Debate 2

KCS scientific congress, 19th Apr 2014, Gwangju

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Debating ?

Case

- **18 Years old Female.**
- **Recurrent Syncope With QTc 495ms.**
- **Strong Family History of SCD.**

  (Mother - SCD, Elder Sister - SCD Even on BB Therapy)

Question 1

본 환자의 진단은 ?

Inherited Long QT Syndrome

How do you know?

- **Diagnositic criteria for long QT syndrome**

ECG finding	Points
QTc	
≥0.48 s	3
0.46-0.47 s	2
0.45 s	1
Torsade de pointes	2
T wave alternans	1
Notched T wave in three leads	1
Low heart rate for age	0.5

Schwartz PJ et al. Circulation. 1993:88;782-784

Clinical History	point
Syncope	
with stress	2
without stress	1
Congenital deafness	0.5

Family history	
Family members with definte LQTS	1
Unexplained sudden cardiac death before age 30 among immediate family members	0.5

Scoring :

≤ 1 point	: low probability of LQTS
2-3 points	: intermediate probability
4 points	: high probability of LQTS

Long QT syndrome 진단시 유의점

1. Physician misread the QT interval

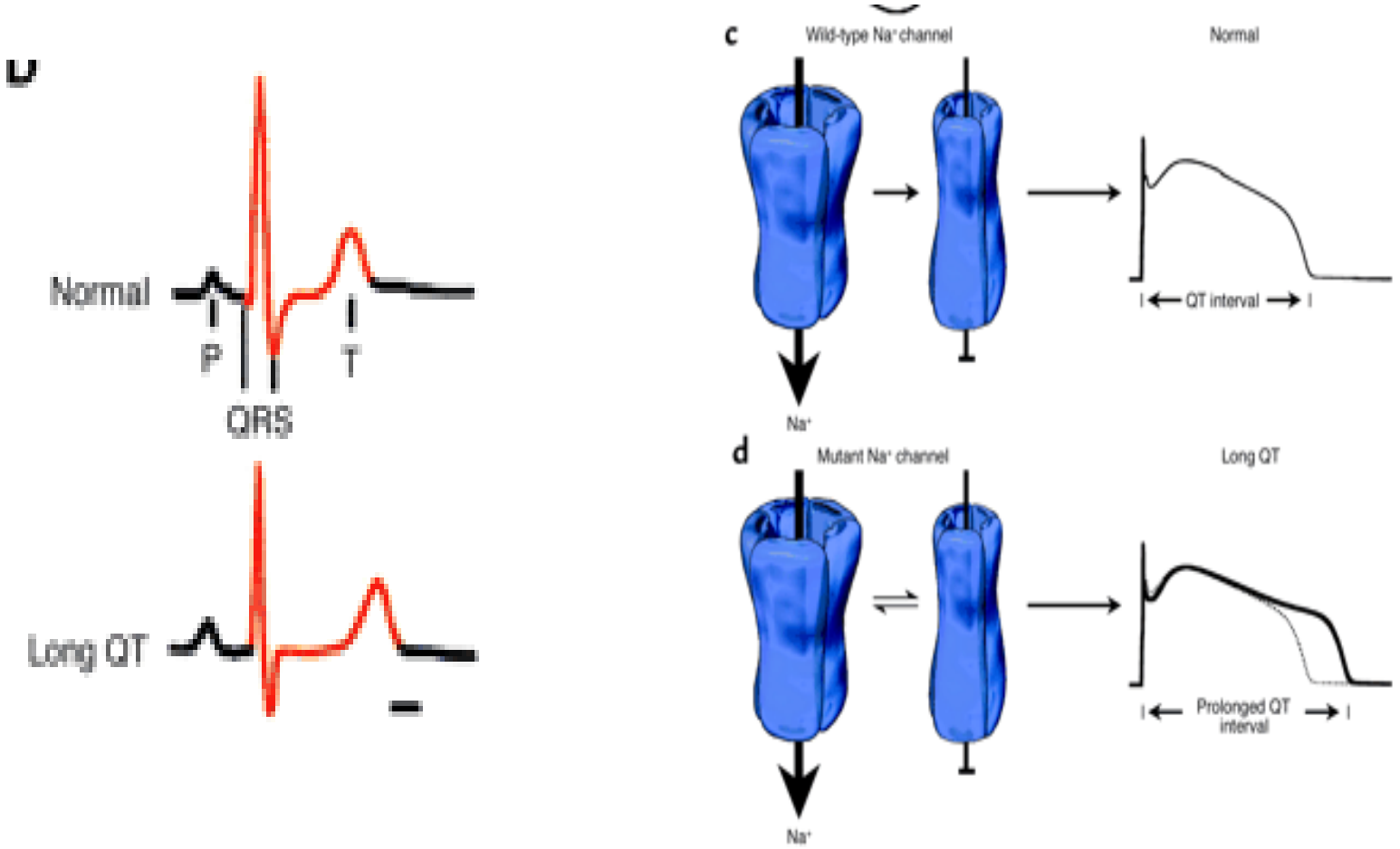
2. Misdiagnosis of vasovagal syncope as long QT syndrome

3. Genetic testing

4. Screening for acquired causes

5. Detailed family history

    Drowning, sudden infant death SD, car accident



- **Mutation-induced ion channel dysfunction**

Repolarization prolongation due to mutations of Na+ and K+ channel genes

→ prolonged intracellular positivity

→ early afterdepolarization → Torsade de pointes

Molecular and cellular mechanisms

Disease	Gene (alternate name)	Protein
LQT-1	*KVLQT1(KCNQ1)*	I_{Ks} K^+ channel α subunit
LQT-2	*HERG(KCNH2)*	I_{Kr} K^+ channel α subunit
LQT-3	*SCN5A*	I_{Na} K^+ channel α subunit
LQT-4	*ANKB*	ANKRIN-β
LQT-5	*minK(KCNE1)*	I_{Ks} K^+ channel β subunit
LQT-6	*MiRP1(KCNE2)*	I_{Kr} K^+ channel β subunit
LQT-7	*KCNJ2*	I_{Kr} K^+ channel α subunit
LQT-8	*CACNA1C*	I_{ca} Ccv1.2
LQT-9	*CAV3*	I_{Na} Caveolin-3
LQT-10	*SCN4B*	I_{Na} NaVB4

- Incidence : LQT1 and LQT2 > LQT3
- Lethality : LQT3 > LQT1 and LQT2

Robert S. Kass et al. J. Clin. Invest. 2003. 112:810-815

Question 2

본 환자는 위험한 환자인가요?

High risk patient

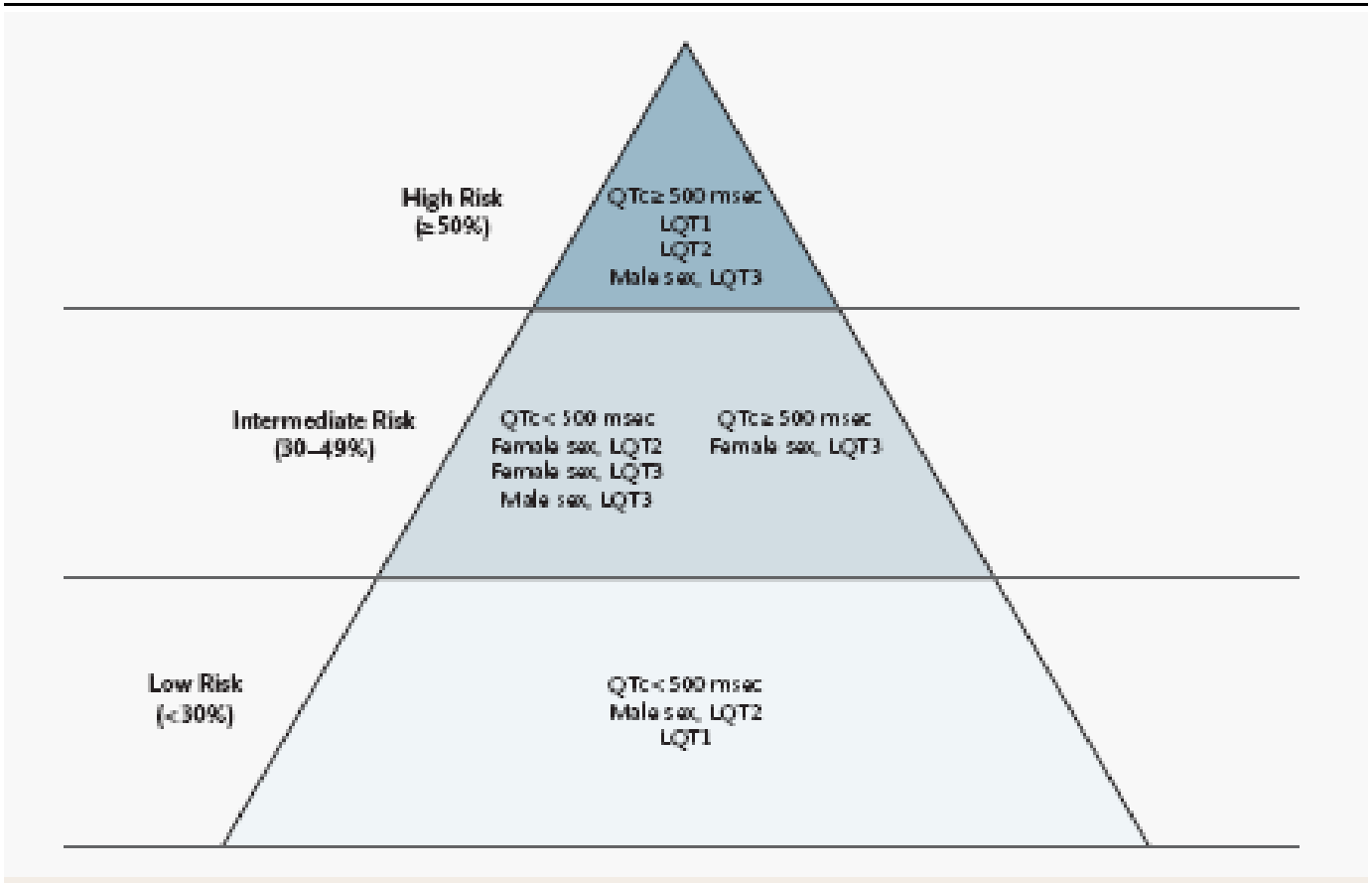
Risk Factors for SCD in Long QT SD

- Syncope
- Hx of Torsades de pointes
- Family Hx of sudden cardiac death
- Excessive QT prolongation or T wave alternans on ECG
- Deafness
- Geno-type

The most powerful predictor of risk is the QTc duration.

Dan M Roden, NEJM 2008

Risk-Stratification of long QT Syndrome



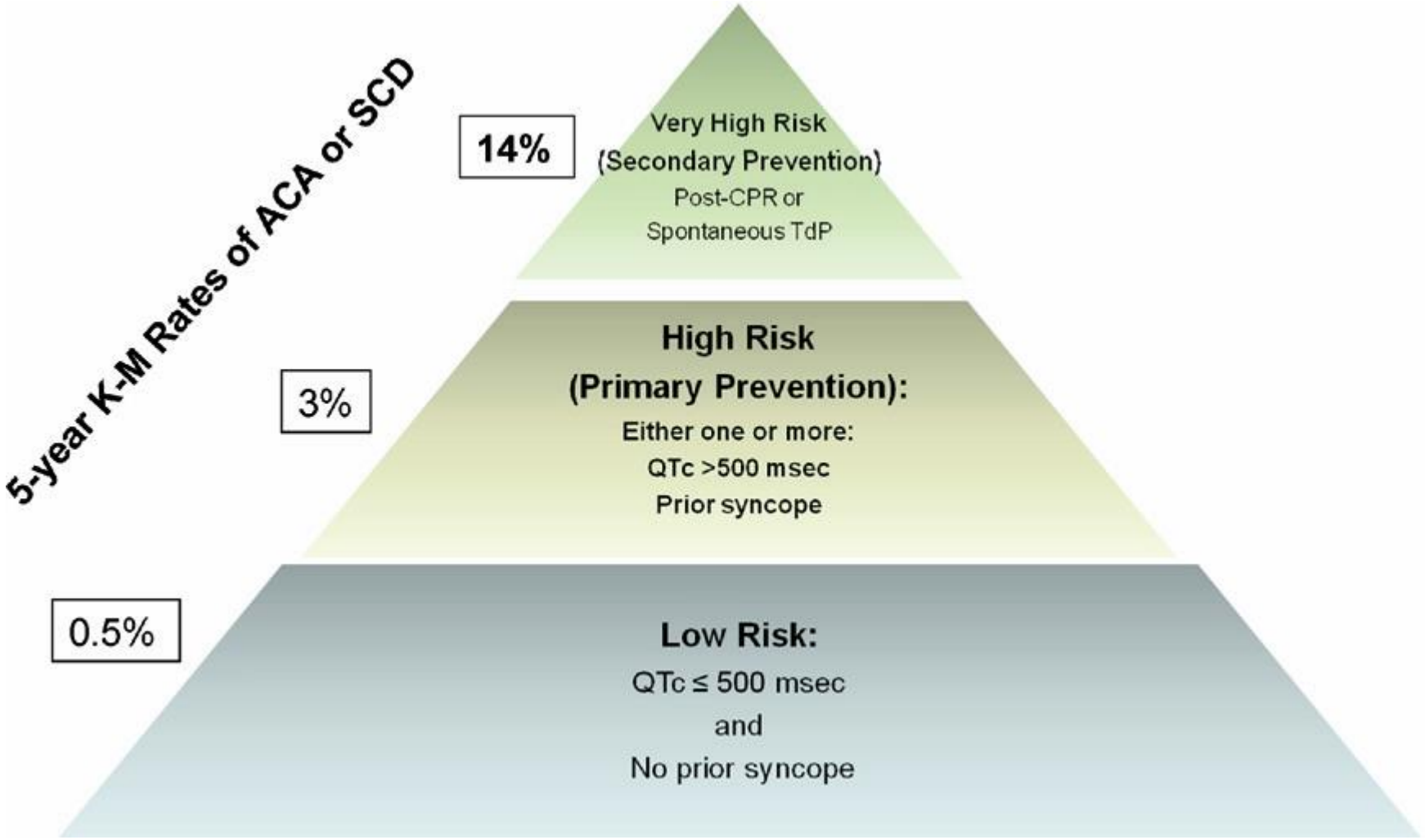
Silva G et al. N Eng J Med. 2003. 348:1866-76

Age-Specific Risk Factors for Life-Threatening Cardiac Events in LQT SD

Age Group (Ref. #)	Risk Factor	Hazard Ratio (p Value)
Childhood (1–12 yrs) (33) Circulation 2008	Male gender	3.96 (<0.001)
	QTc >500 ms	2.12 (0.02)
	Prior syncope	
	Recent (<2 yrs)	14.34 (<0.001)
	Remote (≥2 yrs)	6.45 (<0.001)
Adolescence (10–20 yrs) (28) JAMA 2006	QTc >530 ms	2.3 (<0.001)
	Syncope	
	≥2 syncopal events in past 2 yrs	18.1 (<0.001)
	1 syncopal event in past 2 yrs	11.7 (<0.001)
	≥2 syncopal events in past 2–10 yrs	5.8 (<0.001)
	1 syncopal events in past 2–10 yrs	2.7 (<0.001)
Adulthood (18–40 yrs) (29) JACC 2007	Female gender	2.68 (<0.05)
	QTc duration	
	QTc ≥500 ms	6.35 (<0.01)
	QTc 500–549 ms	3.34 (<0.01)
	Prior syncope	5.10 (<0.01)
Adulthood (41–60 yrs) (53)† Circulation 2008	Recent syncope (<2 yrs)	9.92 (<0.001)
	QTc >530 ms	1.68 (0.06)
	LQT3 genotype	4.76 (0.02)

Goldenberg and Moss, et al. JACC. 2008.

Suggested Risk-Stratification Scheme

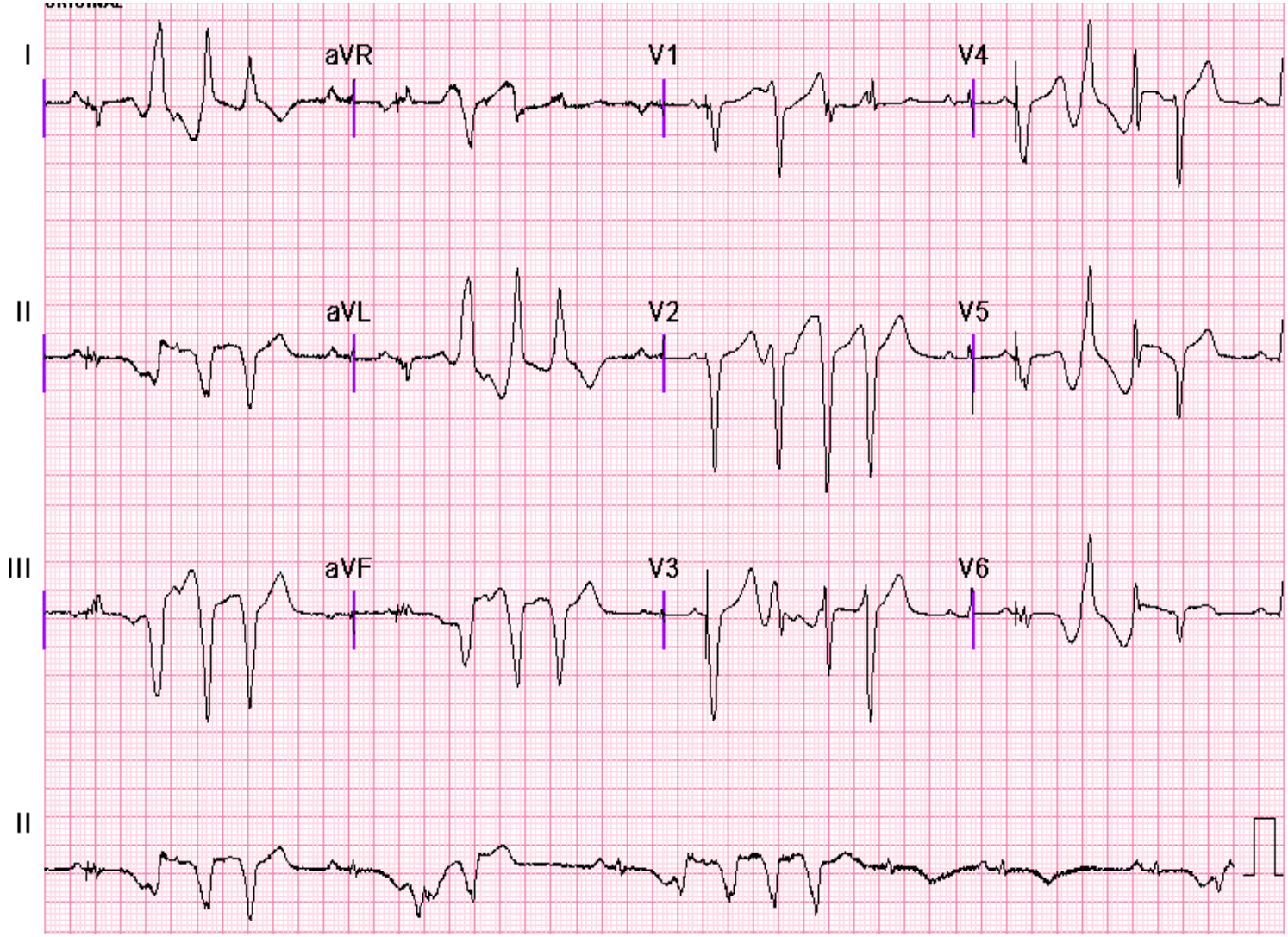


Goldenberg and Moss. JACC. 2008.

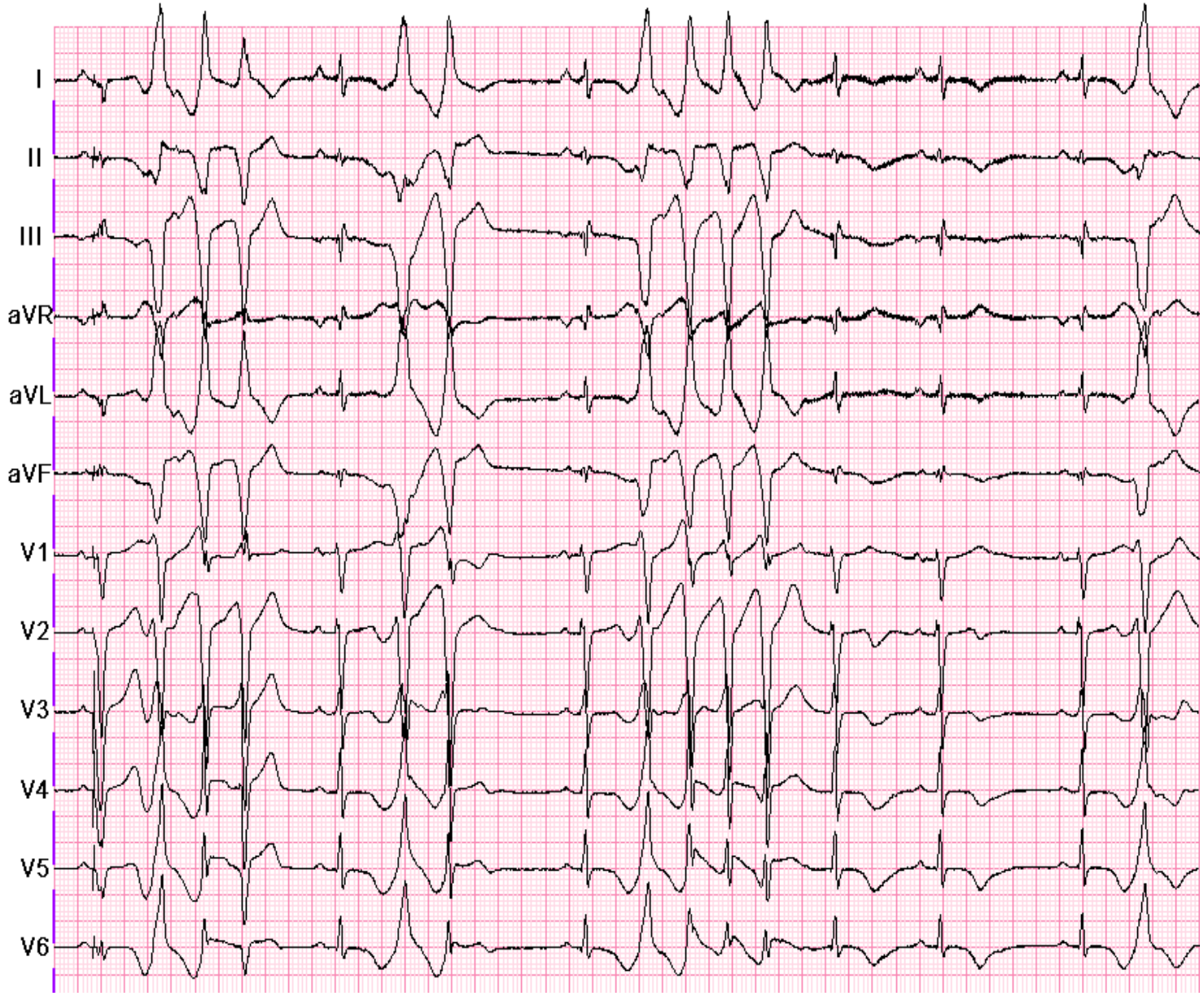
Case Review

38 F, s/p ICD implantation due to ACA with long QT SD

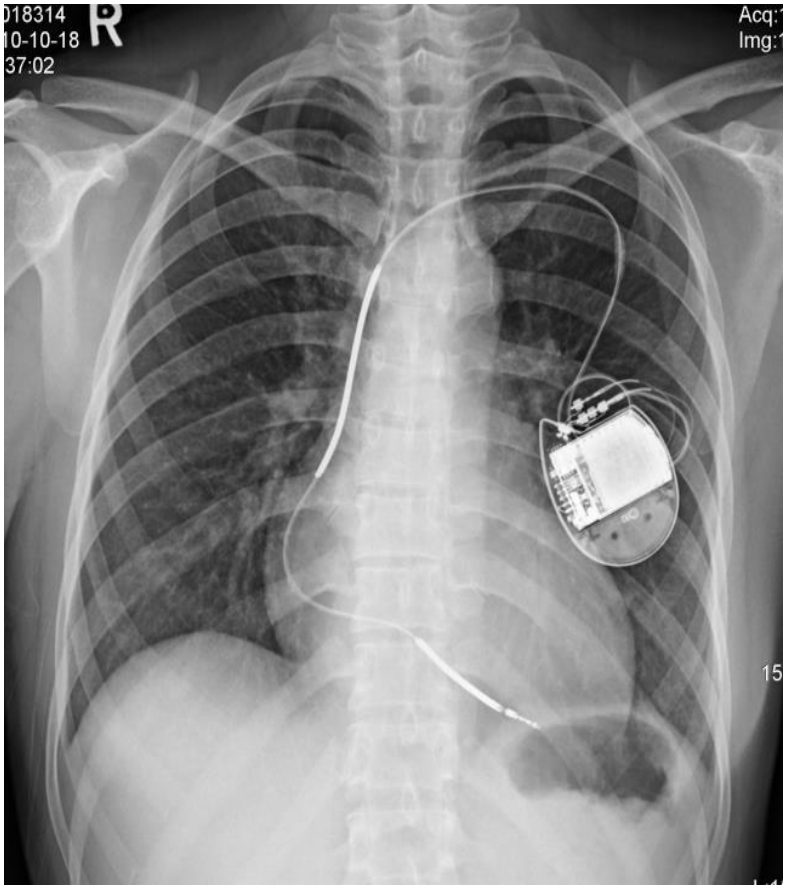
ECG on admission



ECG on admission



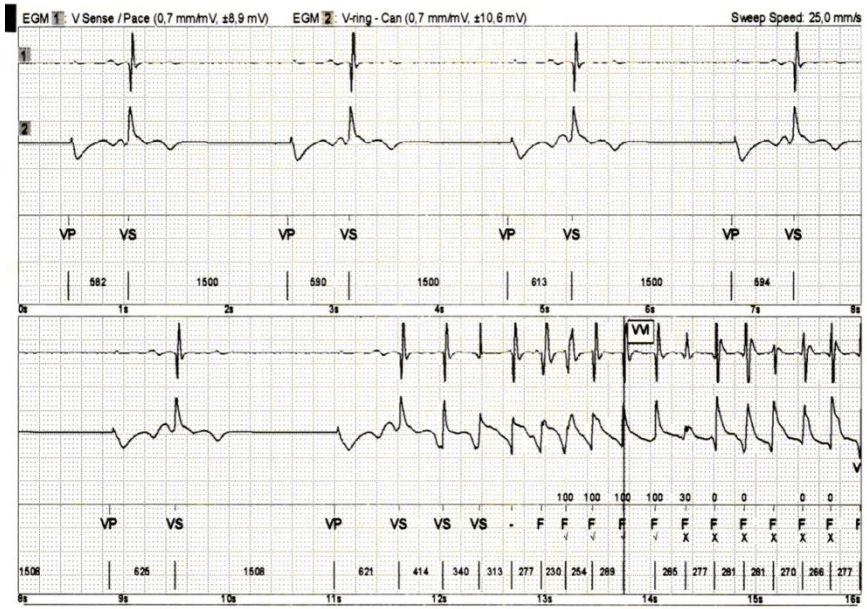
Chest PA on admission

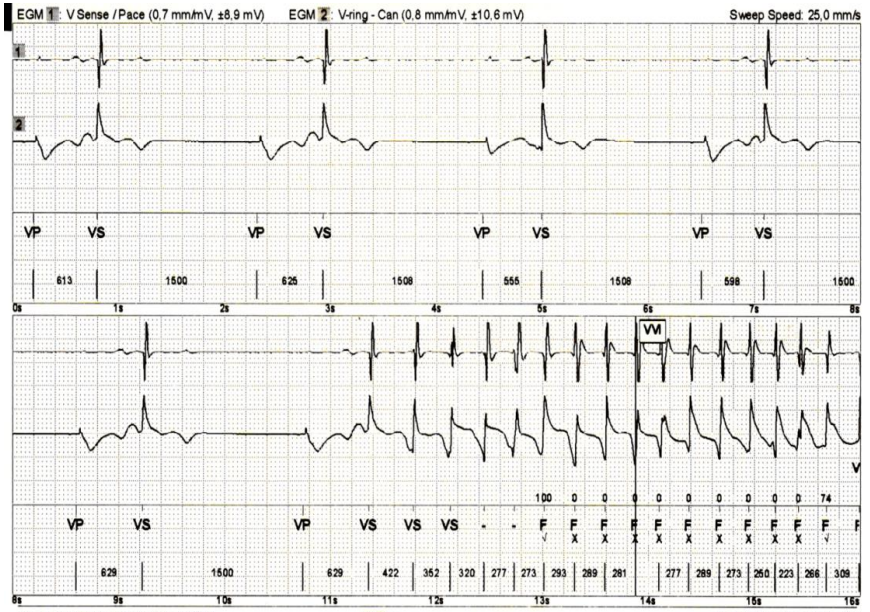


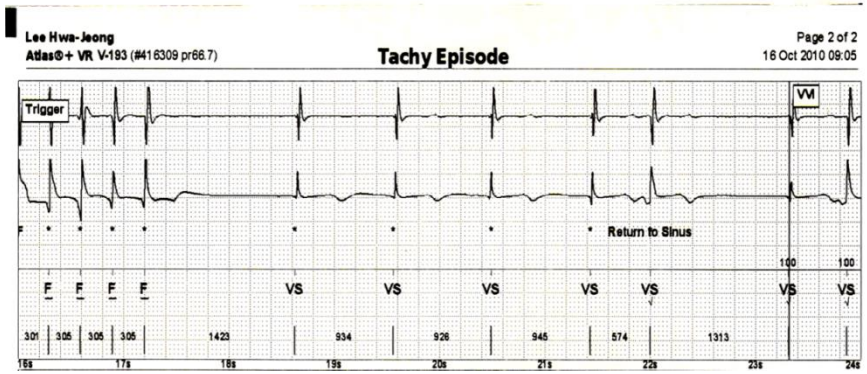
Echo

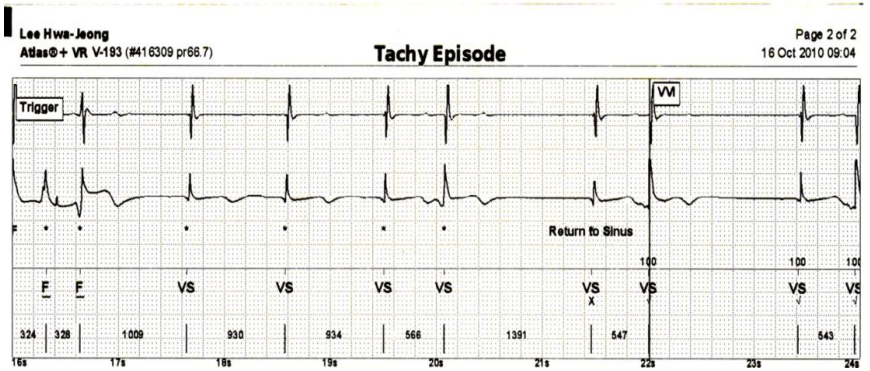
1) Midely enlarged LA
(LAVI = 29 ml/m2)
2) Normal LV systolic function / No RWMA
3) Thickened AV/ Minimal MR, TR.

ICD interrogation – episode 1,2

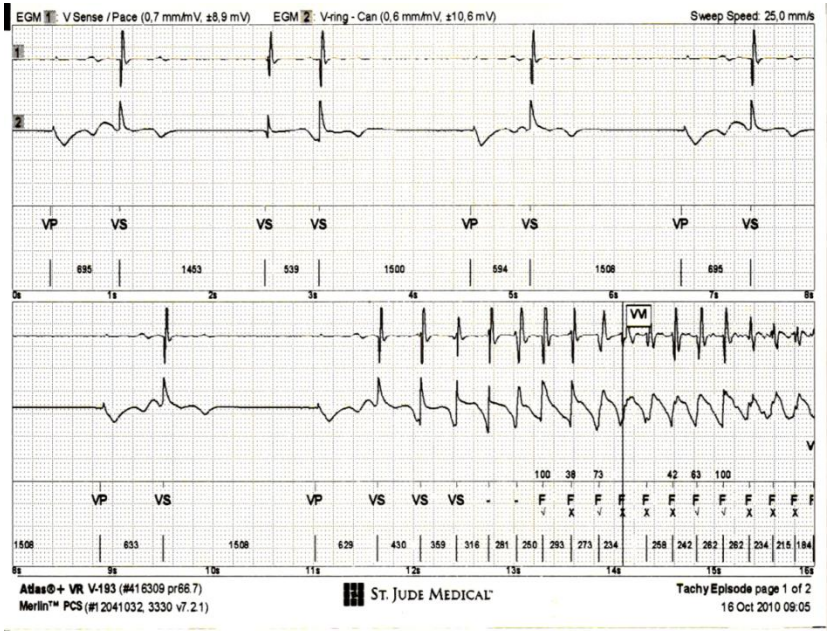


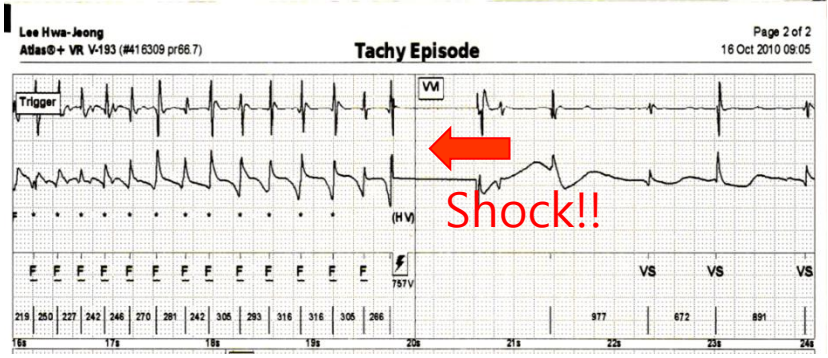


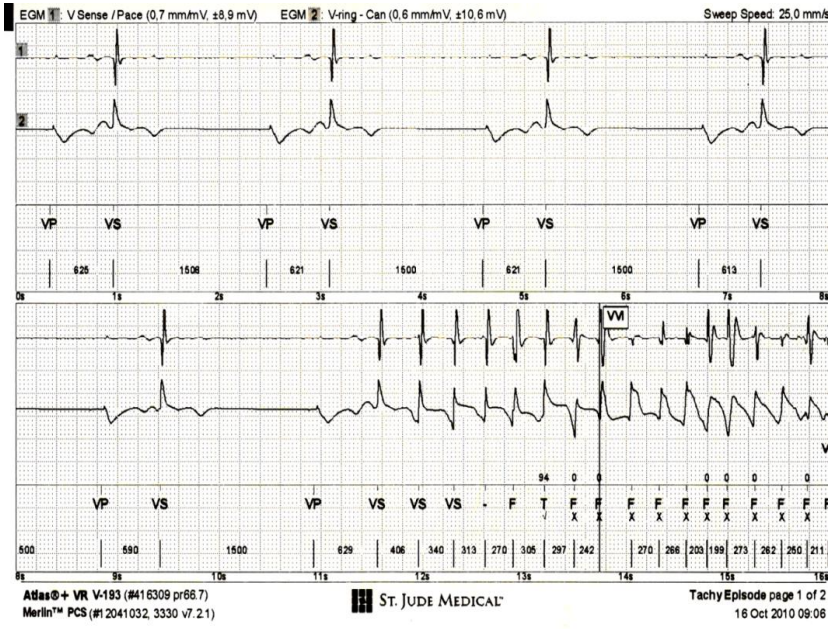


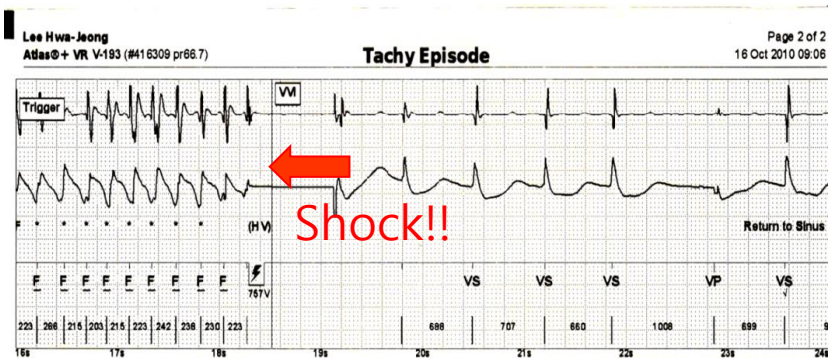


ICD interrogation – episode 3,4









ICD previous setting

Bradycardia backup : VVI 40/min

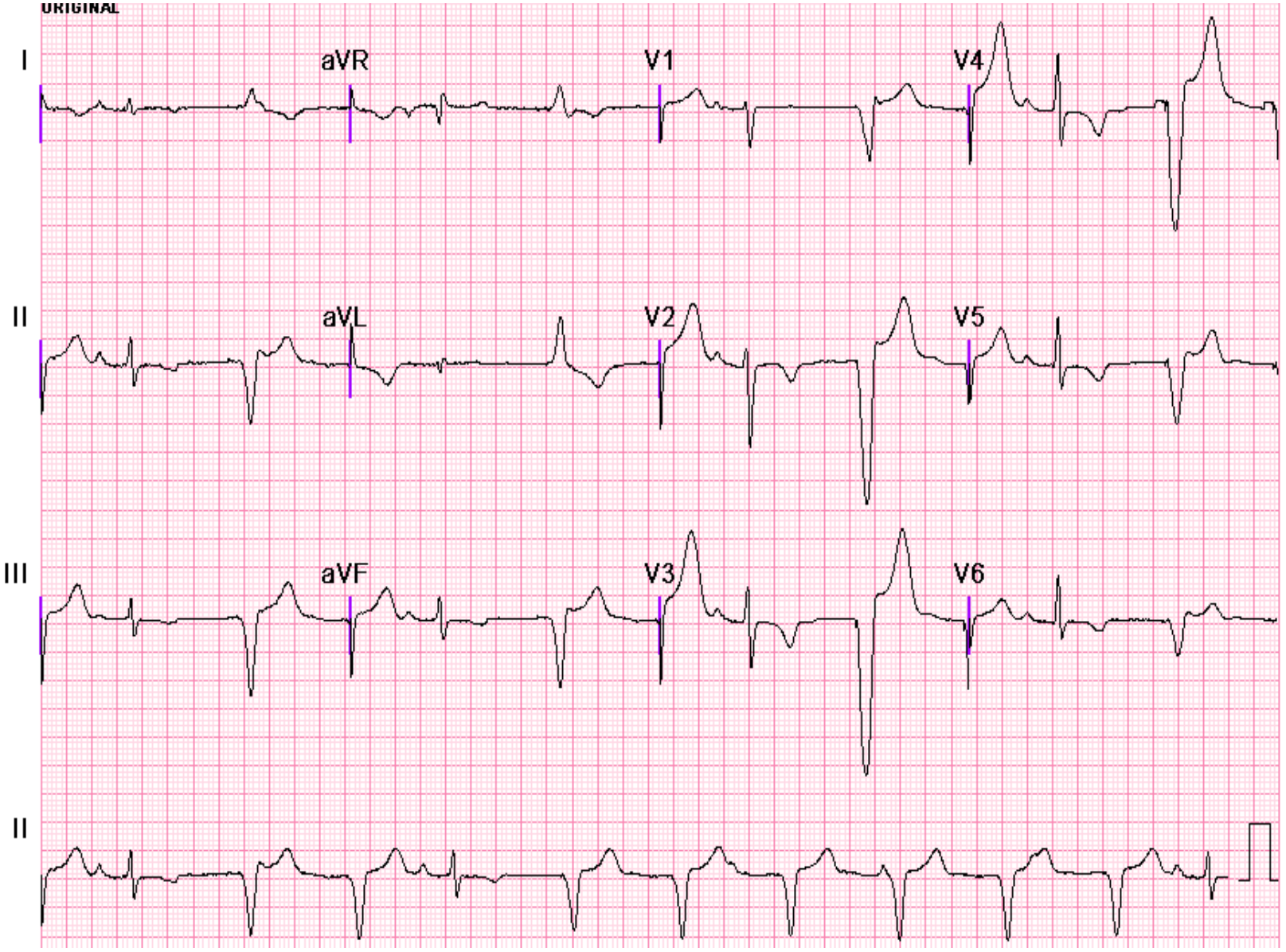
Detection

VF	Detection cutoff 200 bpm (300ms)	
	1st	11 J
	2nd	21 J
	3-8th	31 J
VT	Detection cutoff 165 bpm (363ms)	
	Monitor	

ICD setting

Lower rate 40 ➔ 70 bpm

ECG after ICD resetting



Holter after ICD resetting

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(02)958-8171

PATIENT DEMOGRAPHICS

Last Name	이희정	Physician	
First Name		Scanned By	
Middle Initial		Reading Physician	
ID Number	12018314	Test Date	2010-10-18
Date Of Birth		Analysis Date	2010-10-19
Sex	F	Hookup Time	PM 2:48
Source		Recording Time	18 hr 30 min
Billing Code		Analysis Time	18 hr 30 min
Recorder Format	Philips Recorder:	User Field #1	
Reason for Test		User Field #2	
Medications			

Heart Rate Data

Total Beats	: 70833
Min HR	: 65 BPM at 오전 12:35:59
Avg HR	: 70 BPM
Max HR	: 82 BPM at 오후 6:58:09

Heart Rate Variability

ASDNN 5	: 35.1 msec	SDNN	: 40.7 msec
SDANN 5	: 8.0 msec	RMSSD	: 64.8 msec

QT Analysis

QT Min	: 416 msec	QTc Min	: 463 msec
QT Avg	: 493 msec	QTc Avg	: 533 msec
QT Max	: 535 msec	QTc Max	: 579 msec

QTc > 450 msec : 100%

ST Episode Analysis

	Ch1	Ch2	Ch3
Min ST Level	-1.4	-1.7	-1.4
Max ST Level	3.9	4.9	1.5
ST Episodes	8	14	1

Pacer Analysis

Sinus Beats	: 70342 (99.3%)	FTO	: 2
Paced Beats	: 0 (0.0%)	FTS	: 0
Atrial Paced	: 0 (0.0%)	FTC	: 0
Ventricular Paced	: 0 (0.0%)		
Dual Paced Beats	: 0 (0.0%)		
Fusion Beats	: 0 (0.0%)		

Ventricular Ectopy

Total VE Beats	: 491 (0.7%)
Vent Runs	: 0
Beats	: 0
Longest	: 0
Fastest	: 0 BPM
Triplets	: 0 Events
Couplets	: 1 Event
Single/Interp PVC	: 269/5
R on T	: 0
Single/Late VE's	: 4/0
Bi/Trigeminy	: 211/0 Beats

Supraventricular Ectopy

Total SVE Beats	: 473 (0.7%)
Atrial Runs	: 0
Beats	: 0
Longest	: 0
Fastest	: 0 BPM
Atrial Pairs	: 0 Events
Drop/Late	: 0/0
Longest R-R	: 1.3 sec at 오전 12:36:01
Single PAC's	: 473
Bi/Trigeminy	: 0/0 Beats

Atrial Fibrillation

AFib Beats	: 6 (0.0%)
Duration	: 0.1 min
Events	: 2

INTERPRETATION

Basically pacing rhythm with PVC's
No VT.

Prof: 김진배

Question 3

치료는 어떻게 해야 하나요?

Medical Tx, first.

Therapeutic consideration in Long QT SD

- Beta blocker
- Implantable cardioverter defibrillator
- Surgical left cervicothoracic sympathetic denervation

Beta blocker in Long QT SD

- beta-blockers is considered to be first-line prophylactic therapy.
- should be administered to all intermediate- or high-risk affected individuals and considered on an individual basis in low-risk patients

Hobbs JB, et al. JAMA 2006;296:1249 –54.
Sauer AJ, Moss AJ, et al. JACC 2007;49:329 –37.
Goldenberg I, Moss AJ, et al. Circulation 2008;117:2184 –91.
Dan M Roden. NEJM 2008;358;169-76.

Beta blocker in long QT SD

Age Group (Ref. #)	Risk Factor	Hazard Ratio (p Value)	Beta-Blocker Efficacy, % Reduction (p Value)
Childhood (1–12 yrs) (33)	Male gender	3.96 (<0.001)	73% (0.002)
	QTc >500 ms	2.12 (0.02)	
	Prior syncope		
	Recent (<2 yrs)	14.34 (<0.001)	
	Remote (≥2 yrs)	6.45 (<0.001)	
Adolescence (10–20 yrs) (28)	QTc >530 ms	2.3 (<0.001)	64% (0.01)
	Syncope		
	≥2 syncopal events in past 2 yrs	18.1 (<0.001)	
	1 syncopal event in past 2 yrs	11.7 (<0.001)	
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Adulthood (18–40 yrs) (29)	Female gender	2.68 (<0.05)	60% (<0.01)
	QTc duration		
	QTc ≥500 ms	6.35 (<0.01)	
	QTc 500–549 ms	3.34 (<0.01)	
	Prior syncope	5.10 (<0.01)	
Adulthood (41–60 yrs) (53)†	Recent syncope (<2 yrs)	9.92 (<0.001)	42% (0.40)‡
	QTc >530 ms	1.68 (0.06)	
	LQT3 genotype	4.76 (0.02)	

Goldenberg and Moss, et al. JACC. 2008.

Recurrent Syncope as a Preditor of ACA/SCD

	Adjusted Risk			Time-Dependent Beta-Blocker Effect†		
Variable	HR‡	95% CI	p Value	HR§	95% CI	p Value
First syncope event vs. no events	6.54	3.96–10.80	<0.001	0.25	0.11–0.55	0.001
Second syncope event vs. no events	6.69	6.65–12.25	<0.001	0.28	0.11–0.72	0.008
Third syncope event vs. no events	12.51	7.03–22.28	<0.001	0.22	0.08–0.57	0.002
≥4 Syncope events vs. no events	14.65	8.02–26.76	<0.001	0.20	0.10–0.44	<0.001

Data from International registry, JACC. 2011.

Beta blocker in long QT SD

- ✓ Data of patient from birth through age 20 years among 1,648 patients from the International Long QT Syndrome Registry.
- ✓ International registry data confirms that beta-blocker therapy is associated with a significant reduction in the risk of a first cardiac event in children and adolescents with LQTS
- ✓ Registry findings extend previous data and demonstrate that treatment with beta-blockers is associated with a pronounced (70%) reduction in the risk of subsequent ACA or SCD among patients who experienced any number of previous syncope episodes.

Data from International registry, JACC. 2011.

ACC/AHA/ESC guideline

Recommendation	Level of Evidence†	Comment
No participation in competitive sports	I	Includes patients with the diagnosis established by means of genetic testing only
Beta-blockers	I	For patients who have QTc-interval prolongation (>460 msec in women and >440 msec in men)
	IIa	For patients with a normal QTc interval
Implantable cardioverter–defibrillator	I	For survivors of cardiac arrest
	IIa	For patients with syncope while receiving beta-blockers
	IIb	For primary prevention in patients with characteristics that suggest high risk; these include LQT2, LQT3, and QTc interval >500 msec‡

국내 guideline

ICD 인정 기준

Long QT 증후군 환자에서 베타 차단제에 반응이 없을 경우

보험 인정

One more thing to be considered

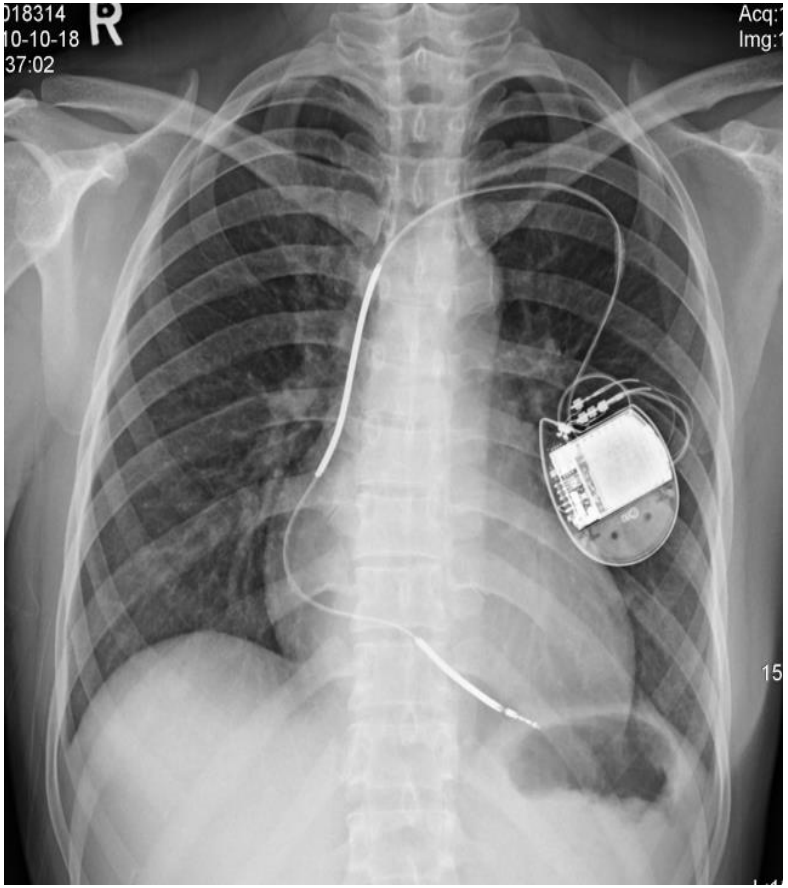
- Drawback of ICD

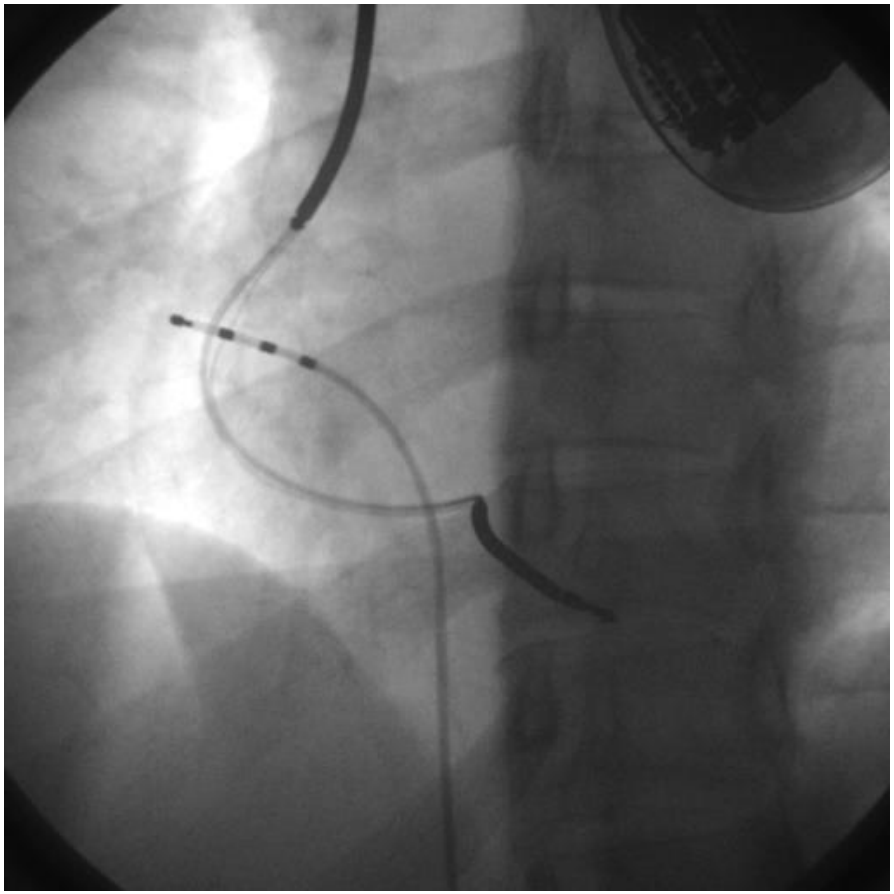
1. Device related complication.

2. It cannot prevent SCD completely.

Case Review

38 F, s/p ICD implantation due to ACA with long QT SD





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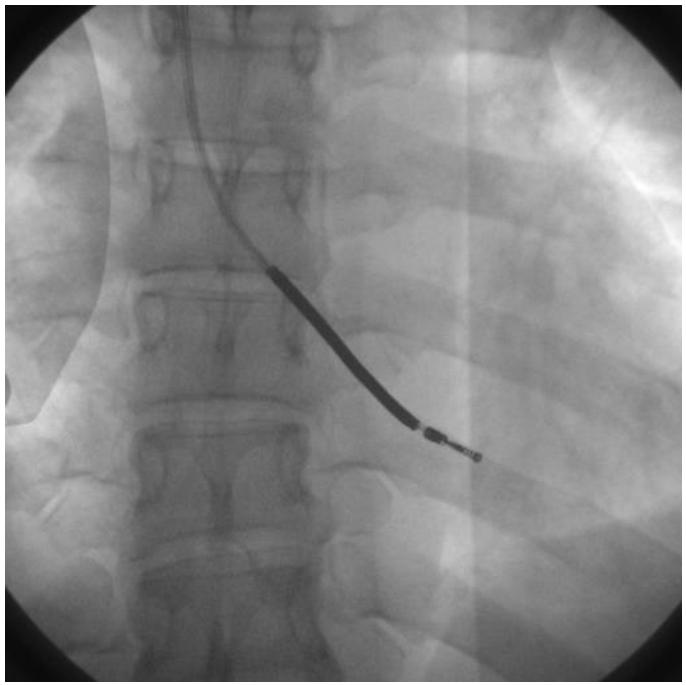
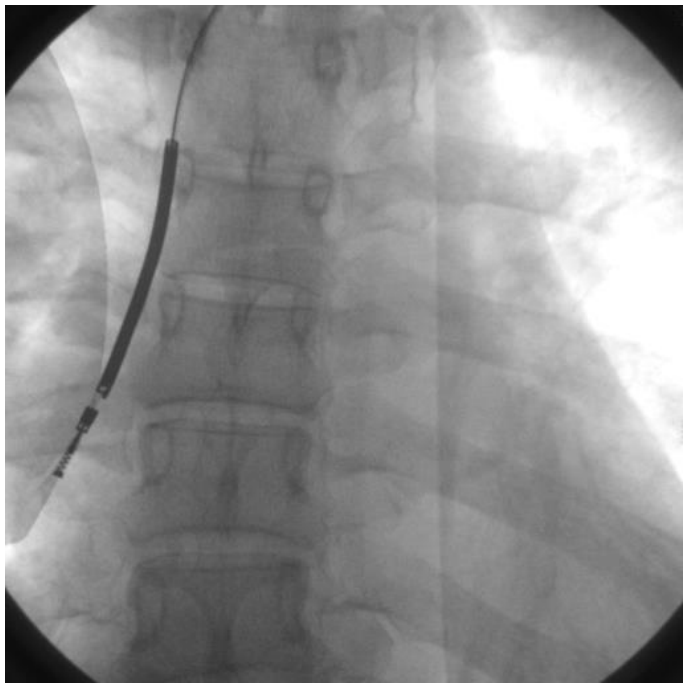
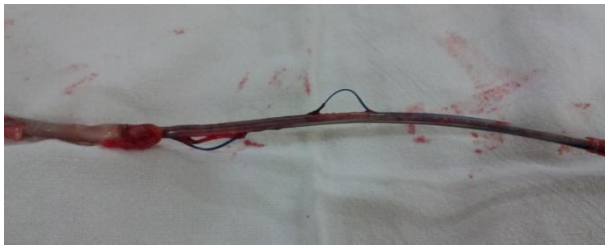
Lead extraction







Chest PA after new ICD implantation

Thank you for your attention