

2015 Venice Arrhythmia

Core Curriculum:

Arrhythmogenic genetic syndrome: what's new?

Brugada Syndrome: What's new?

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**Variants of Brugada Syndrome:
the evolving picture**

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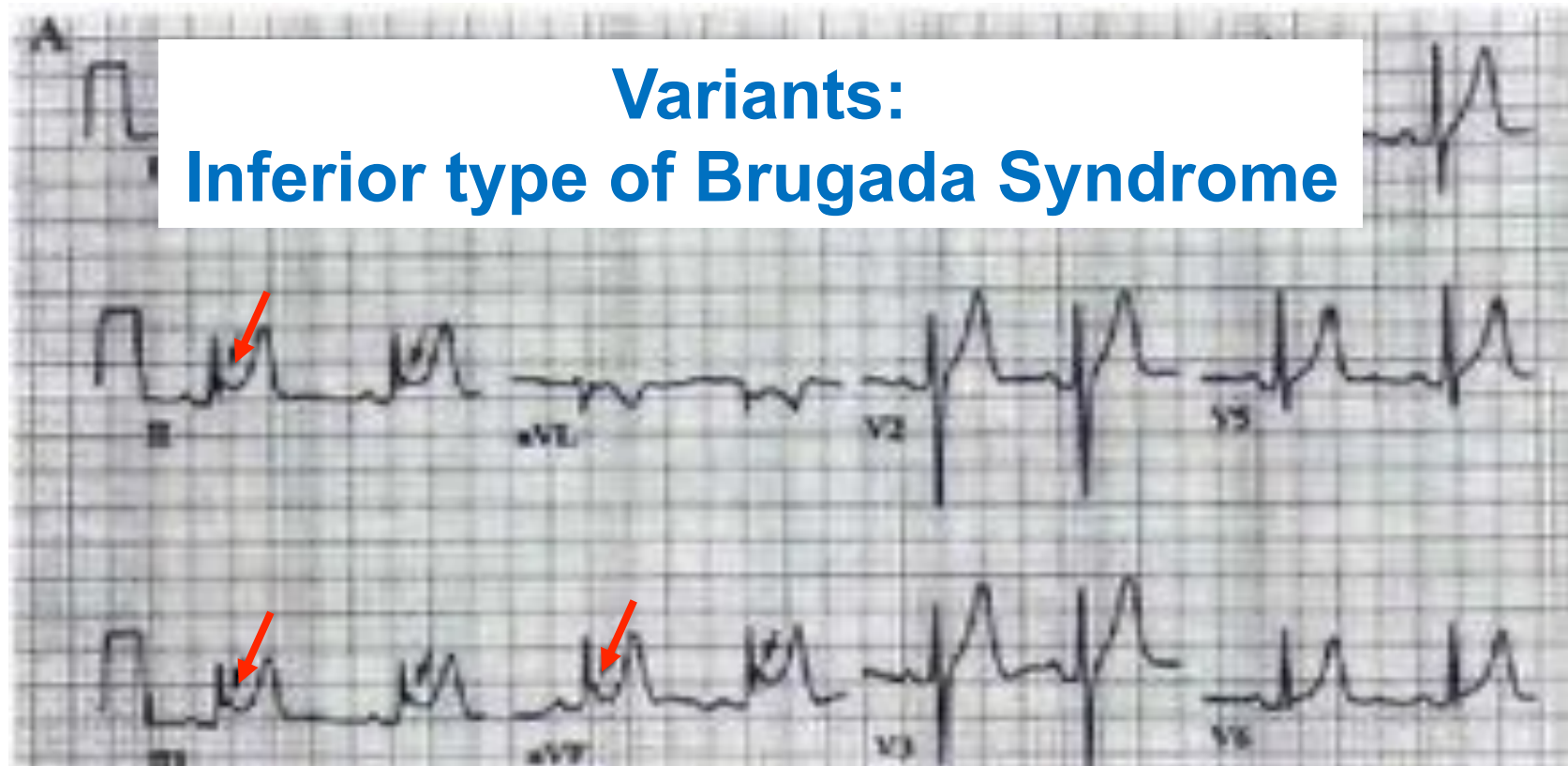


Conflicts of Interest: Wataru Shimizu

- | | |
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Idiopathic VF with J wave and ST elevation in the inferior leads: Brugada Syndrome Variants ?

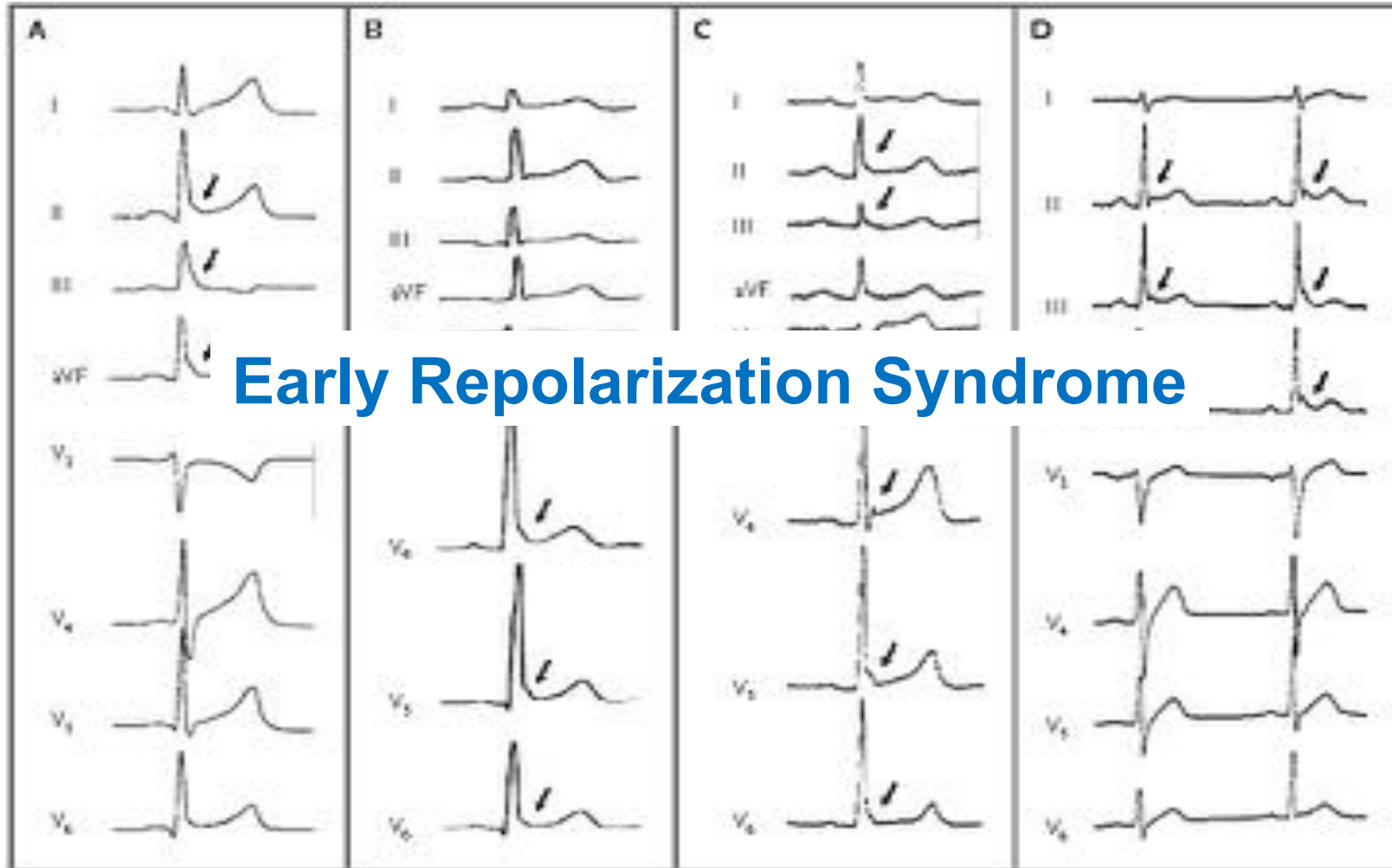
- Takagi M, Shimizu W. et al JCE 2000
- Kalla H. et al JCE 2000



Early repolarization pattern in infero/lateral leads

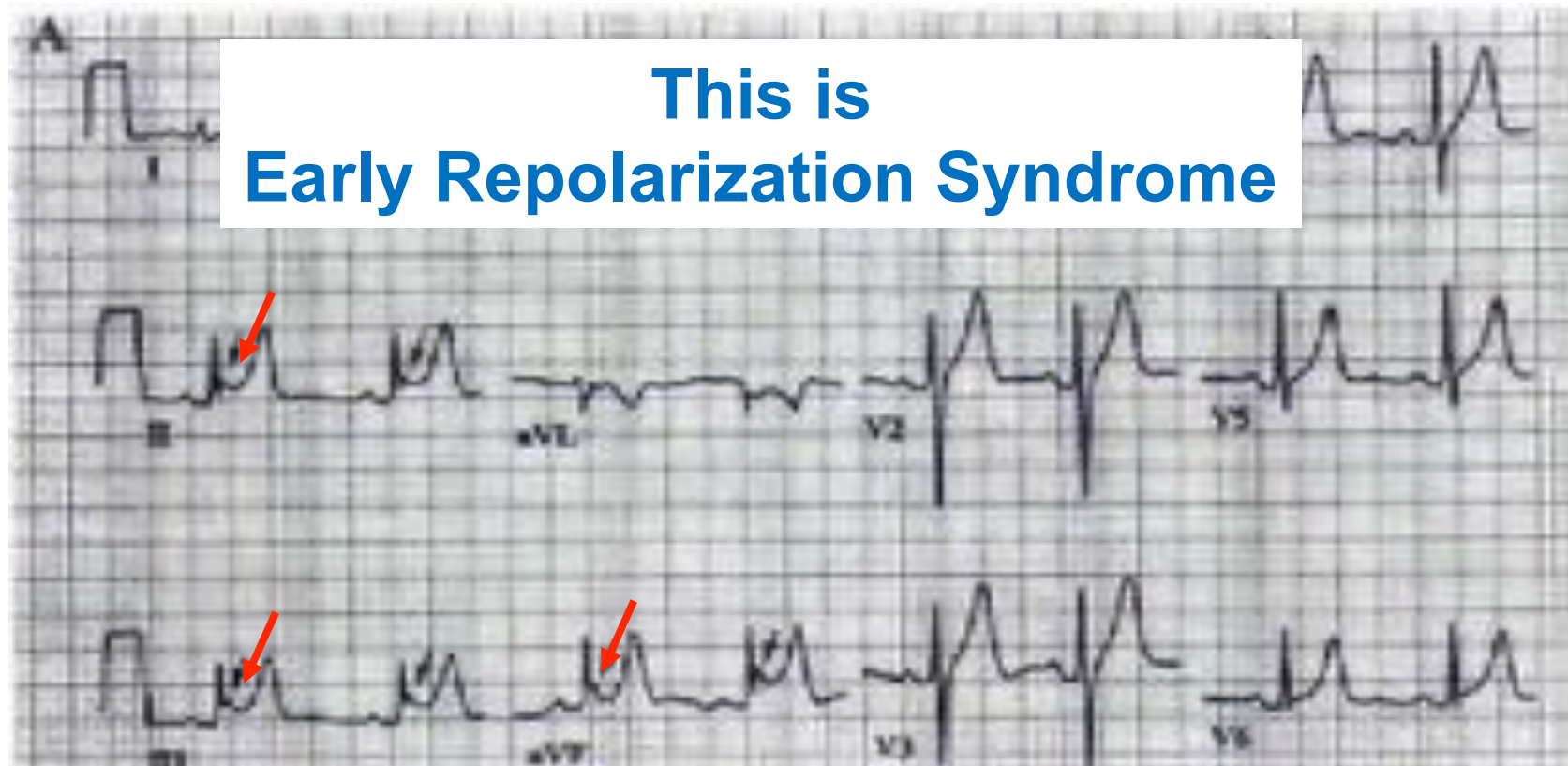
- Sudden cardiac arrest associated with early repolarization

(Haissaguerre M. et al NEJM 2008)



Idiopathic VF with J wave and ST elevation in the inferior leads: Brugada Syndrome Variants ?

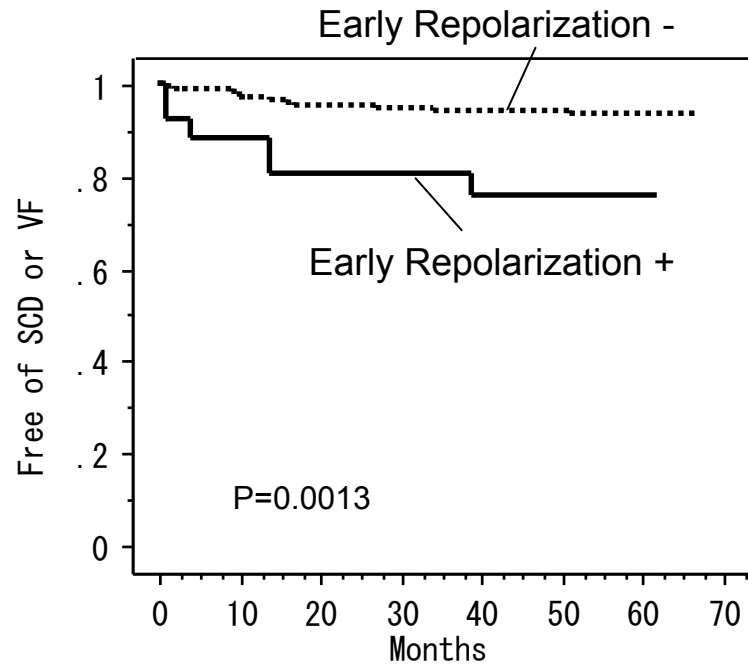
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Japanese Brugada Registry

Kamakura S, Shimizu W, et al. Circ Arrhythm Electrophysiol 2009; 2: 495-503.

Early Repolarization in infero-lateral leads



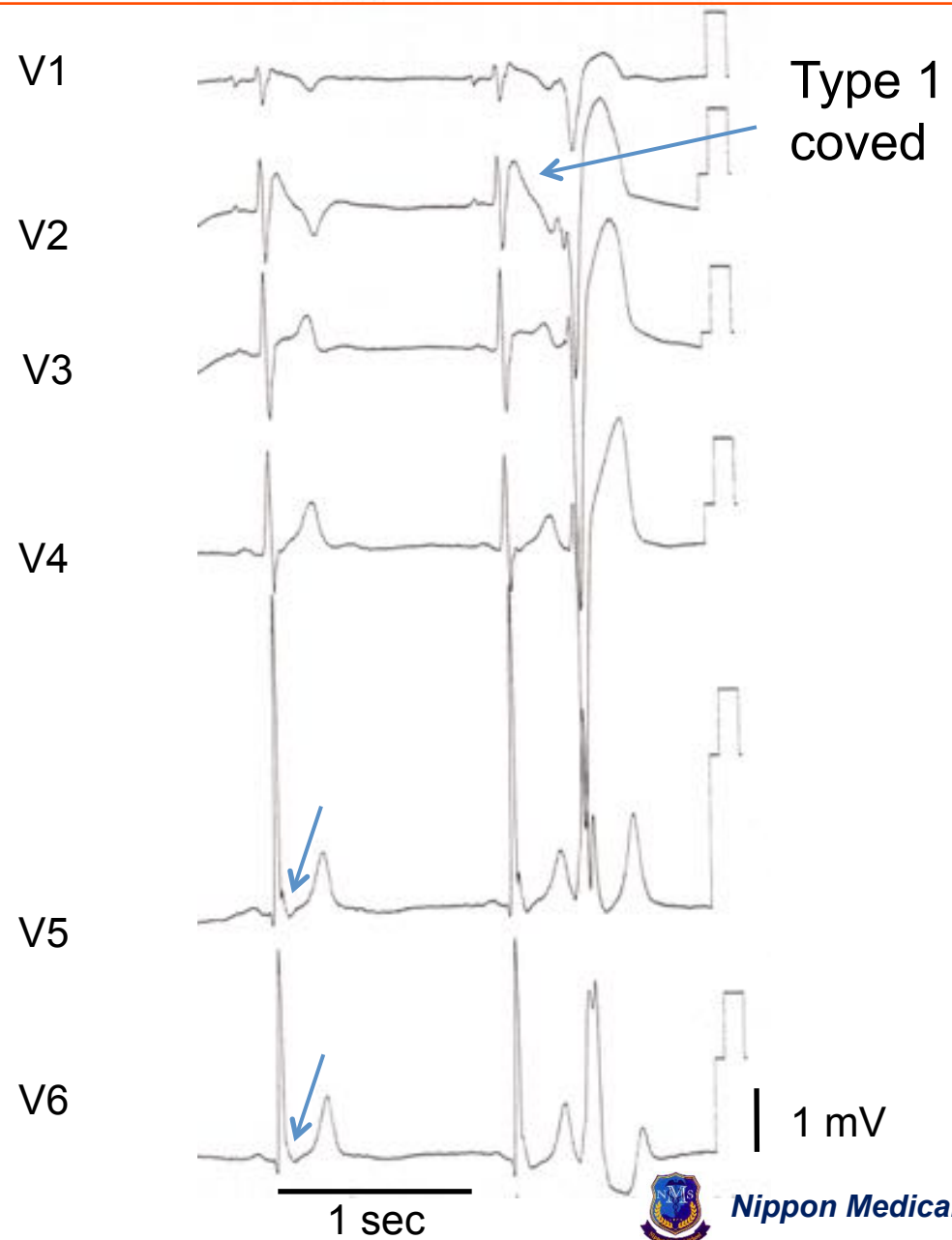
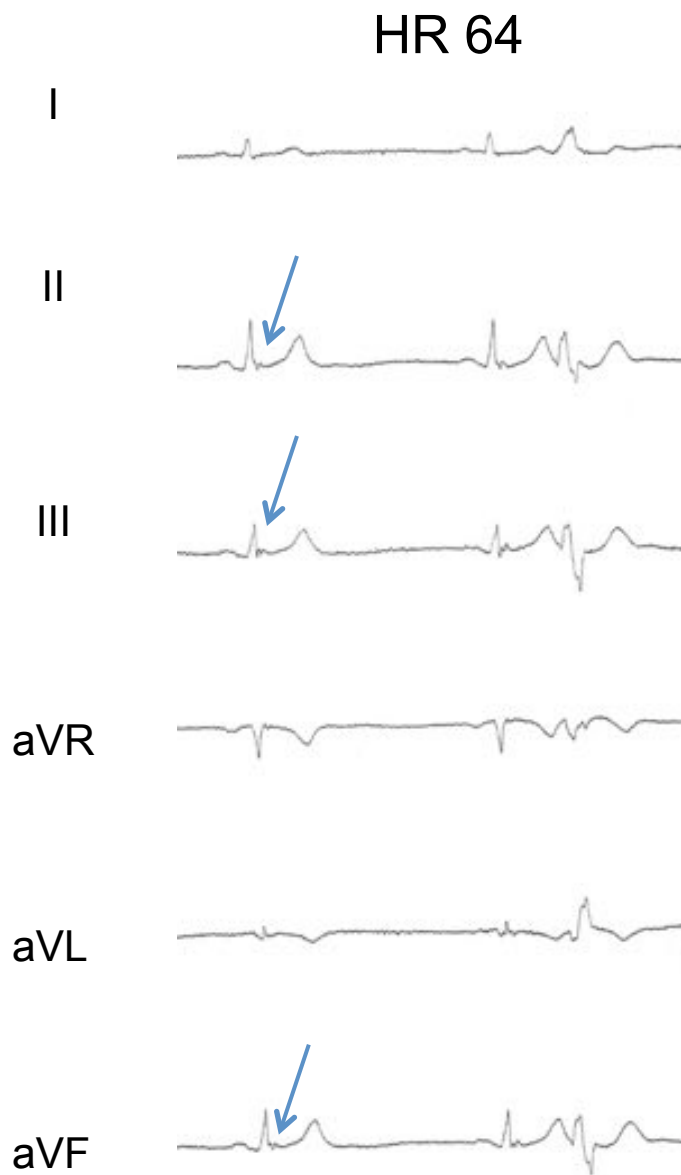
- Brugada patients associated with early repolarization in infero-lateral leads showed poorer prognosis than those without.

N. of pts. with early repolarization

Early Rep -	219	214	197	166	155	127	63
Early Rep +	26	23	19	19	17	12	9

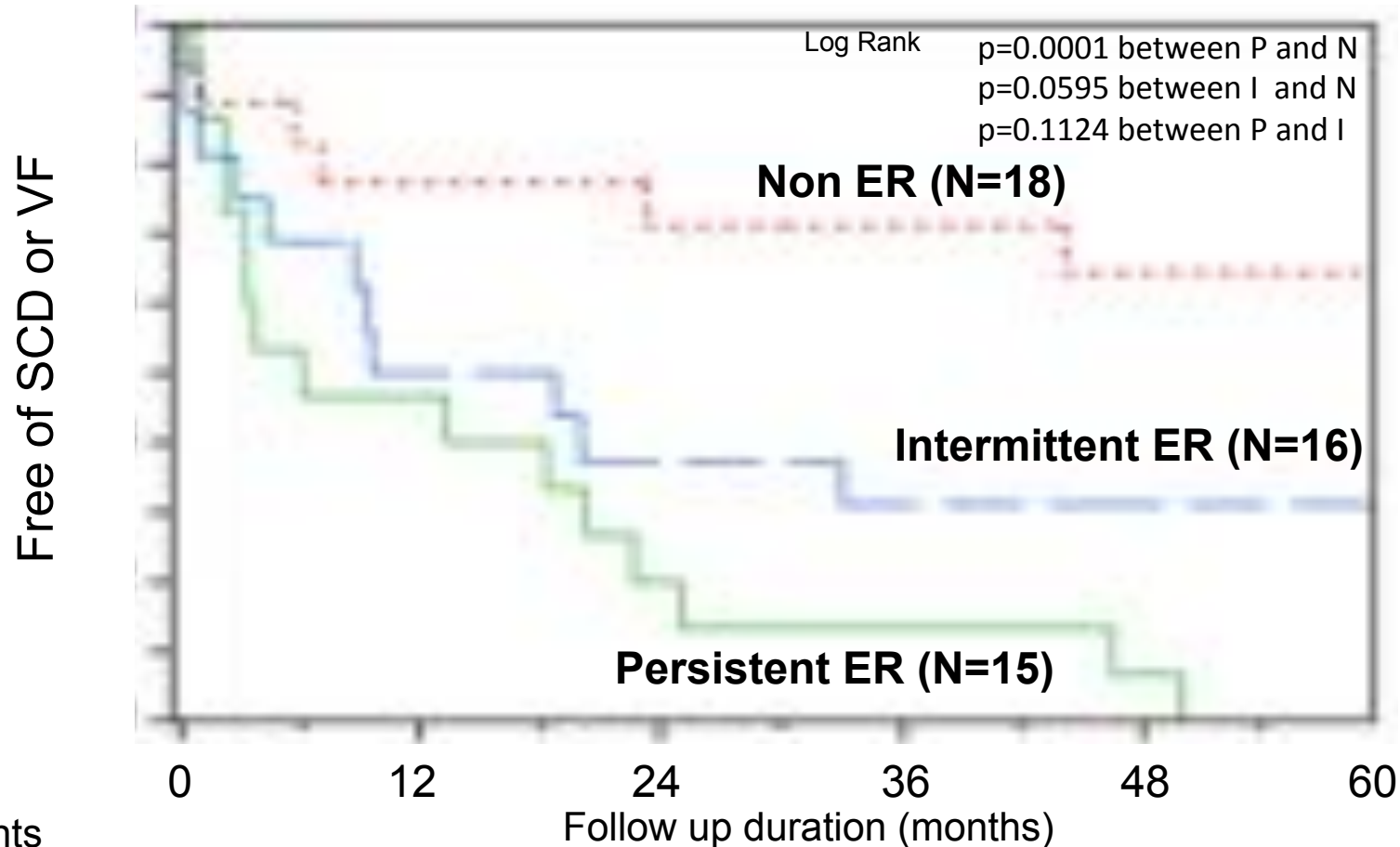
Type 1 Brugada patient with infero-lateral ER

Kawata H, Shimizu W et al. Heart Rhythm 2013;10:1161-1168



Survival Curve of Brugada patients with VF document depending on presence and frequency of infero-lateral ER

Kawata H, Shimizu W et al. Heart Rhythm 2013;10:1161-1168



Number of patients

Persistent	15	8	4	3	2	0
Intermittent	16	9	7	6	5	4
Non	18	14	13	12	11	10

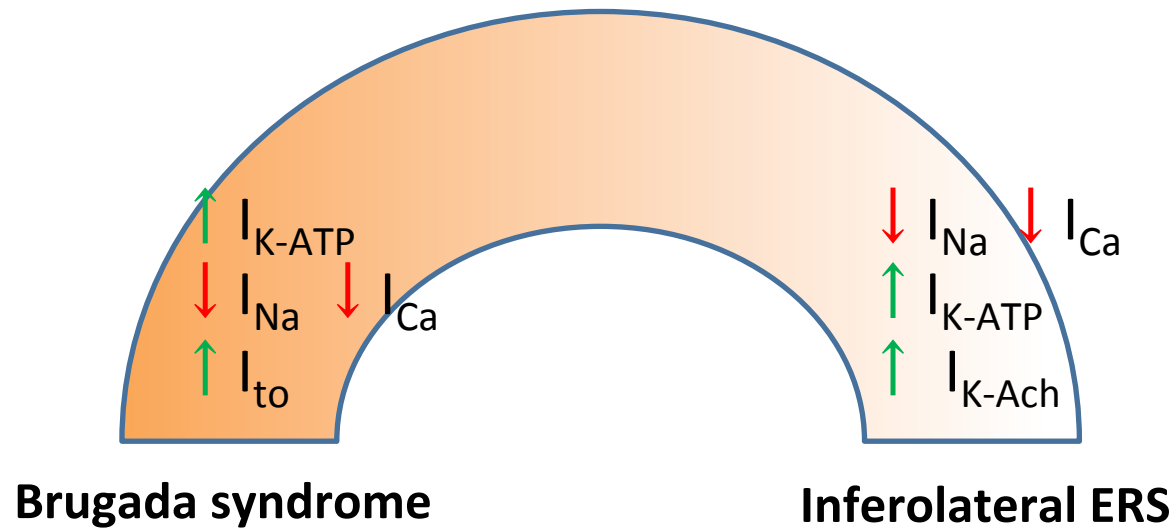
Similarities between Brugada syndrome and ERS

Shimizu W et al. Unpublished data

- Male predominance
- Late adulthood onset
- Genotype
- More frequent ventricular arrhythmias during sleep and rest than during physically active periods
- Dynamicity of the J-point elevation in an ER pattern and ST-segment elevation in a Brugada ECG
- Pause- and bradycardia-dependent augmentation of the J-point elevation in the ER pattern and ST-segment elevation in the Brugada ECG
- Response to pharmacological therapy (Isoproterenol, Quinidine, Bepridil, Denopamine, Cilostazol)

J wave syndrome

Antzelevitch C. Heart Rhythm. 2010; 7: 549-558.

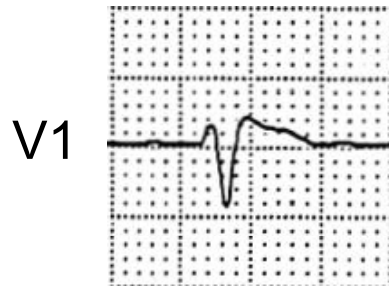


- Brugada syndrome (BrS) and ERS are considered to share a similar characteristics and to represent a continuous spectrum of phenotypic expression termed J-wave syndrome.

Japanese Brugada Registry

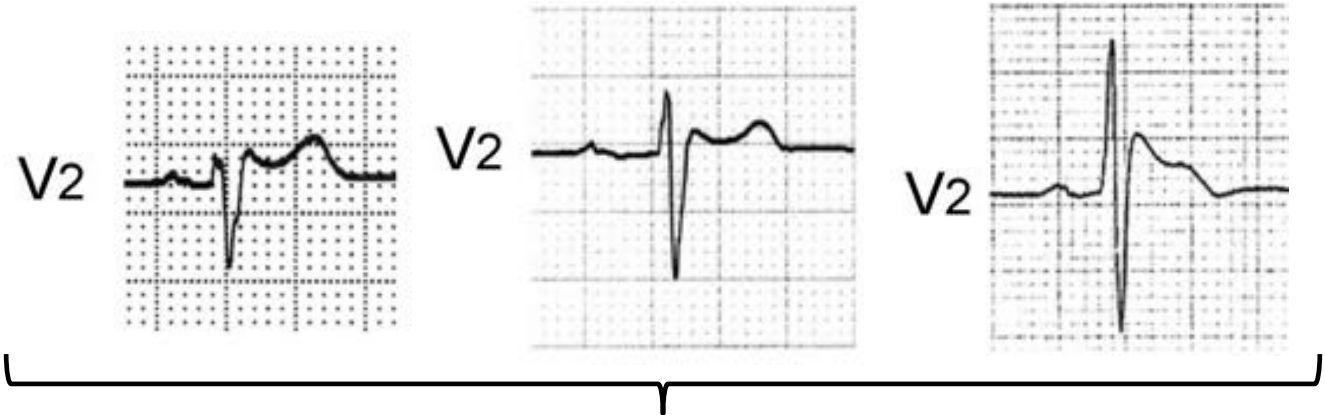
Kamakura S, Shimizu W, et al. Circ Arrhythm Electrophysiol 2009; 2: 495-503.

J wave amplitude =
1.6mm (< 2.0mm)



Coved type

Non type 1 ECG



Saddleback type

- We also reported in Japanese Brugada Registry that patients with **non-type 1 ST-segment elevation (ER pattern) in standard V1-V2 leads** even after drug provocation test show poor prognosis, just as patients with type 1 Brugada syndrome.

Diagnosis of Brugada Syndrome

Priori SG, Wilde AA, Krahn A, Shimizu W, et al. *Europace* 15(10): 1389-1406, 2013.

BrS is diagnosed when a type-1 ST-segment elevation is observed

Diagnostic criteria 2005

- At least **2** right precordial leads (V₁ to V₃)
- Standard 12-lead ECG
- Spontaneously or after drug challenge test by a sodium channel blocking agent

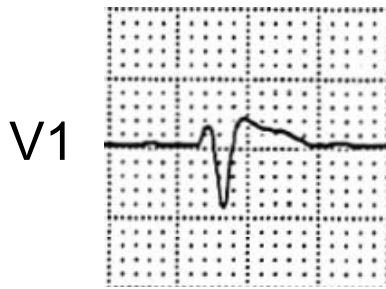
Consensus statement in 2013

- At least **1** right precordial lead (V₁ and V₂)
- Standard or **a higher position** (up to the 2nd intercostal space)
- Spontaneously or after drug challenge test by a sodium channel blocking agent

Hypothesis

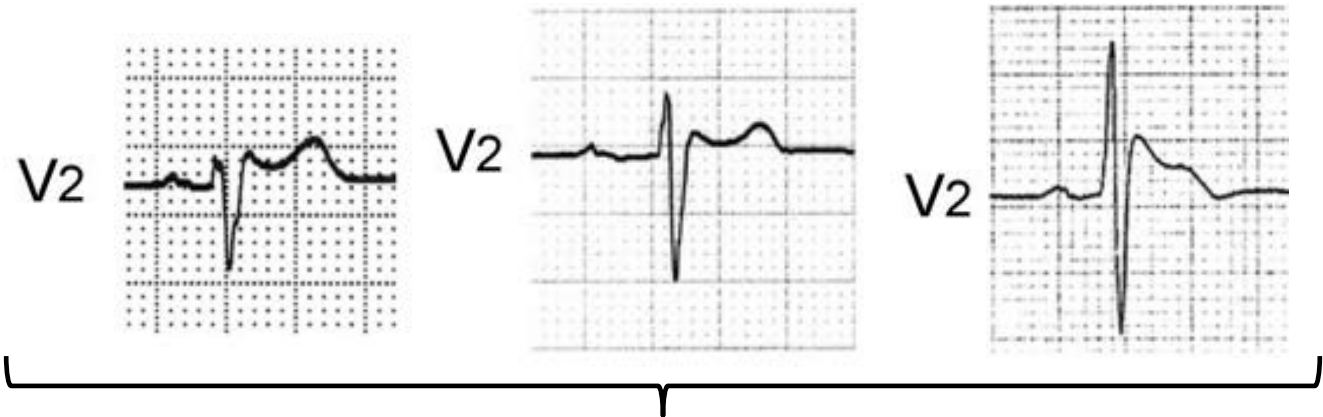
Kamakura S, Shimizu W, et al. Circ Arrhythm Electrophysiol 2009; 2: 495-503.

J wave amplitude =
1.6mm (< 2.0mm)



Coved type

Non type 1 ER pattern



Saddleback type

- Patients with **non-type 1 ER (NT1-ER) in high costal (2nd and 3rd) ECG recordings** may be another variant of Brugada syndrome.
- Therefore, we compared the clinical profile and long-term prognosis between patients with and without **NT1-ER in high costal (2nd and 3rd) ECG** among infero-lateral ERS patients.

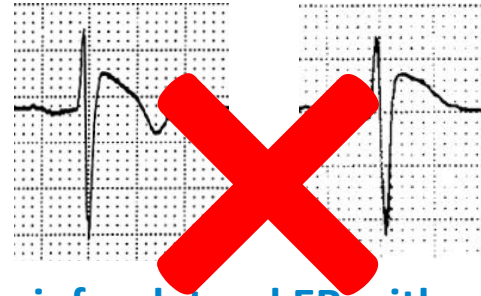
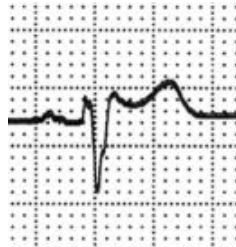
Methods

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.

- 31 patients (27 men, mean age: 42.0 ± 14.1 years) with infero-lateral ERS and a prior episode of VF were divided into 2 groups.
 - ❑ baseline and high costal (2nd and 3rd) ECG recordings
 - ❑ drug provocation tests with a sodium channel blocker (pilsicainide 1mg/kg)

- ✓ **ERS[A]-group (n=12): patients with an inferolateral ER combined with NT1-ER**

V₁-V₃
standard + high costal

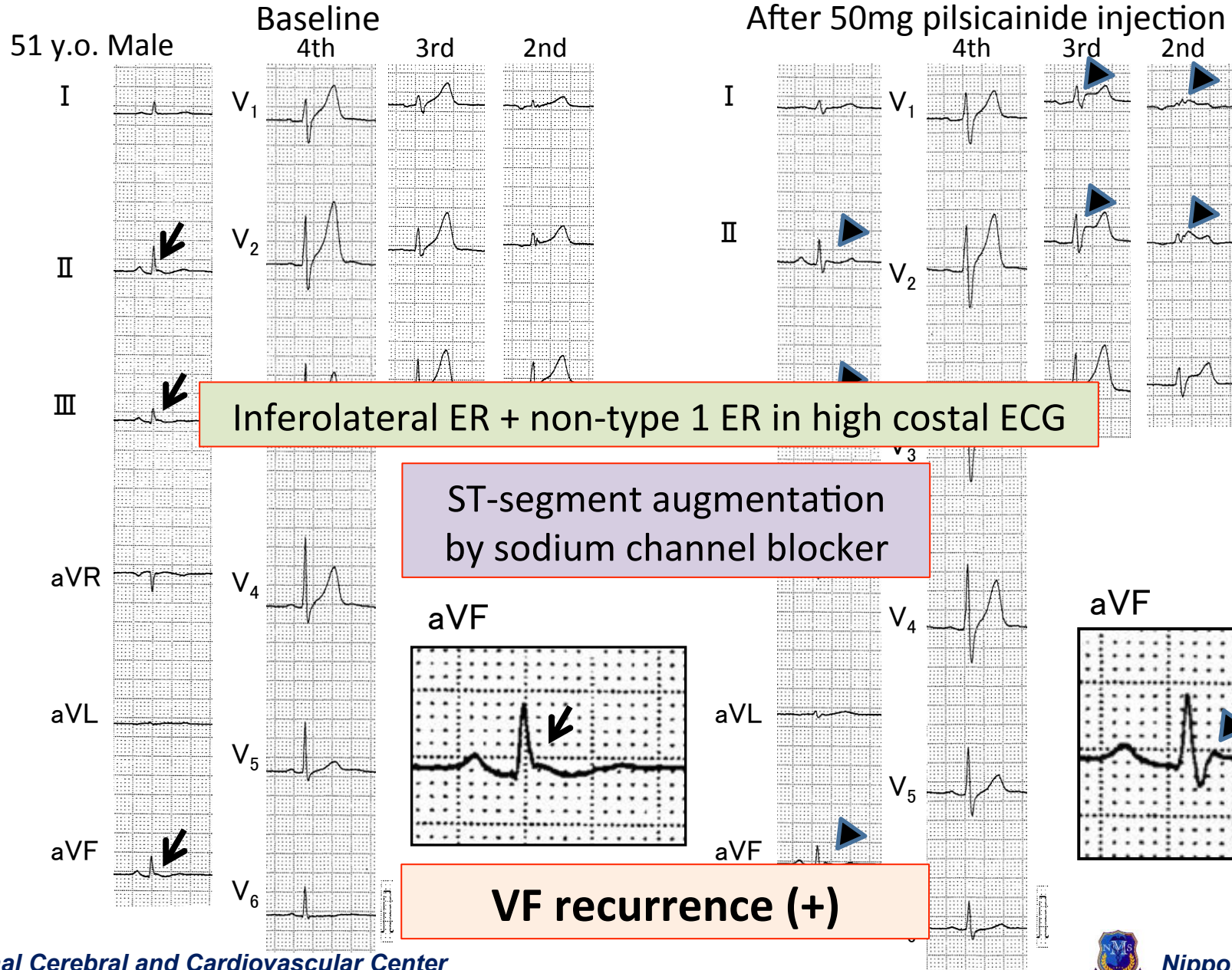


- ✓ **ERS[B]-group (n=19) : patients with pure inferolateral ER without NT1-ER**

- Clinical profiles and VF recurrences during follow-up were compared among ERS(A) group, ERS(B) group, 40 patients with Brugada syndrome and a history of VF (BS group), and 13 patients with idiopathic VF without J waves (IVF group).

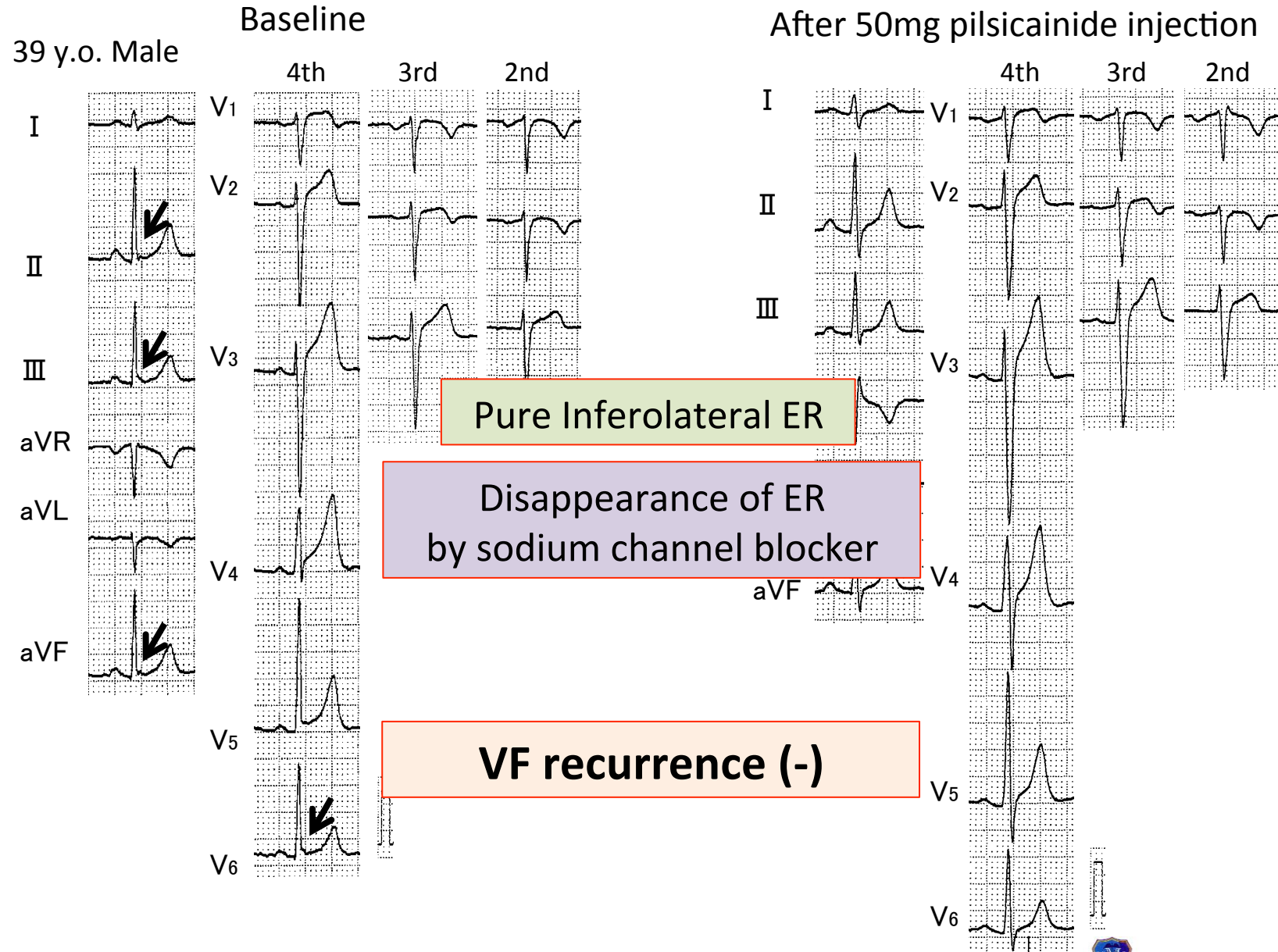
ERS (A) group

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.



ERS (B) group

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.



Clinical Characteristics

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.

Group	ERS (n=31)				P value (A) vs. (B)
	ERS (A) (n=12)	ERS(B) (n=19)	BS (n=40)	IVF (n=13)	
Age (years)	41.2 ± 11.4	42.5 ± 15.8	43.0 ± 12.2	46.1 ± 12.7	0.60
Men n, (%)	9 (75%)	18 (95%)	40 (100%)	8 (62%)	0.27
FH of SCD n, (%)	1 (8%)	0 (0%)	8 (20%)	2 (15%)	0.39
VF/CA during sleep (%)	10 (8, 2) (83%)	2 (2, 0) (11%)	22 (17, 5) (55%)	1 (1, 0) (8%)	< 0.0001

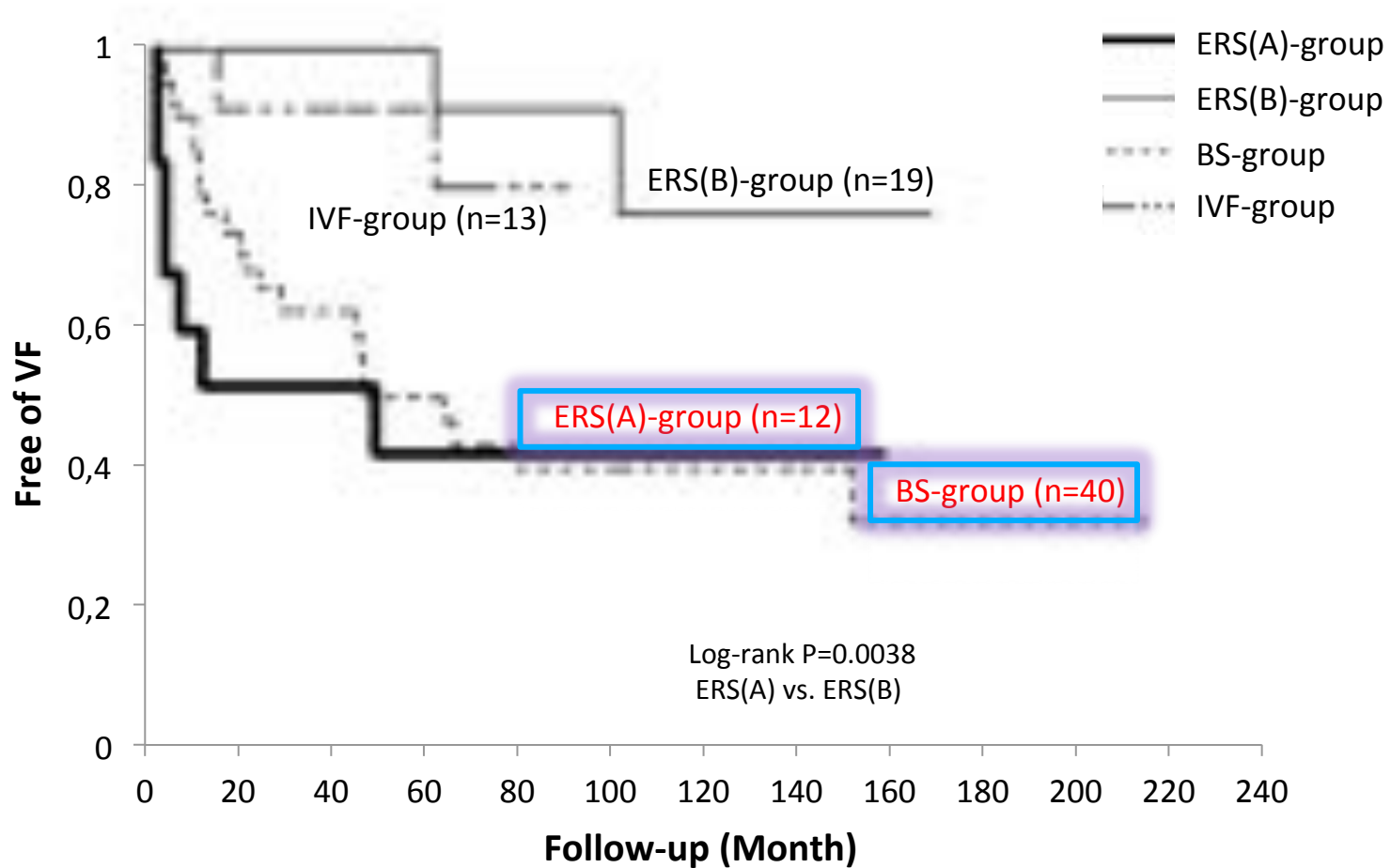
Clinical Course

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.

Group	ERS (n=31)				P value (A) vs. (B)
	ERS (A) (n=12)	ERS(B) (n=19)	BS (n=40)	IVF (n=13)	
Follow-up (months)	90 ± 57	76 ± 46	104 ± 63	82 ± 50	0.76
VF recurrence n, (%)	7 (58%)	2 (11%)	22 (55%)	2 (15%)	0.012
VF storm n, (%)	5 (42%)	0 (0%)	10 (25%)	0 (0%)	0.0047
ICD implantation n (%)	12 (100%)	18 (95%)	38 (95%)	10 (77%)	1.0

Kaplan-Meier analysis of free of VF

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.



Summary

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.

- Infero-lateral ERS patients can be divided into 2 heterogeneous groups:
 - Patients with pure infero-lateral ER
 - Patients with infero-lateral ER + non-type 1 ER pattern in high costal ECG.
- Non-type 1 ER pattern in high costal ECG seems to be a key predictor of poor outcome in patients with inferolateral ERS.

Patients with non-type 1 ER pattern in high costal ECG may be another variant of Brugada syndrome

J wave syndrome

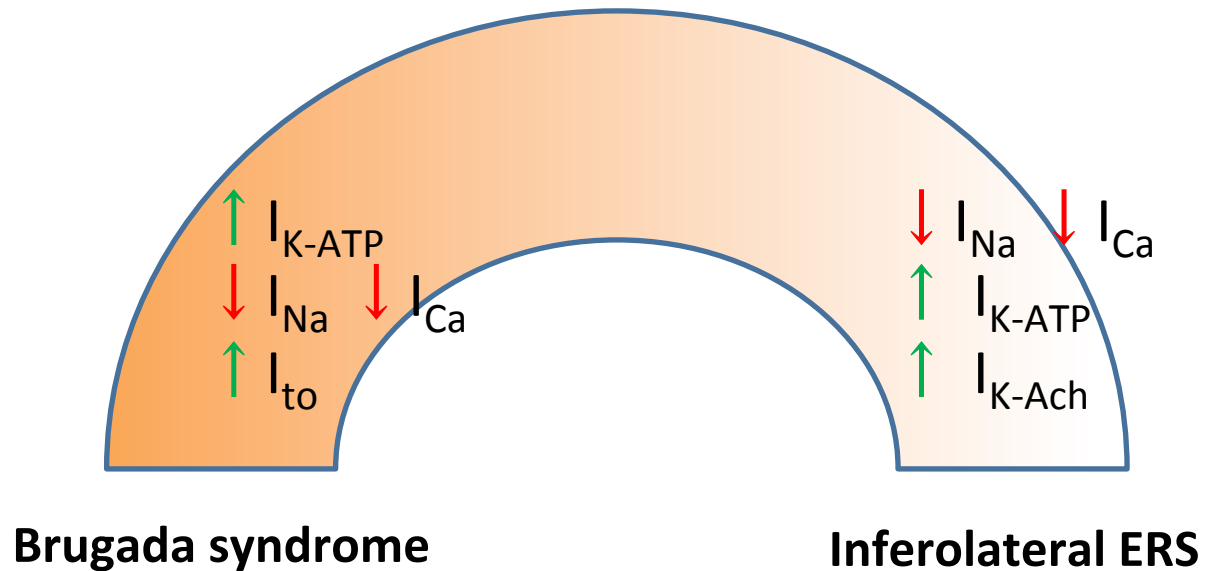
Antzelevitch C. Heart Rhythm. 2010; 7: 549-558.

ERS

ERS1 (lateral- I, V4-V6): good prognosis

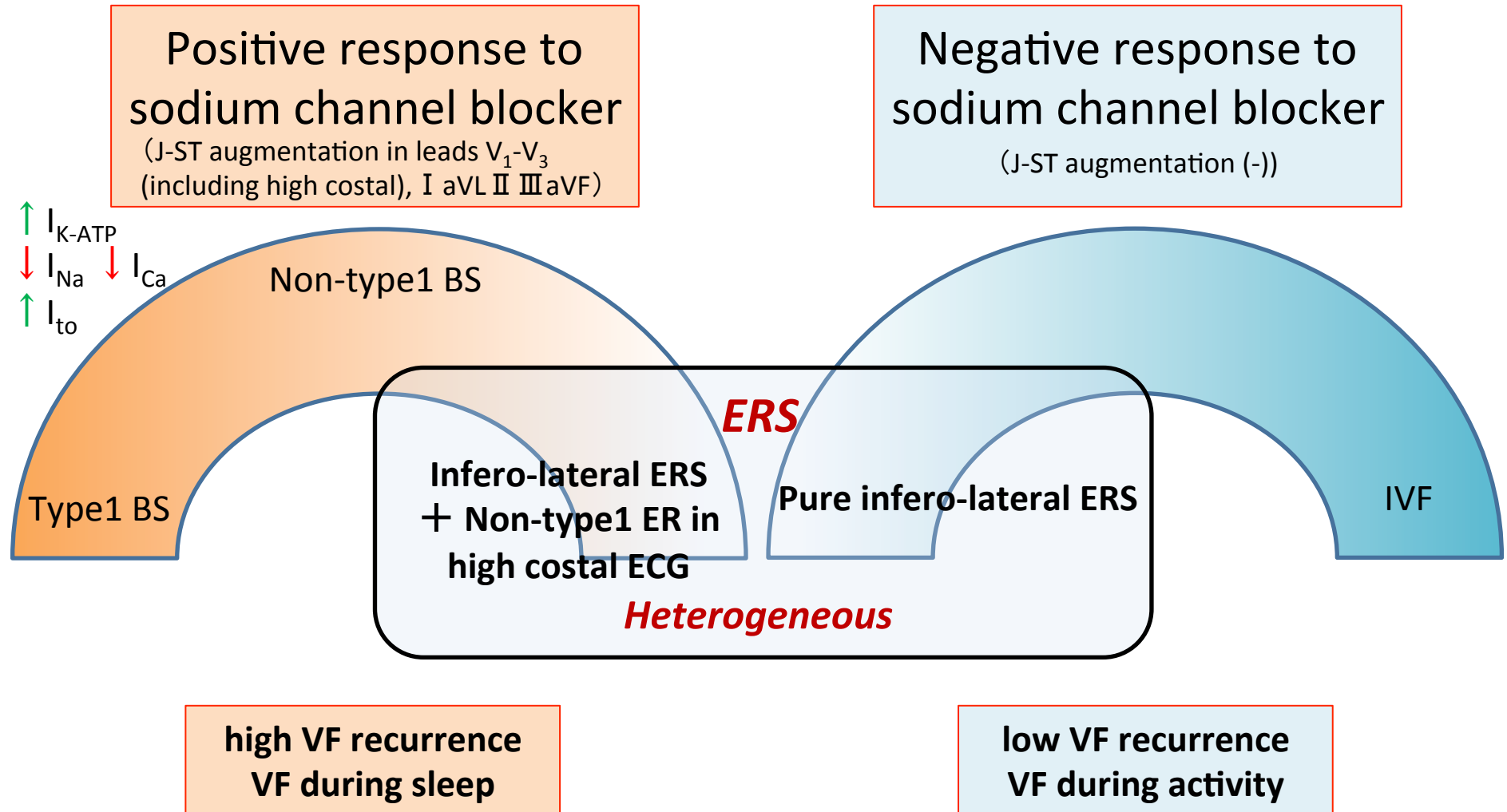
ERS2 (inferior- II, III, aVF)

ERS3 (global): poor prognosis



Early repolarization syndrome (ERS)

Kamakura T, Shimizu W et al. J Am Coll Cardiol 2013; 62:1610-1618.



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