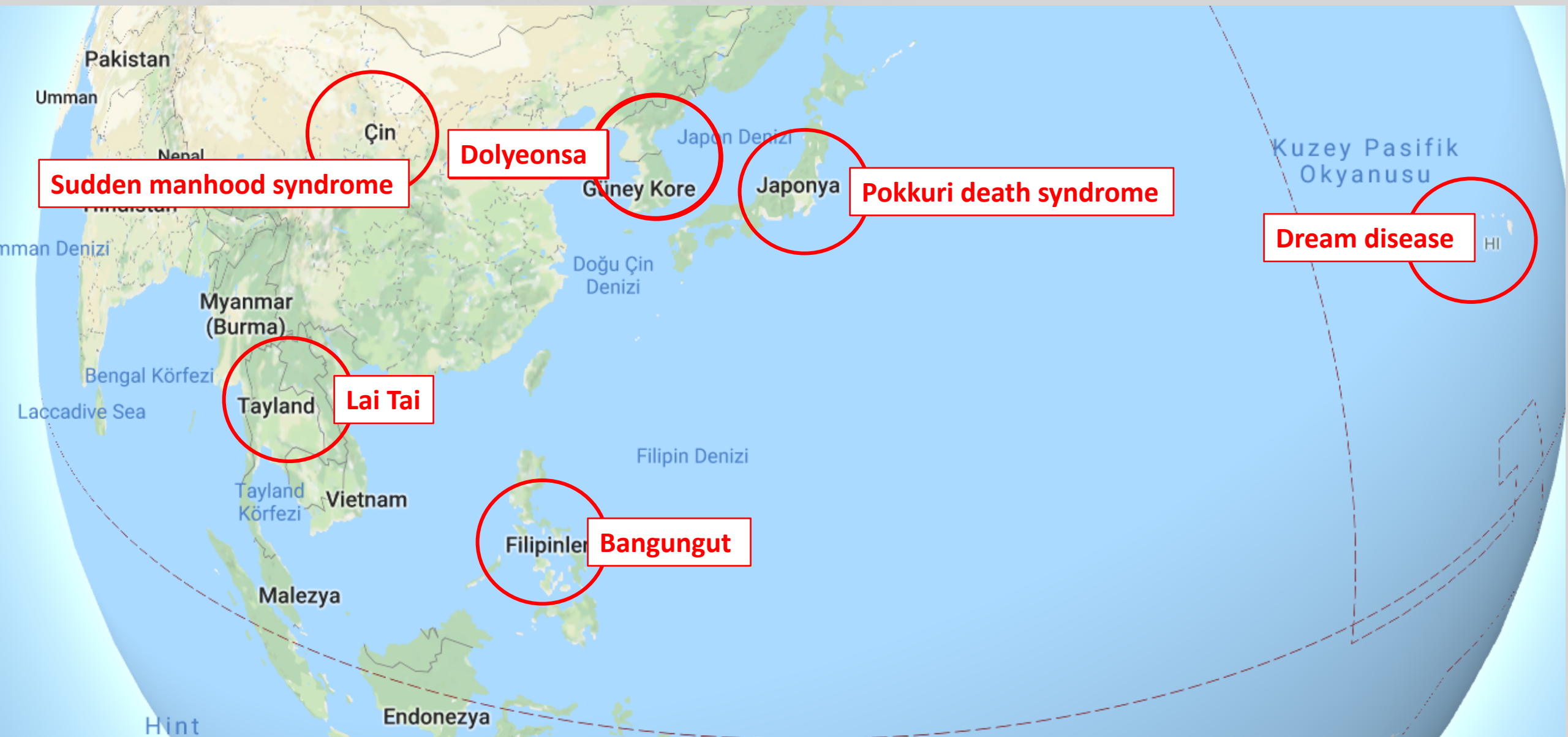


BRUGADA SENDROMU KİME ICD TAKALIM

DR. SELİM EKİNCİ

İZMİR SAĞLIK BİLİMLERİ ÜNİVERSİTESİ

TEPECİK EĞİTİM VE ARAŞTIRMA HASTANESİ



Sudden manhood syndrome

Dolyeonsa

Pokkuri death syndrome

Dream disease

Lai Tai

Bangungut

Tarihçe

- 1953, Osher ve Woff, sağ precordial ST segment yükselmesi +RBBB
- 1975 yılında Calo, bugünkü triada benzer bir tabloyu tarif etti
- 1986'da Prof. Pedro Brugada, ilk hasta
- 1992'de Pedro ve Josep Brugada kardeşlerin ilk serisi; N:8
- 1996 yılında, Yan, Antzelevitch ve Miyazaki, sendromu tanımlamak için ilk kez Brugada adını kullandı.
- Hastalığın SCN5A ile ilişkisi ilk defa 1998 de keşfedildi.

**Right Bundle Branch Block, Persistent ST Segment Elevation
and Sudden Cardiac Death: A Distinct Clinical and
Electrocardiographic Syndrome**

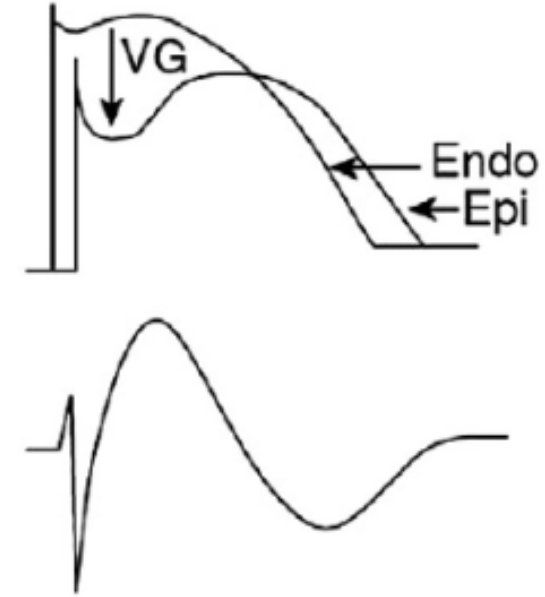
A Multicenter Report

PEDRO BRUGADA, MD, JOSEP BRUGADA, MD*†

Aalst, Belgium and Barcelona, Spain

İSTATİSTİK

- Tüm SCD nin %4-12
- Normal yapısal kalpte SCD nin %20
- Prevelans : 1/5000-1/2000
- İnsidans: %0,12-%0,8
- E/K: 8-10



Brugada's pattern

Fig. 1. In BrS, the heterogeneous dispersion of repolarization takes places between the endocardium and the epicardium of the RV at the beginning of phase 2 (voltage gradient [VG]) because of the transient predominance of outward I_{to} current. Epi indicates epicardium; Endo, endocardium.

SENDROM MU? – PATTERN Mİ?

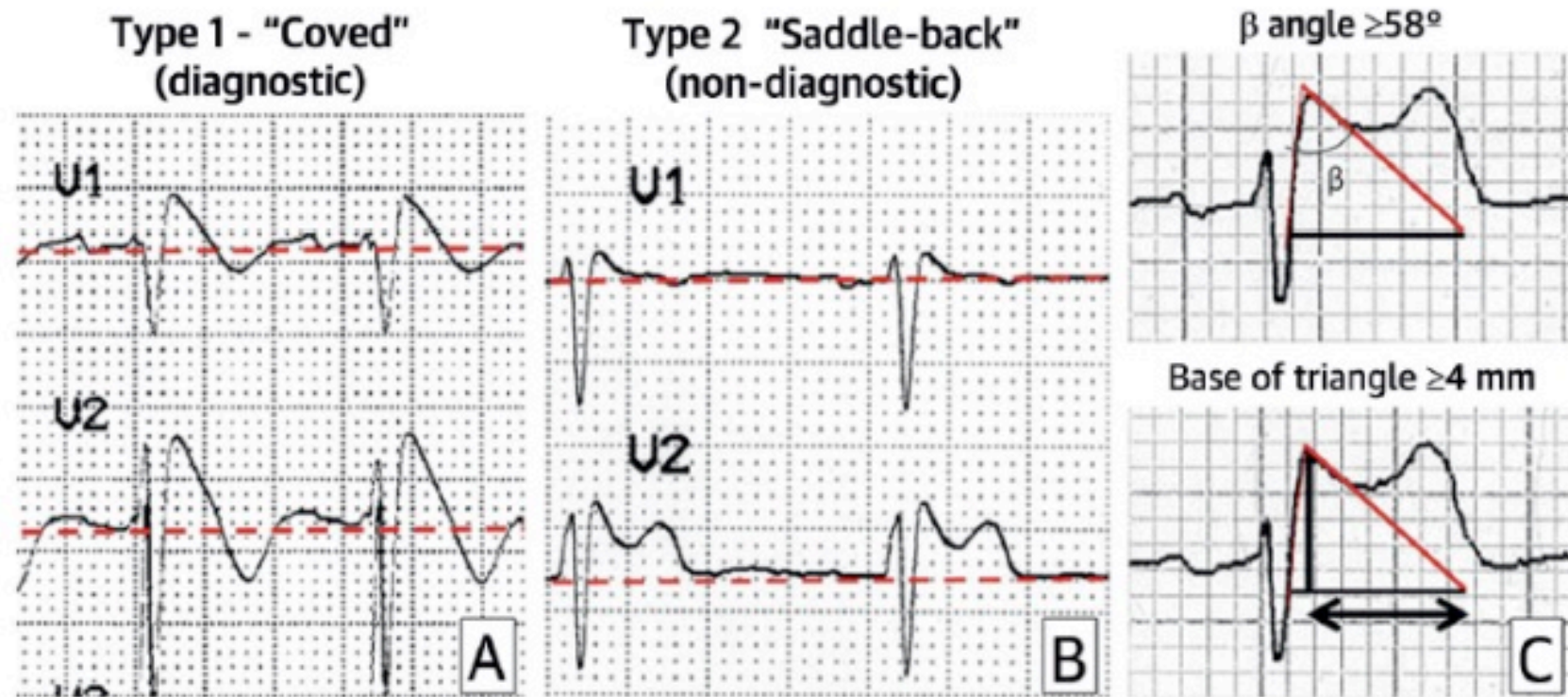
İLİŞKİLİ SEMPTOMLAR:

SCD- SENKOP- NOKTURNAL AGONAL SOLUNUM - NÖBET

- Asemptomatiklerde yıllık olay riski %0.5
- Semptomatiklerde yıllık olay riski %1.9
- Orta yaş erkek erişkinde herhangi nedenle ölüm riski %0.4

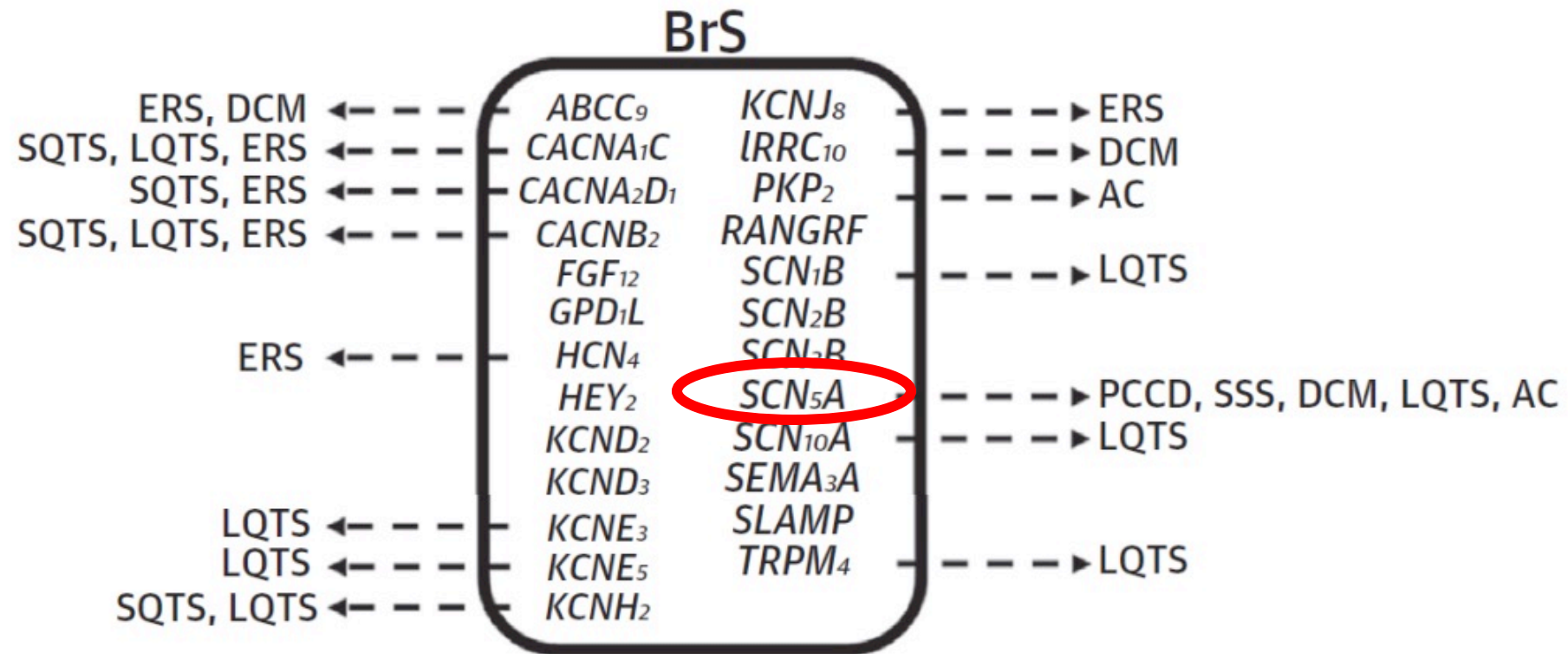
- Asemptomatik hastalarda 10 yıllık ICD terapi oranı %12
- Spontan tip 1 EKG azalmış survive ve artmış ve erken ICD terapisi ile ilişkili
- Asemptomatiklerde patern kelimesi sadece ilaç ile indüklenenlere mi saklanmalı?

FIGURE 1 Electrocardiographic Patterns in Brugada Syndrome



(A) Type 1 Brugada electrocardiogram pattern showing a concave ST-segment elevation ≥ 2 mm in ≥ 1 right precordial lead, followed by a negative T-wave. (B) Type 2 Brugada electrocardiogram pattern showing a convex ST-segment elevation ≥ 0.5 mm (generally ≥ 2 mm) in ≥ 1 right precordial lead followed by a positive T-wave. (C) Additional criteria for the diagnosis of Brugada electrocardiogram pattern type 2 (**top**: the β angle, described by Chevallier et al. (18); **bottom**: the length of the base triangle of the r' wave 5 mm below the maximum rise point).

FIGURE 3 Genes Associated With BrS



All genes currently associated with BrS. Some of these genes are also associated with other arrhythmogenic disease. AC = arrhythmogenic cardiomyopathy; BrS = Brugada syndrome; DCM = dilated cardiomyopathy; ERS = early repolarization syndrome; LQTS = long QT syndrome; PCCD = progressive conduction cardiac disease; SQTS = short QT syndrome; SSS = sick sinus syndrome.

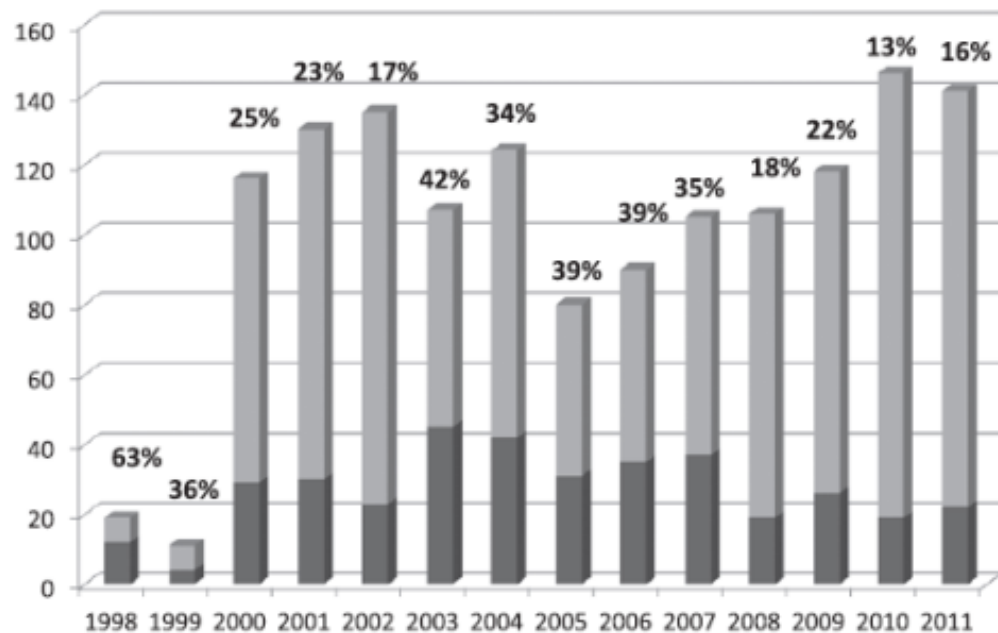
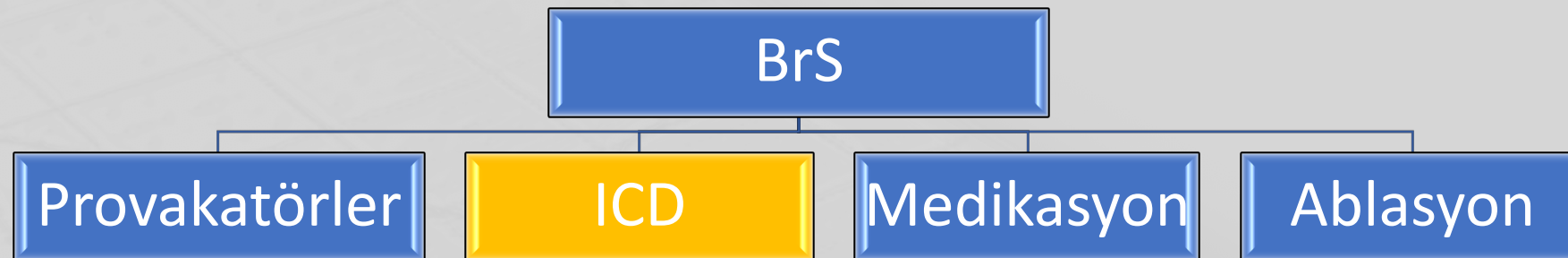


Figure 1. Percentage of implantable cardioverter-defibrillator (ICD) implantation in Brugada syndrome (BrS) patients over the years. The number of patients implanted with an ICD per year is in dark gray; the number of patients diagnosed with BrS but not implanted with an ICD is in light gray. Rate of ICD implantation is displayed on the top of the column. The graph starts in 1998 because very few ICDs were implanted for BrS before this date (n=5).

Table 3. Rate of Events After ICD Implantation

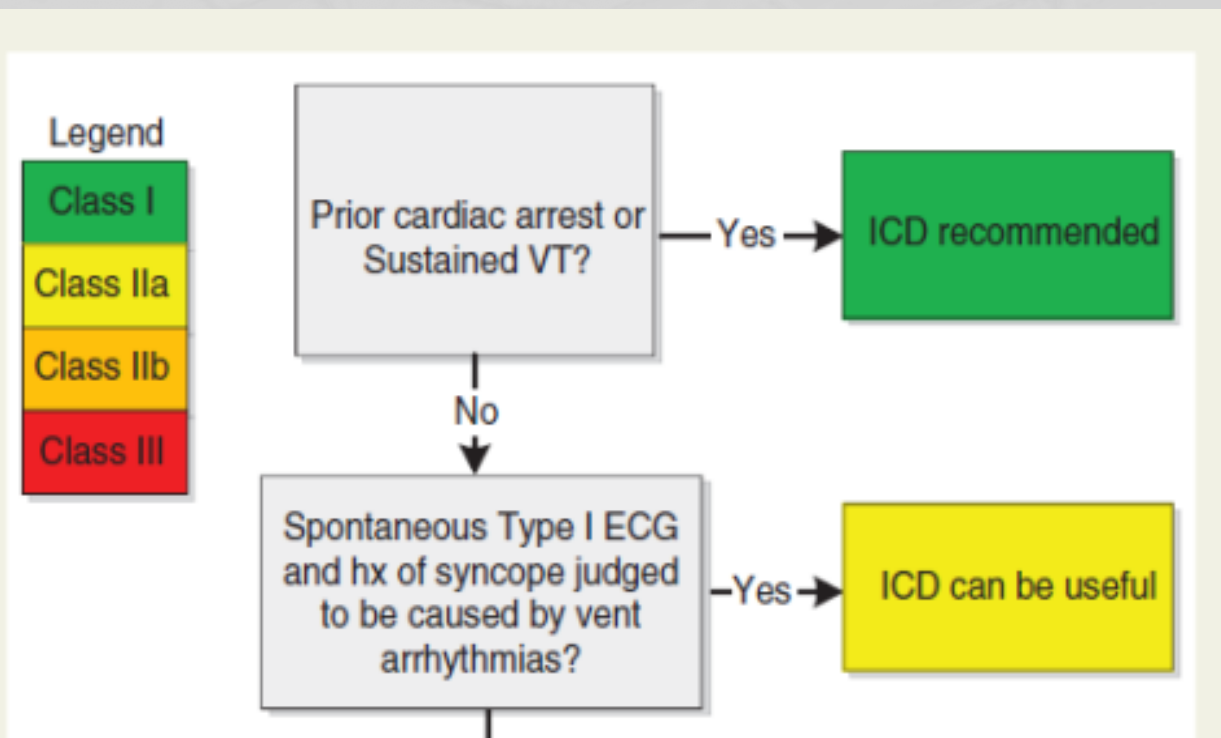
Year	Appropriate Shock Rate, %			Inappropriate Shock Rate, %	Lead Failure Rate, %
	Aborted SCA	Syncope	Asymptomatic		
1	25	3	1	8	1
2	30	6	2	13	2
3	36	7	4	15	5
4	41	10	6	18	7
5	48	11	6	23	13
10	48	19	12	37	29

ICD indicates implantable defibrillator-cardioverter; and SCA, sudden cardiac arrest.

Outcome after implantation of a cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study-part 2. Frédéric Sacher, Vincent Probst, Philippe Maury, Dominique Babuty, Jacques Mansourati, Yuki Komatsu, Christelle Marquie, Antonio Rosa, Abou Diallo, Romain Cassagneau, *et al.* *Circulation*. 2013 Oct 15; 128(16): 1739–1747. Published online 2013 Aug 30. doi: 10.1161/CIRCULATIONAHA.113.001941



RISK SINIFLAMA



2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

ICD implantation is recommended in patients with a diagnosis of Brugada syndrome who (a) Are survivors of an aborted cardiac arrest and/or (b) Have documented spontaneous sustained VT.	I	C	451
ICD implantation should be considered in patients with a spontaneous diagnostic type I ECG pattern and history of syncope.	IIa	C	451

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

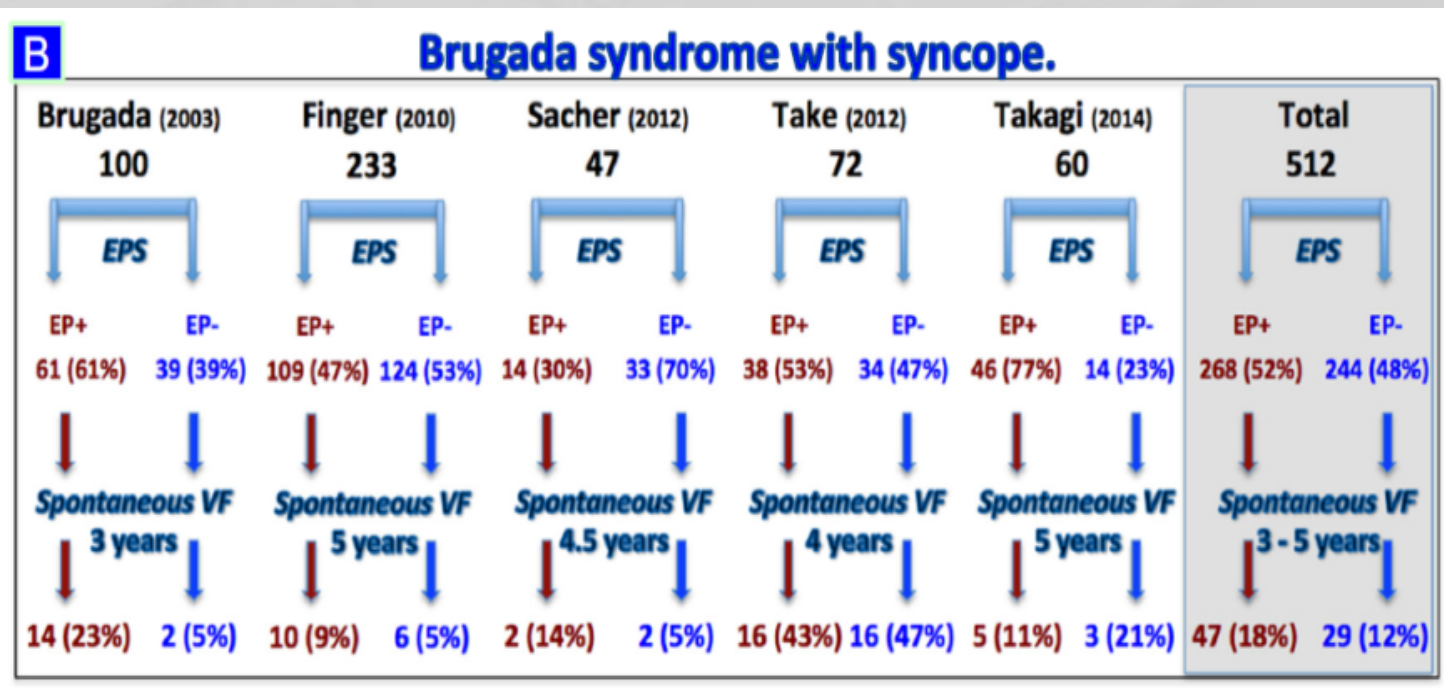
SENKOP

- Hastaların 1:3 ü bu şekilde tanı alır

- Olay riski senkop yokluğuna göre 4 kat daha fazla SCD varlığına göre 4 kat daha azdır.
- Senkop tartışılmaz bir risk faktörüdür

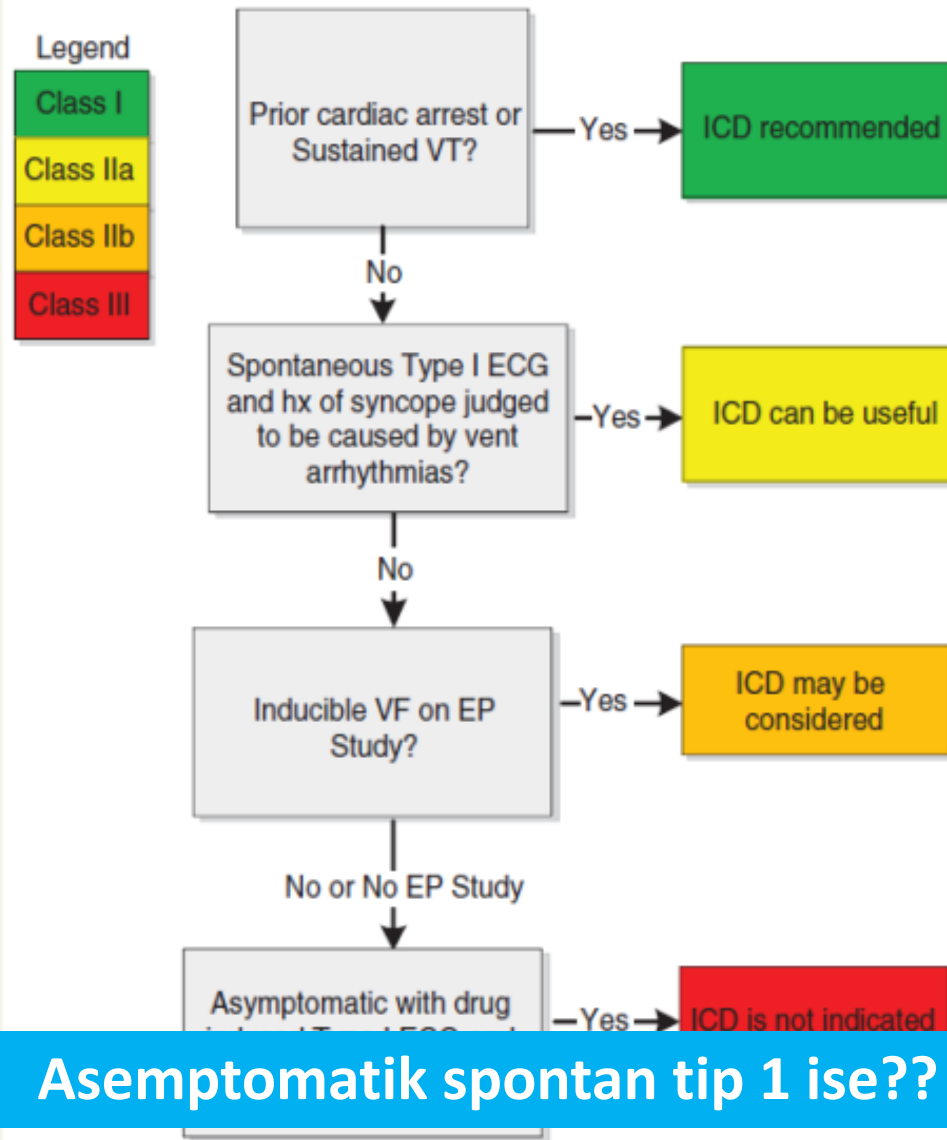
- Spontan tip 1 EKG paterni + senkop daha kötü prognoz:
 - hastaların% 6 ila% 19'u takip eden 24 ila 39 ay içerisinde aritmik bir olaya sahip olacaktır

- VAGAL SENKOP OLMADIĞINDAN EMİN OL!



Priori SG, Gasparini M, Napolitano C, et al. Risk stratification in Brugada syndrome: results of the PRELUDE (PRogrammed Electrical stimulation preDICTive value) registry. J Am Coll Cardiol 2012; 59:37–45.

Milman A, Andorin A, Gourraud JB, et al. Profile of patients with Brugada syndrome presenting with their first documented arrhythmic event: data from the Survey on Arrhythmic Events in BRUGada Syndrome (SABRUS). Heart Rhythm 2018;15: 716–24.



Asemptomatik spontan tip 1 ise??

Figure 2 Consensus recommendations for ICDs in patients diagnosed with Brugada syndrome.

Asemptomatik hastalarda risk sınıflandırması

- Olguların %60'ı asemptomatik.
- Bildirilen yıllık asemptomatik BrS olaylarının oranı zaman içinde azalmıştır.
- Daha yakın tarihli çalışmalarda bile, asemptomatik BrS hastalarında aritmik olayların oranı ihmal edilemez
 - % 0,5 ila % 1,2 oranında insidans,
 - 10 yıllık takipte % 12 malign ventriküler aritmi oranına yol açmaktadır.

Table 1 Variables identified as being associated with sudden cardiac death in Brugada syndrome.

Variables	Definition	Effect on SCD	Main publications
Aborted SCD	—	Increased risk ^a	[2,5,10]
Syncope	Cause by arrhythmia	Increased risk ^a	[2,5,10]
Spontaneous ECG pattern	Type 1 ECG	Increased risk	[2,5,10]
Old age	Aged > 60 years	Decreased risk, but needs to be confirmed ^b	[37]
Sex	Female sex	Decreases risk ^b	[32,37]
EPS	VF occurrence	Increased risk, with conflicting data, particularly with three extra stimuli ^b	[2,10,52]
Sinus dysfunction	In females	Increased risk, but needs to be confirmed ^b	[33]
S wave in D1	S wave > 0.1 mV and/or > 40 ms	Increased risk, but needs to be confirmed ^b	[38]
QRS fragmentation	At least four spikes in one or at least eight spikes in all of the precordial leads	Increased risk, but needs to be confirmed ^b	[10,40]
Inferior type 1	Type 1 ECG in inferior or lateral leads	Increased risk, but needs to be confirmed ^b	[47]
Tpeak–Tend interval	Maximum Tpeak–Tend interval > 100 ms in precordial lead	Increased risk, but needs to be confirmed ^b	[48]
Early repolarization	J wave > 0.1 mV in two inferolateral leads	Increased risk, with conflicting data ^b	[39,45]
Post-exercise ST-segment elevation	≥0.05 mV in V1–V3 post exercise	Increased risk, but needs to be confirmed ^b	[56]
Type 1 ECG burden	24-h Holter monitoring	Increased risk, but needs to be confirmed ^b	[31]
Young age	Aged < 18 years	Conflicting data ^c	[34,36]
Family history of SCD	SCD in first-degree relatives	Conflicting data ^c	[2,10,39]
Genetic	SCN5A mutations	Conflicting data ^c	[2,10,34]
Atrial fibrillation	—	Conflicting data ^c	[2,9,10,38]
PR duration	PR > 200 ms	Conflicting data ^c	[41,44]
QRS duration	QRS > 120 ms	Conflicting data ^c	[41,44]
Late potentials	Two of three positive criteria	Conflicting data ^c	[42,44]
aVr sign	R wave ≥ 0.3 mV or R/q ≥ 0.75 in aVr	Conflicting data ^c	[2,10,43]

ECG: electrocardiogram; EPS: electrophysiological study; SCD: sudden cardiac death; VF: ventricular fibrillation.

^{a–c} An indication of the strength of data associating the variable with SCD (from ^a for consistent and prospective data to ^c for conflicting results).

YAŞ VE CİNSİYET

- İnkomplet penetranslı otozomal dominant bir hastalık
- Gen taşıyıcılarının oranı cinsiyetler arasında benzer olsa da semptomatiklerin çoğu erkektir
- Erkeklerde spontan tip 1 EKG ve EPS de VF indüksiyon sıklığı 3 kat fazladır.
- Kardiyak arrest riski 7 kat fazladır
- Büyük registry'lerde SCD hastalarının %64-94 i erkektir
- Uygun ICD şok alanların %86'sı erkektir

- Diğer taraftan asemptomatik hastaların da çoğu erkektir ve spontan tip1 EKG yi dikkate aldığımızda cinsiyetin SCD riskinde bir anlamı yoktur

TABLE 1			
Electrocardiographic Characteristics of Patients with Severely Symptomatic Brugada Syndrome According to Gender			
	Male (n = 50)	Female (n = 8)	P-Value
Spontaneous type 1 ECG	36 (72%)	2 (25%)	P = 0.02
Maximal ST elevation (mm)	3.7 ± 1.3	2.4 ± 0.7	P = 0.007
Mean ST elevation in patients with spontaneous type 1 pattern (mm)	2.8 ± 1 (36 pts)	2.3 ± 0.9 (2 pts)	P = 0.54
PR (ms)	185 ± 31	192 ± 50	P = 0.63
QTc (ms)	408 ± 40	440 ± 63	P = 0.08

Implantable Cardioverter-Defibrillator Therapy in Brugada Syndrome

A 20-Year Single-Center Experience

Giulio Conte, MD,* Juan Sieira, MD,* Giuseppe Ciconte, MD,* Carlo de Asmundis, MD,* Gian-Battista Chierchia, MD,* Giannis Baltogiannis, MD,* Giacomo Di Giovanni, MD,* Mark La Meir, MD,† Francis Wellens, MD,† Jens Czapla, MD,†

TABLE 3 Univariate Cox Regression Analysis Among Patients Experiencing Appropriate Shocks

	β Coefficient	HR (95% CI)	p Value
Age	−0.02	0.98 (0.96–1.0)	0.12
Male	1.08	2.95 (1.02–8.53)	0.04
Proband	−0.35	0.71 (0.33–1.53)	0.38
Spontaneous type 1 ECG pattern	0.91	2.50 (1.16–5.39)	0.02
Symptoms	0.97	2.63 (1.40–4.92)	<0.01
Syncope	−0.08	0.93 (0.32–2.67)	0.89
Aborted SCD	1.51	4.53 (1.57–13.0)	<0.01
Family history of SCD	−0.42	0.66 (0.31–1.42)	0.29
Previous AF	−0.31	0.73 (0.22–2.44)	0.61
Previous SND	0.57	1.77 (0.42–7.50)	0.44
EPS inducibility	0.90	2.44 (1.18–6.02)	0.04
SCN5A mutation	0.29	1.33 (0.24–7.45)	0.74
Implantation during or after 2005	−1.18	0.31 (0.12–0.77)	0.01

The HR for age considers every year increase.

AF = atrial fibrillation; CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

Multivariate analizde sadece EPS de ventrikler aritmi indüksiyonu ve SCD anlamlı olarak kaldı

Çocuk hastalar

- Hormonların etkisi?
 - Kastrasyon sonrası cinsiyet ilişkili farklar minimize olur
 - Çocuklarda erkek predominansı yok
- Hasta sayıları düşük
- Atrial aritmi varlığı riski artırır
- Ateş erişkinde SCD için nadir tetikleyici ancak çocuklarda daha sık dikkat çeker
- Ajmalinle tanı alan çocuklarda risk düşük ancak ajmalin sırasında VF çocuklarda daha sık

İleri Yaş grubu

- Prognoz hakkında kesin yargı verecek yeterli kanıt yok
- Büyük bir seride >70 yaş grubunda benign prognoz gösterdi
- Taiwan dan yapılan br çalışmada 55 yaş üzerinde BrS prevelansı fazla bulundu ancak bunlarda genel popülasyona göre mortalite farkı saptanmadı

Table 3 Prevalence and annual event rates (ventricular fibrillation or sudden death) of Brugada ECG patterns in community-based elderly cohort studies throughout the world

Population	Country/city	Authors	Sample size, n	Male, n (%)	Age (year)	BrP-1, n (%) (M/F)	BrP-2 n (%) (M/F)	BrP-3 n (%) (M/F)	Event/year (%) BrP-1	Event/year (%) BrP-2 and 3
Asia	Japan/Moriguchi	Miyasaka et al. 2001 ⁸	13 929	3691 (26)	58 ± 10	17 (0.12) (NA)	81 (0.58) (NA)	NA	0	1.2
	Japan/Moriguchi	Tsuji 2008 ¹²	13 904	3686 (27)	58 ± 10	37 (0.27) (31/6)	61 (0.44) (48/13) ^a		0	1.6
	Taiwan	Present study	5214	2530 (49)	69.3 ± 8	4 (0.077) (3/1)	68 (1.30) (53/15)	101 (1.94) (56/45)	0	0
Europe	Finland	Junttila 2004 ²⁰	542	542 (100)	50 ± 6	0 (0)	3 (0.55) (3/0) ^a		0	0
	Germany	Sinner et al. 2009 ²⁴	4149	2034 (49)	50.6 ± 13.9	11 (0.27) (9/2)	3 (0.07) (3/0)	0 (0)	NA	
America	US (Japanese American)	Ito 2006 ¹³	8006	8006	53.9 ± 4.5	12 (0.150)	11 (0.137)		0	0

AİLE ÖYKÜSÜ VE GENETİK TEMEL

Table 1 Value of familial and genetic data on risk stratification in Brugada syndrome (data from largest studies)

Study	Population	Association with arrhythmic events
Priori ³⁸	200	Family history of sudden death: sensitivity 22%, specificity 65%, PPV 7%, NPV 87% Presence of <i>SCN5A</i> mutation: sensitivity 32%, specificity 57%, PPV 8.3%, NPV 87%
Kamakura ¹²	330*	Family history of sudden death was predictive of arrhythmic events (hazard ratio 3.25, 95% confidence interval 1.42–7.6 on multivariate analysis)
Probst ¹¹	1029	No association between family history of sudden death or <i>SCN5A</i> mutation and arrhythmic event during follow-up
Maury ³⁷	325†	<i>SCN5A</i> mutation correlated with a history of ventricular fibrillation on univariate but not multivariate analysis
Conte ⁸	176	No association between family history of sudden death or <i>SCN5A</i> mutation and symptoms before ICD implantation or appropriate shocks during follow-up

NPV = negative predictive value; PPV = positive predictive value.

*Study included only probands or only patients who underwent implantable cardioverter-defibrillator (ICD) implantation.

†Patients here were also included in the study by Probst.



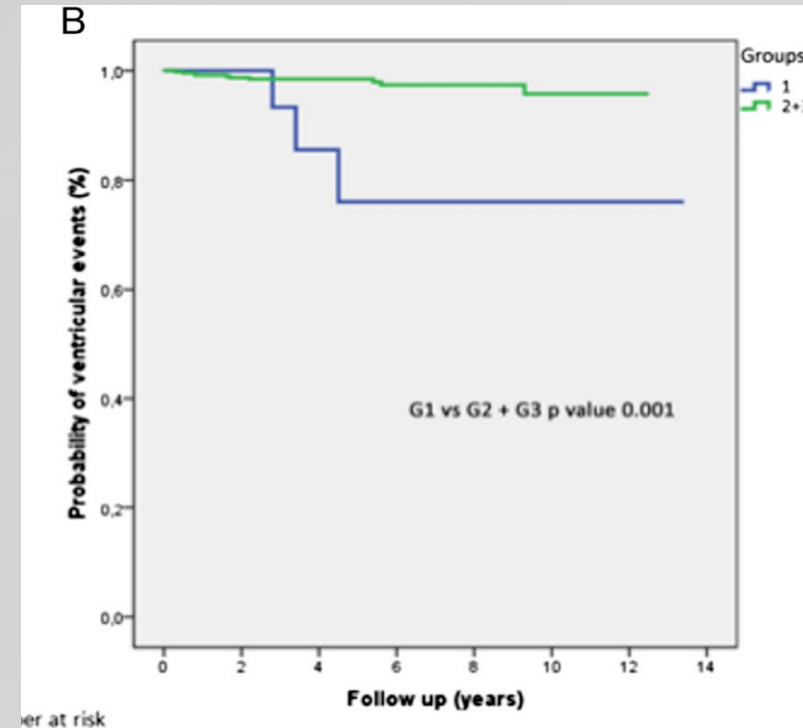
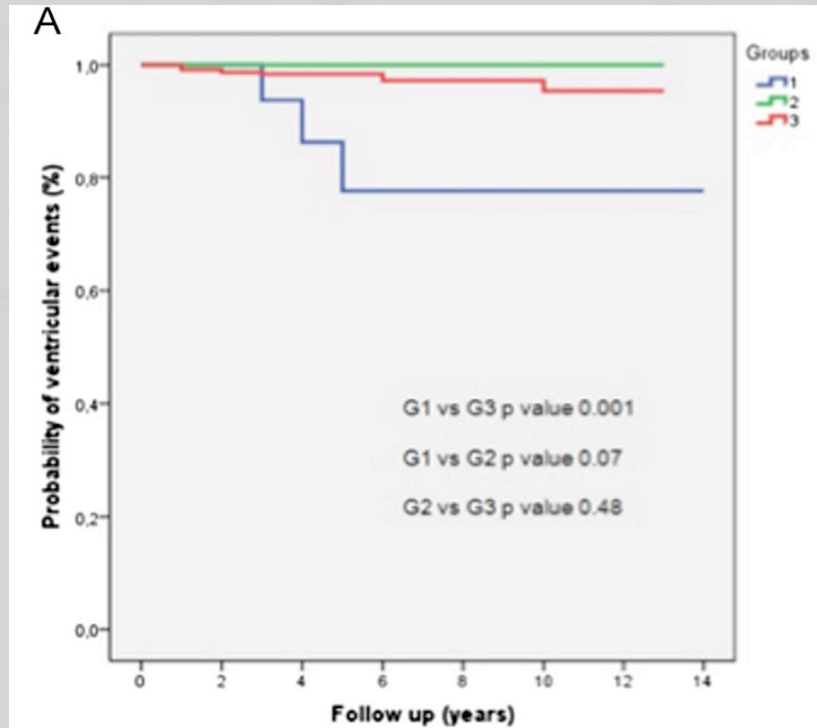
ARTICLE

Genetics can contribute to the prognosis of Brugada syndrome: a pilot model for risk stratification

Elena Sommariva¹, Carlo Pappone², Filippo Martinelli Boneschi³, Chiara Di Resta¹, Maria Rosaria Carbone⁴, Erika Salvi^{5,6}, Pasquale Vergara⁷, Simone Sala⁷, Daniele Cusi^{5,6,8}, Maurizio Ferrari^{1,4,9} and Sara Benedetti^{*,9}

ATRIAL FİBİLASYON / FLUTTER VARLIĞI

- BrS de daha sık
- Malign seyirle ilişkili
- Ancak bağımsız bir gösterge değil
 - Spontan tip1 EKG ve repol/depol anormalliklerine göre kontrol yapılıncı değerini yitiriyor

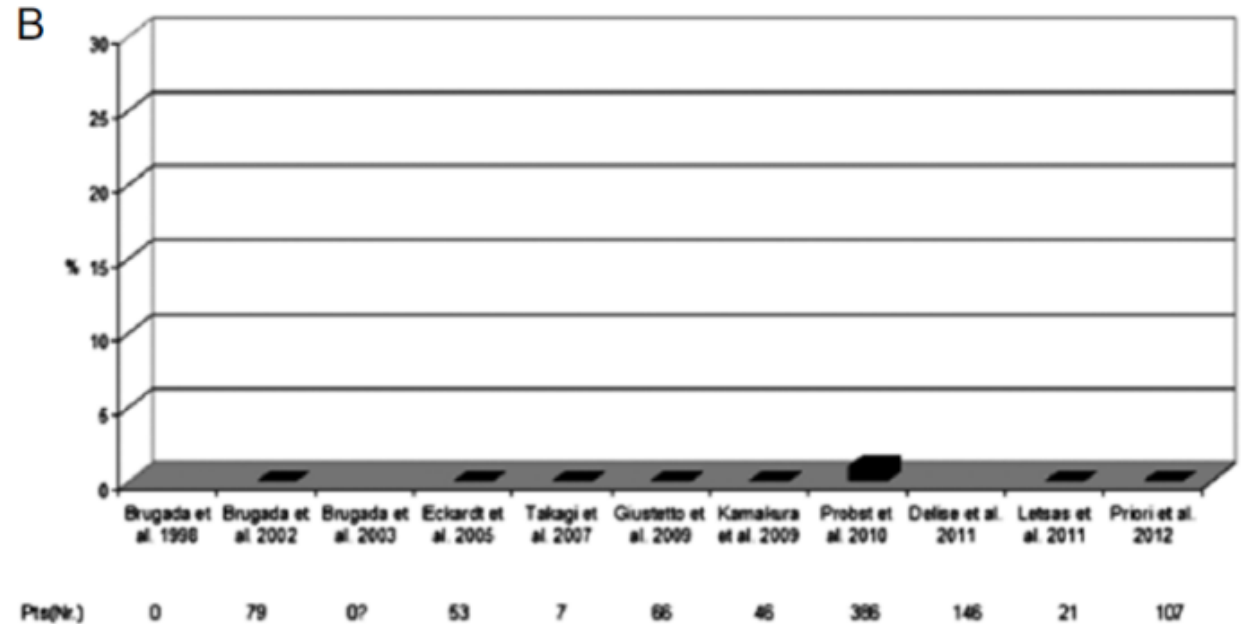
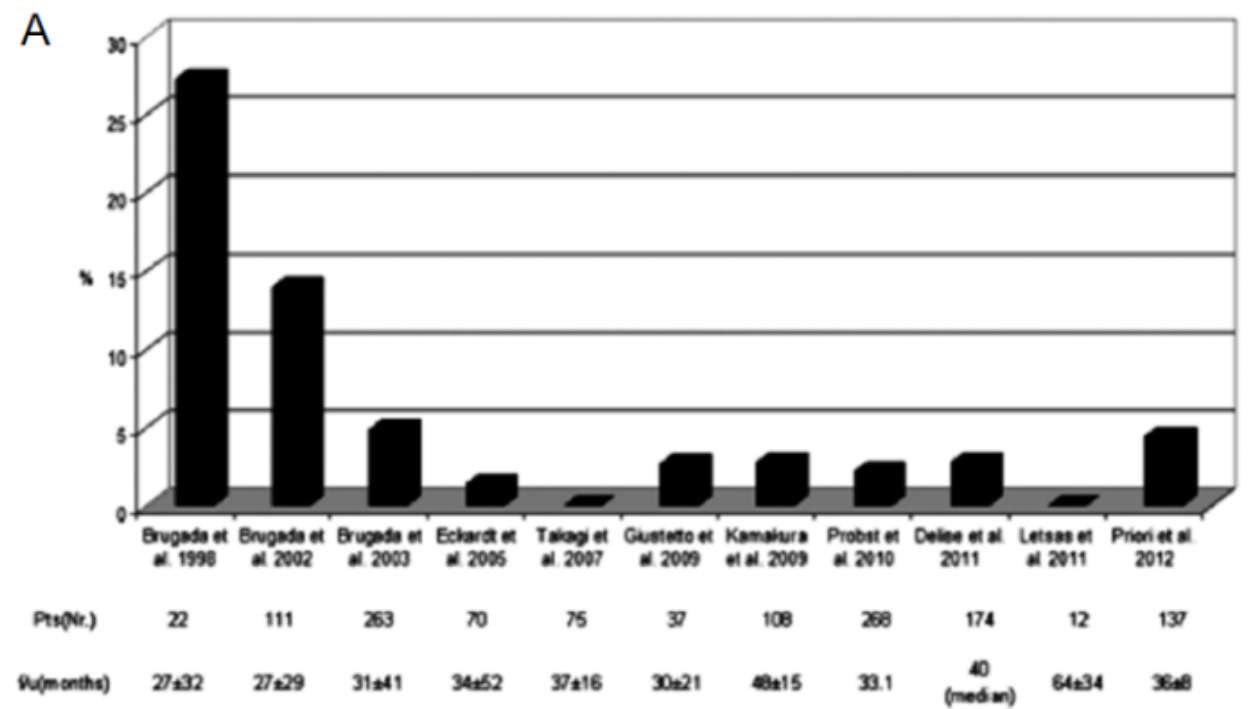


EKG PARAMETRELERİNİN PROGNOSTİK ROLÜ

SPONTAN TİP 1 EKG

- Daha az kümülatif sağ kalım
- İki kat artmış aritmik olay
- Daha kısa ilk aritmik olay süresi
- Bu gözlem hem semptomlu hem semptomsuz hastalar için geçerli.

Başlangıçta Sx(-) hastalarda spontan tip1 EKG varlığı(A), ve yokluğunda (B) aritmik olay sıklığı

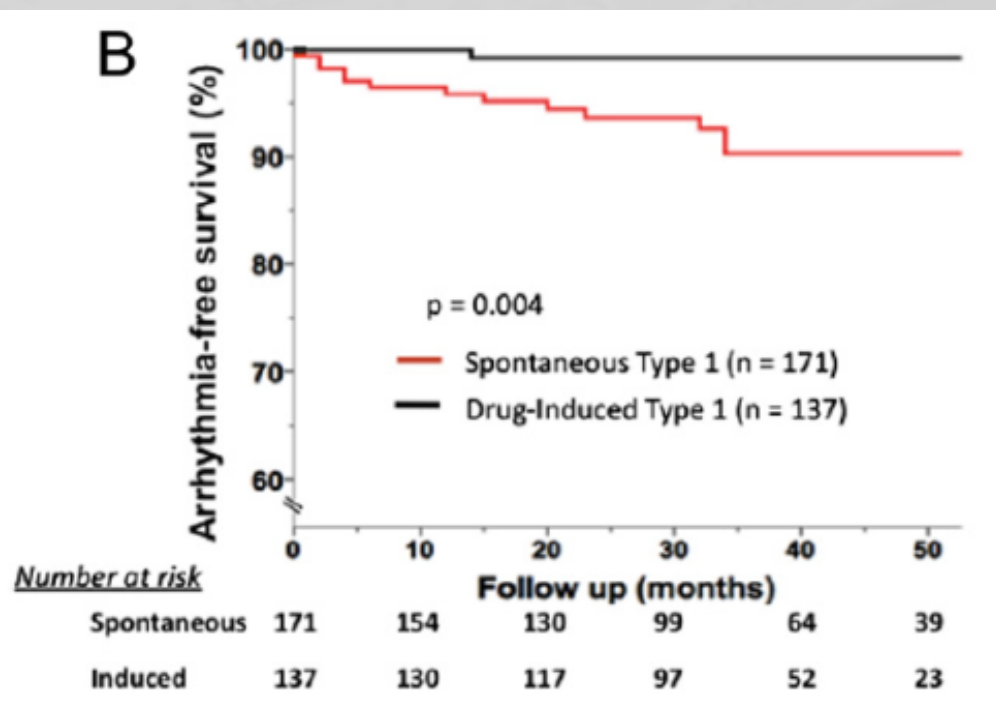


Honarbaksh S, Providencia R, Lambiase PD. Risk Stratification in Brugada Syndrome: Current Status and Emerging Approaches. *Arrhythm Electrophysiol Rev.* 2018;7(2):79-83.

Risk stratification in Brugada syndrome: Clinical characteristics, electrocardiographic parameters, and auxiliary testing. Arnon Adler, Raphael Rosso, Ehud Chorin, Ofer Havakuk, Charles Antzelevitch, Sami Viskin Heart Rhythm. 2016 Jan; 13(1): 299–310. Published online 2015 Sep 1. doi: 10.1016/j.hrthm.2015.08.038

Table 3 Prognostic Accuracy of Predictors of Outcome

	Inducibility* (Full Protocol)	Inducibility (With 1 or 2 Extra Stimuli)	Spontaneous Type 1 ECG Pattern	History of Syncope	Spontaneous Type 1 ECG and Syncope	QRS-f	VRP <200 ms
Sensitivity	35.7 (14–64)	25.0 (5.8–50)	92.9 (65–99)	50.0 (25–76)	42.9 (19–69)	42.9 (20–69)	78.6 (49–94)
Specificity	58.8 (58–60)	74.2 (78–81)	45.7 (45–47)	80.6 (79–82)	90.5 (89–92)	93.5 (92–95)	62.9 (62–64)
NNT	102.3 (20–200)	—	14.5 (12–58)	12.4 (6.7–108)	6.8 (3.7–26)	4.7 (2.7–14)	13.2 (9.4–50)
Univariate log-rank (p value)	0.67	0.89	0.004	0.011	0.000105	0.000001	0.002



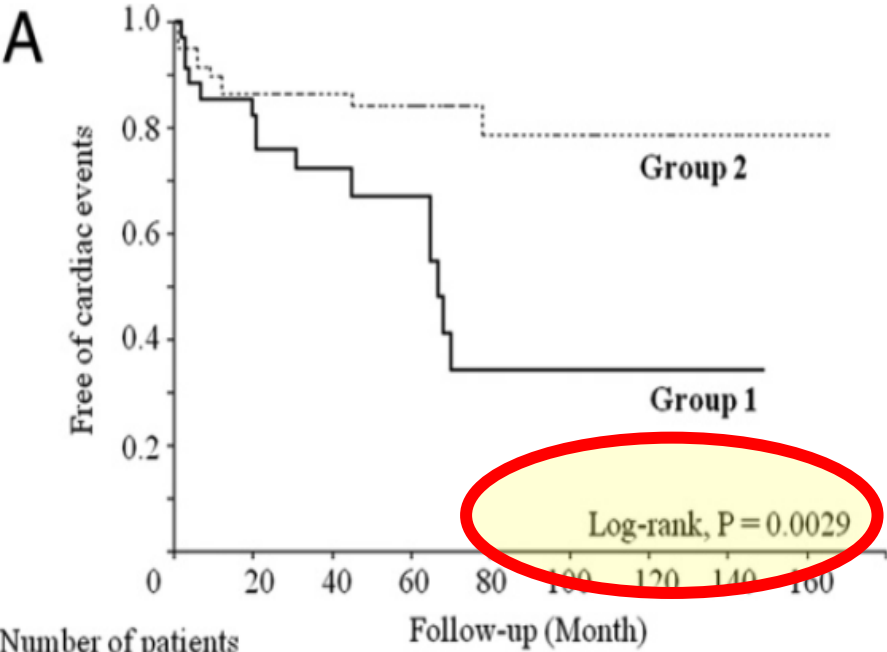
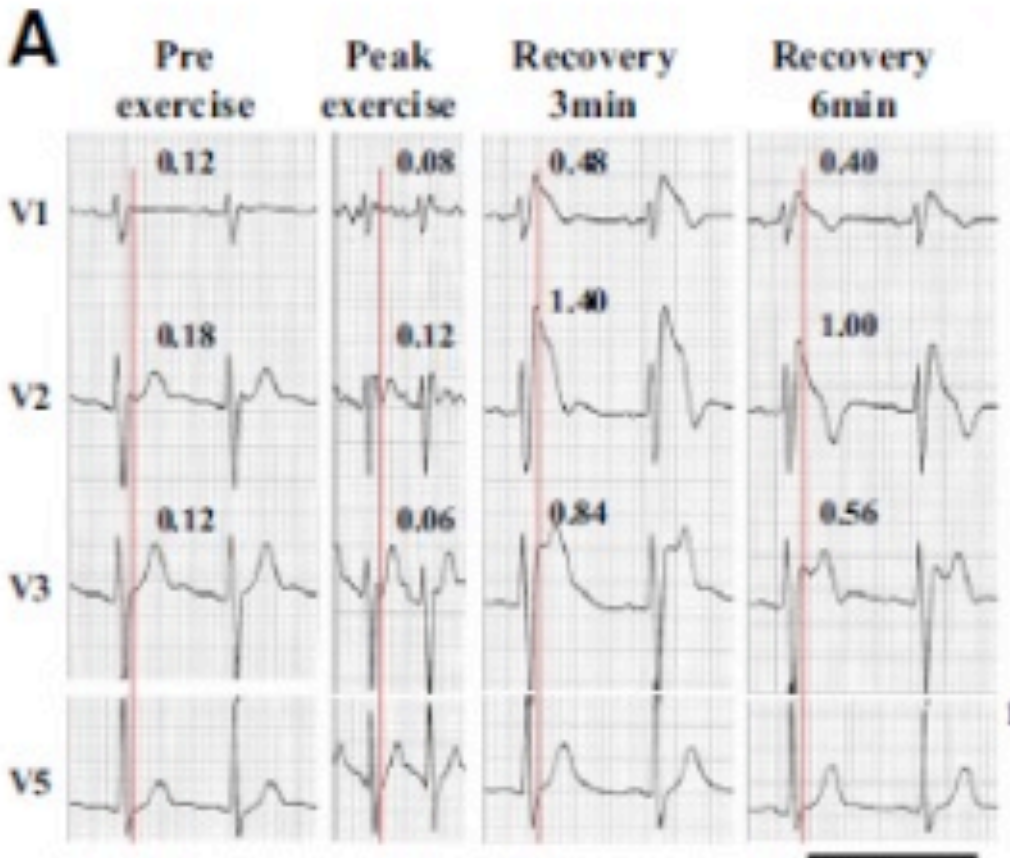
Risk Stratification in Brugada Syndrome

Results of the PRELUDE (PRogrammed
ELectrical stimUlation preDictive valuE) Registry

Priori SG, Gasparini M, Napolitano C, et al. Risk stratification in Brugada syndrome: results of the PRELUDE (PRogrammed ELectrical stimUlation preDictive valuE) registry. J Am Coll Cardiol 2012; 59:37–45.

Augmented ST-Segment Elevation During Recovery From Exercise Predicts Cardiac Events in Patients With Brugada Syndrome

Hisaki Makimoto, MD,* Eiichiro Nakagawa, MD, PhD,† Hiroshi Takaki, MD, PhD,*
Yuko Yamada MD,* Hideo Okamura, MD,* Takashi Noda, MD, PhD,* Kazuhiro Satomi, MD, PhD,*



Number of patients							
Group 1							
34	26	16	11	4	4	1	1
Group 2							
59	51	41	28	11	9	6	3

AJMALİN PROGNOSTİK Mİ?

EDITORIAL COMMENTARY

Everybody has Brugada syndrome until proven otherwise?

Sami Viskin, MD,^{*} Raphael Rosso, MD,^{*} Limor Friedensohn, MD,^{*} Ofer Havakuk, XX,^{*} Arthur Wilde, MD[†]

From the ^{}Tel Aviv Sourasky Medical Center and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, and [†]Heart Center, Academic Medical Center, Amsterdam, The Netherlands.*

- Sensitivitesi %100 olarak belirtilmekle birlikte spesivitesinin ne olduğu konusundaki veriler sorgulanmış.
- Negatif testin oldukça iyi prognozla ilişkisi olduğu vurgulanmış
- Test + saptandığında ek olarak prognoStik bulguların elde edildiği söylenmiş.
 - Ekstremitte leadlerinde Coved type ST elevasyonu
 - Makroskopik T dalga alternansının gelişmesi.
 - Test sırasında VF indüksiyonu(%0,15-1,8)(prognostik anlamı bilinmiyor.)

QRS FRAGMENTASYONU

Table 2 Correlation between QRS fragmentation and arrhythmic events in Brugada syndrome*

Study	Population	Definition of QRS fragmentation (<i>f</i> -QRS)	Association of QRS fragmentation with arrhythmic events
Morita ⁶²	115 patients with Brugada syndrome and 80 controls with RBBB	≥ 4 spikes in the QRS in V_1 , V_2 , or V_3 or ≥ 8 spikes in V_1 , V_2 , and V_3	<i>f</i> -QRS more common among Brugada syndrome patients with cardiac arrest (85%) than among asymptomatic Brugada patients (34%) or controls with RBBB (3%)
Take ²³	84 Brugada patients presenting with syncope	Mean number of spikes in the 3 leads (V_1 – V_3) was 7 ± 2	<i>f</i> -QRS associated with VF during follow-up in patients with syncope (HR 2.3, 95% CI 1.1–.6)
PRELUDE ²⁴	Brugada syndrome: 65 with syncope, 243 asymptomatic	≥ 2 spikes in the QRS in V_1 , V_2 , or V_3	<i>f</i> -QRS was an independent predictor of arrhythmic events in this prospective study (HR 8.9, 95% CI 3–6)
Maury ³⁷	325 Brugada patients, mainly probands	As in Morita et al ⁶²	<i>f</i> -QRS associated with a history of cardiac arrest but not with ICD shocks during follow-up
Tokioka ⁵⁰	Brugada syndrome [†] : 43 with VF or syncope, 183 asymptomatic	As in Morita et al ⁶²	<i>f</i> -QRS associated with wider QRS complexes and spontaneous type I ECG
Sakamoto ⁶³	129 Brugada patients (103 asymptomatic)	As in Morita et al ⁶²	Independent predictor of VF during follow-up <i>f</i> -QRS <i>not</i> associated with a history of VF or with arrhythmic events during follow-up

CI = confidence interval; *f*-QRS = fragmented QRS complex; HR = hazard ratio; ICD = implantable cardioverter-defibrillator; VF = ventricular fibrillation.

* Morita defined QRS fragmentation as ≥ 4 spikes in the QRS complex because 2–3 spikes were often seen in controls with right bundle branch block (RBBB).
Priori²⁴ defined QRS fragmentation as ≥ 2 spikes in the QRS of V_1 , V_2 , or V_3 .

[†]The populations of patients studied by Morita⁶² and Tokioka⁵⁰ overlap.

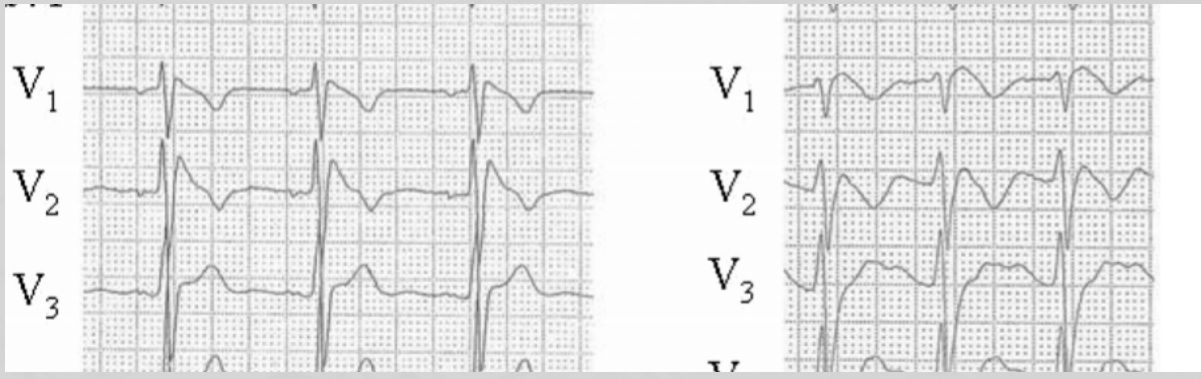
Risk Stratification in Brugada Syndrome

Results of the PRELUDE (PRogrammed
ELectrical stimUlation preDictive valuE) Registry

Table 3 Prognostic Accuracy of Predictors of Outcome

	Inducibility* (Full Protocol)	Inducibility (With 1 or 2 Extra Stimuli)	Spontaneous Type 1 ECG Pattern	History of Syncope	Spontaneous Type 1 ECG and Syncope	QRS-f	VRP <200 ms
Sensitivity	35.7 (14–64)	25.0 (5.8–50)	92.9 (65–99)	50.0 (25–76)	42.9 (19–69)	42.9 (20–69)	78.6 (49–94)
Specificity	58.8 (58–60)	74.2 (78–81)	45.7 (45–47)	80.6 (79–82)	90.5 (89–92)	93.5 (92–95)	62.9 (62–64)
NNT	102.3 (20–200)	—	14.5 (12–58)	12.4 (6.7–108)	6.8 (3.7–26)	4.7 (2.7–14)	13.2 (9.4–50)
Univariate log-rank (p value)	0.67	0.89	0.004	0.011	0.000105	0.000001	0.002

- Henüz kılavuzlar fQRS i ICD kararı vermede önermiyor ancak VF ile ilişkisi 1 çalışma hariç tüm çalışmalarda gösterilmiştir.
- Ancak çalışmalar arasında fQRS tanımları farklıdır ve EKG filtre ayarlarının durumu nasıl etkileyeceği net değildir.



QRS genişliği

- 2 çalışma olumlu sonuçlandı da sonraki büyük kayıt çalışmalarında ve PRELUDE'de değeri gösterilemedi.

'aVr Sign'

- aVr de $> 3\text{mm}$ R dalgası veya
- R/q oranı > 0.75 ise artmış risk?
- Büyük çalışmalarda konfirme edilemedi.

PERİFERAL LEADLERDE TİP 1 PATTERN

- Ajmalin testinde vakaların %10'u

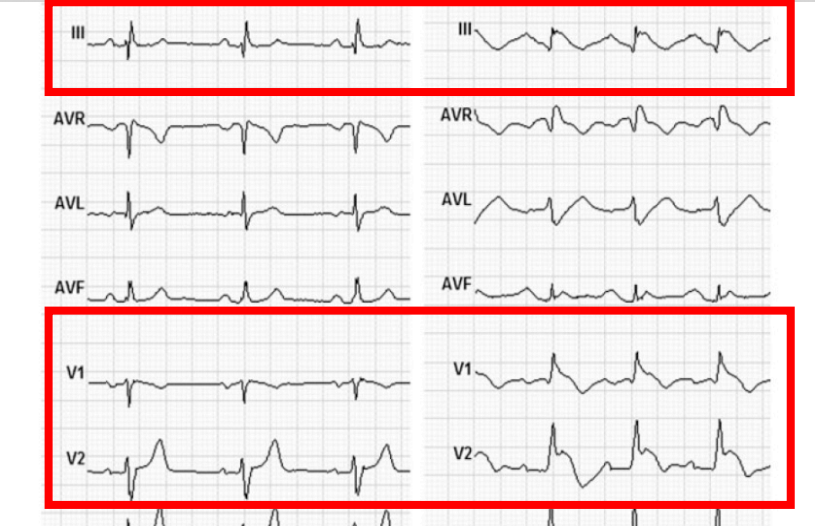


Table 3 Correlations between type 1 ST elevation in the peripheral leads and symptoms or ventricular arrhythmias

	Type 1 ST elevation in the peripheral leads (n = 30, 9%)	No type 1 ST elevation in the peripheral leads (n = 293, 91%)	P
Syncopal	13 of 30 (43%)	72 of 293 (26%)	.02
SCD	4 of 30 (13%)	8 of 293 (3%)	.003
AT in patients with ICD	5 of 18 (28%)	12 of 116 (10%)	.03
SCD and/or AT	8 of 30 (27%)	18 of 293 (6%)	<.0001
Syncopal/SCD/AT	17 of 30 (57%)	81 of 293 (28%)	.001

Prevalence, characteristics, and prognosis role of type 1 ST elevation in the peripheral ECG leads in patients with Brugada syndrome

A. Rollin,^{*} F. Sacher,[†] J.B. Gourraud,[‡] J.L. Pasquié,[§] F. Raczk,[§] A. Duparc,^{*} P. Mondoly,^{*} C. Cardin,^{*} M. Delay,^{*} S. Chatel,[‡] N. Derval,[†] A. Denis,[†] M. Sadron,^{*} J.M. Davy,[§] M. Hocini,[†] P. Jaïs,[†] L. Jesel,[†] M. Haïssaguerre,[†] V. Probst,[‡] P. Maury^{*}

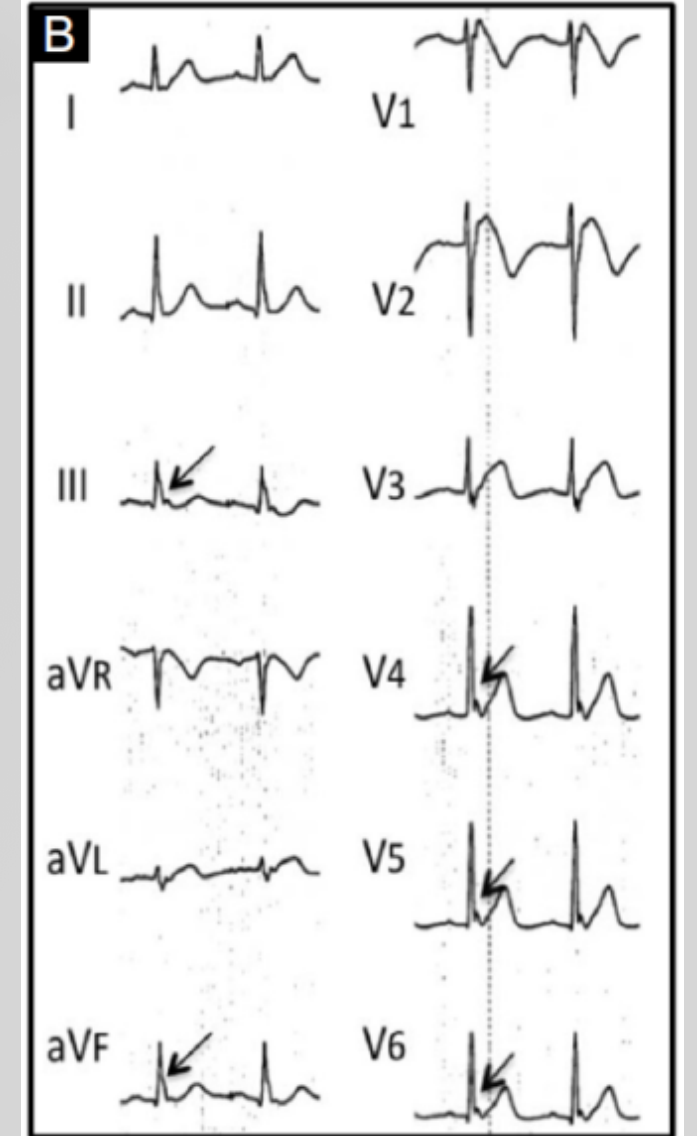
Table 4 Parameters related to SCD and/or AT in univariate and multivariate analyses

Parameters	OR (95% CI)	P
<i>Univariate analysis</i>		
Type 1 ST elevation in the peripheral leads	5.55 (2.17–14.21)	.0003
Syncopal	3.12 (1.39–7.04)	.006
Spontaneous type 1 ST elevation	2.63 (1.13–6.10)	.023
SCN5A mutations	3.06 (1.06–8.80)	.037
Familial SCD	2.27 (1.01–5.12)	.047
Inducibility	2.39 (0.83–6.31)	.10
<i>Multivariate analysis</i>		
Type 1 ST elevation in the peripheral leads	4.58 (1.70–12.32)	.0025
Spontaneous type 1 ST elevation	2.43 (1.01–5.84)	.047
Syncopal	2.34 (0.99–5.50)	.051
Familial SCD	1.99 (0.84–4.69)	.11

SCN5A mutations or inducibility not included in the multivariate analysis because of missing data in a significant part of the population. AT = appropriate implantable cardioverter-defibrillator therapy; CI = confidence interval; OR = odds ratio; SCD = sudden cardiac death.

PERİFERAL LEADLERDE ERKEN REPOLARİZASYON

- BrS de inferolateral erken repol. %11-15
- VF riski 4 kat daha fazla
- Başka bir çalışmada horizontal ST de EP varsa risk 11 kat fazla
- EP persistan ise risk en yüksek

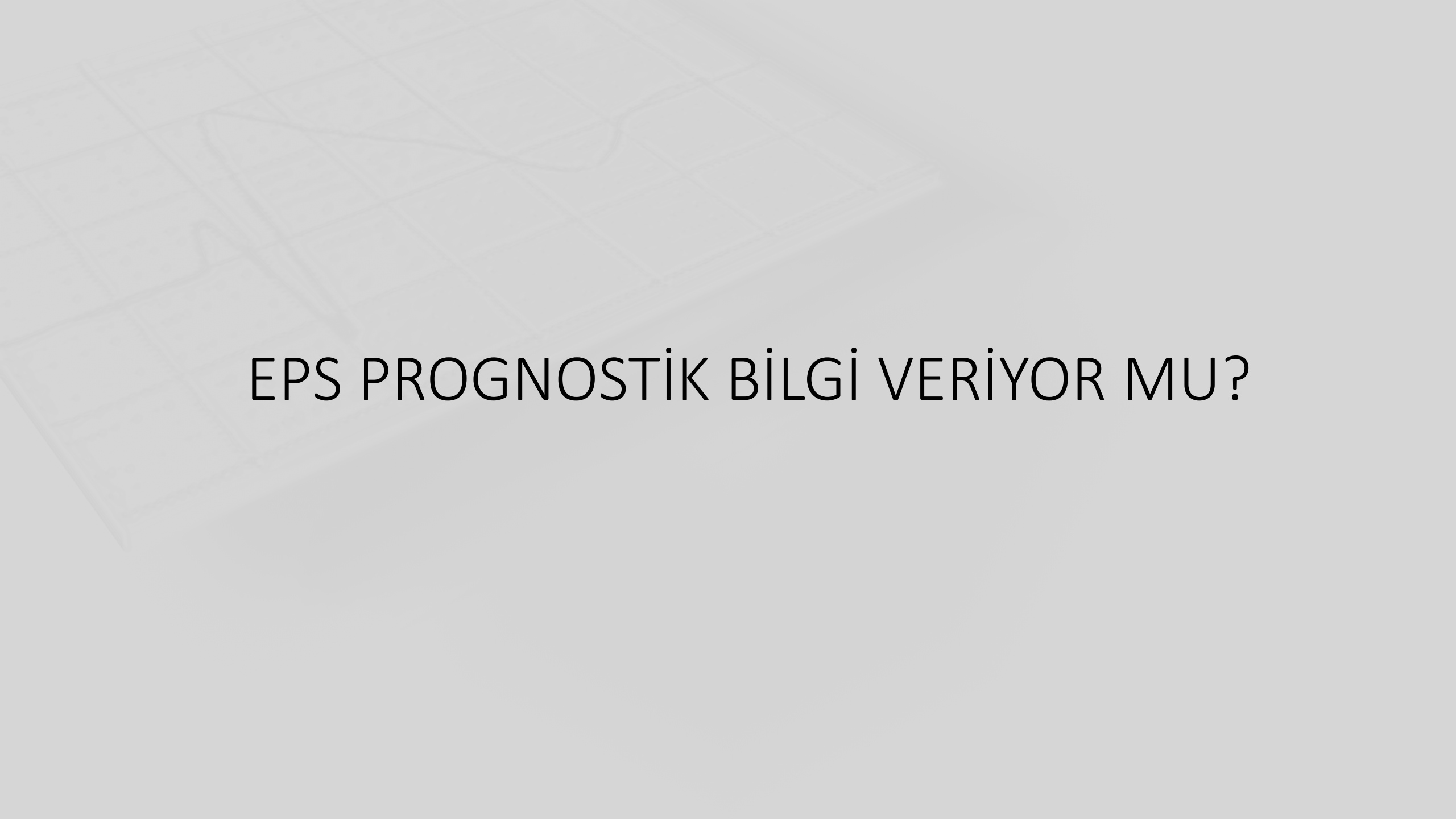


saEKG DE GEÇ POTANSİYELLER

- Ikeda et al. LP varlığının aritmik olayları öngördüğünü univariate analizde gösterdi. (konfirme edilmedi)

Makroskopik TWA

- Bir çalışmada pilsicainid testi sırasında görülmesi VF için 22 kat artmış riski gösterdi (konfirme edilmedi)
- Mikrovolt TWA brugada için yeterli veriye sahip değil.



EPS PROGNOSTİK BİLGİ VERİYOR MU?

- Tüm serilerde EPS indüklenebilirliği
 - SCD öyküsü olanlarda en yüksek
 - Senkop varlığında intermediate
 - Asemptomatiklerde düşük saptanıyor
- Ancak soru EPS nin aritmik olaylarla ne kadar korele olduğu değil
- Soru EPS ICD kararı verdirebilecek kadar güçlü bir veri sağlıyor mu?

A **Asymptomatic Brugada syndrome.**

Japanese Study		Europe FINGER Study		Latest Brugada series		All 3 studies combined	
Spontaneous type I	Drug-induced type I	Spontaneous type I	Drug-induced type I	Spontaneous type I	Drug-induced type I	Spontaneous type I	Drug-induced type I
57	34	172	197	40	281	269	582
↓ Inducible VF	↓	↓ Inducible VF	↓	↓ Inducible VF	↓	↓ Inducible VF	↓
32 (56%)	20 (58%)	63 (37%)	74 (37%)	11 (27%)	21 (7%)	106 (39%)	115 (20%)
↓ Spontaneous VF at 4 years	↓	↓ Spontaneous VF at 5 years	↓	↓ Spontaneous VF At 6 years	↓	↓ Spontaneous VF At 4-6 years	↓
1/32=3%	0/20=0	1/63=2%	3/74=4%	3/11=27%	2/21=10%	5/106=5%	5/115=4%
1/52 = 2%		4/137 = 3%		5/32 = 16%		10/221 = 4.5%	
Spontaneous type I	Drug-induced type I	Spontaneous type I	Drug-induced type I	Spontaneous type I	Drug-induced type I	Spontaneous type I	Drug-induced type I
57	34	172	197	40	281	40	281
↓ Negative EPS	↓	↓ Negative EPS	↓	↓ Negative EPS	↓	↓ Negative EPS	↓
25	14	109	123	29	260	163	407
↓ Spontaneous VF at 4 years	↓	↓ Spontaneous VF at 5 years	↓	↓ Spontaneous VF at 5 years	↓	↓ Spontaneous VF At 4-6 years	↓
2/25=8%	0/14=0	2/109=2%	1/123=1%	0/29=0	3/260=1%	4/163=2.5%	4/397=1%
2/39 = 5%		3/232 = 1%		3/289 = 1%		8/560 = 1.4%	

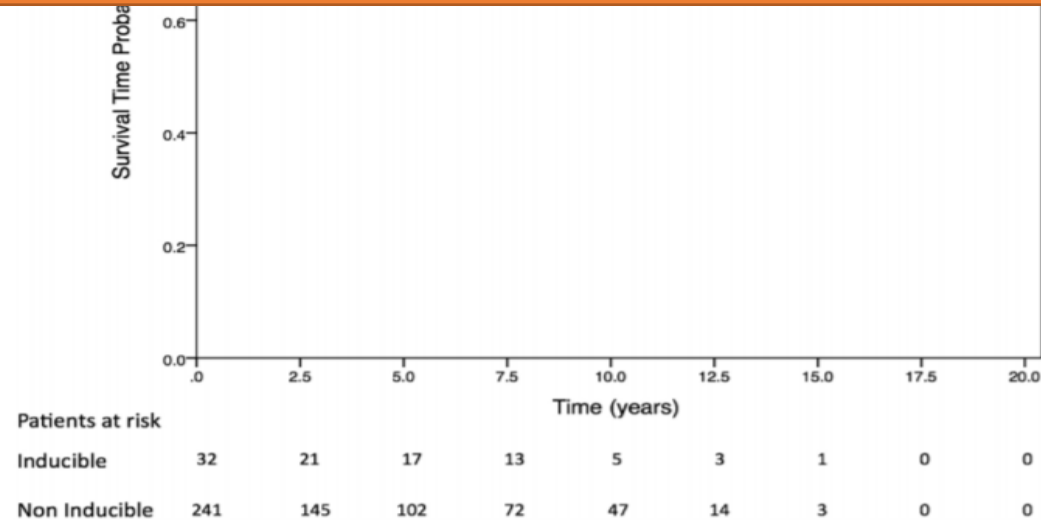
Totalde %1,4 e %4,5 gibi bir fark olsa da bu güvenle bir öneri yapabilmek için düşük bir fark
Ayrıca veriler arasında belirgin bir uyumsuzluk mevcut

Original Article

Prognostic Value of Programmed Electrical Stimulation in Brugada Syndrome 20 Years Experience

Juan Sieira, MD; Giulio Conte, MD; Giuseppe Ciconte, MD; Carlo de Asmundis, MD;
Gian-Battista Chierchia, MD; Giannis Baltogiannis, MD; Giacomo Di Giovanni, MD;
Yukio Saitoh, MD; Ghazala Irfan, MD; Ruben Casado-Arroyo; Justo Juliá, MD;
Mark La Meir, MD; Francis Wellens, MD; Kristel Wauters, MD; Sophie Van Malderen, MD;

137 hasta brugadanın serisinde de alınmış
Ancak indüklenebilirlik azalmış
Yıllık olay oranları da azalma göstermiş.
Ayrıca bu azalma benzer çalışmalar ile uyumlu düzeyde
Bu bias olasılığı ve ilk vakaların yüksek riski ile açıklanıyor.



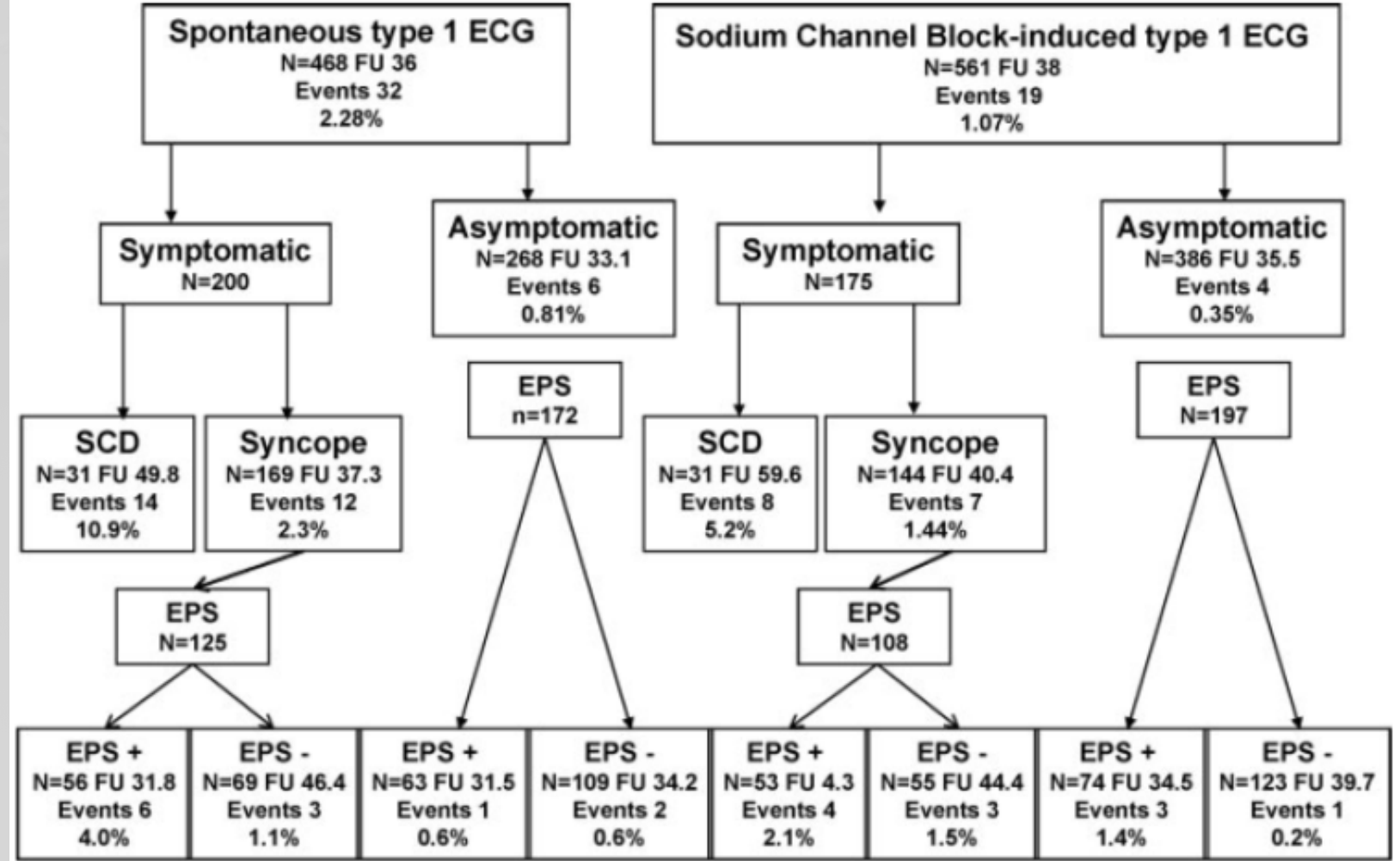
Event-free survival in asymptomatic patients according to Kaplan–Meier method.

Long-Term Prognosis of Patients Diagnosed With Brugada Syndrome

Results From the FINGER Brugada Syndrome Registry

V. Probst, MD, PhD*; C. Veltmann, MD*; L. Eckardt, MD*; P.G. Meregalli, MD*; F. Gaita, MD; H.L. Tan, MD, PhD; D. Babuty, MD, PhD; F. Sacher, MD; C. Giustetto, MD; E. Schulze-Bahr, MD, PhD; M. Borggrefe, MD, PhD; M. Haissaguerre, MD; P. Mabo, MD, PhD; H. Le Marec, MD, PhD; C. Wolpert, MD, PhD; A.A.M. Wilde, MD, PhD

- **FINGER çalışması**
- 654 asemptomatik hasta
- indüklenebilirlik lehine her grupta bir artış rapor etti ancak multivariate analizde etkinliği anlamlı düzeye ulaşamadı.
- Asemptoatiklerde sıklık %0,5



Risk Stratification in Brugada Syndrome

N: 273

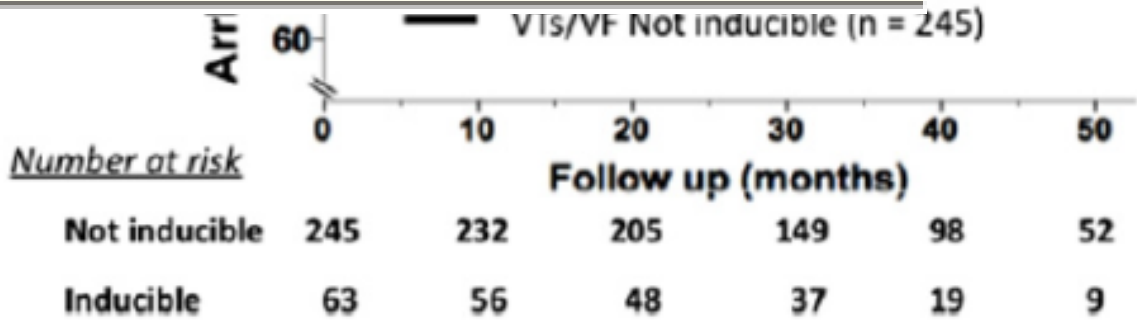
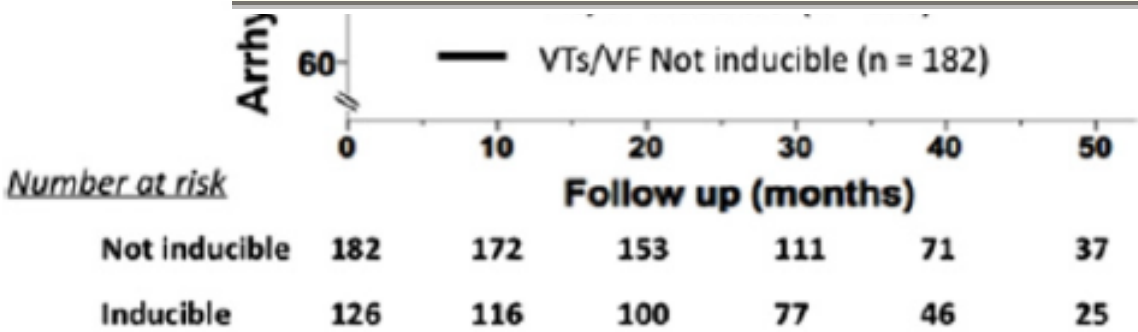
Results of t
ELectrical s

Table 3 Prognostic Accuracy of Predictors of Out

Silvia G. Prior
Paolo Della Be

A

	Inducibility* (Full Protocol)	Inducibility (With 1 or 2 Extra Stimuli)	VRP <200 ms
Sensitivity	35.7 (14-64)	25.0 (5.8-50)	78.6 (49-94)
Specificity	58.8 (58-60)	74.2 (78-81)	62.9 (62-64)
NNT	102.3 (20-200)	—	13.2 (9.4-50)
Univariate log-rank (p value)	0.67	0.89	0.002



Systematic Review for the 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

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

Part 1: For Asymptomatic Patients With Brugada Syndrome, What Is the Association Between an Abnormal Programmed Ventricular Stimulation Study and Sudden Cardiac Death and Other Arrhythmia Endpoints?

Table 1. Summary of Electrophysiological Study Protocols and Inducibility Rates by Study Included

Study, Year, Reference	Positive EP Study	Protocol
Sieira, et al 2015 (15)	32/241 (13%)	Single site, 3 cycle lengths, 3 ES (≥ 200 ms)
Priori 2012, et al (12)	97/243 (40%)	2 sites (RVA, RVOT), 2 cycle lengths, 3 ES (≥ 200 ms)
Kamakura 2009, et al (11)	61/123 (50%)	2 sites (RVA, RVOT), 2 cycle lengths, 3 ES (does not mention a minimum CL)
Takagi, et al 2007 (16)	50/63 (79%)	Unspecified in the methods
Probst, et al 2010 (14)	137/369 (37%)	2 sites (unspecified), 2 cycle lengths, 3 ES (≥ 200 ms for a “positive” study)
Priori, et al 2000 (12)	6/19 (32%)	unspecified in the methods but several sites and up to 3 ES (not uniformly specified by the protocol)
Brugada, et al 2003 (10)	91/263 (35%)	Single site (not RVOT), 2 cycle lengths, ≥ 2 ES (VERP)

EP indicates electrophysiological; ES, extra stimulus; RVA, right ventricular apex; RVOT, right ventricular outflow tract; and VERP, ventricular effective refractory period.



Figure 1.2. Forest Plot for Risk of All Arrhythmic Events Excluding Brugada P, et al. (2003) (10)

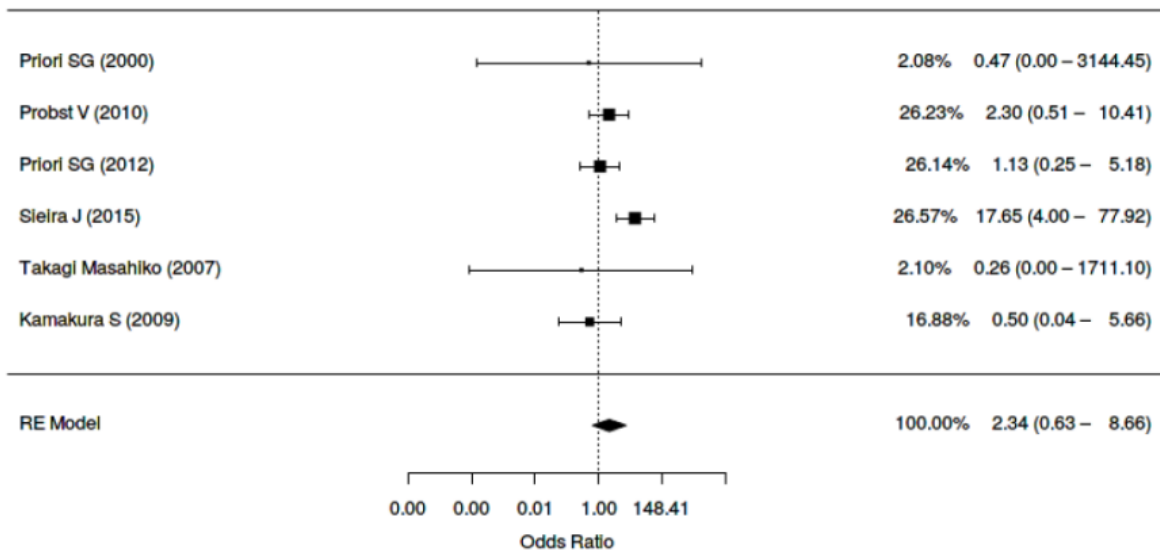
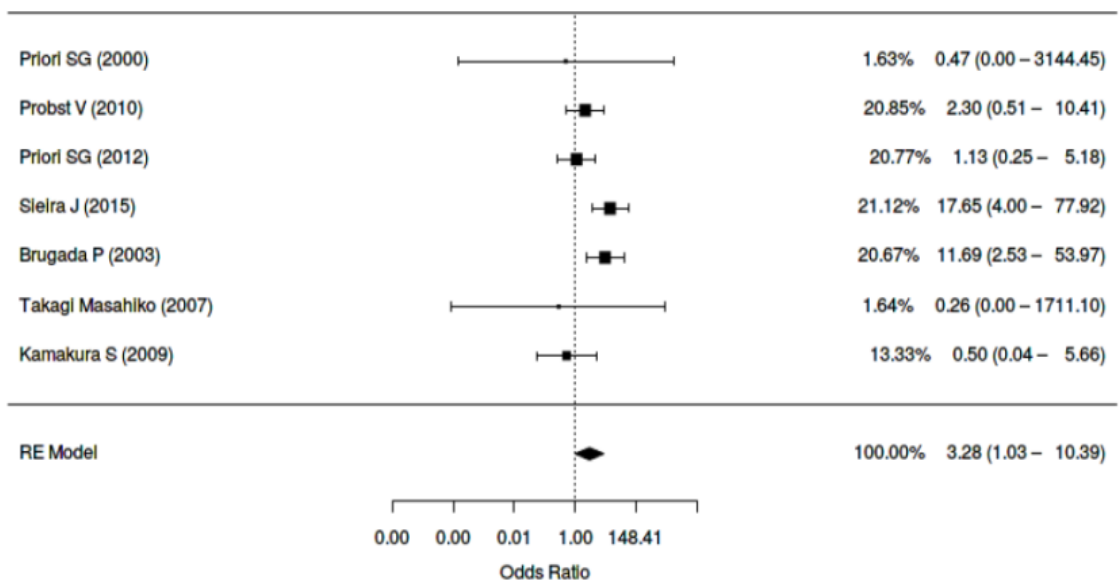


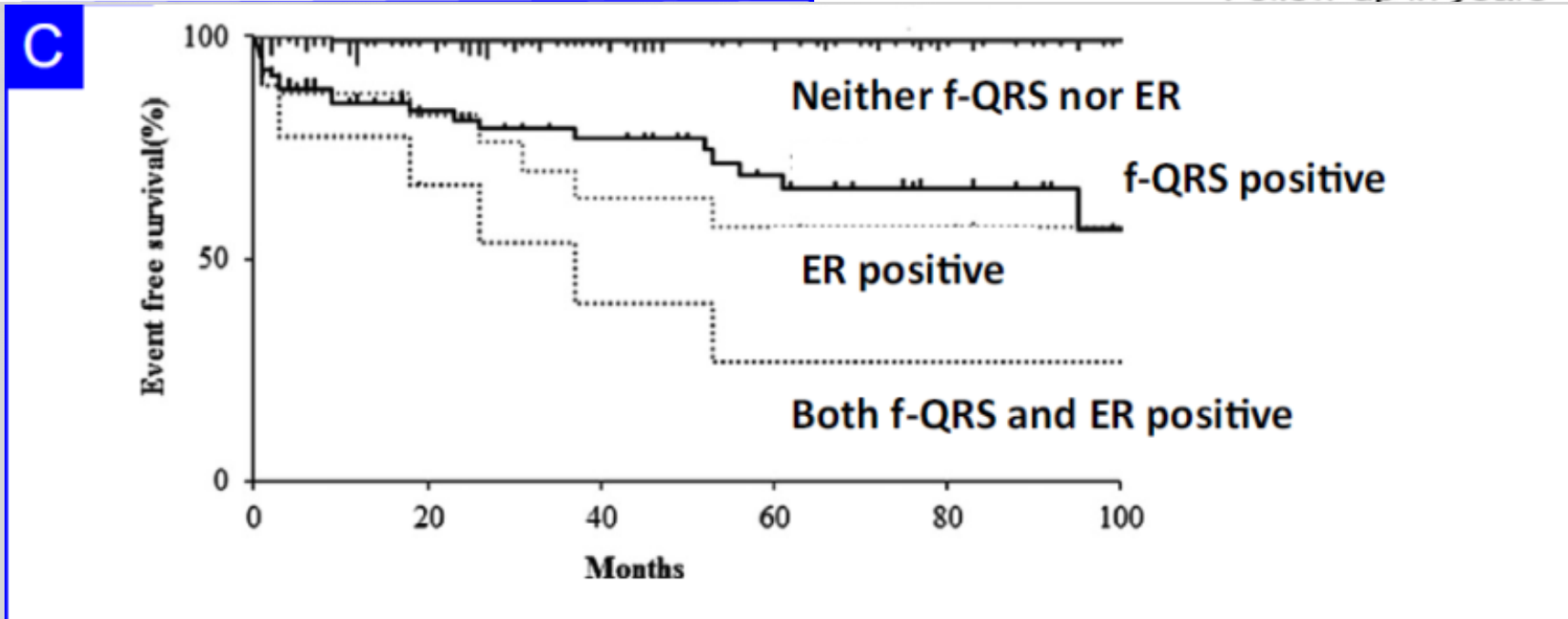
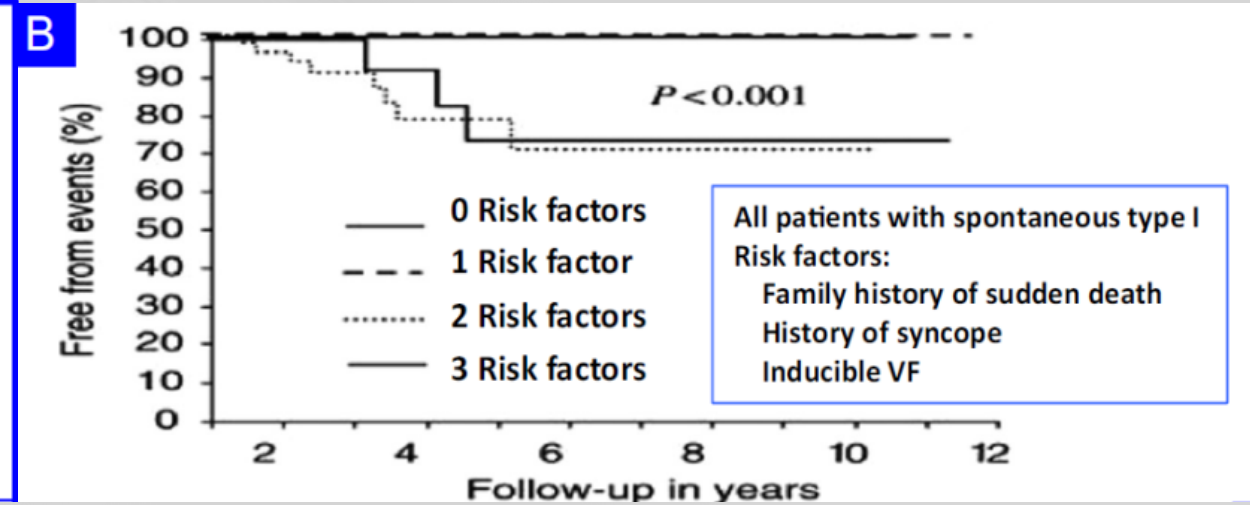
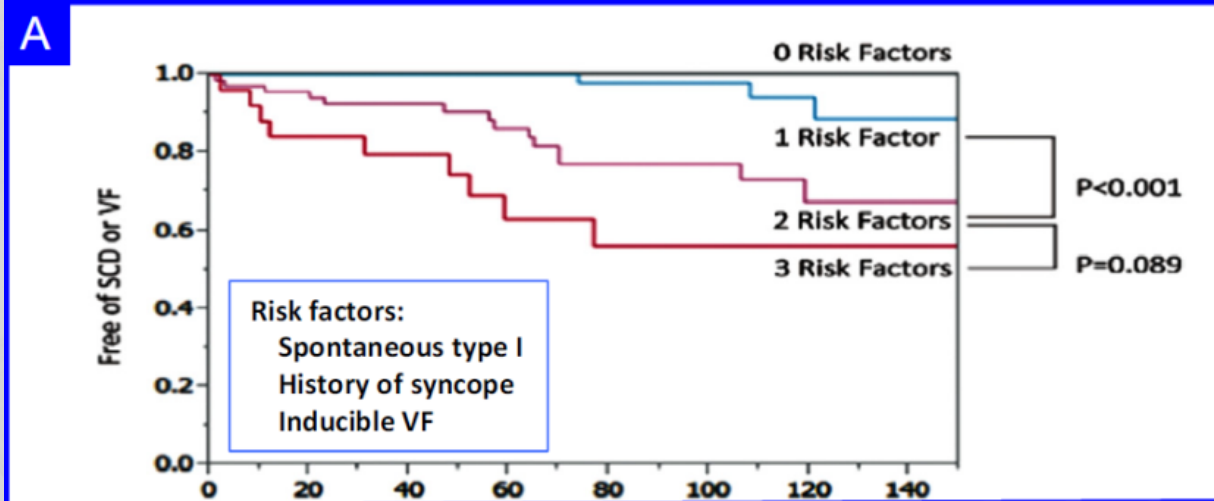
Figure 1.3. Forest Plot for Risk of All Arrhythmic Events Including Brugada P, et al. (2003) (10)



- Total 1138 hasta
- EPS de VA+: %34.3 (n:390)
- Aritmik olay: %3,3 (13/390)
- EPS de VA -: %65,7 (n:748)
- Aritmik olay: %1,6 (12/748)

- OR:2.3 (95% confidence interval [CI]: 0.63–8.66; p=0.2)

RISK FAKTÖRLERİNİ KOMBİNE EDELİM Mİ?



Brugada Syndrome Phenotype Elimination by Epicardial Substrate Ablation

Josep Brugada, MD*; Carlo Pappone, MD, PhD*; Antonio Berrueto, MD, PhD;
Gabriele Vicedomini, MD; Francesco Manguso, MD, PhD; Giuseppe Ciconte, MD;
Luigi Giannelli, MD; Vincenzo Santinelli, MD

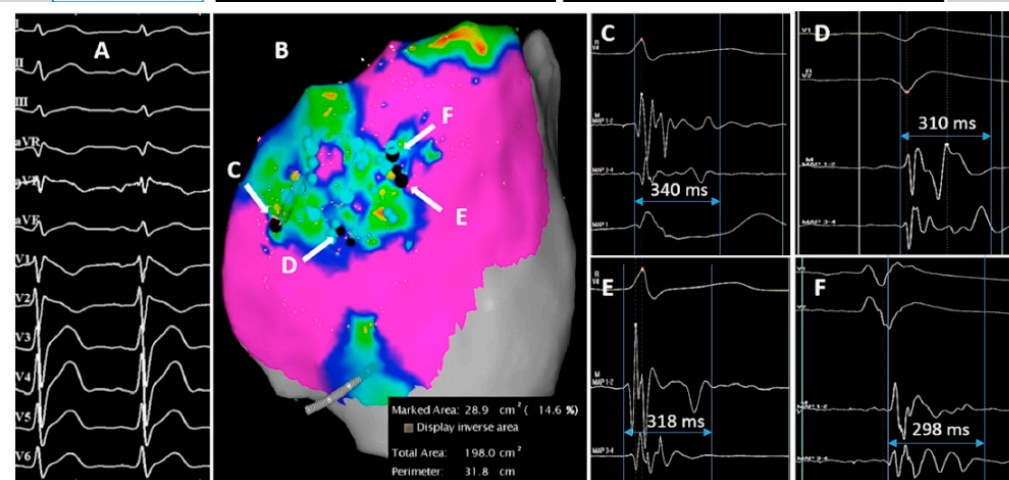
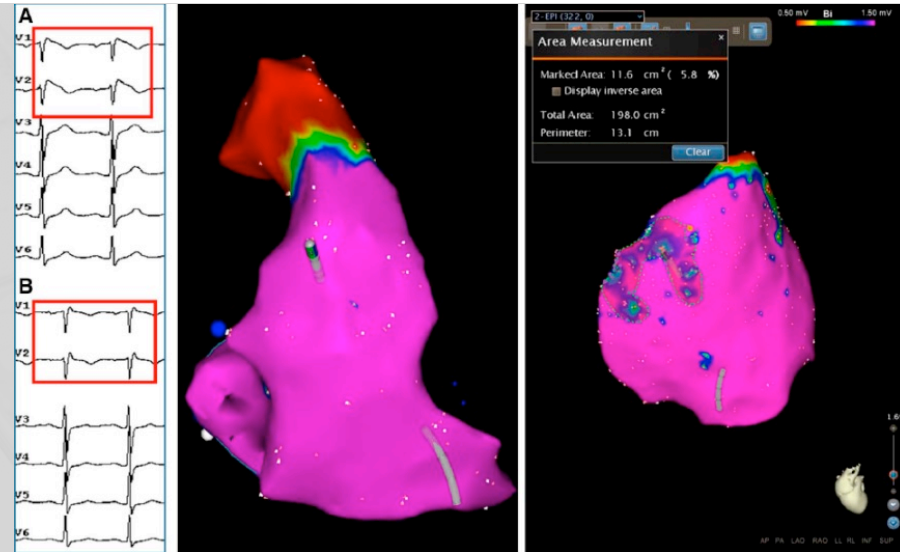
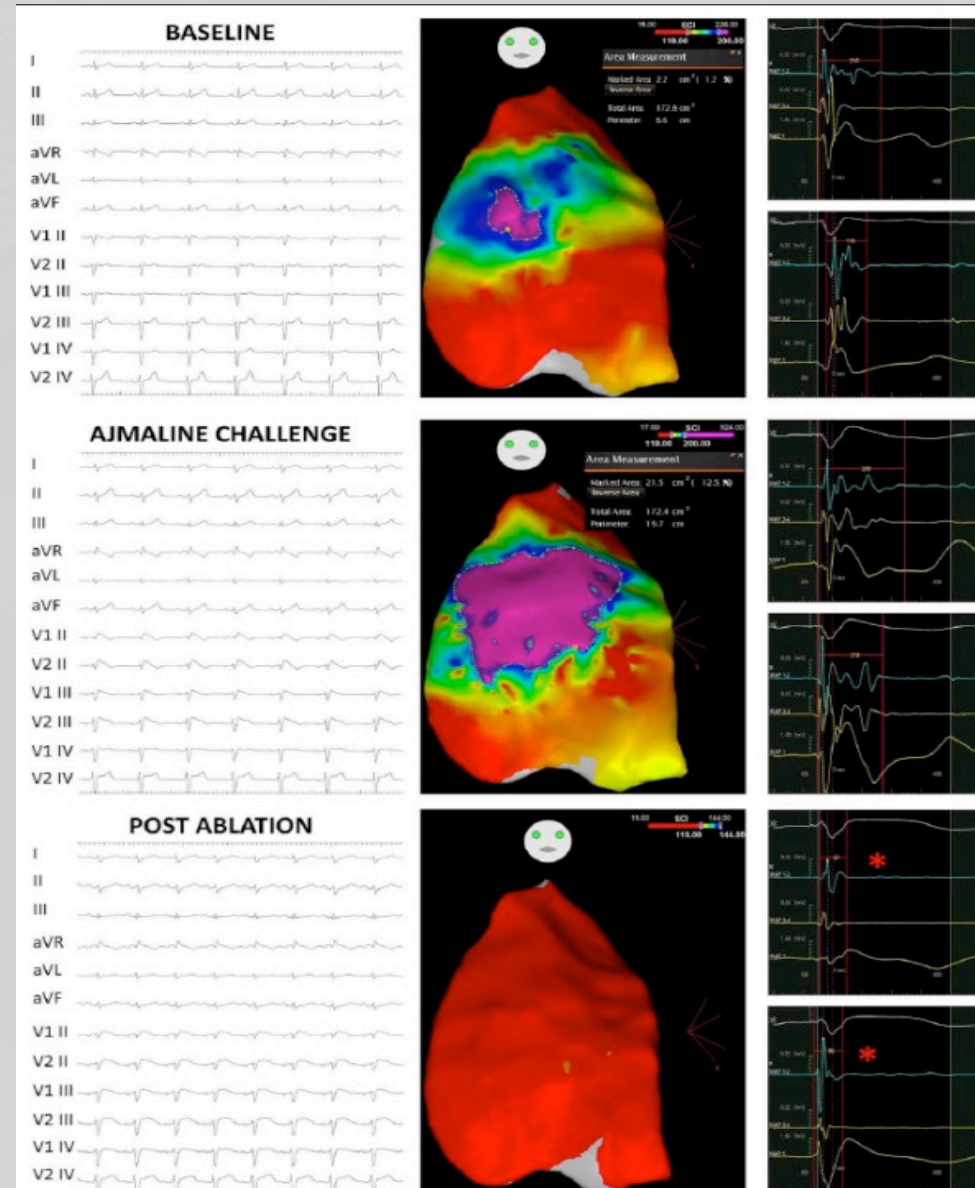
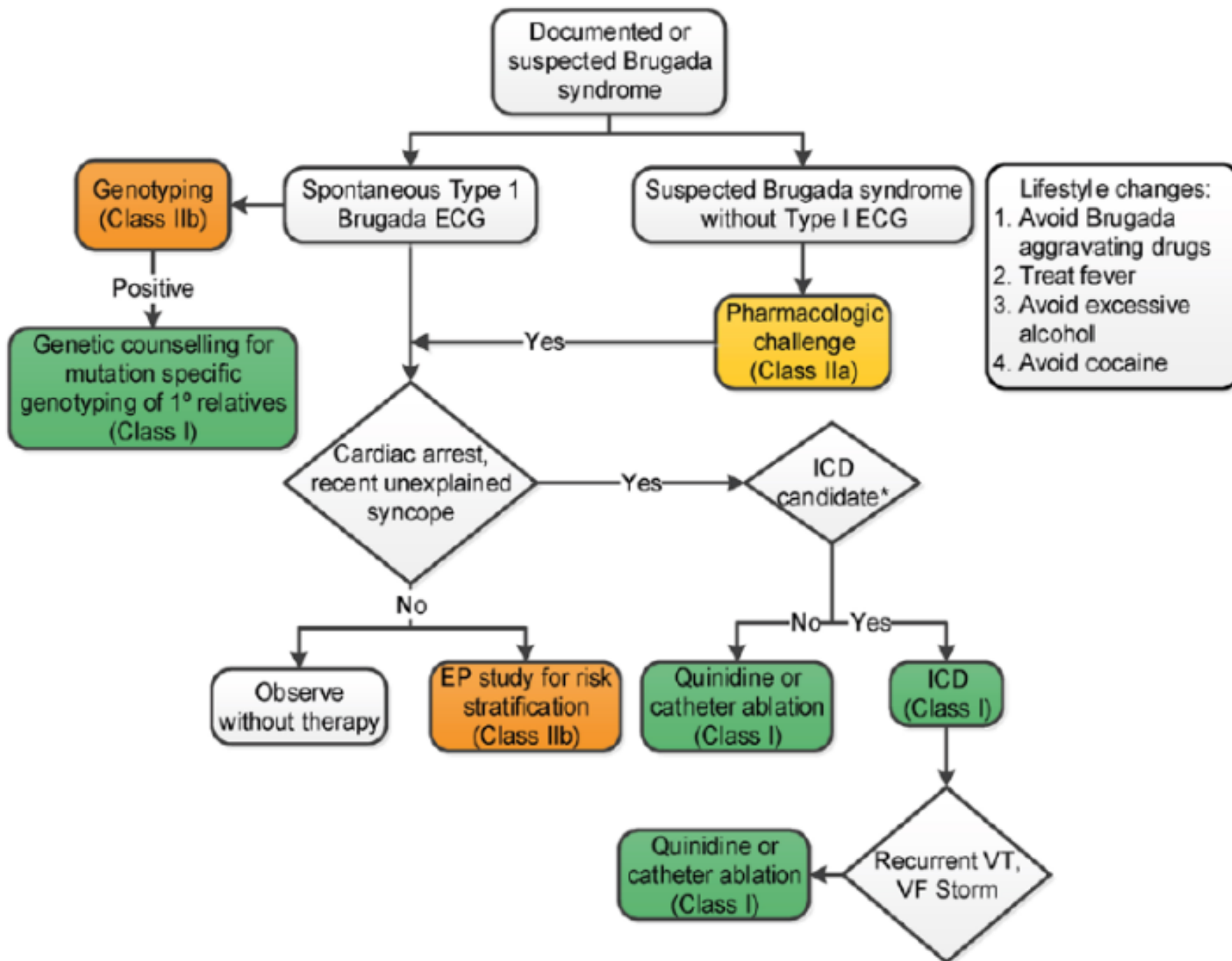


Figure 2. Same patient as in Figure 1. After administration of flecainide, 12-lead ECG shows a typical coved pattern in V1–V2 (A), and the epicardial map (B) shows an increased area (from 11.6 cm² to 28.9 cm²) of high frequency low-voltage potentials characteristically located on the right ventricular outflow tract (C and D). In this area, there are also low-frequency low voltage potentials (E and F; arrows). Endocardial map remained unaltered after flecainide infusion (not shown).

ABLASYON







TEŞEKKÜRLER.....