2006	7 (14%)	19 (36%)	12 (23%)	9 (17%)	5 (10%)	52
2007	4 (17%)	8 (33%)	10 (42%)	1 (4%)	1 (4%)	24
2008	6 (24%)	8 (32%)	10 (40%)	1 (4%)	0	25
2009	19 (28%)	25 (36%)	19 (28%)	5 (7%)	1 (2%)	69
2010	19 (36%)	19 (36%)	9 (17%)	6 (11%)	0	53
2011	25 (36%)	26 (37%)	16 (23%)	3 (4%)	0	70
2012	37 (32%)	39 (33%)	32 (27%)	8 (7%)	1 (1%)	117
Total	**119 (28%)**	**149 (35%)**	**112 (27%)**	**36 (8%)**	**8 (2%)**	**424**

Figure 3. (**A**) The gradual improvement in 1-year atrial fibrillation (AF)-free survival in each subsequent year was associated with (**B**) the gradual fall in Atrial fibrillation type, Left Atrium size, Renal insufficiency, Metabolic syndrome, cardiomyopathy (ALARMEc) risk score in successive patients in consecutive years.

M. Wojcik, et al. Circ Journal. 2014;78:1612

CBA: Learning Curve



ALARMEc risk score	Total	Events	Censored	
			N	%
0	99	17	82	82,8%
1	133	40	93	69,9%
2	104	42	62	59,6%
3	35	21	14	40,0%
4	7	5	2	28,6%
Total	378	125	253	66,9%

M. Wójcik. Et al.Cardiology Journal.2015

Erken CBA ?

- M. Namdar,et al. Isolating the pulmonary veins as first-line therapy in patients with lone paroxysmal atrial fibrillation using the Cryoballoon. Europace.2012: 14, 197–203

- 18 Lone PAF → 14 ay takipte % 89 AFsiz hayat !

About the Cryo-FIRST Trial

The Cryo-FIRST trial is led by principal investigators Dr. Malte Kuniss of the Kerckhoff-Klinik Heart Center, and Dr. Gian Battista Chierchia, of the Heart Rhythm Management Centre, UZ Brussel-VUB. It is a multicenter, prospective, randomized study designed to assess the procedural feasibility and clinical outcomes of patients undergoing cryoballoon ablation as a first-line treatment for PAF as compared to antiarrhythmic drugs.

CBA: özofagus

- A. Fürnkranz,et al.Esophageal Endoscopy Results After Pulmonary Vein Isolation Using the Single Big Cryoballoon Technique. JCEp.2010:21
  - 38 CBA + Luminal özfg. Isı takibi
  - 3 aylık f-up: Endoskopi: ETL (özfg termal lezyon) Ø AÖF Ø

- A. Metzner,et al. Increased Incidence of Esophageal Thermal Lesions Using the Second-Generation 28-mm Cryoballoon.CAE.2013:6
  - 50 CBA (2.kuşak CB-A) + Luminal özfg. Isı takibi
  - 2. günde Endoskopi: % 12 ETL + (prosedürel özfg ıs < 3.0 °C)
  - 7. günde Endoskopi: hepsi iyileşmekte

- Atriyo Özofageal Fistül
  - F. Stöckigt,et al.JCEp.2012:23 → İlk olgu. CBA sonrası 4. Hafta.Nöro sekelle taburcu.
  - H.W. Lim.,et al. JCEp.2014:25 → CBA sonrası 4. Hafta. Fatal.
  - R. Kawasaki, et al. JCEp.2014:25 → 3 fatal olgu

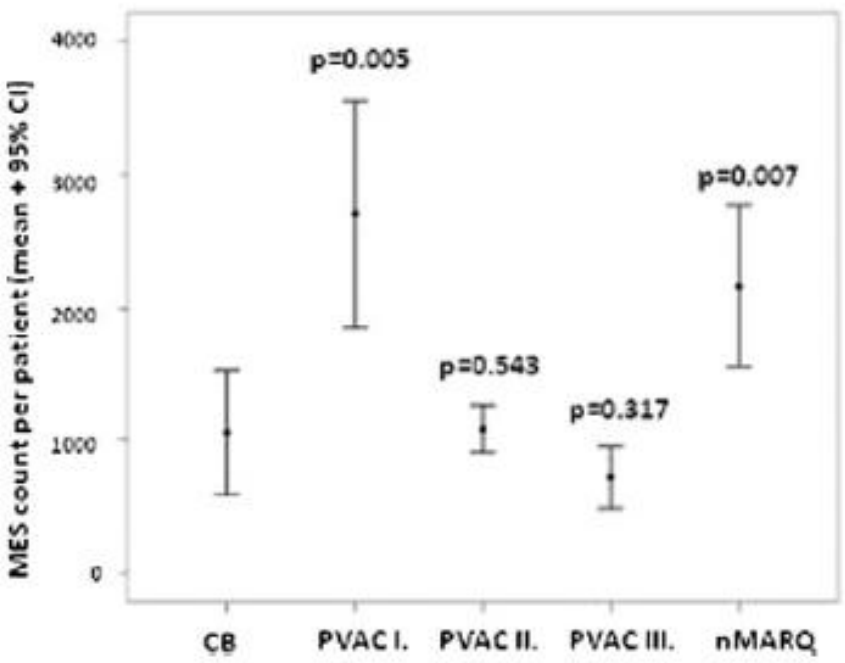
CBA: PNP

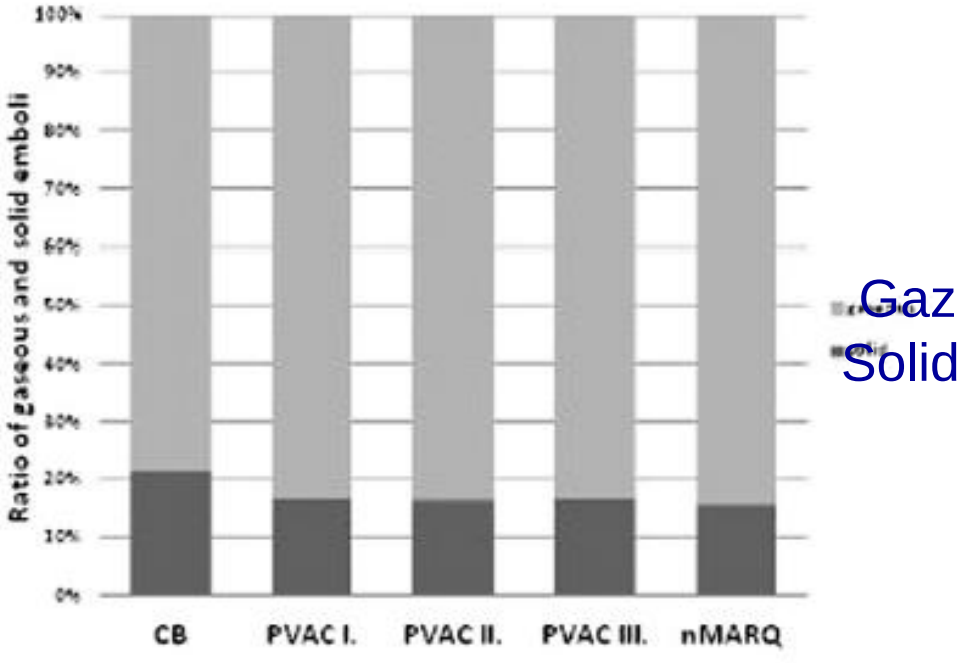
- A. Fürnkranz,et al. Incidence and characteristics of phrenic nevre palsy following pulmonary vein isolation with the second-generation as comparedwith the firstgeneration cryoballoon in 360 consecutive patients. Europace.2015:17
  - N=360 hasta: 106 vs 254 (CB vs CB-A)
  - Geçici PNP: % 3,8 vs % 5,9
  - Kalıcı PNP: % 1,9 vs % 2,8
  - Tam recovery ort 280 gün

- U Canpolat,et al. Imaging before cryoablation of atrial fibrillation: is phrenic nerve palsy predictable. Europace.2014
  - 162 hasta : % 2,75 geçici- kalıcı YOK.
  - BT ile RP arter-RUPV ostium mesafe kısalığıyla ilişkili

- A. Metzner,et al. The Incidence of Phrenic Nerve Injury During Pulmonary Vein Isolation Using the Second-Generation 28 mm Cryoballoon. JCEp.2014:25
  - N=115 hasta → % 3,5 (1'i 10 ayda düzelmiş, 3'ünde f-up< 10 ay)

CBA: sessiz serebral mikroemboli



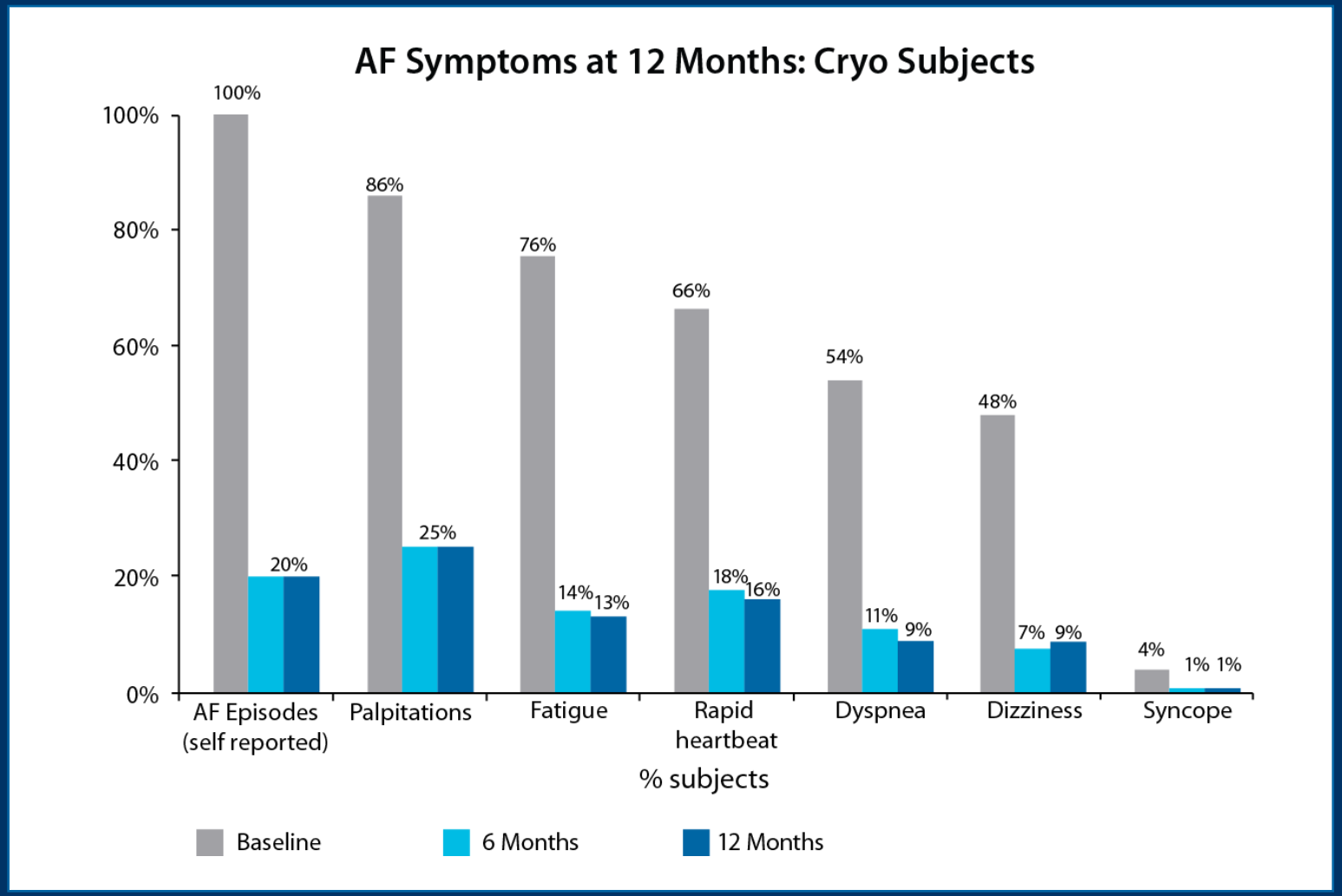


%	İrrg RFA	PVAC	CBA	Laser Bl.	nMARQ	Mesh	Robotik
Flair +	7,4-8,3	1,7-38,9	4,3-5,6	NA	0	27	NA
Difussion +	6,8-24	20-42	5,0-29	11,4-42	24-33	NA	18

A.Kiss,et al.Int J Cardiol.2014:174
T. Deneke,et al.JCEp.2015

CBA: hayat kalitesine etki (QoL)

(STOP-AF): subjektif semptom bildirimleri



CBA: hayat kalitesine etki (QoL)

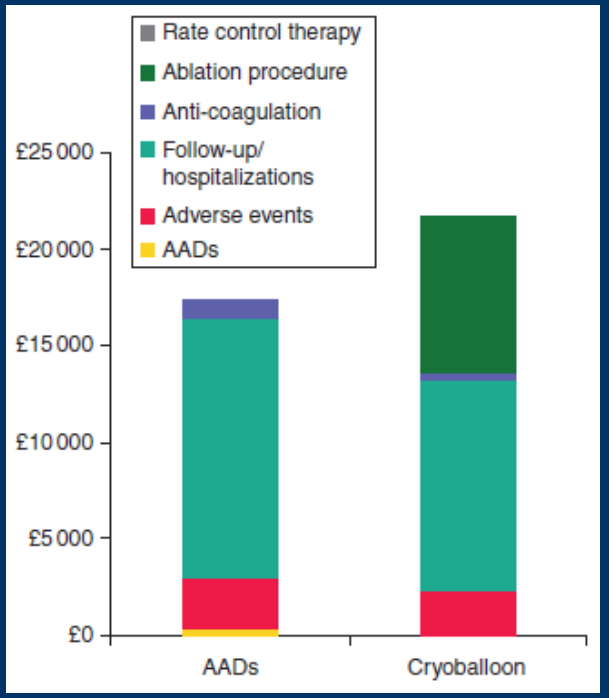
(STOP-AF): SF-36 ölçeği bileşenleri

CBA: maliyet-etkinlik

Table 2 Deterministic cost-effectiveness results

Treatment arm	Total costs	Total QALYs
Anti-arrhythmic drugs	£17 627	3.404
Cryoballoon ablation	£21 162	3.565
Incremental	£3535	0.161

QALYs, quality-adjusted life-years.



We developed a state-transition (Markov) model to calculate the total costs and quality-adjusted life-years (QALYs) associated with cryoablation and AAD therapy in patients with PAF. A 5-year horizon was used for the base-case. Data from a recent study of cryoballoon ablation in patients with PAF were used to model short-term health outcomes and costs, together with longer term external evidence to populate subsequent time periods. Total discounted costs were £21 162 and £17 627 for the cryoballoon ablation and AAD arms, respectively. Total QALYs of 3.565 and 3.404 therefore led to an incremental cost-effectiveness ratio of £21 957 per QALY gained. Sensitivity analysis suggested that the key drivers of the results were the model time horizon, the costs of follow-up care in patients with recurrent AF, and the costs of the ablation procedure.

Cryoballoon ablation provides increased quality-adjusted life expectancy compared with AAD at reasonable additional cost, representing good value for money in patients with PAF.

M.R. reynolds, et al. Cost effectiveness of CBA for the management of PAF. Europace.2014:16:652

Objective quality assessment of atrial fibrillation ablation: A nove scoring system

$$AFA\ Score = \frac{\left(\frac{Number\ of\ procedures}{Redo\ Rate + PV\ Reconnection\ Rate}\right)}{1 + (deaths\ x\ 1.0) + (life\ threatening\ complications\ x\ 0.6) + (non - life\ threatening\ complications\ x\ 0.1)}$$

Definitions

Number of procedures = Total number of atrial fibrillation ablations performed in a group (excluding all repeated procedures)

Redo rate = Number of 1st repeat ablations / number of patients undergoing atrial fibrillation ablation

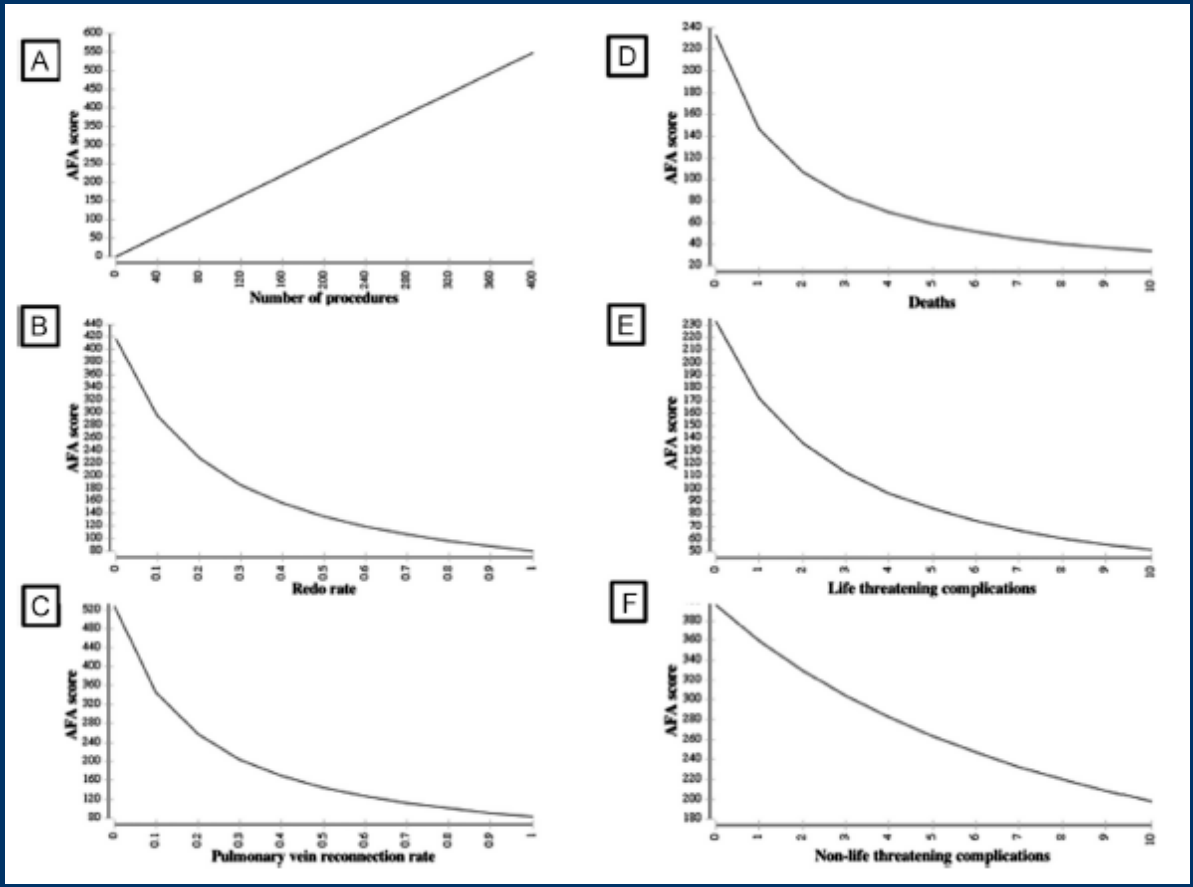
Pulmonary vein reconnection rate = Number of PVs demonstrating electrical connection to the left atrium/ total number of PVs (assessed during redo procedures)

Deaths = Number patients who died of any procedure-related cause within 30 days

Life threatening complications = Stroke/TIA/peripheral embolism, atrio-esophageal fistula, or cardiac perforation/tamponade requiring open heart surgery

Non-life threatening complications = Hematoma or retroperitoneal bleed requiring transfusion, pseudoaneurysm or AV fistula, PV stenosis requiring intervention, pericardial effusions requiring pericardiocentesis, or phrenic nerve paralysis

J.S. Chinitz, et al. Heart Rhythm.2013:10



A.Aryana,et al.2014.

Table 3 The calculated AFA score for each of the groups

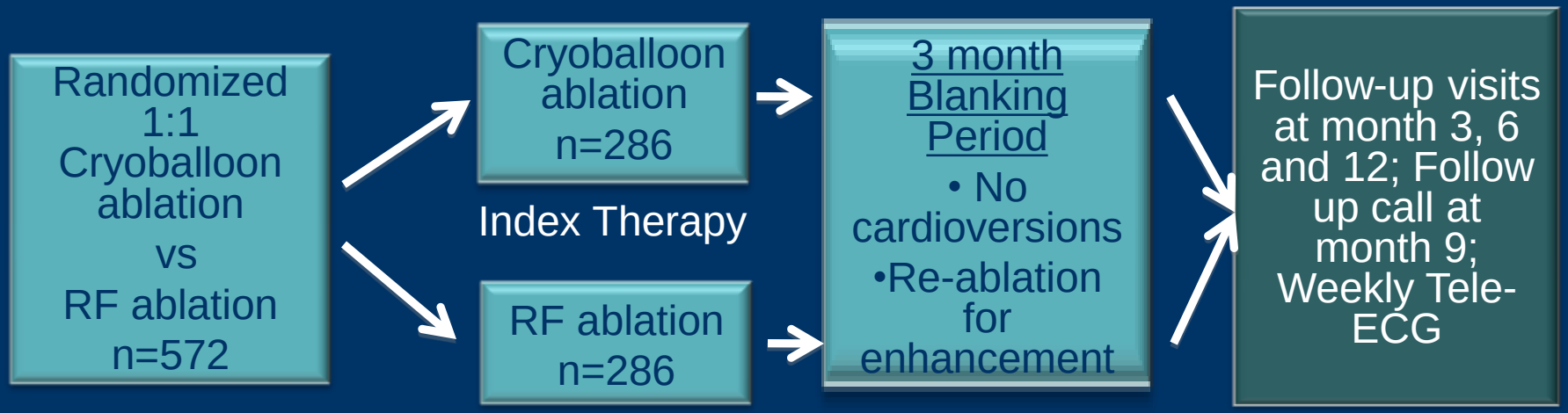
Treatment group	Number	Redo rate	Rate of PV reconnection	Complications			AFA score
				Death	Life-threatening	Nonlife-threatening	
CB-1	140	0.20	0.302	1	0	1	133
CB-2	200	0.16	0.130	0	0	8	383
$CB\text{-}1_{80}$	80	0.15	0.250	1	0	1	95
$CB\text{-}2_{80}$	80	0.11	0.083	0	0	5	276

CBA: head to head RCT

FIRE AND ICE Trial Design

<u>Key Inclusion Criteria</u>

- Symptomatic paroxysmal atrial fibrillation (PAF) with ≥ 2 episodes
- Treatment failure of ≥ 1 AAD



<u>Key Exclusion Criteria</u>

- LA diameter > 55 mm
- EF < 35%
- ≥2 cardioversions within 2 years
- Any previous LA ablation or surgery
- Recent cardiac surgery or PCI, MI

Cryobalon Ablasyon: sonuç/özet

- CBA ablasyon işlem süresini azaltabilir ve özellikle lezyon bölgesinde trombüs oluşumu ile kateter travması ya da kateter/doku temas noktasında aşırı ısınmaya bağlı kardiyak perforasyon gibi RF kaynaklı komplikasyonları azaltabilir.

- CBA ile PV izolasyonunun durabilitesi, etkinliği ve güvenirliği hem eski hem de yeni kuşak cryobalonlar için klinik çalışmalarda değerlendirilmiş ve erken ve geç dönem başarı oranları RFA ile kıyaslanabilir şekilde olumlu bulunmuştur

- CBA ile görülen komplikasyonlar görece RFA'a göre daha farklıdır:

TEŞEKKÜRLER