

# 12-lead ECG에서 관찰될 수 있는 여러 질환들의 마커와 그 임상적 의미

서울대학교병원 순환기내과 권순일

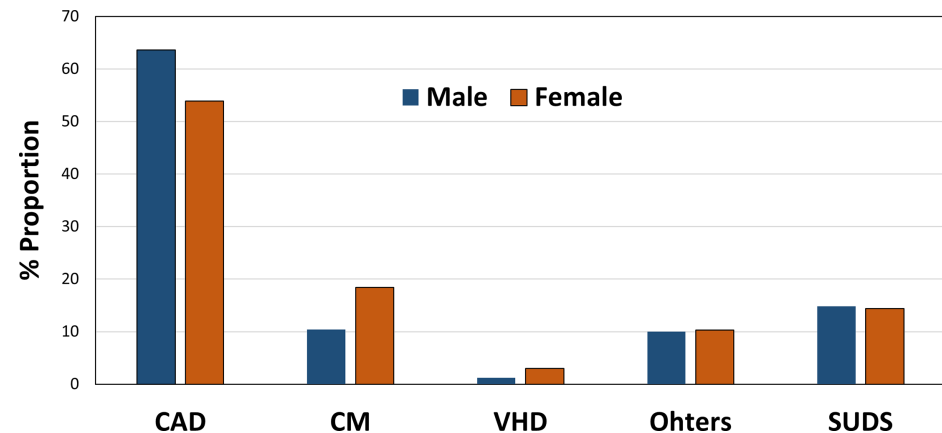
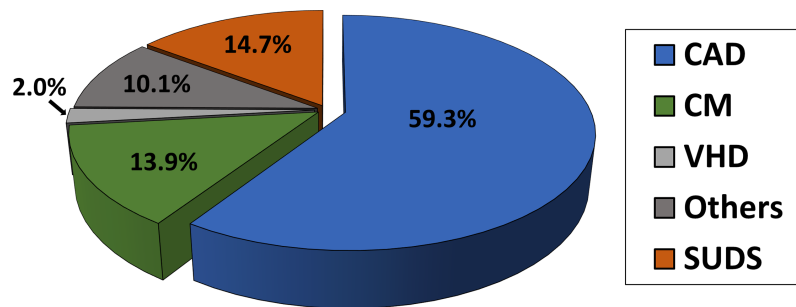
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- Summary

# Causes of sudden cardiac arrest in Korea

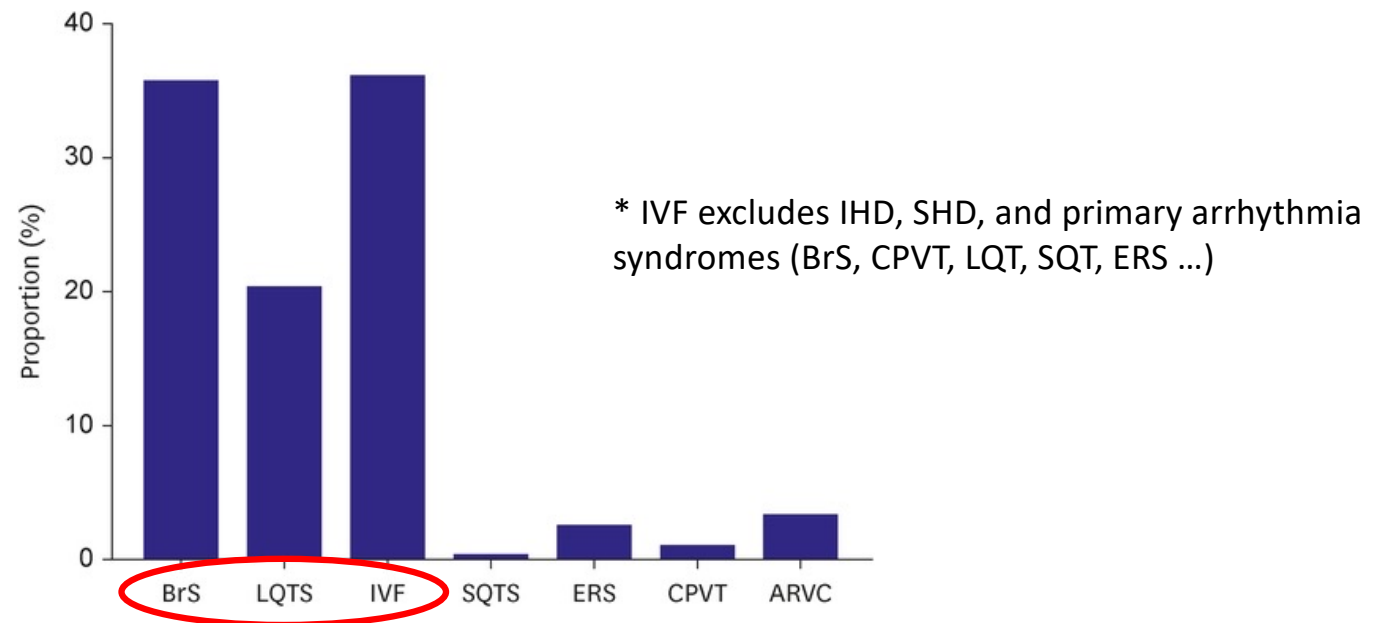
- 2002~2013 Korean SCA data from NHIS database
- SCA incidence: 16.1 per 100,000 PY



\* SUDS: sudden unexplained death syndrome  
Roh SY et al. PLoS One. 2020 Nov 25;15(11):e0242799

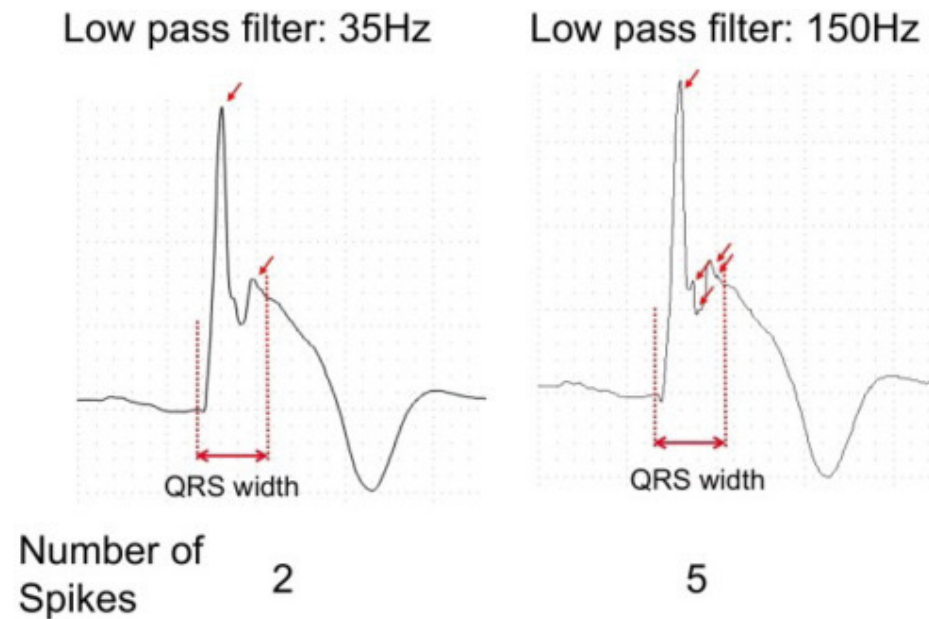
# Inherited arrhythmias in Korean

- 2014~2017 Korean IA Registry
- NGS performed in 265 IA probands



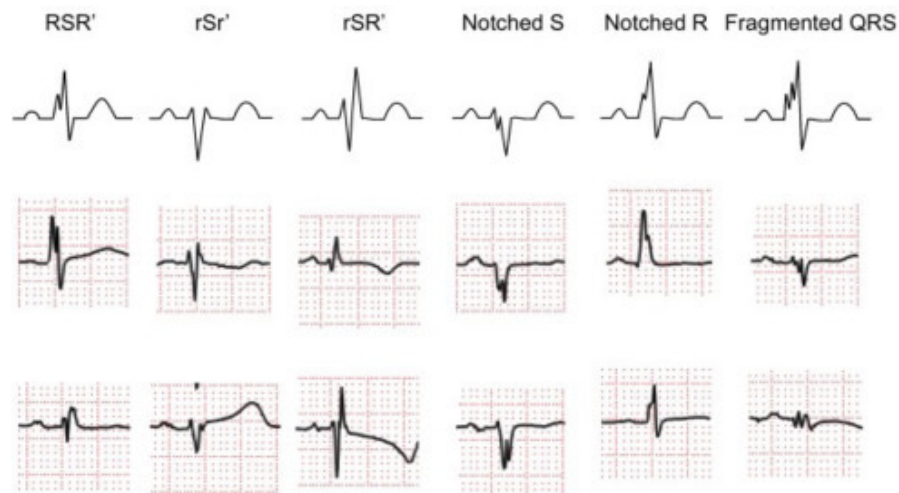
# Fragmented QRS: *impact of bandpass filter setting*

- Usual 12-lead ECG setting
  - High-pass filter: 0.05–20 Hz
  - Low-pass filter: 100–150 Hz
  - AC filter: 50 or 60 Hz



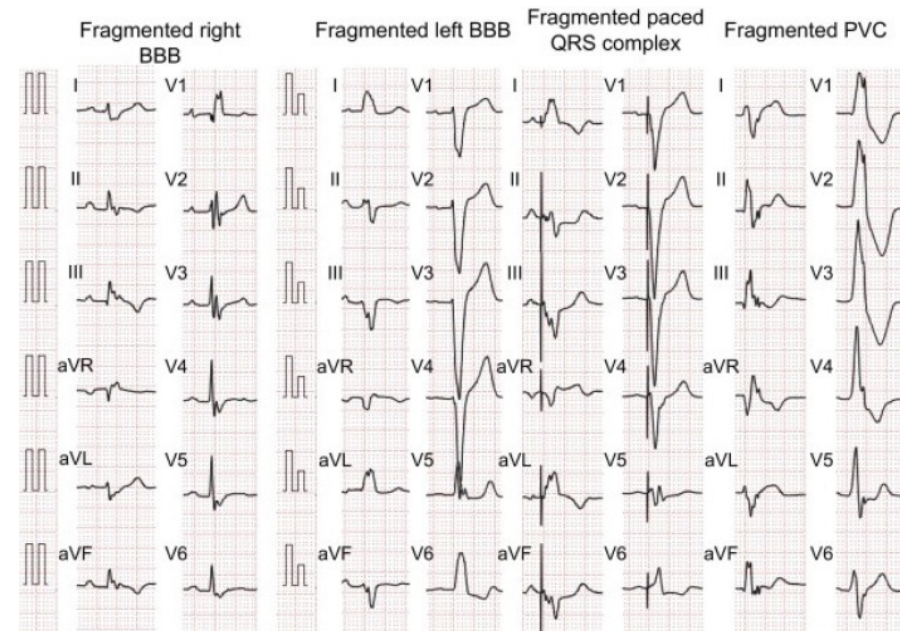
# Fragmented QRS: *definition*

## <Narrow QRS complex>



- Additional R wave (R')
- Notching in S wave or R wave
- Presence of more than one R' (fragmentation) in two contiguous leads

## <Wide QRS complex>



- > 2 R' waves or notches in the R or S wave in a wide QRS complex of BBB, or paced QRS, or PVC in 2 contiguous leads
- If PVC only has 2 notches in the R waves, fQRS-positive when the notches were > 40 ms apart and present in 2 contiguous leads

Take Y, et al. Indian Pacing Electrophysiol J. 2012 Sep;12(5):213-25

Das MK, et al. Circulation. 2006 May 30;113(21):2495-501

Das MK, et al. Circ Arrhythm Electrophysiol. 2008 Oct;1(4):258-68

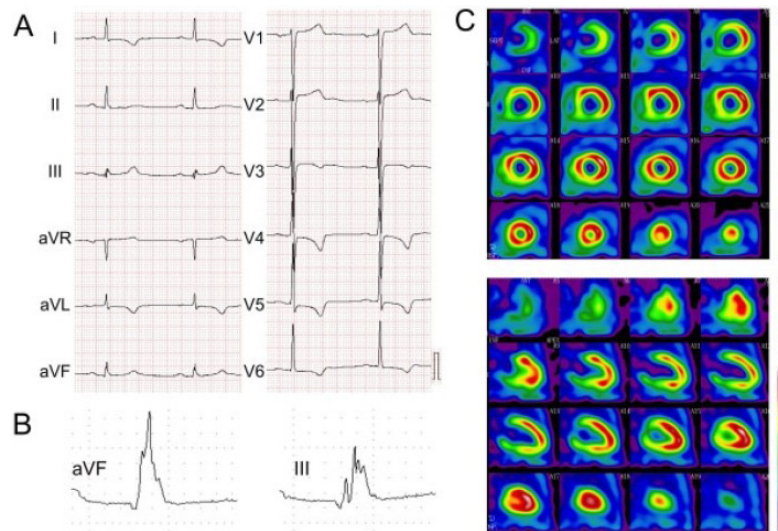
# Fragmented QRS: *mechanism*

Myocardial scar  
Intracardiac conduction abnormality

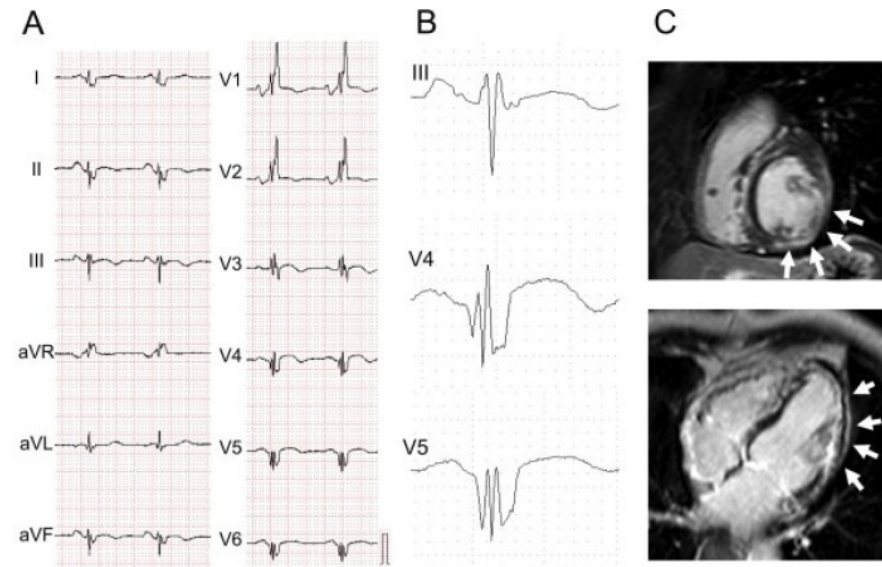


Substrate for ventricular arrhythmia

## <MI with inferior perfusion defect>

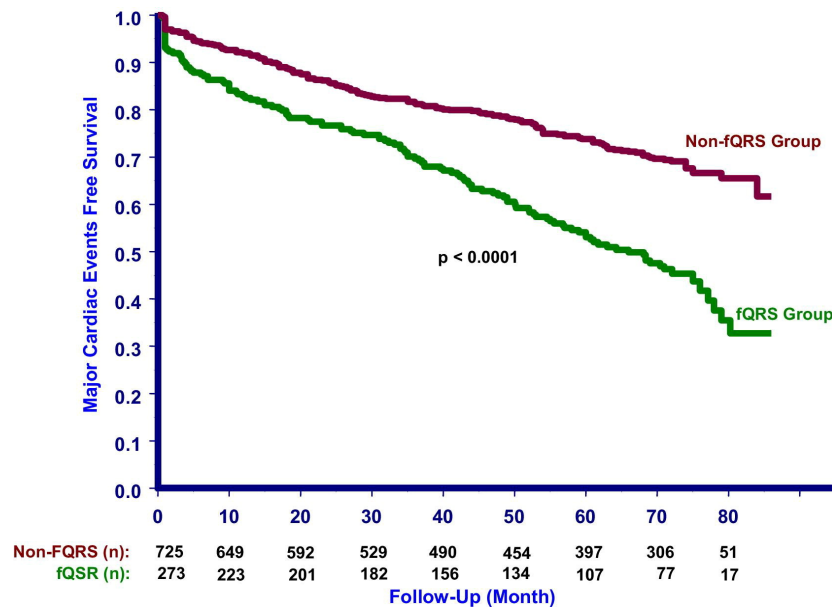


## <DCM with inferolateral LGE >

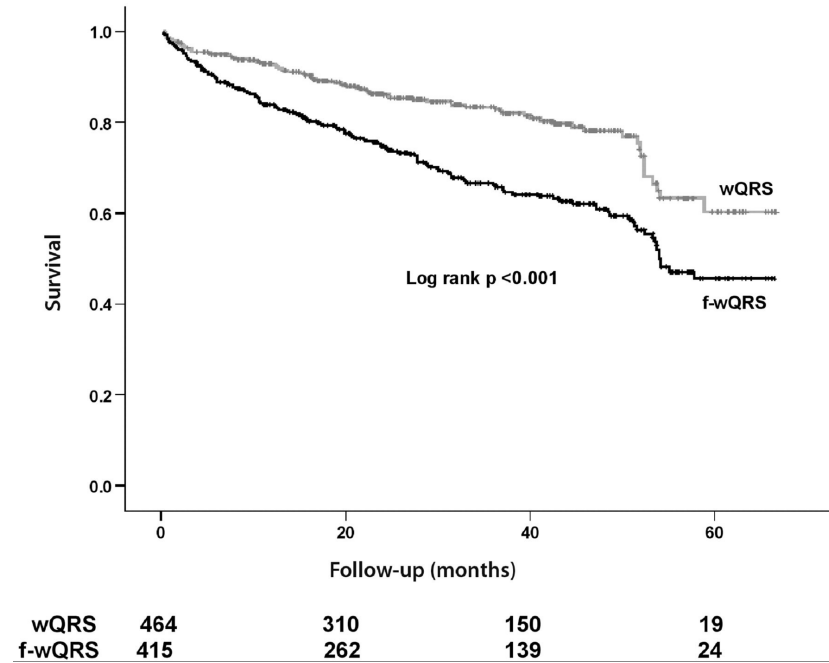


# Fragmented QRS: *clinical impact*

<MI: Narrow QRS complex>



<MI: Wide QRS complex>

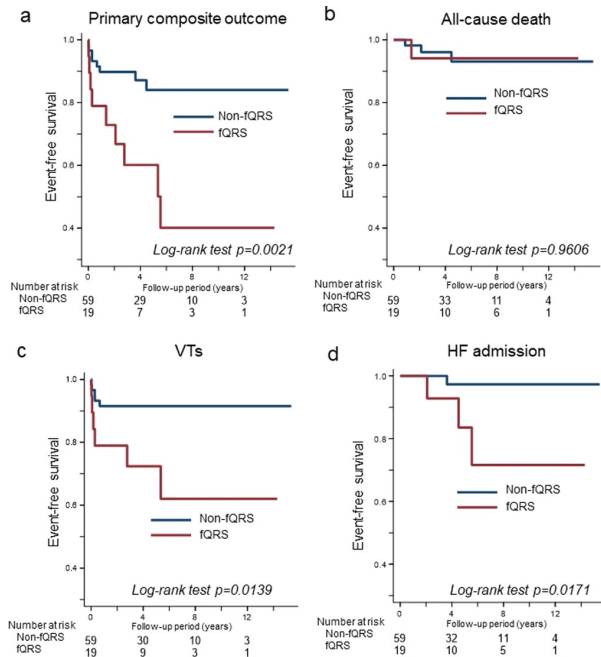


Das MK, et al. Circulation. 2006 May 30;113(21):2495-501  
 Das MK, et al. Heart Rhythm. 2007 Nov;4(11):1385-92  
 Das MK, et al. Circ Arrhythm Electrophysiol. 2008 Oct;1(4):258-68

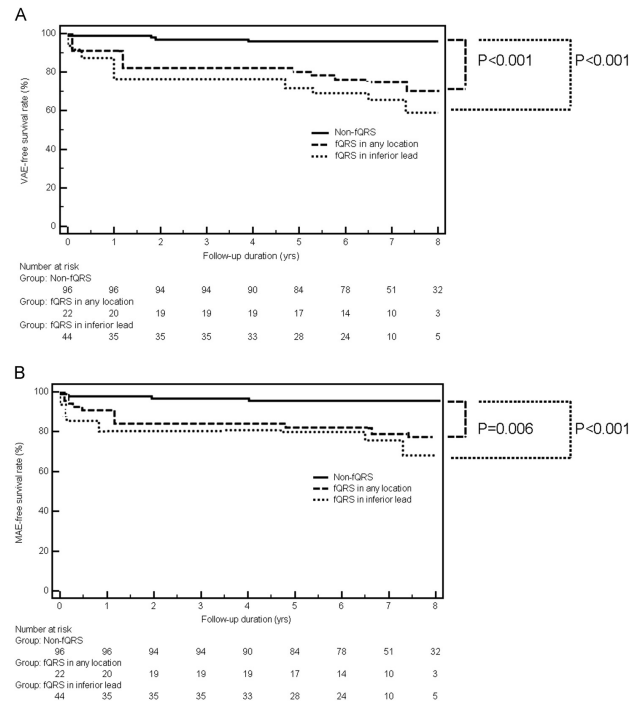


# Fragmented QRS: *clinical impact*

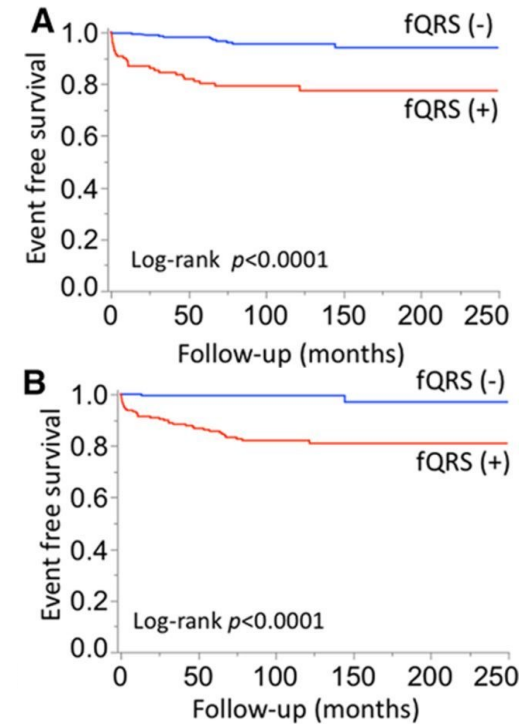
## <Cardiac sarcoidosis>



## <HCM>



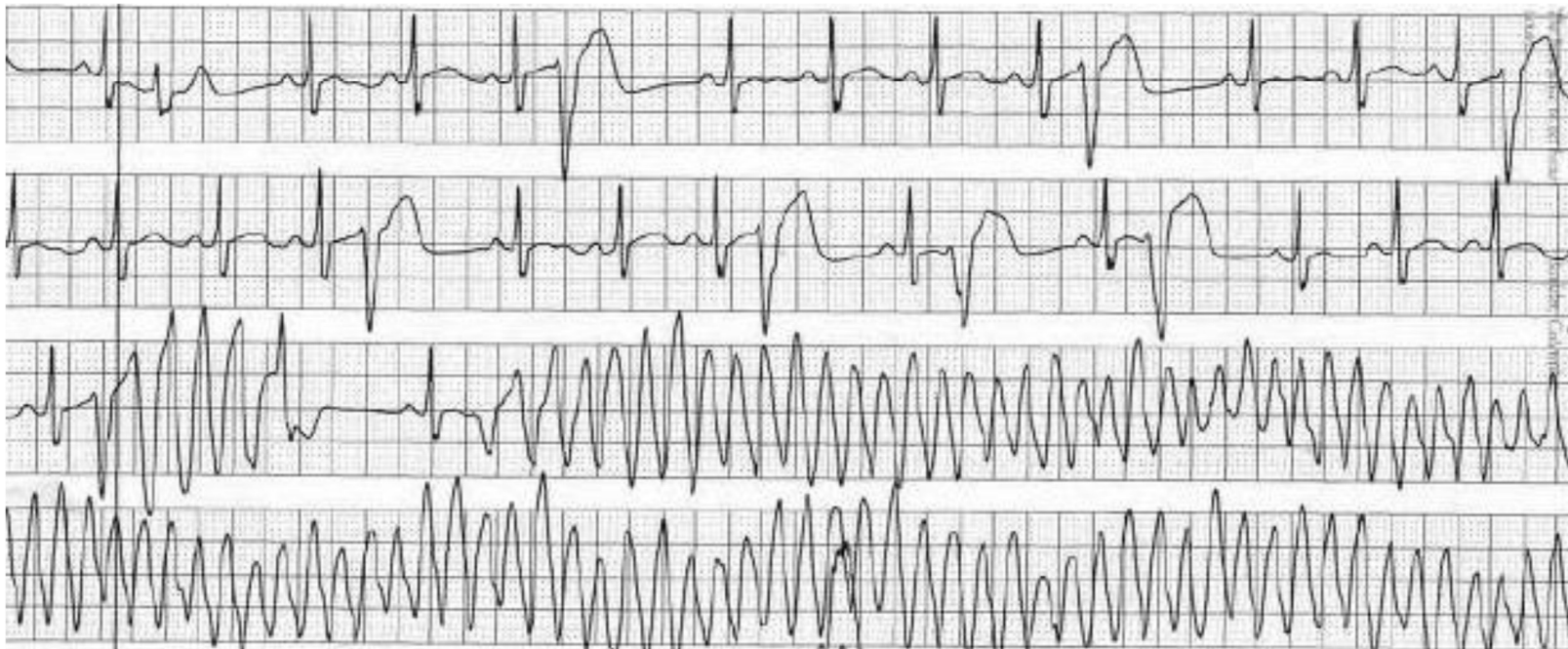
## <BrS>



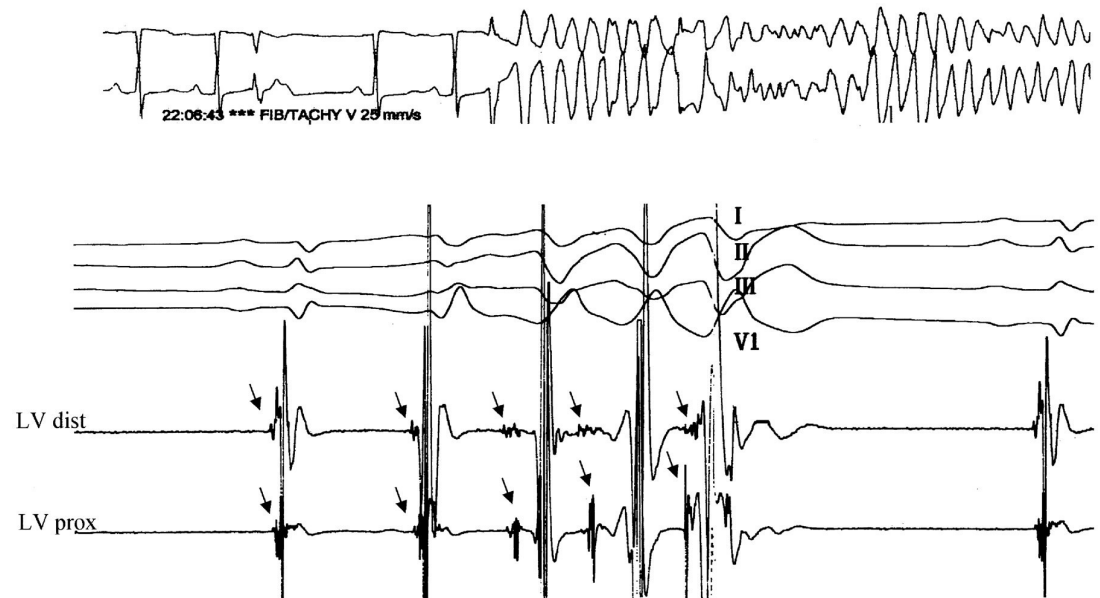
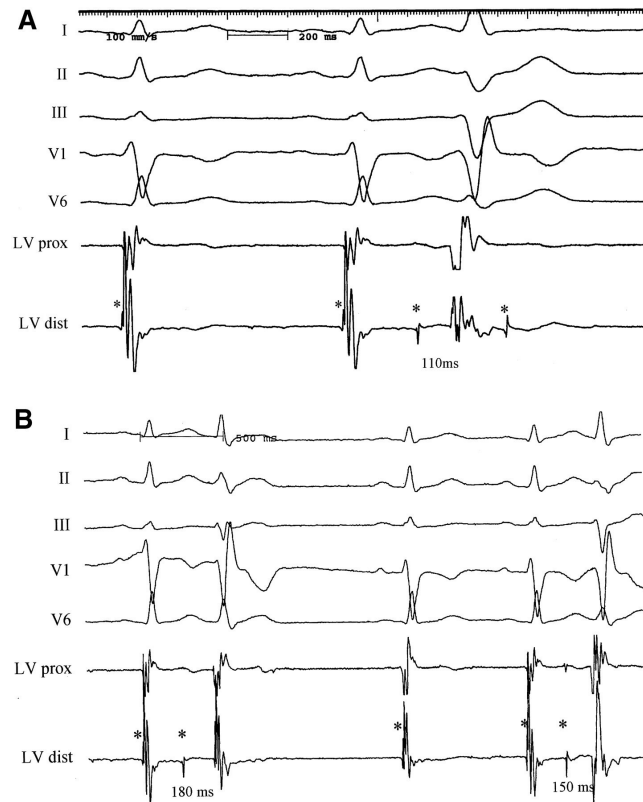
Hagiwara H, et al. Heart Vessels. 2023 Jun;38(6):803-816  
 Morita H, et al. Circ Arrhythm Electrophysiol. 2017 Mar;10(3):e004765  
 Kang KW, et al. Heart Rhythm. 2014 Aug;11(8):1433-40

# Short-coupled PVC

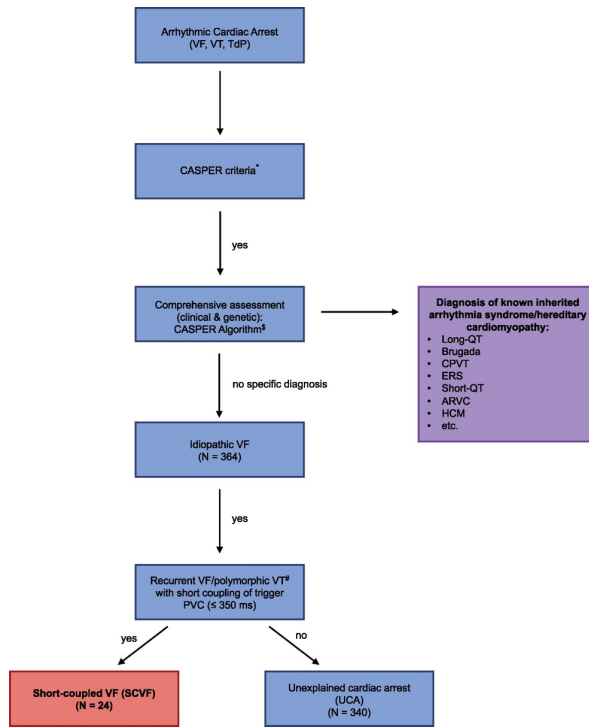
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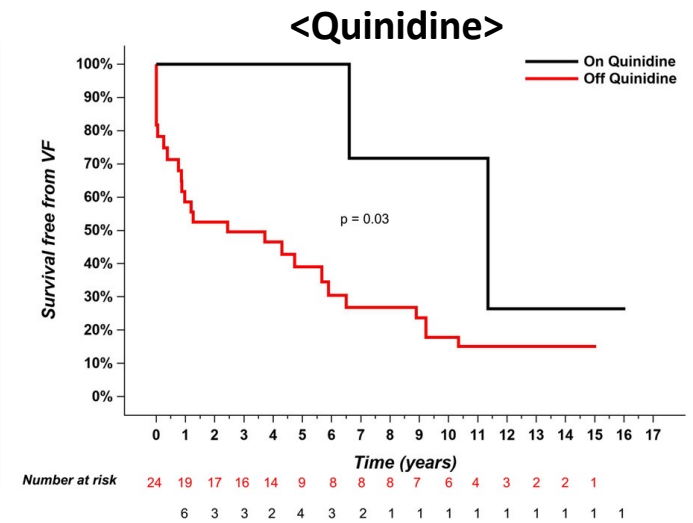
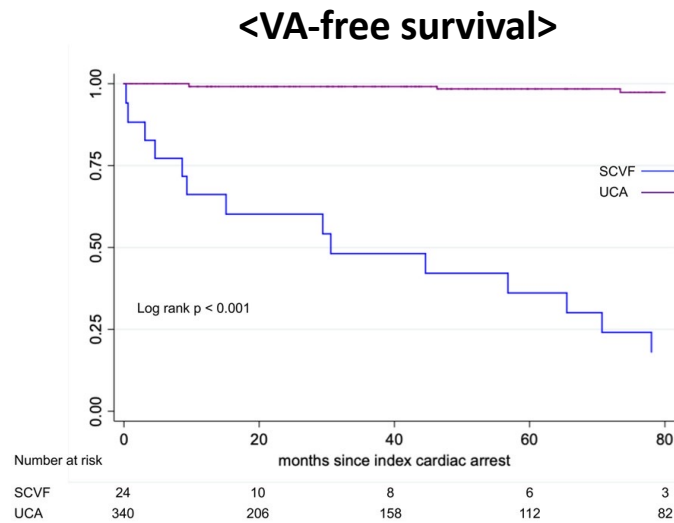
# Short-coupled PVC: *scPVC-induced VT/VF, mechanism*



# Short-coupled PVC: *clinical significance*



24/350 (6.9%)

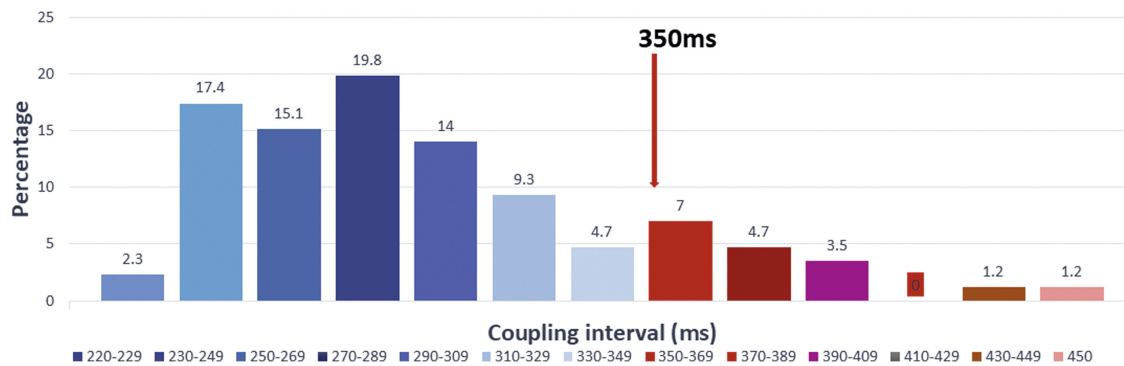


\* UCA: unexplained cardiac arrest  
Steinberg C, et al. Eur Heart J. 2021 Jul 31;42(29):2827-2838

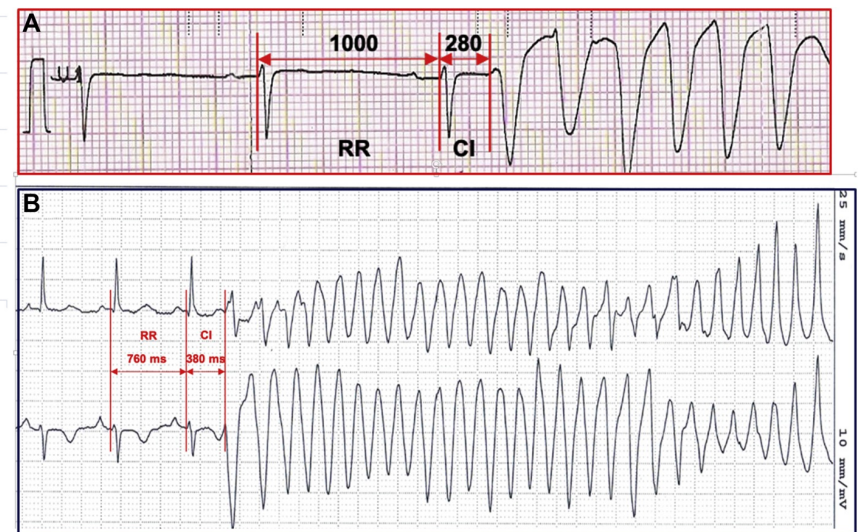
# Short-coupled PVC: *how short is 'short'?*

- Review of 86 case reports

<Distribution of CI of PVCs triggering PVT/VF>

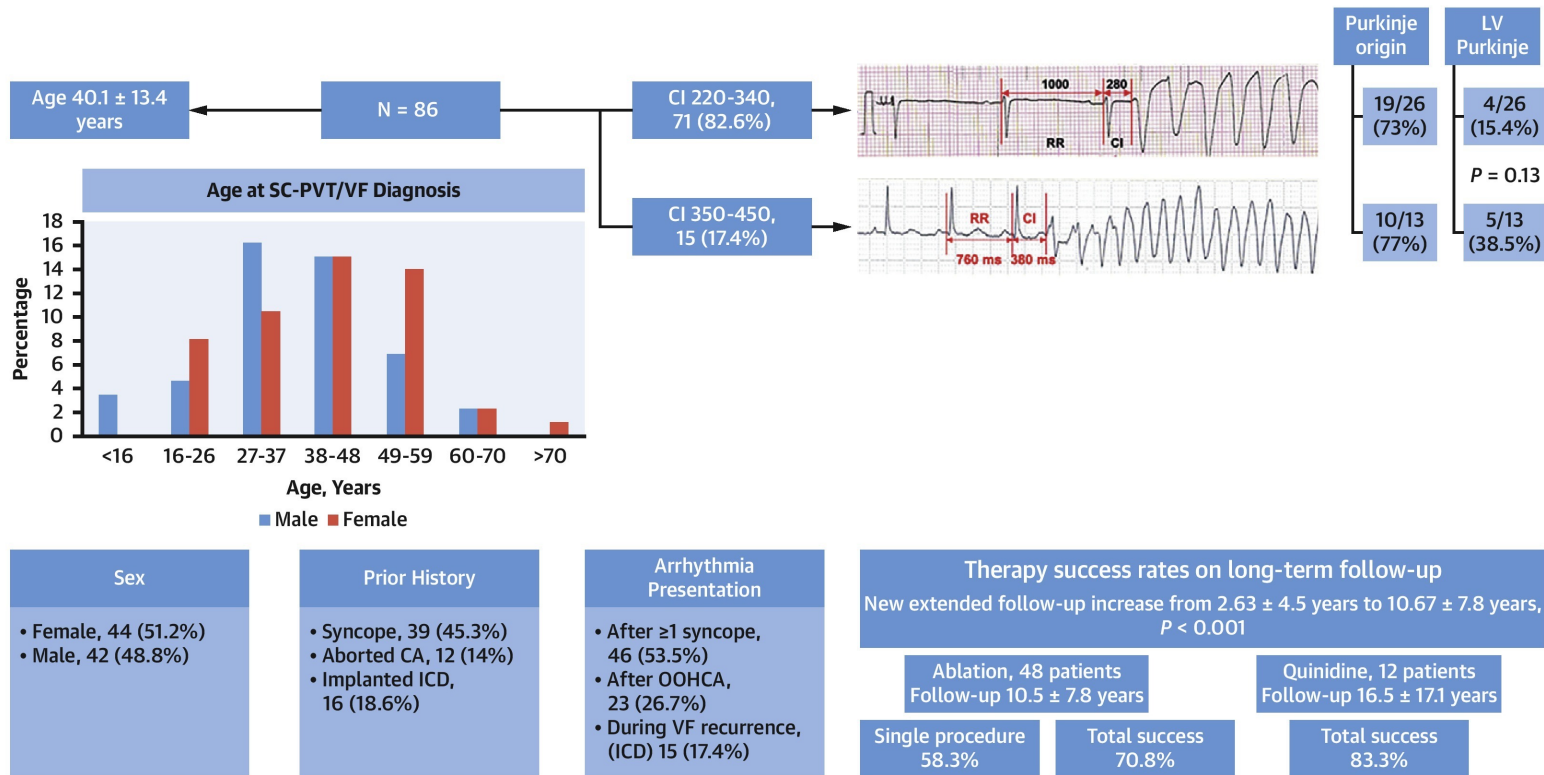


<Examples of scPVC induced PVT/VF>



# Short-coupled PVC: *long-term follow-up data*

## Short-Coupled Idiopathic Ventricular Fibrillation: Literature Review With New Extended Follow-Up



# Short-coupled PVC: *medical treatment*

PO Drug	N	Success Rate (%)	P Value
Beta blockers	30	13.30	<0.001
Verapamil	24	50	0.053
Procainamide	15	26.70	0.003
Quinidine	12	83.30	
Amiodarone	5	60	0.30
Flecainide	5	60	0.30
Cibenzoline	3	0	
Pilsicainide	1	100	
Sotalol	1	0	
Disopyramide	1	0	
Bepridil	1	Acute success late failure	
Propafenone	1	100	

# Short-coupled PVC

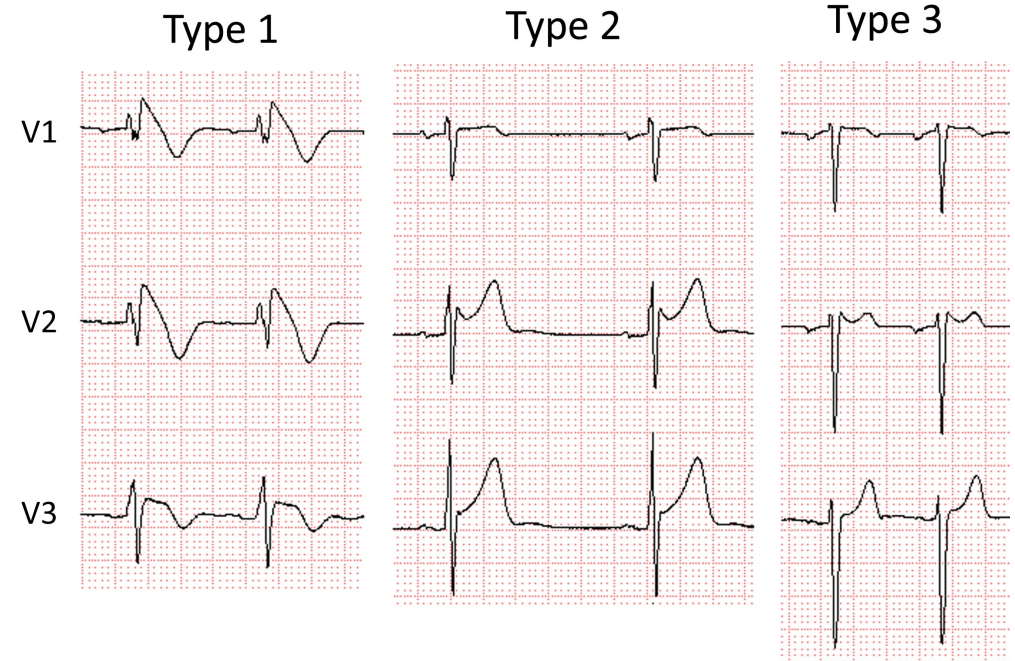
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- Short-coupled premature ventricular contractions (scPVCs) leading to ventricular fibrillation (VF) is an uncommon etiology of cardiac arrest in patients without structural heart disease
- The arrhythmia is characterized by a PVC coupling interval of <350 ms, a relatively short QRS duration, and a normal QT interval
- Genetic and electrophysiologic testing have increasingly implicated the Purkinje system as the source of scPVCs
- Verapamil and quinidine have demonstrated efficacy in reducing the arrhythmogenic burden, with catheter ablation having additional long-term success



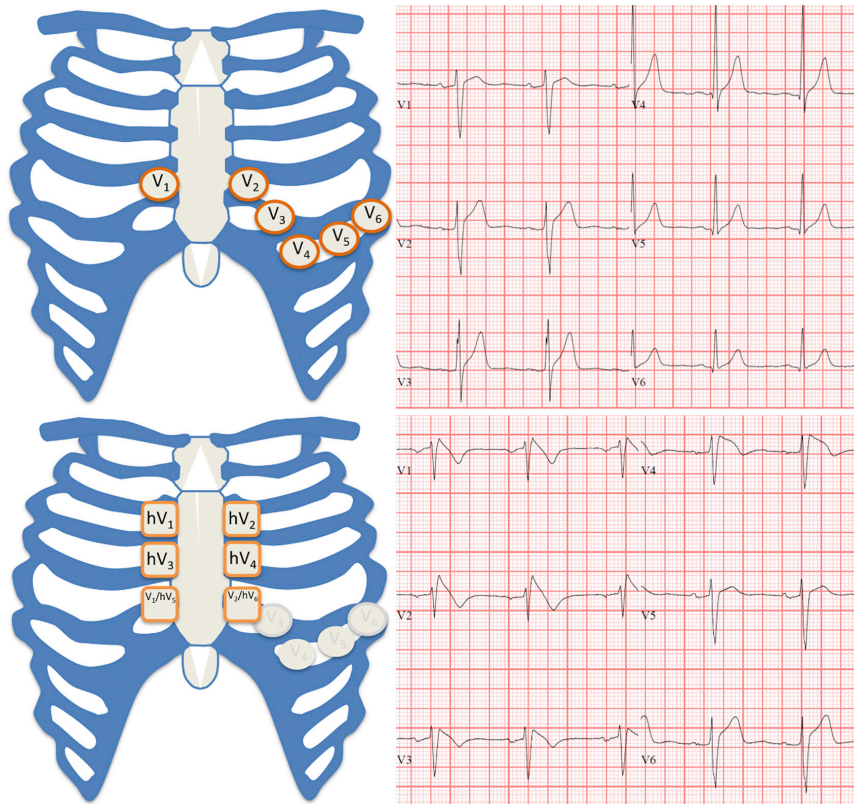
# Brugada syndrome: *diagnosis*

- Type 1 is the only ECG criterion that is diagnostic of BrS (Type 2 and 3 needs SCB provocation test)
- J elevation  $\geq 0.2$  mV, a coved type ST segment followed by a negative T wave
- Brugada syndrome is definitively diagnosed when a type 1 ST-segment is observed in  $>1$  right precordial lead (V1 to V3) in the presence or absence of a sodium channel–blocking agent, and in conjunction with one of the following:
  - PMT, VF
  - a family history of sudden cardiac death at  $<45$  years old
  - coved-type ECGs in family members
  - inducibility of VT with programmed electrical stimulation
  - syncope
  - nocturnal agonal respiration



# Brugada syndrome: *diagnosis*

<High-lead ECG>



<Sodium channel blocker provocation test>

Baseline

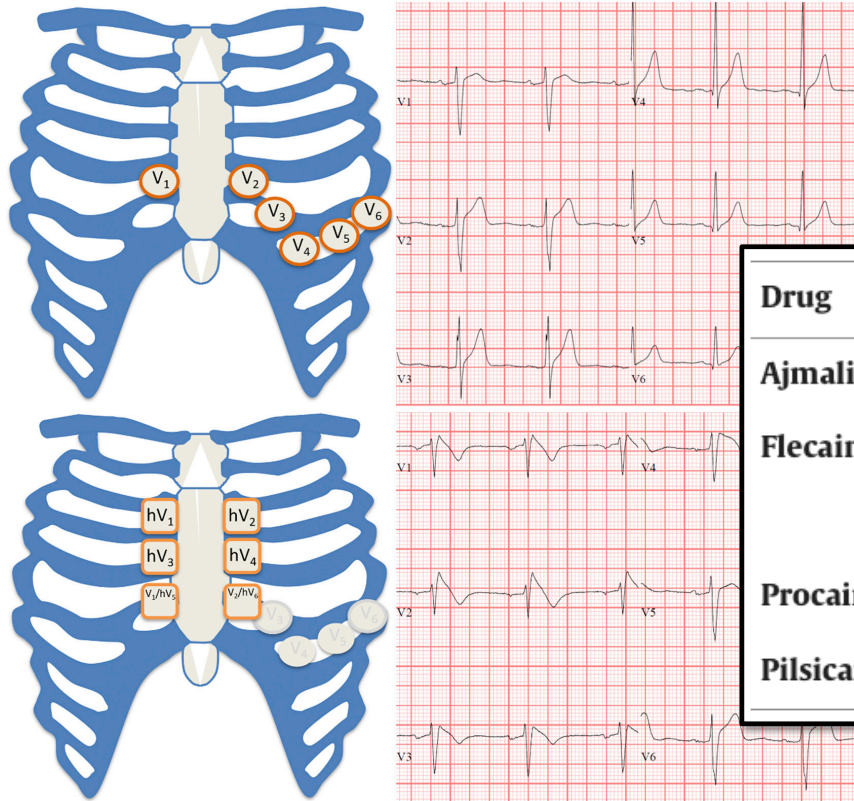


Procainamide (end-infusion)



# Brugada syndrome: *diagnosis*

## <High-lead ECG>



## <Sodium channel blocker provocation test>

### Baseline



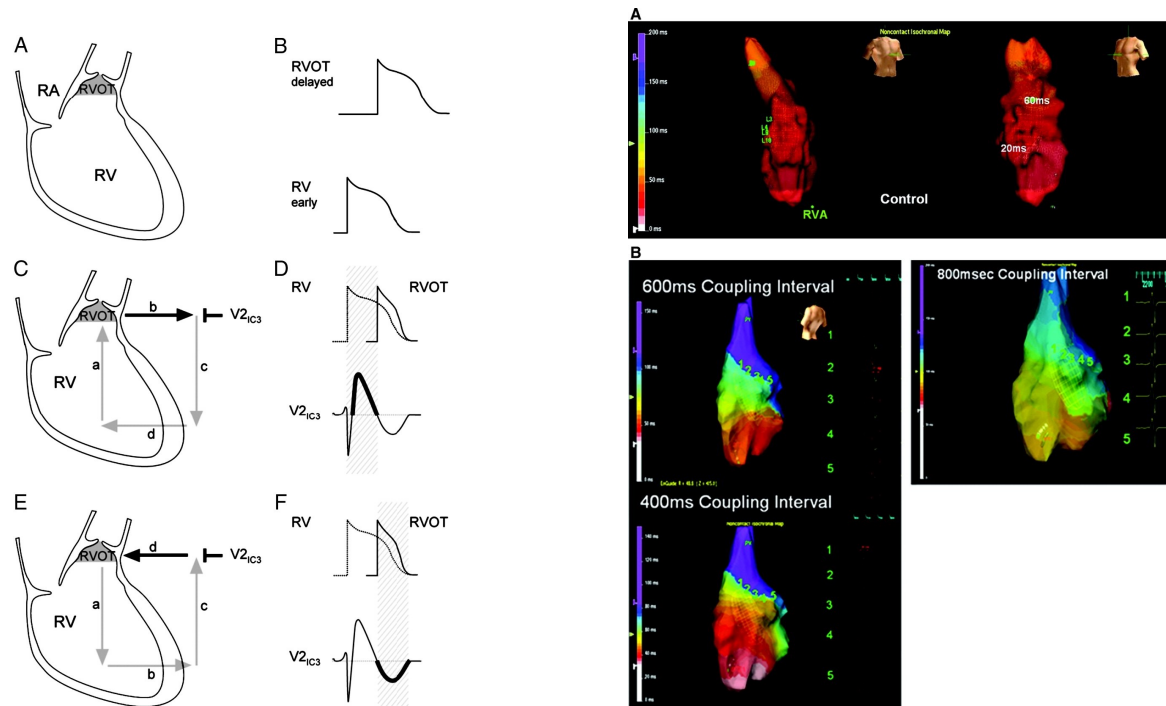
### Procainamide (end-infusion)



Drug	Dose	Administration
<b>Ajmaline</b>	1 mg/kg over 10 minutes	Intravenous
<b>Flecainide</b>	2 mg/kg over 10 minutes	Intravenous
<b>Procainamide</b>	200–300 mg	Oral (>1 hour)
<b>Procainamide</b>	10 mg/kg over 10 minutes	Intravenous
<b>Pilsicainide</b>	1 mg/kg over 10 minutes	Intravenous

# Brugada syndrome: *two hypotheses*

- Hypothesis 1: Primary depolarization disorder d/t reduced  $I_{Na}$ 
  - Conduction delay in RVOT → heterogeneity of depol. around RVOT → Arrhythmogenic

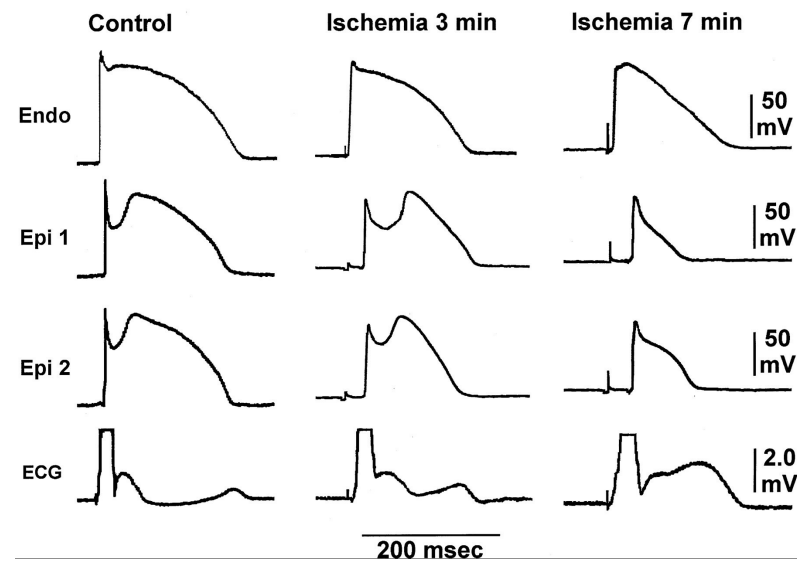
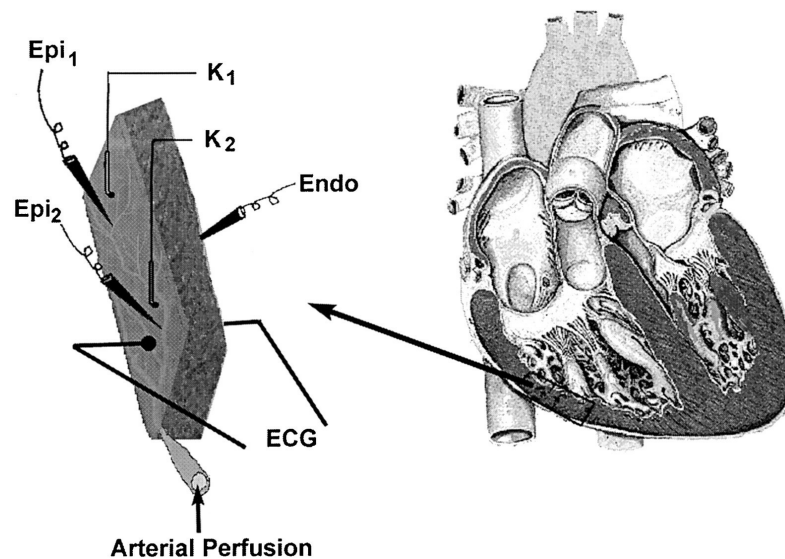


Wilde AA, et al. J Mol Cell Cardiol. 2010 Oct;49(4):543-53  
 Lambiase PD, et al. Circulation. 2009 Jul 14;120(2):106-17

# Brugada syndrome: *two hypotheses*

- Hypothesis 2: Primary repolarization disorder d/t increased  $I_{to}$ 
  - Heterogeneity of repol. between epi and endocardium → arrhythmogenic by phase 2 reentry

Arterially Perfused Canine Right Ventricular Wedge



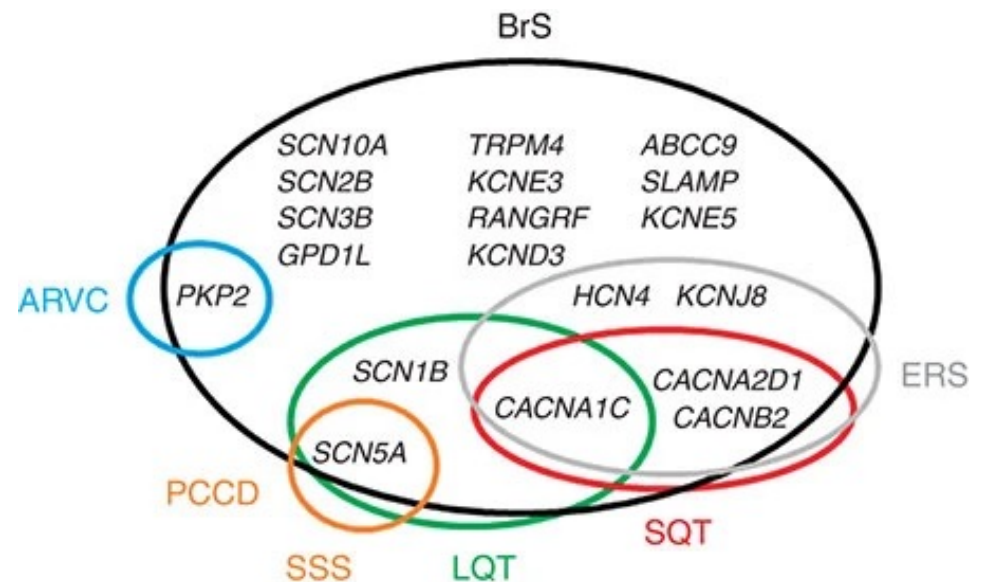
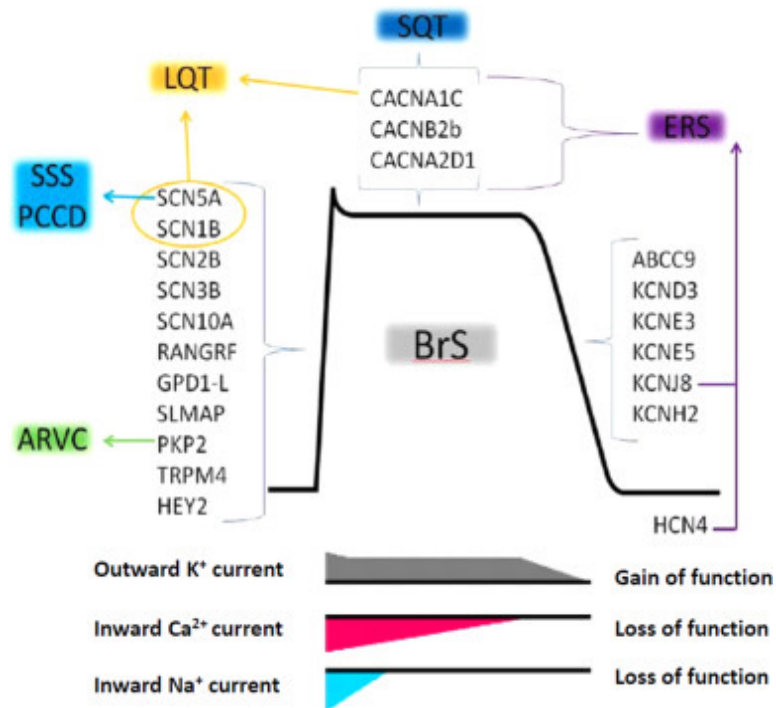
# Brugada syndrome: *genetics*

Genetic Defects Associated with BrS

	Locus	Gene/protein	Ion channel	Percent of probands
<b>BrS1</b>	3p21	<i>SCN5A, Na<sub>v</sub>1.5</i>	↓ I <sub>Na</sub>	11%–28%
<b>BrS2</b>	3p24	<i>GPD1L</i>	↓ I <sub>Na</sub>	Rare
<b>BrS3</b>	12p13.3	<i>CACNA1C, Ca<sub>v</sub>1.2</i>	↓ I <sub>Ca</sub>	6.6%
<b>BrS4</b>	10p12.33	<i>CACNB2b, Ca<sub>v</sub>β2b</i>	↓ I <sub>Ca</sub>	4.8%
<b>BrS5</b>	19q13.1	<i>SCN1B, Na<sub>v</sub>β1</i>	↓ I <sub>Na</sub>	1.1%
<b>BrS6</b>	11q13-14	<i>KCNE3, MiRP2</i>	↑ I <sub>to</sub>	Rare
<b>BrS7</b>	11q23.3	<i>SCN3B, Na<sub>v</sub>β3</i>	↓ I <sub>Na</sub>	Rare
<b>BrS8</b>	12p11.23	<i>KCNJ8, Kir6.1</i>	↑ I <sub>K-ATP</sub>	2%
<b>BrS9</b>	7q21.11	<i>CACNA2D1, Ca<sub>v</sub> α2δ1</i>	↓ I <sub>Ca</sub>	1.8%
<b>BrS10</b>	1p13.2	<i>KCND3, K<sub>v</sub>4.3</i>	↑ I <sub>to</sub>	Rare
<b>BrS11</b>	17p13.1	<i>RANGRF, MOG1</i>	↓ I <sub>Na</sub>	Rare
<b>BrS12</b>	3p21.2-p14.3	<i>SLMAP</i>	↓ I <sub>Na</sub>	Rare
<b>BrS13</b>	12p12.1	<i>ABCC9, SUR2A</i>	↑ I <sub>K-ATP</sub>	Rare
<b>BrS14</b>	11q23	<i>SCN2B, Na<sub>v</sub>β2</i>	↓ I <sub>Na</sub>	Rare
<b>BrS15</b>	12p11	<i>PKP2, Plakophilin-2</i>	↓ I <sub>Na</sub>	Rare
<b>BrS16</b>	3q28	<i>FGF12, FHAF1</i>	↓ I <sub>Na</sub>	Rare
<b>BrS17</b>	3p22.2	<i>SCN10A, Na<sub>v</sub>1.8</i>	↓ I <sub>Na</sub>	5%–16.7%
<b>BrS18</b>	6q	<i>HEY2 (transcriptional factor)</i>	↑ I <sub>Na</sub>	Rare

Major: Loss-of-mutation of SCN5A

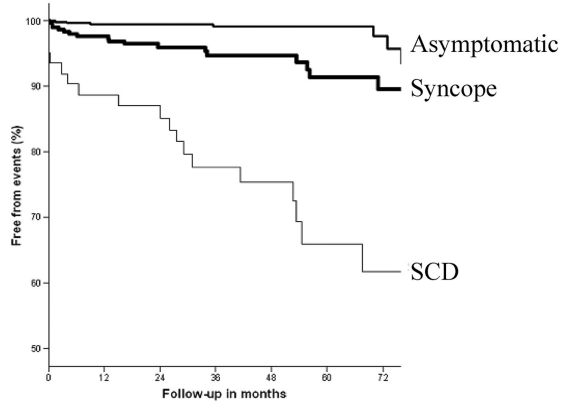
# Brugada syndrome: *genetics*



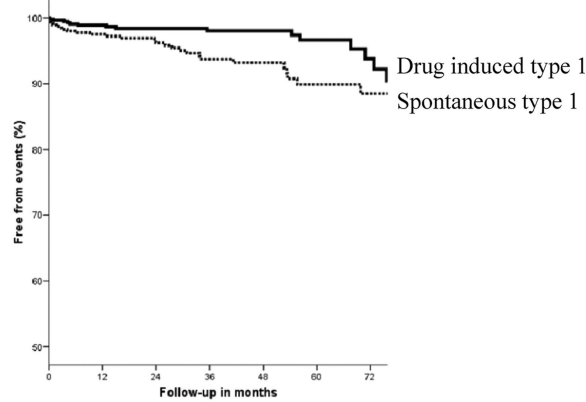
Sarquella-Brugada G, et al. Genet Med. 2016 Jan;18(1):3-12  
 Juang JJ, et al. J Arrhythm. 2016 Oct;32(5):418-425

# Brugada syndrome: *clinical significance*

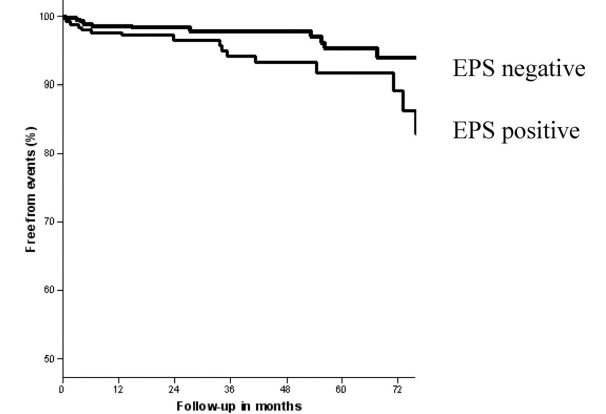
## <FINGER Brugada Syndrome Registry>



	0	12	24	36	48	60	72
group A	62	54	47	36	29	18	15
group B	313	244	192	148	99	73	49
group C	654	505	379	275	195	109	54



	0	12	24	36	48	60	72
type 1	468	350	269	200	135	88	58
no type 1	561	453	349	259	188	112	60

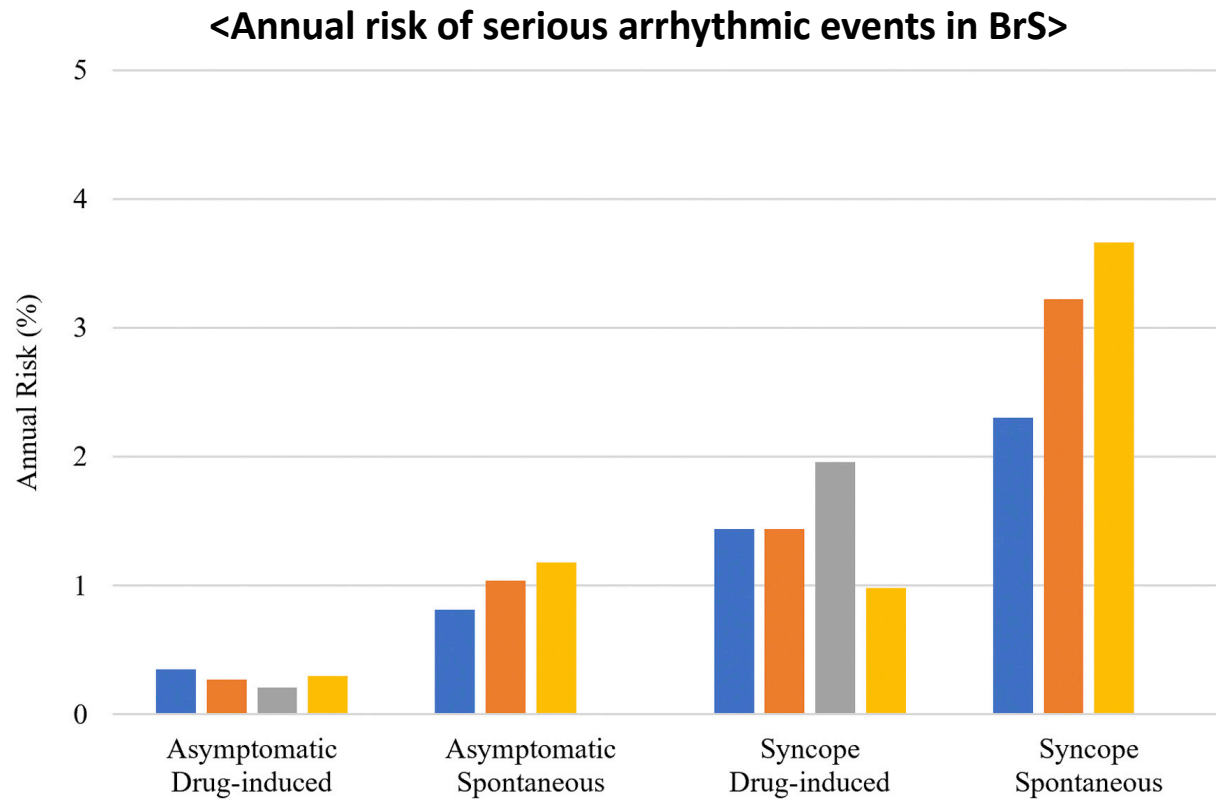


	0	12	24	36	48	60	72
negative	376	301	237	187	136	94	59
positive	262	212	161	113	81	52	34

- Significant predictors
  - Symptoms and spontaneous type 1 BrS ECG
- Nonsignificant factors
  - Gender, Family history of SCD, Inducibility of VT/VF by EPS, SCN5A mutation



# Brugada syndrome: *clinical significance*

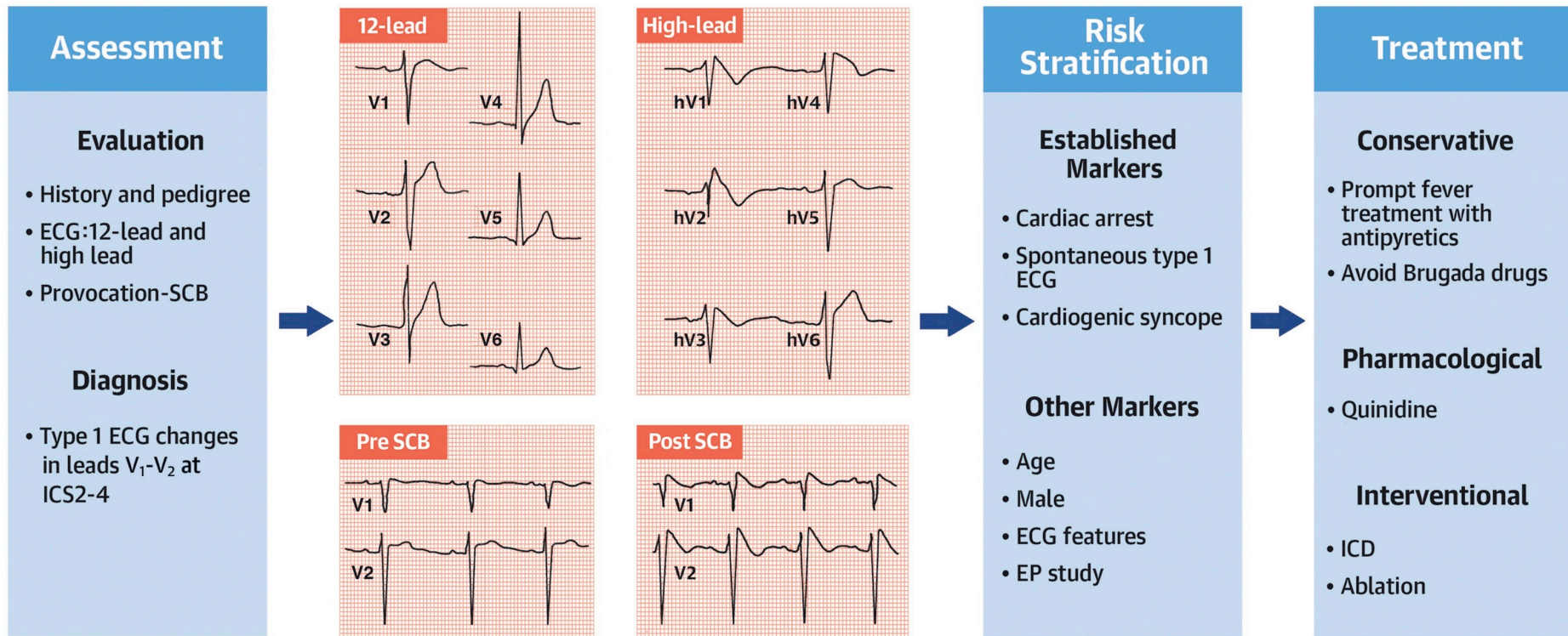


# Brugada syndrome: *Shanghai score*

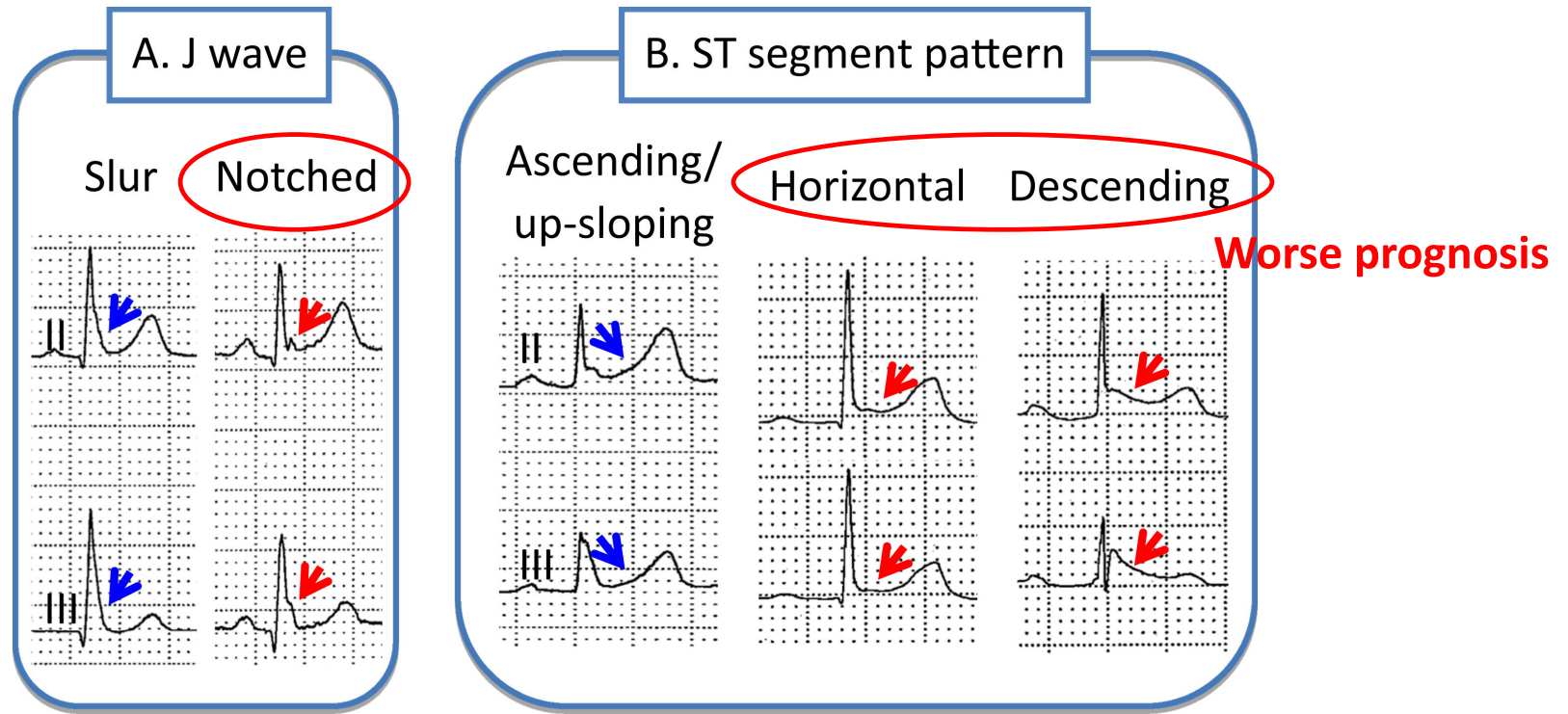
		Points
ECG findings <sup>a,b</sup>		
A	Spontaneous type 1 ECG	3.5
B	Fever-induced type 1 ECG	3
C	Type 2/3 ECG that converts to type 1 ECG with SCB provocation	2
Clinical history <sup>a</sup>		
A	Unexplained cardiac arrest or documented VF/polymorphic VT	3
B	Nocturnal agonal respirations	2
C	Suspected arrhythmic syncope	2
D	Syncope of unclear etiology	1
E	AF/flutter age <30 y without clear etiology	0.5
Family history <sup>a</sup>		
A	First- or second-degree relative with definite BrS	2
B	Suspicious SCD (fever, nocturnal, Brugada-aggravating drug) in a first- or second-degree relative	1
C	Unexplained SCD age <45 y in first- or second-degree relative with negative autopsy	0.5
Genetic testing		
A	Probable pathogenic mutation in BrS susceptibility gene	0.5

- Requires  $\geq 1$  ECG finding
- $\geq 3.5$  points: Probable/definite BrS
- 2-3 points: Possible BrS
- $< 2$  points: Nondiagnostic

# Brugada syndrome: *clinical approach*



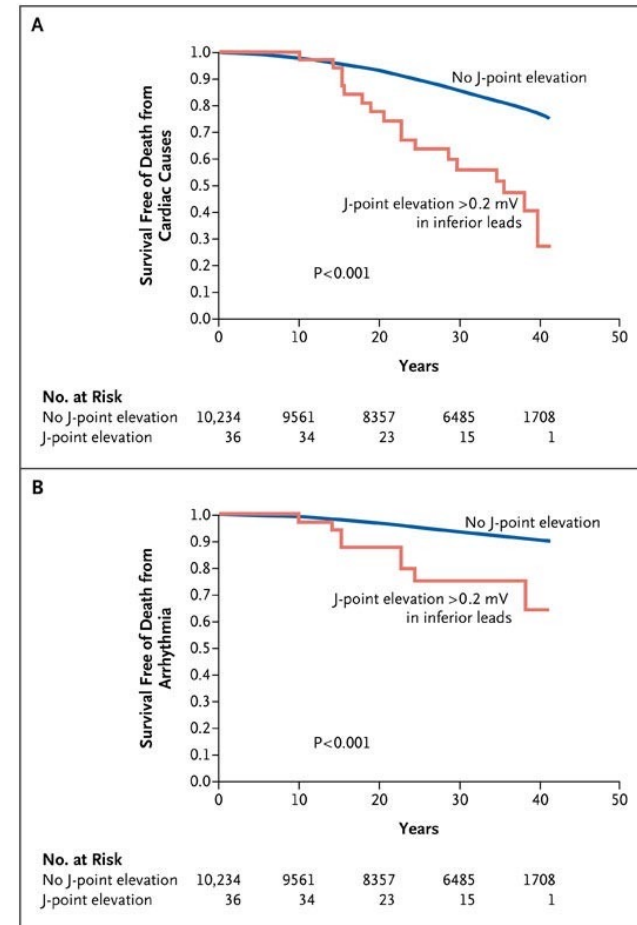
# ERS / J-wave syndrome: *diagnosis*



# ERS / J-wave syndrome: *clinical significance*

**Table 3. Adjusted Relative Risk of Death from Cardiac Causes in the Secondary Analysis.\***

Variable	No. of Subjects	Relative Risk (95% CI)	P Value
Prolonged QTc interval	668	1.20 (1.02–1.42)	0.03
Left ventricular hypertrophy according to Sokolow–Lyon criteria	3410	1.16 (1.05–1.27)	0.004
J-point elevation in inferior leads			
$\geq 0.1$ mV	384	1.28 (1.04–1.59)	0.03
$>0.2$ mV	36	2.98 (1.85–4.92)	$<0.001$



## ERS / J-wave syndrome: *clinical significance*

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- 조기 재분극이 있으면 누구나 심급사의 위험이 있는가?

### Diagnostic power of J-point elevation

As mentioned previously (see “Statistics”), the estimated risk for idiopathic VF in the **general population**, ages 35 to 45 years, is roughly **3.4 of 100,000** individuals. On the basis of the results of our study, the **probability of having J-point elevation is 0.42 for idiopathic VF patients and 0.13 for control subjects**. According to the Bayes' formula of conditional probabilities, finding a J-wave in the ECG of an individual in the 35 to 45 years age range increases the chances of having idiopathic VF from **3.4 of 100,000 individuals to only 11 of 100,000**.

# ERS / J-wave syndrome: *genetics*

Genetic Defects Associated with ERS				
	Locus	Gene/protein	Ion channel	Percent of Probands
ERS1	12p11.23	<i>KCNJ8, Kir6.1</i>	↑ $I_{K-ATP}$	Rare
ERS2	12p13.3	<i>CACNA1C, Ca<sub>v</sub>1.2</i>	↓ $I_{Ca}$	4.1%
ERS3	10p12.33	<i>CACNB2b, Ca<sub>v</sub>β2b</i>	↓ $I_{Ca}$	8.3%
ERS4	7q21.11	<i>CACNA2D1, Ca<sub>v</sub>α2δ1</i>	↓ $I_{Ca}$	4.1%
ERS5	12p12.1	<i>ABCC9, SUR2A</i>	↑ $I_{K-ATP}$	Rare
ERS6	3p21	<i>SCN5A, Na<sub>v</sub>1.5</i>	↓ $I_{Na}$	Rare
ERS7	3p22.2	<i>SCN10A, Na<sub>v</sub>1.8</i>	↓ $I_{Na}$	Rare

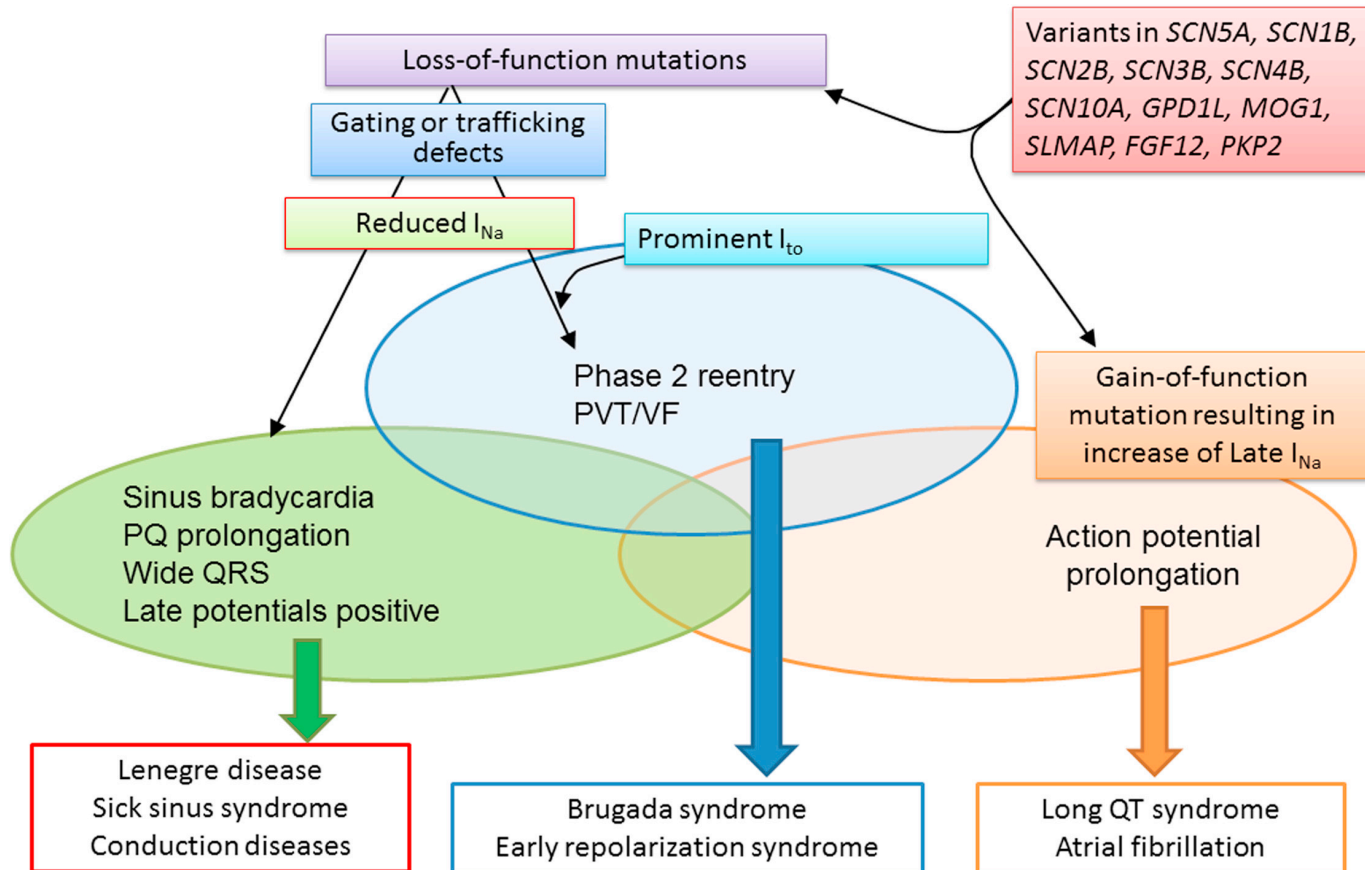
Genetic Defects Associated with BrS				
	Locus	Gene/protein	Ion channel	Percent of probands
BrS1	3p21	<i>SCN5A, Na<sub>v</sub>1.5</i>	↓ $I_{Na}$	11%–28%
BrS2	3p24	<i>GPD1L</i>	↓ $I_{Na}$	Rare
BrS3	12p13.3	<i>CACNA1C, Ca<sub>v</sub>1.2</i>	↓ $I_{Ca}$	6.6%
BrS4	10p12.33	<i>CACNB2b, Ca<sub>v</sub>β2b</i>	↓ $I_{Ca}$	4.8%
BrS5	19q13.1	<i>SCN1B, Na<sub>v</sub>β1</i>	↓ $I_{Na}$	1.1%
BrS6	11q13-14	<i>KCNE3, MiRP2</i>	↑ $I_{to}$	Rare
BrS7	11q23.3	<i>SCN3B, Na<sub>v</sub>β3</i>	↓ $I_{Na}$	Rare
BrS8	12p11.23	<i>KCNJ8, Kir6.1</i>	↑ $I_{K-ATP}$	2%
BrS9	7q21.11	<i>CACNA2D1, Ca<sub>v</sub> α2δ1</i>	↓ $I_{Ca}$	1.8%
BrS10	1p13.2	<i>KCND3, K<sub>v</sub>4.3</i>	↑ $I_{to}$	Rare
BrS11	17p13.1	<i>RANGRF, MOG1</i>	↓ $I_{Na}$	Rare
BrS12	3p21.2-p14.3	<i>SLMAP</i>	↓ $I_{Na}$	Rare
BrS13	12p12.1	<i>ABCC9, SUR2A</i>	↑ $I_{K-ATP}$	Rare
BrS14	11q23	<i>SCN2B, Na<sub>v</sub>β2</i>	↓ $I_{Na}$	Rare
BrS15	12p11	<i>PKP2, Plakophilin-2</i>	↓ $I_{Na}$	Rare
BrS16	3q28	<i>FGF12, FHAF1</i>	↓ $I_{Na}$	Rare
BrS17	3p22.2	<i>SCN10A, Na<sub>v</sub>1.8</i>	↓ $I_{Na}$	5%–16.7%
BrS18	6q	<i>HEY2 (transcriptional factor)</i>	↑ $I_{Na}$	Rare

# ERS / J-wave syndrome: *ERS vs. BrS*

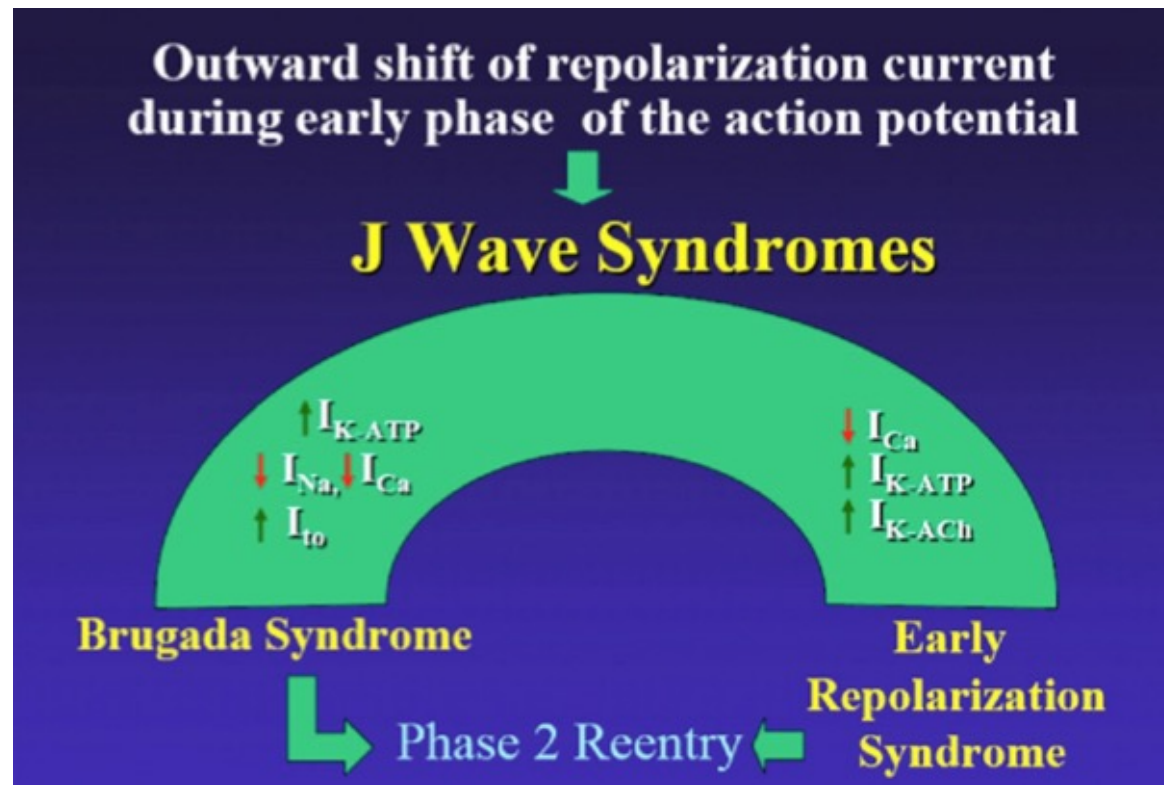
Differences	BrS	ERS	Possible mechanisms
Region most involved	RVOT	Inferior LV wall	Higher levels of $I_{to}$ and/or differences in conduction
Leads affected	V <sub>1</sub> -V <sub>3</sub>	II, II a, VF, V <sub>4</sub> , V <sub>5</sub> , V <sub>6</sub> ; I, aVL, Both: inferolateral	
Regional difference in prevalence			Europe: BrS = ERS Asia: BrS > ERS
Incidence of late potential in signal-averaged ECG	Higher	Lower	Reduction of J wave in the setting of ER is thought to be due largely to prolongation of QRS. Accentuation of repolarization defects predominates in BrS, whereas accentuation of depolarization defects predominates in ERS. Some investigators have hypothesized that some of these changes may be the result of, rather than the cause of the BrS substrate, which may create a hibernation-like state due to loss of contractility in the RVOT secondary to loss of the AP dome.
Prevalence of atrial fibrillation	Higher	Lower	
Effect of sodium channel blockers on surface ECG	Increased J-wave manifestation	Reduced J-wave manifestation	
Structural changes, including mild fibrosis and reduced expression of Cx43 in RVOT or fibrofatty infiltration in cases of arrhythmogenic right ventricular cardiomyopathy. Imaging studies have also revealed wall motion abnormalities and mild dilation in the region of the RVOT.	Higher in some forms of the syndrome	Unknown	



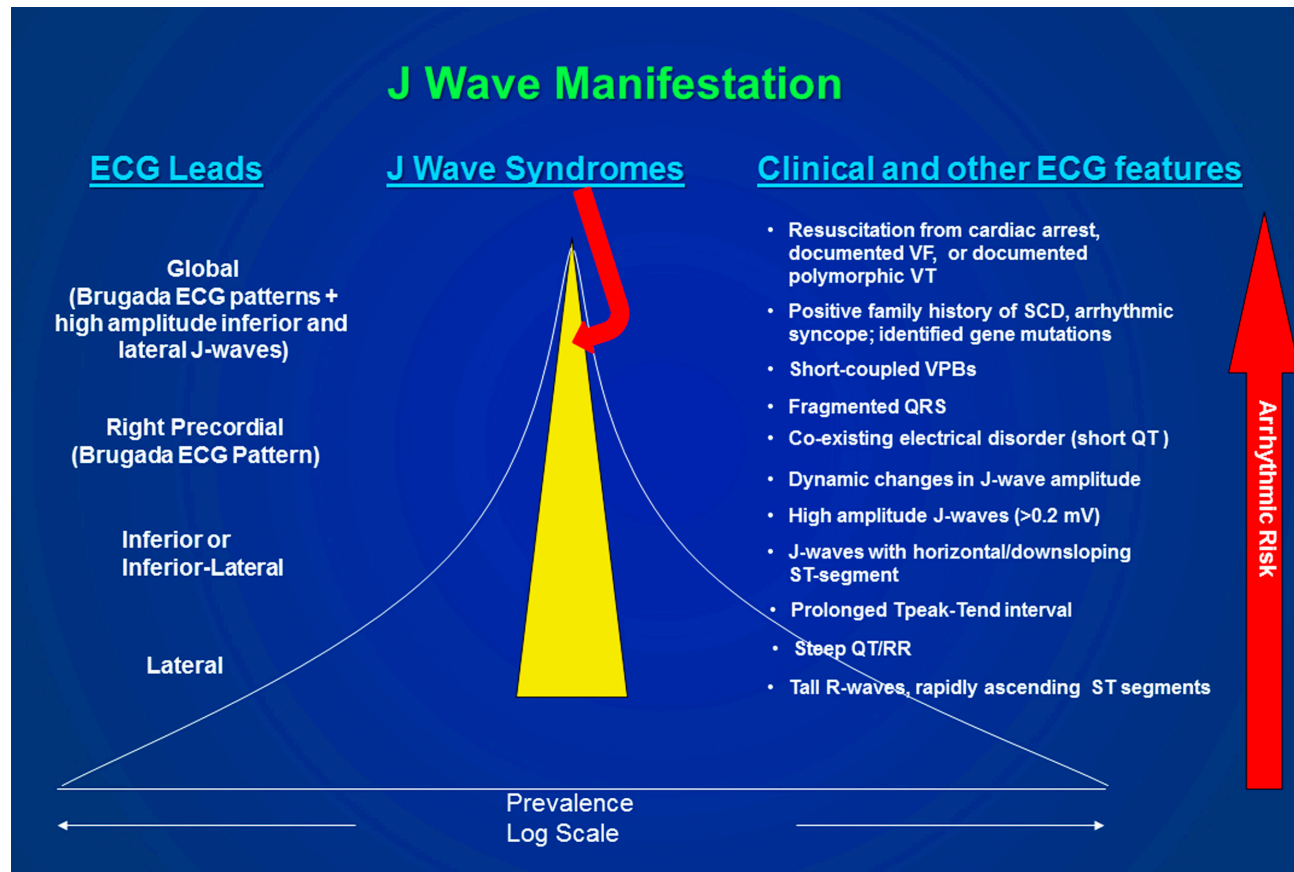
# ERS / J-wave syndrome: *current concept*



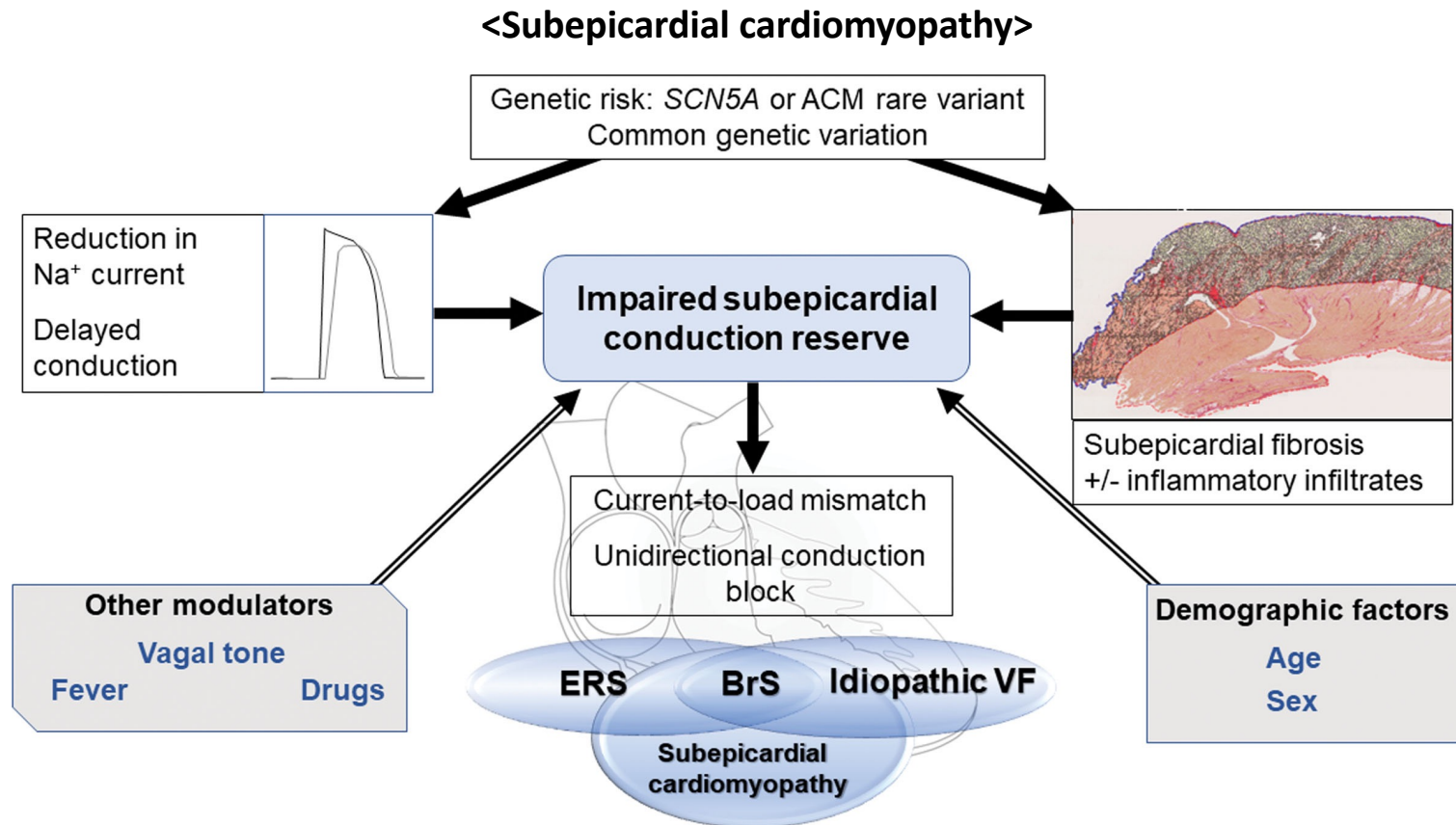
# ERS / J-wave syndrome: *current concept*



# ERS / J-wave syndrome: *current concept*

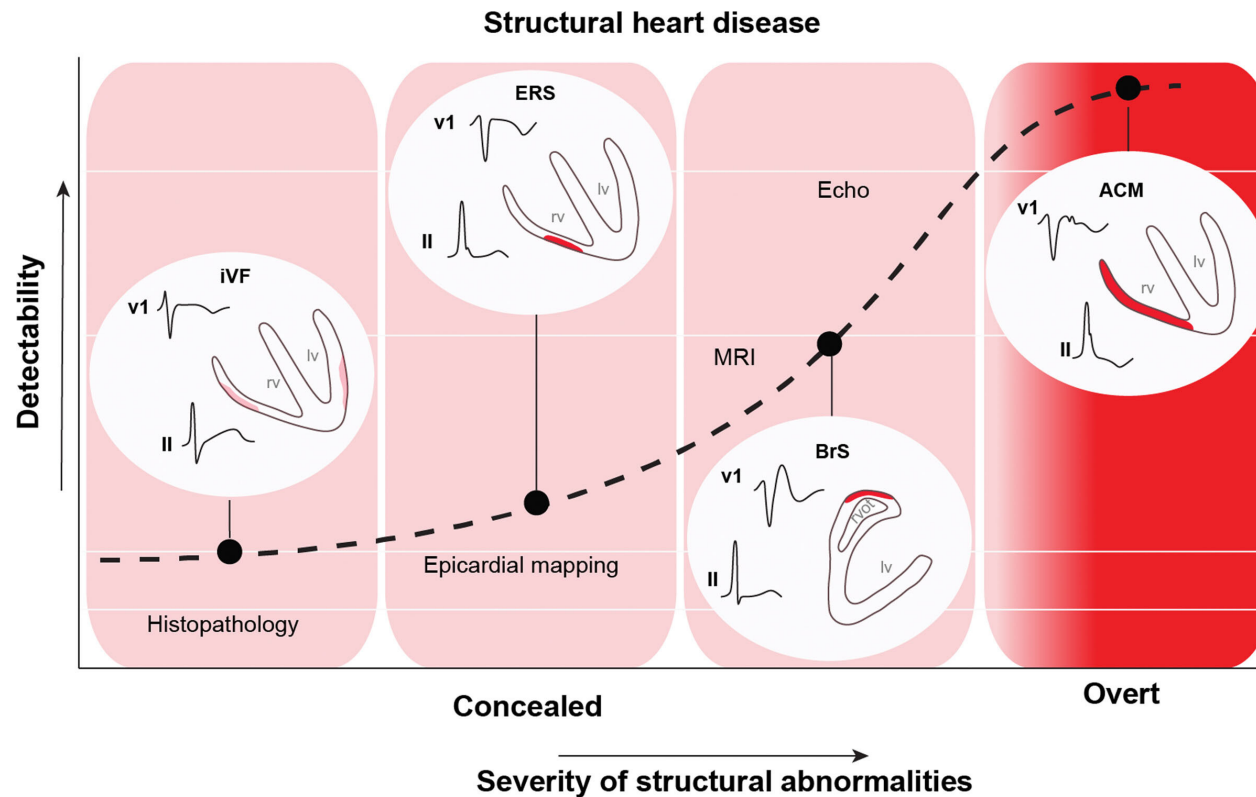


# ERS / J-wave syndrome: *new concept*



\* ACM: arrhythmogenic cardiomyopathy  
Miles C, et al. Circulation. 2023 May 23;147(21):1622-1633

# ERS / J-wave syndrome: *new concept*



\* ACM: arrhythmogenic cardiomyopathy  
 Miles C, et al. Circulation. 2023 May 23;147(21):1622-1633

# Summary

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- 한국인에서 가장 흔한 심인성 심정지 원인은 심혈관질환, 심근병증, 부정맥 순이다
- 한국인에서 가장 흔한 유전성 부정맥질환 3가지는 특발성심실세동, 브루가다증후군, QT연장증후군이다
- fQRS는 심장내 전도이상으로 발생하며 심근경색 뿐 아니라 다양한 심근병증에서 심장돌연사의 위험인자이다
- scPVC는 coupling interval 이 <350 ms 인 경우로 정의할 수 있으며 퍼킨지섬유 전도이상을 통해 심실부정맥을 일으킬 수 있고 심장돌연사의 위험인자이다
- 브루가다증후군은 주로 SCN5A 의 기능상실변이와 관련이 있으나 최근 다양한 유전자가 관여하는 것으로 알려지고 있다
- 브루가다증후군의 예후를 결정하는 가장 중요한 위험인자는 제1형 심전도 특징과 실신이다
- 조기재분극증후군이나 J파증후군은 다양한 유전자변이와 관련이 있으며 심장돌연사의 위험인자이나 절대위험도가 매우 낮기 때문에 증상이나 급사의 가족력이 없는 경우 심장돌연사의 고위험군으로 해석하면 안된다
- 최근에는 기존 질환을 포괄하는 개념으로 심외막하 심근병증 혹은 부정맥성 심근병증 개념이 등장하고 있다



*Thank you for your attention*