Syncope with HCM: Hemodynamic or Arrhythmic?

2016.4.16.

최 의 근

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Case

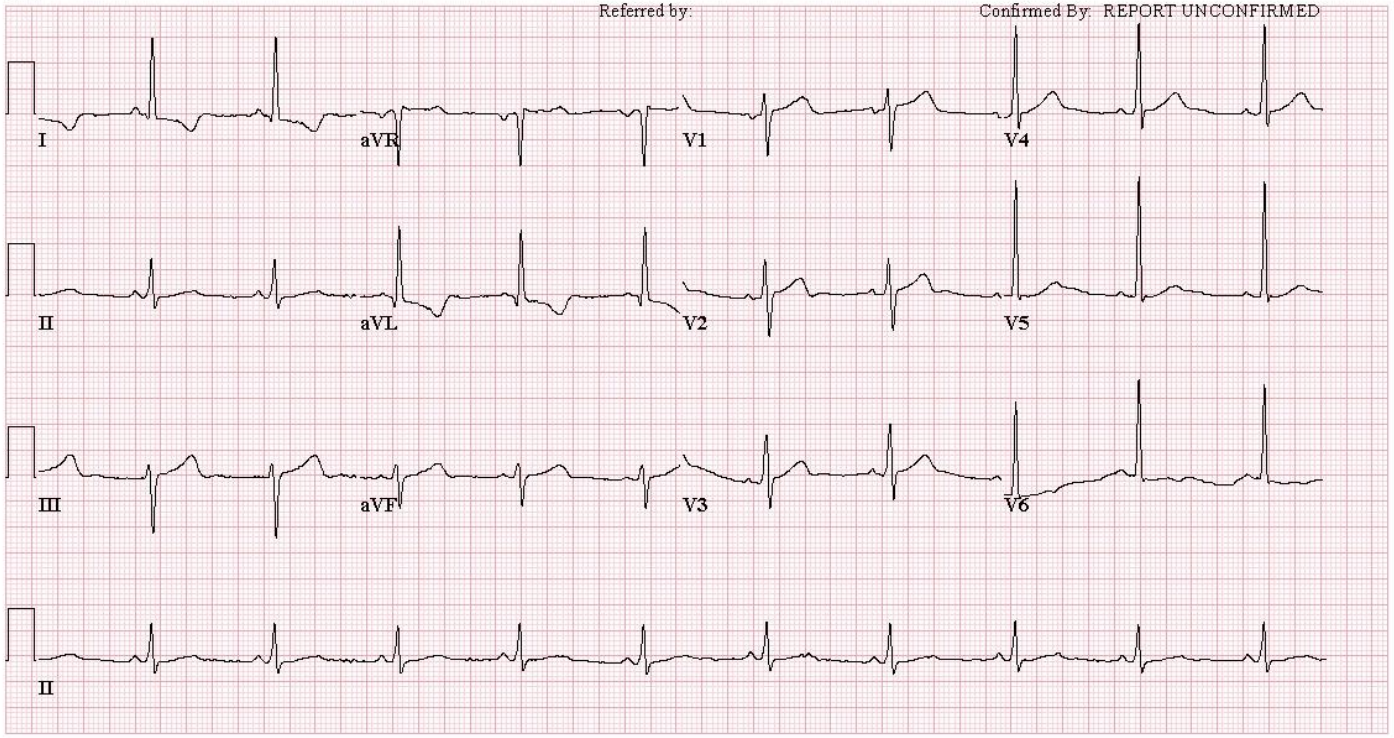
- M/52
- 2014.12 syncope during driving (가슴답답하고 어지러움후 의식 소실). 앞니 부러짐
- 2015.1 presyncope episode (어지러움, 쓰러질 거 같은 기분)
- FHx of SCD: denied
- HTN/DM/hyperchol: all denied
- Panic disorder on medication (alprozolam, tianeptin)

ECG

		Vent. rate	62	BPM	Normal sinus rhythm
Male	Unknown	PR interval	130	ms	Left ventricular hypertrophy with repolarization abnormality
		QRS duration	100	ms	Abnormal ECG
Room:		QT/QTc	458/464	ms	
Loc: 6		P-R-T axes	29 -9	128	

Technician:
Test ind:
Med:

Referred by: Confirmed By: REPORT UNCONFIRMED



25mm/s 10mm/mV 40Hz 8.0.1 12SL 231 CID: 6

EID:14 EDT: 15:49 09-JAN-2015 ORDER:

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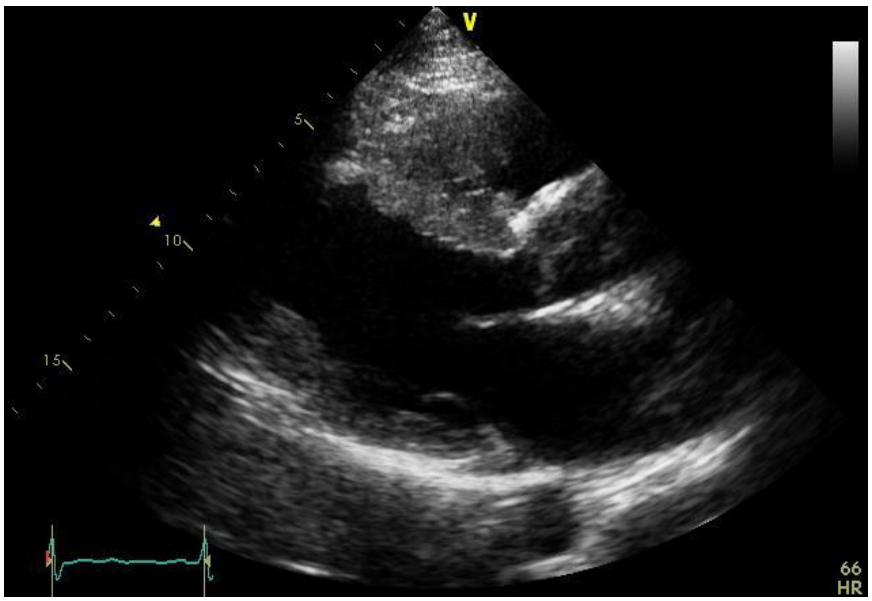
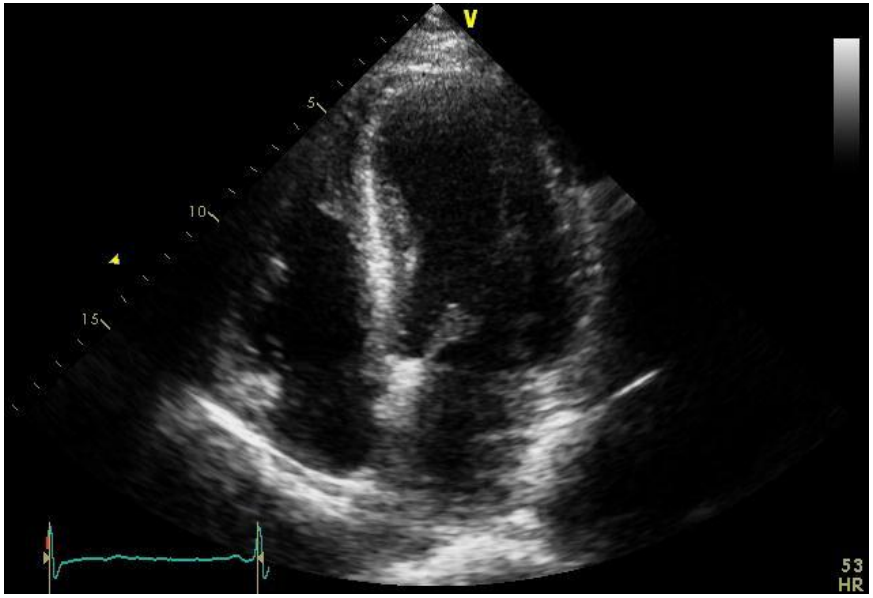
EchoCG

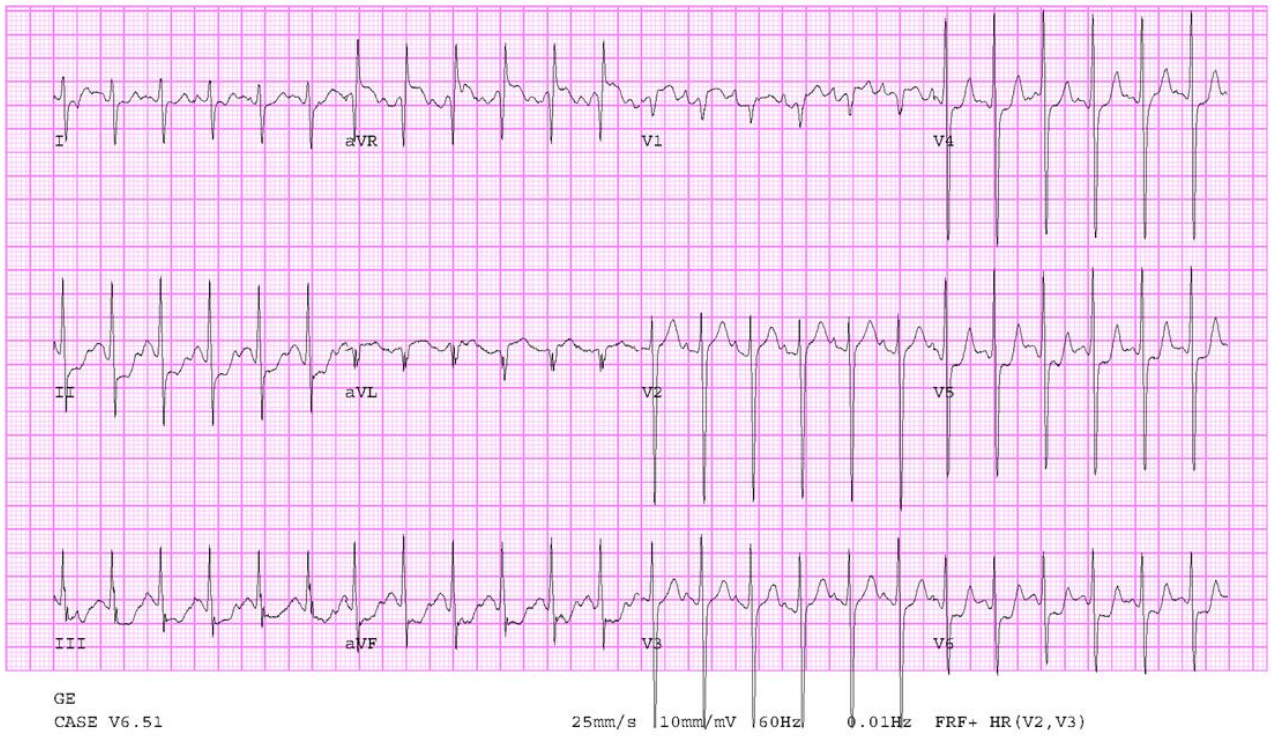
- LVEF 66%, LVEDD 53mm
- Asymmetrical septal hypertrophy (16mm)
- No dynamic LVOT obstruction





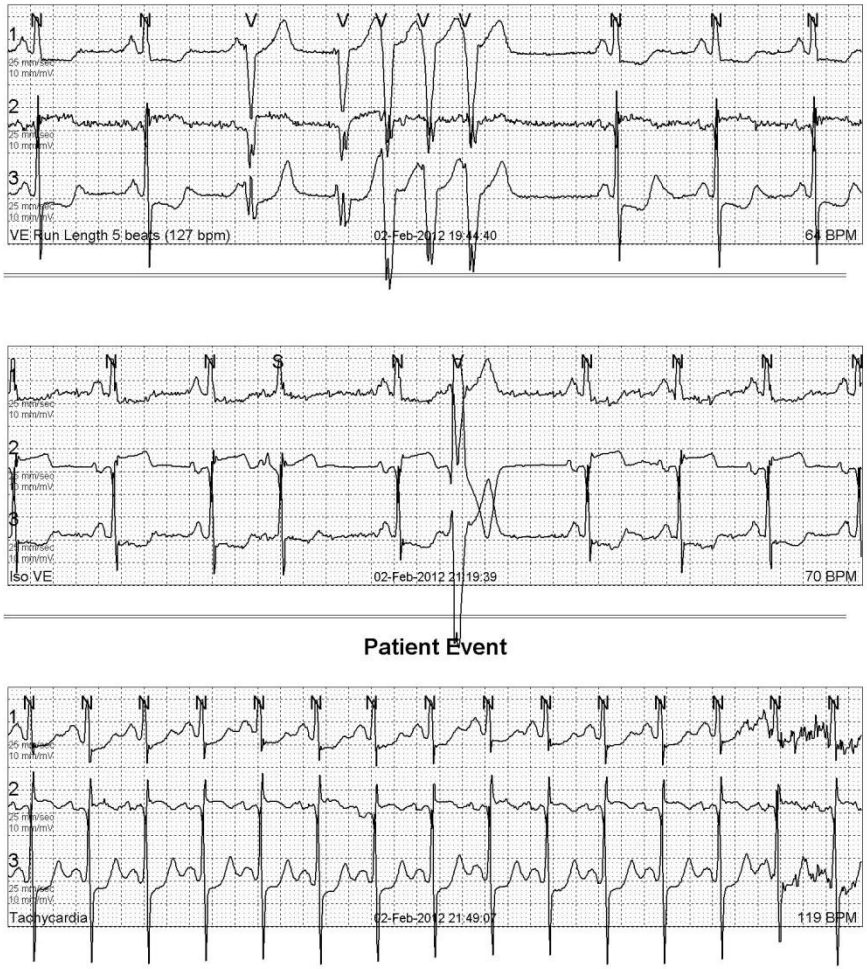
TMT

Phase	Stage	Time in Stage	Speed km/h	Grade %	METS	HR bpm	BP mmHg	RPP	PVC VE/min
PRETEST	SUPINE	0:01			1.0	-1			0
	WARM-UP	2:13	1.0	0.0	1.4	75	105/60	78	1
EXERCISE	STAGE 1	3:00	2.7	10.0	4.6	108	105/53	113	0
	STAGE 2	3:00	4.0	12.0	7.0	127	95/48	120	0
	STAGE 3	3:00	5.4	14.0	10.0	144	112/49	161	0
	STAGE 4	0:29	6.7	16.0	10.7	150			0
RECOVERY		5:07	0.0	0.0	1.0	80	113/63	90	0

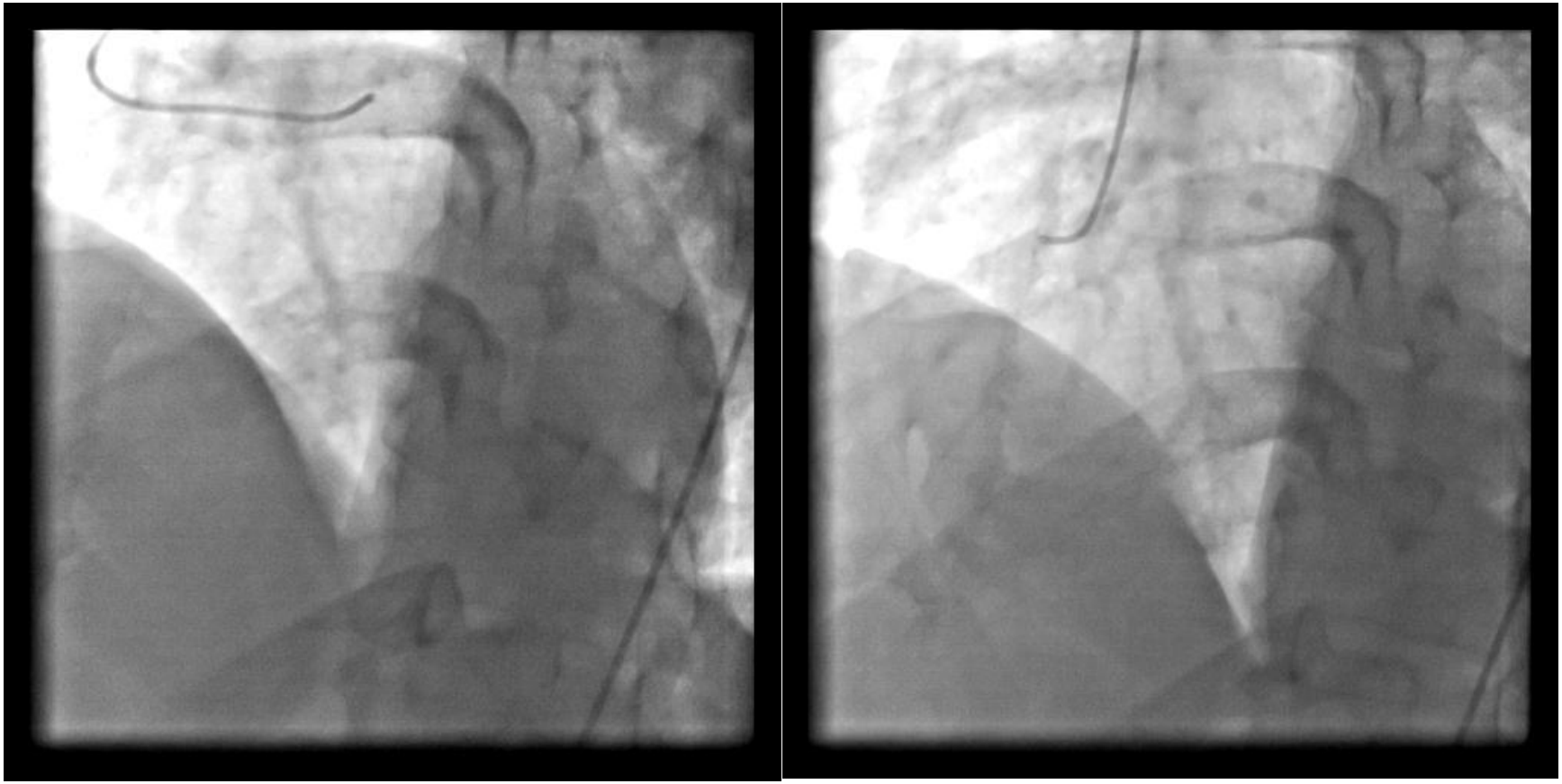


Stage 3
HR 144bpm
BP 112/49mmHg

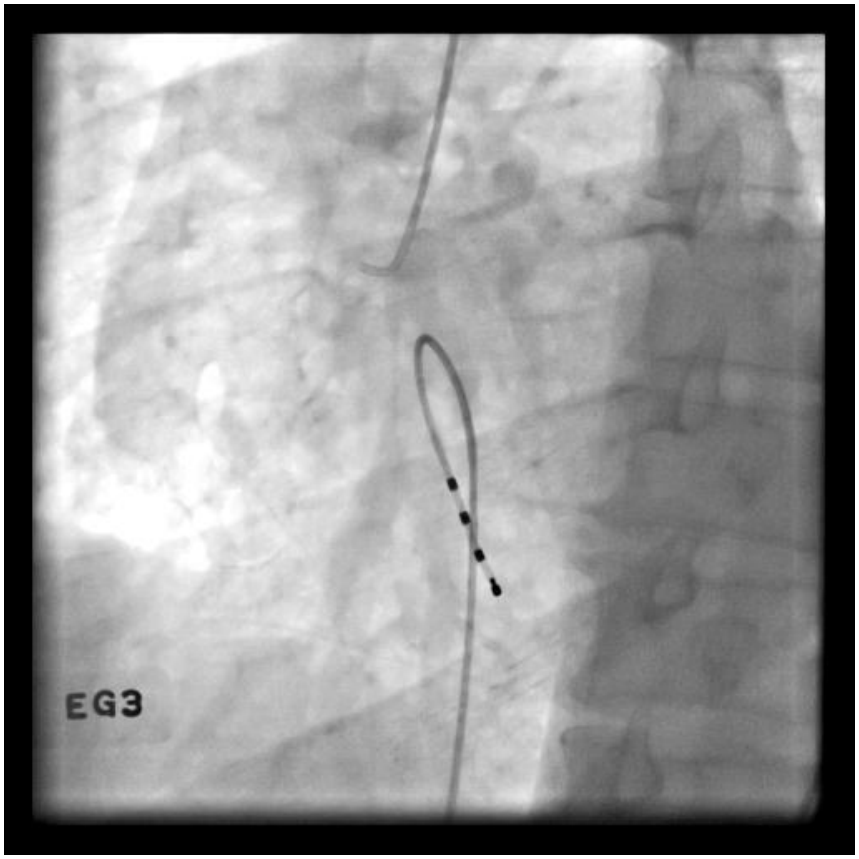
24-hour Holter monitoring

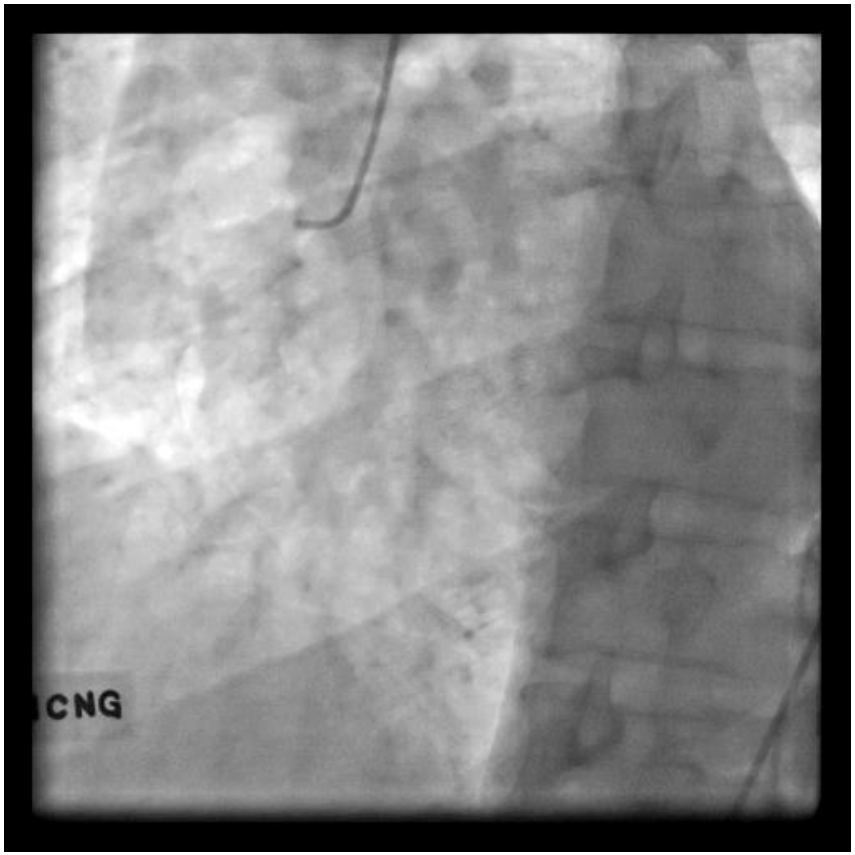


Coronary angiography



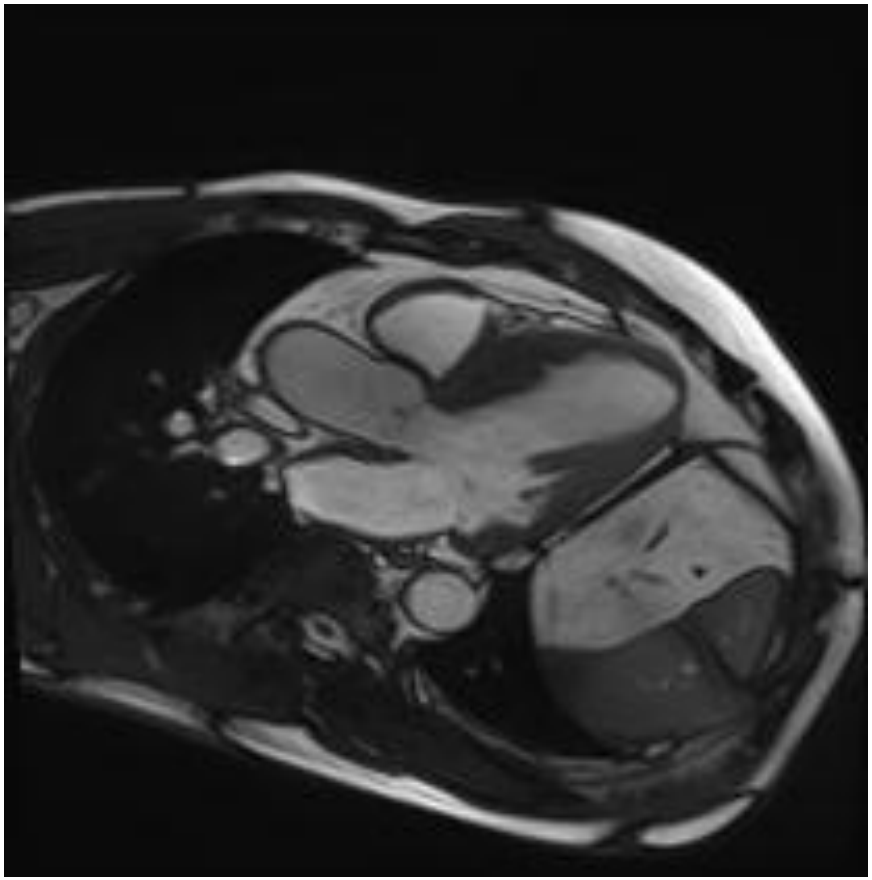
CAG with provocation test

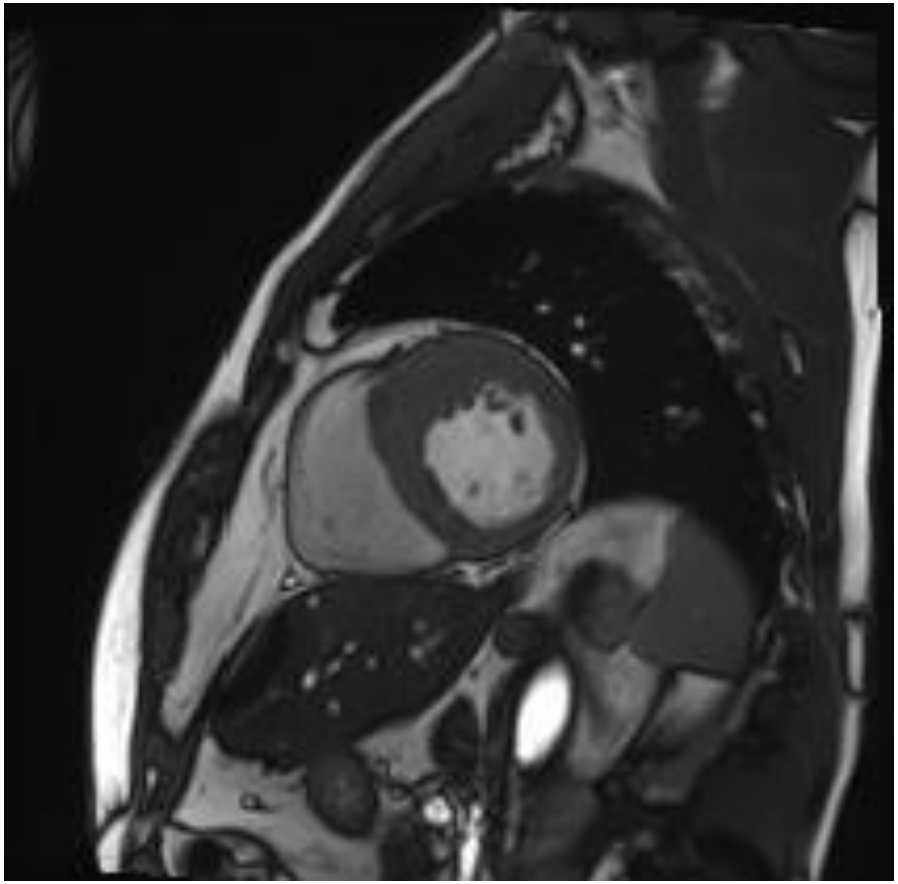




No chest pain, No ST change

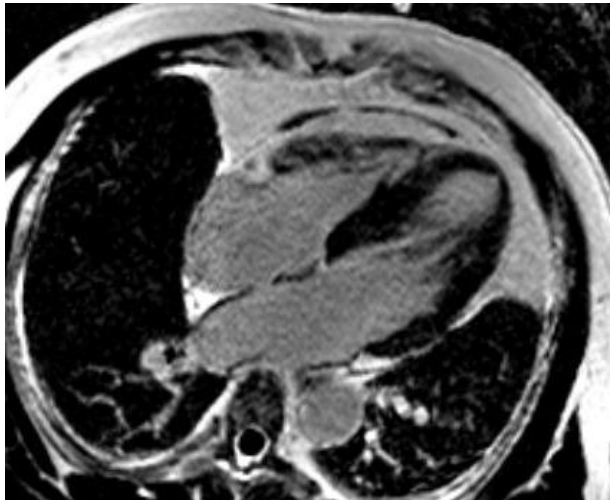
Cardiac MRI :

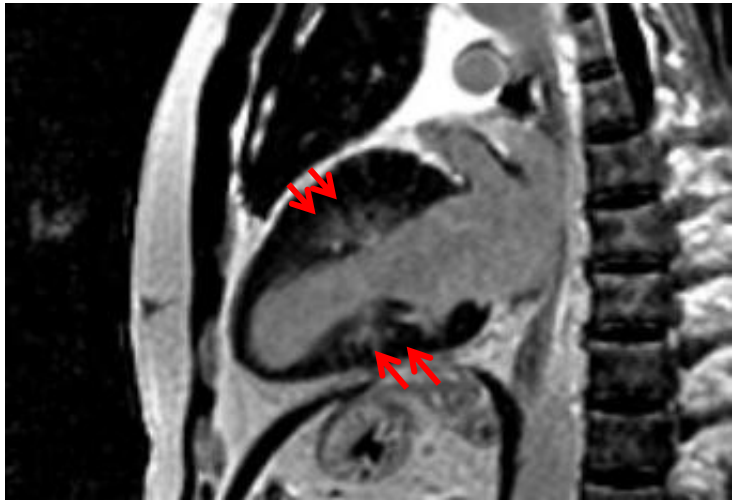


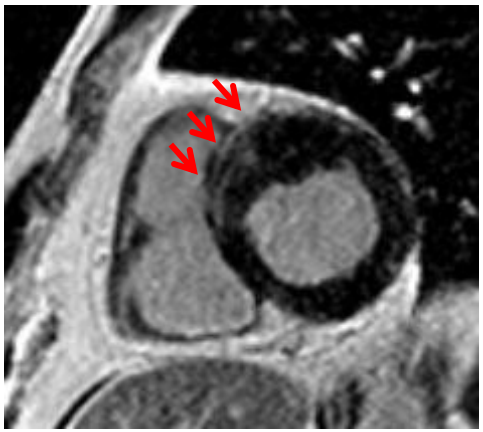


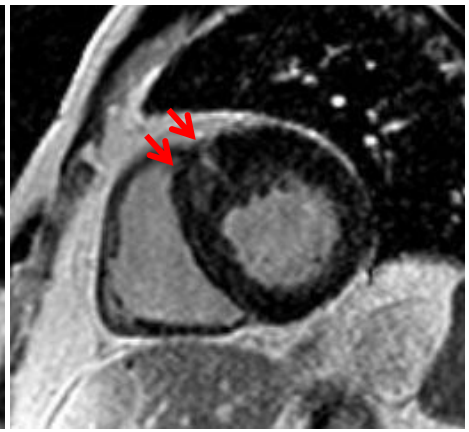
Maximal thickness at mid septal area : 27.9mm

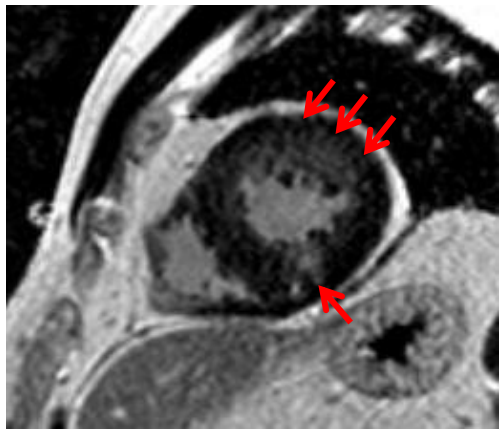
Cardiac MRI : LGE

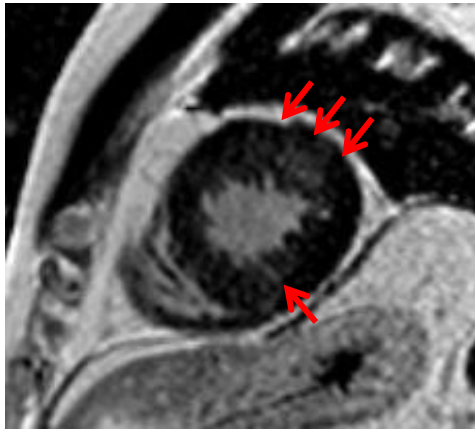




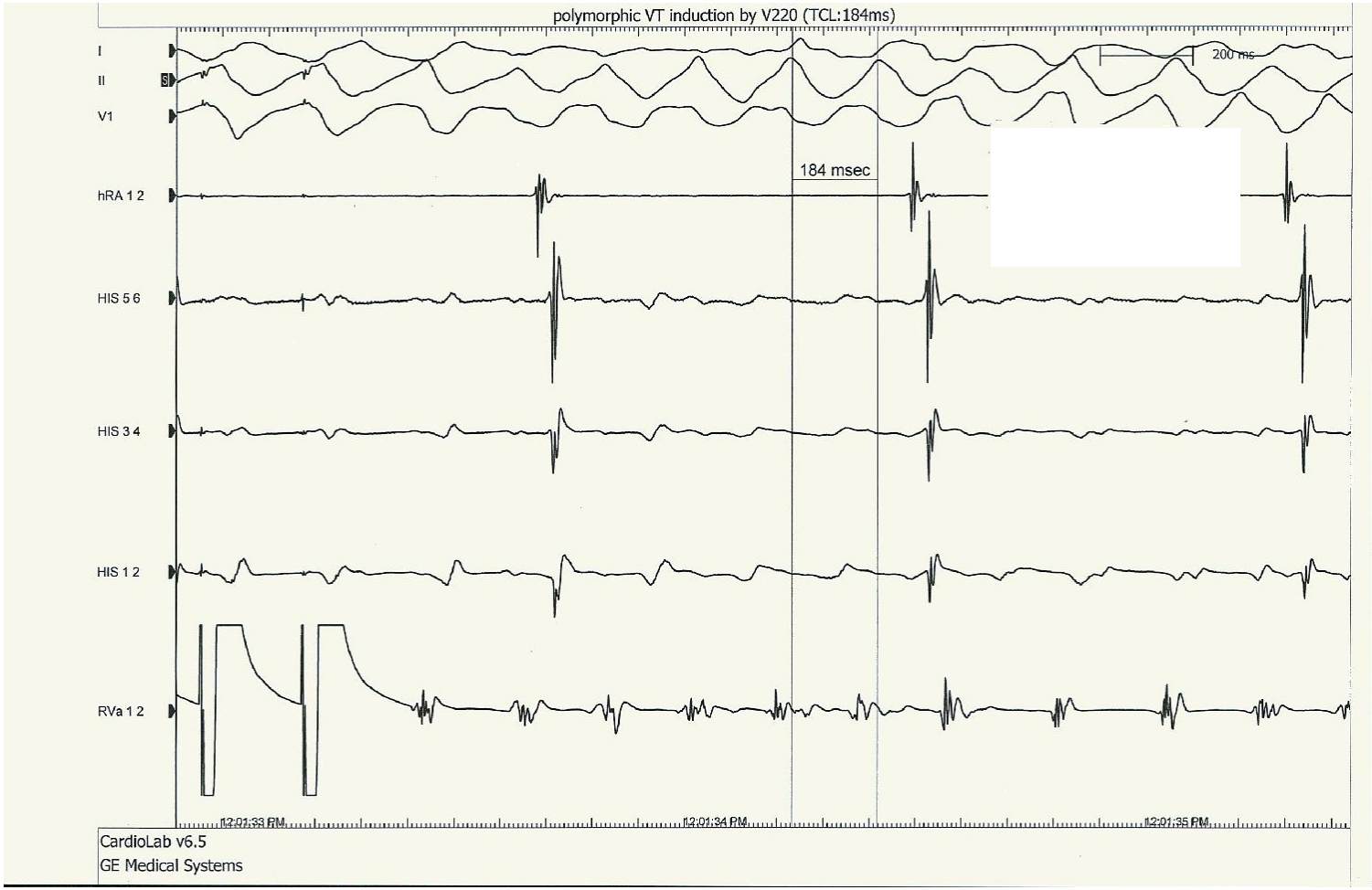




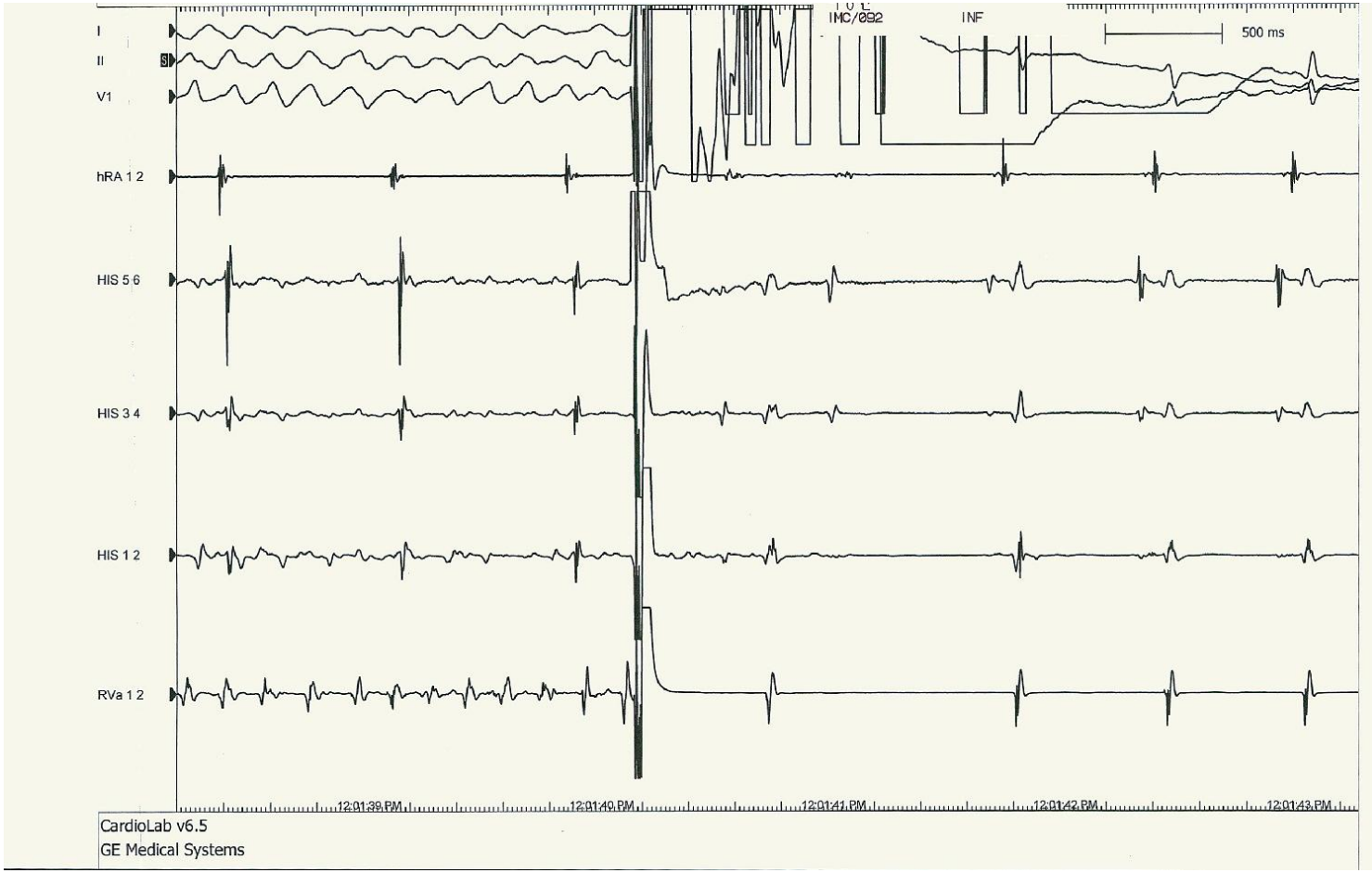




EPS : polymorphic VT induced by RVP 220ms



EPS


I
II
V1
hRA 1 2
HIS 5 6
HIS 3 4
HIS 1 2
RVa 1 2
IMC/092
INF
500 ms
12:01:39 PM
12:01:40 PM
12:01:41 PM
12:01:42 PM
12:01:43 PM
CardioLab v6.5
GE Medical Systems

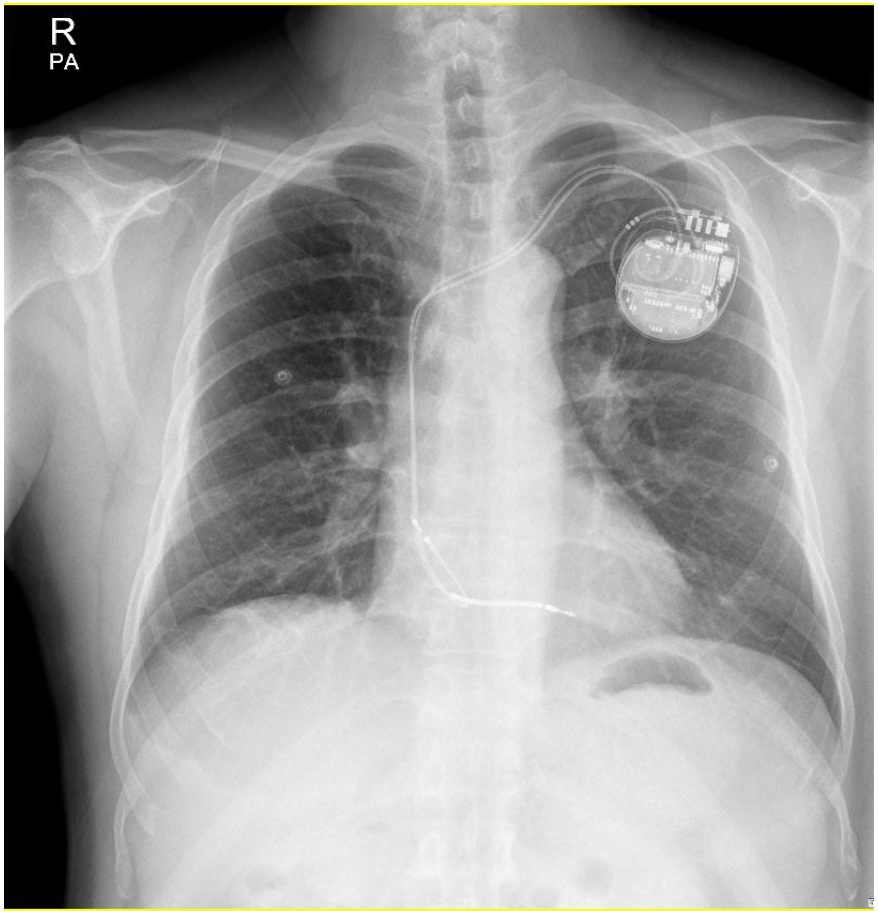
Question 1.

- **What is the reason of syncope in this patient?**
  - LVOT obstruction
  - Abnormal BP response during exercise
  - NS-VT, LGE in cardiac MRI
  - Polymorphic VT in EPS
  - Variant angina

Question 2.

- **Does this patient need ICD?**
  - HCMP
  - Syncope during driving
  - Abnormal BP response during exercise
  - NS-VT
  - FHx of SCD (x)
  - LVH ≥ 30mm (x)

ICD implantation



Ellipse DR (St Jude Medical)
A lead (active) LPA1200M-52
V lead (active) 7122Q

FastPath™ Summary Page 1 of 1

Battery
Longevity: 6,9-7,8 yrs
~ERI > 6 yrs

Implant Date: 2015 Mar 10
Last Max Charge 7,1 sec (2015 Mar 10)
Battery Current 13 uA
Remaining Capacity to ERI 94%

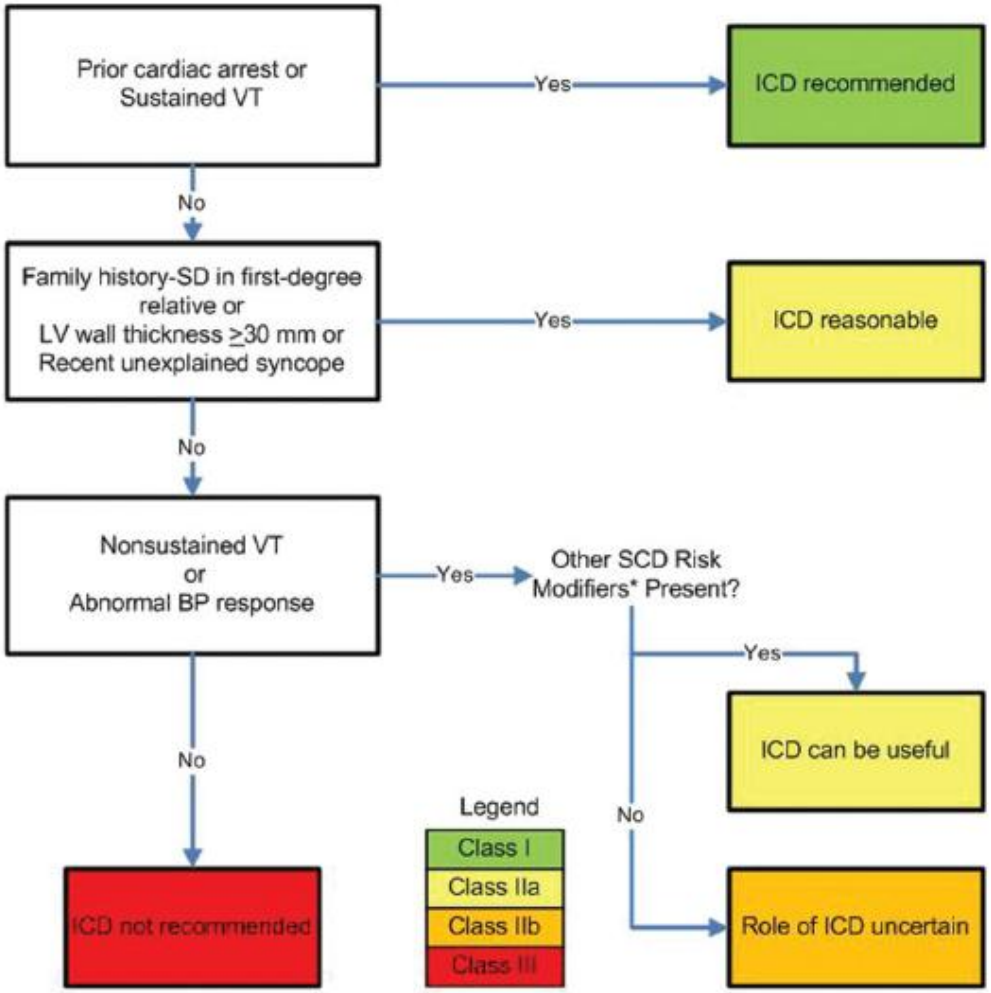
Test Results 2015 Mar 30 (A) Automatic

	Capture	Sense	Lead Impedance
A	**0,375V @ 0,5ms** (Bi) (A) 0,5V @ 0,5ms (Bi) 2015 Mar 16	**4,0mV** (Bi) (A) 4,3mV (Bi) 2015 Mar 16	**430 Ω** (Bi) (A) 450 Ω (Bi) 2015 Mar 15
V	**<0,25V @ 0,5ms** (Bi) 0,5V @ 0,5ms (Bi) 2015 Mar 16	**11,8mV** (Bi) (A) 11,8mV (Bi) 2015 Mar 16	**440 Ω** (Bi) (A) 430 Ω (Bi) 2015 Mar 15
HV			**55 Ω** (RV to Can) (A) 55 Ω (RV to Can) 2015 Mar 16

Parameters

			VT	VF
Mode	DDD	Zone Configuration		
Base Rate	40 min-1	Detection Criteria	171 min-1	214 min-1
Max Track Rate	110 min-1	Therapy **(ENABLED)**	ATP x3	20,0 J
Paced AV Delay	250 ms		20,0 J	30,0 J
Sensed AV Delay	200 ms		30,0 J	36,0 J x4
			36,0 J x2	

SCD in HCM



2011 ACCF/AHA Guideline for HCM

Risk factors of SCD in HCM

- 917 patients with HCM (554 males, 43+15 years)
- During follow-up 61 months, 54 (5.9%) patients died suddenly

Table 3 Predictors of sudden cardiac death on multivariate analysis

	RR (95% CI)	Significance
NSVT	3.84 (2.1–7.0)	0.00001
ABPR	1.42 (0.7–2.8)	0.3
Syncope	2.27 (1.2–4.2)	0.01
FHSCD	1.88 (1.0–3.5)	0.04
Severe LVH	1.70 (0.8–3.8)	0.2
Severe LVOTO	3.82 (1.6–9.2)	0.005

Severe LVH, severe left ventricular hypertrophy (≥30 mm); Severe LVOTO, left ventricular outflow tract obstruction (≥90 mmHg).

Elliott PM et al. Eur Heart J. 2006;27:1933– 41

국내 삽입형제세동기 기준 (HCM)

사. 비후성 심근병증 환자로서 아래의 ①~⑤ 중 두 가지이상에 해당되는 경우

(1) 실신의 증상

(2) 급사의 가족력

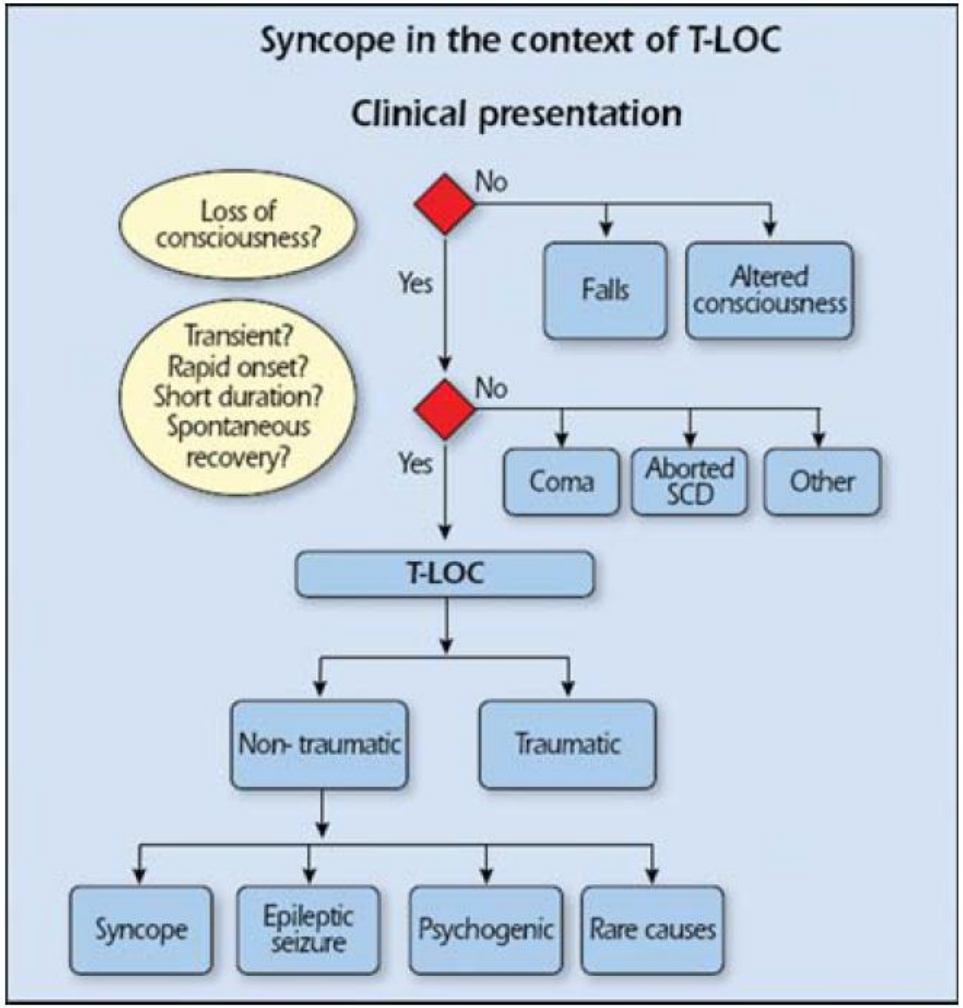
(3) 좌심실중격의 과도한 비후(>30mm)

(4) 24시간 활동 중 심전도에서 나타난 비지속성 심실빈맥

(5) 운동부하검사 상 이상 혈압증가 반응이 없는 경우(충분한 운동부하에도 혈압상승이 < 20mmHg 인 경우)

What is syncope?

- Transient loss of consciousness due to transient global cerebral hypoperfusion characterized by <u>rapid onset, short duration, and spontaneous complete recovery</u>



ESC guildeline for syncope 2009

Prevalence of syncope in HCM

- 1511 consecutive patients with HCM (1983~2005)
- Italy
- Unexplained syncope vs. neurally mediated syncope vs. without syncope
- Unexplained syncope : 153 of 1511 (10.1%)

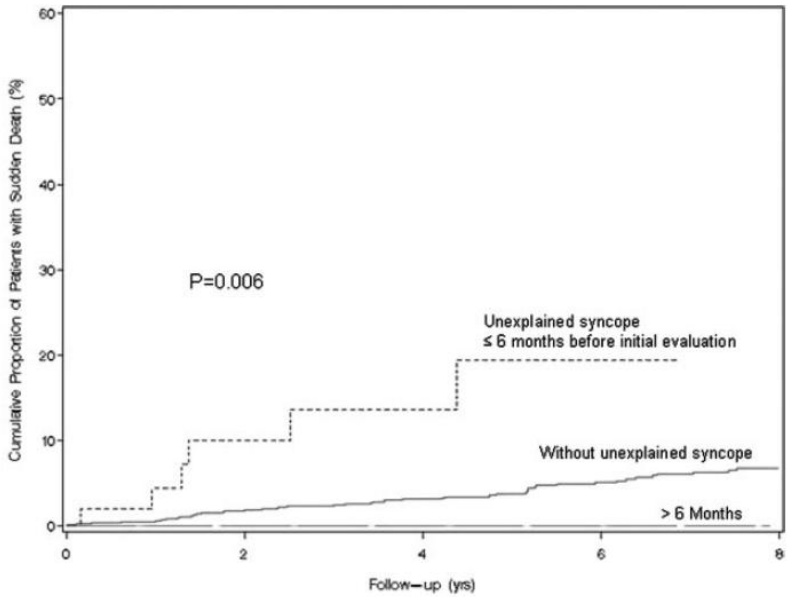
Table 1. Characteristics of the 1511 HCM Study Patients at Initial Evaluation, According to Presence or Absence of a History of Syncope

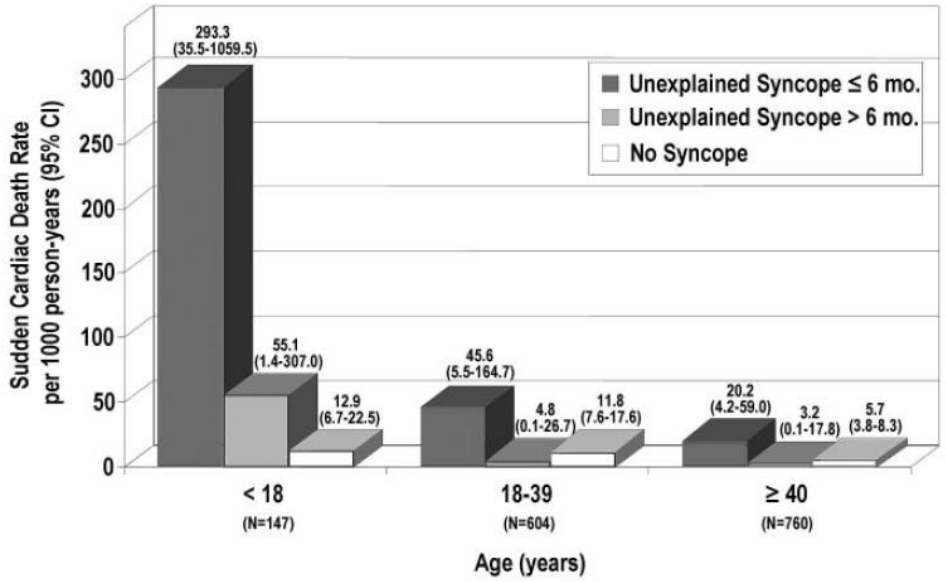
Variable	Overall Patient Population	Patients With Unexplained Syncope	Patients With Neurally Mediated Syncope	Patients Without Syncope	*P**
No. of patients	1511	153	52	1306	
Age, y, mean±SD (median)	46±19.7 (47)	47±18.9 (47)	51±17.0 (56)	46±19.9 (47)	0.12†
Male sex, n (%)	927 (61)	85 (56)	25 (48)	817 (63)	0.03†§
Family history of sudden death, n (%)	288 (19)	36 (24)	17 (33)	235 (18)	0.01†§

Spirito P et al. Circulation. 2009;119:1703-1710

Time between unexplained syncope and first patient evaluation

Time between unexplained syncope and first patient evaluation			0.006
Without unexplained syncope‡	1349	1 (Reference)	
≤6 mo	53	4.89 (2.19–10.94)	
>6 to 12 mo	16	0 (No events)	—
>1 to ≤2 y	13	2.01 (0.27–14.80)	
>2 to 5 y	19	1.04 (0.14–7.57)	
>5 y	50	0.38 (0.05–2.74)	





Spirito P et al. Circulation. 2009;119:1703-1710

Mechanisms for syncope in HCM

- **Arrhythmia**
  - Paroxysmal atrial fibrillation/supraventricular tachycardia
  - Complete heart block/sinus node dysfunction
  - Sustained ventricular tachycardia

- **Primary hemodynamic mechanism**
  - Left ventricular outflow tract obstruction
  - Abnormal vascular control mechanisms leading to episodes of hypotension due to inappropriate vasodilatation
  - Hypotension due to impaired filling when preload is reduced in the setting of diastolic dysfunction

Williams L et al. Europace 2007;9:817-22

Evaluation of syncope in HCM

- 12-lead ECG
- Ambulatory ECG monitoring
- Implantable loop recorder
- Echocardiography
- Treadmill test
- Head-up tilt test
- EPS

Principal causes of syncope in HCM

- Supraventricular arrhythmias
  - AF
- Ventricular arrhythmias
  - NSVT
  - VT (rare)

Electrophysiologic Abnormalities in Patients With Hypertrophic Cardiomyopathy

A Consecutive Analysis in 155 Patients

- EPS in 155 pts with HCM
  - Cardiac arrest in 22 pts, syncope in 55 pts, presyncope in 37 pts
- EPS abnormalities : 126 (81%) pts
- Most common SVT : atrial re-entrant tachycardia (10%) and AF (11%)

TABLE 3. Prevalence of Abnormal Electrophysiologic Findings in the Various Subgroups of Patients With Hypertrophic Cardiomyopathy

HCM subgroup	SN (%)	His-P (%)	SVT (%)	SVA (%)
Cardiac arrest	13/17 (76)	5/22 (23)	4/21 (19)	17/22 (77)
Syncope	19/29 (66)	21/55 (38)	7/51 (14)	27/55 (49)
Presyncope	14/18 (78)	9/33 (27)	12/29 (41)	12/37 (32)
Asymptomatic VT	6/12 (50)	5/21 (24)	5/18 (28)	5/24 (21)
Palpitations (no VT)	6/10 (60)	0/10 (0)	4/10 (40)	1/10 (10)
Malignant FH	3/7 (43)	4/7 (57)	1/7 (14)	4/7 (57)
Total	61/93 (66)	44/148 (30)	35/147 (24)	66/155 (43)

HCM, hypertrophic cardiomyopathy; SN, abnormal sinus node function; His-P, abnormal His-Purkinje conduction; SVT, induced supraventricular tachycardia (atrial or atrioventricular reentrant tachycardia or atrial fibrillation; SVA, induced sustained ventricular arrhythmia; FH, family history.

Fananapazir L et al. Circulation 1989;80:1259–68

Programmed electrical stimulation in hypertrophic cardiomyopathy. Results in patients with and without cardiac arrest or syncope

K.-H. KUCK, K.-P. KUNZE, M. SCHLÜTER, C. A. NIENABER AND A. COSTARD

Department of Cardiology, University Hospital Eppendorf, Hamburg, Federal Republic of Germany

KEY WORDS: Sudden death, hypertrophic cardiomyopathy, electrophysiologic study, ventricular arrhythmias, syncope.

Programmed electrical stimulation was performed in 54 consecutive patients with hypertrophic cardiomyopathy. There were 11 'symptomatic' patients: three had a history of cardiac arrest due to ventricular tachyarrhythmias (group A), and eight had a history of syncope of unknown origin (group B); 43 patients were 'asymptomatic', i.e. they had no documented or suspected symptomatic ventricular arrhythmias (group C). There were no differences among the groups with respect to electrocardiographic, echocardiographic or hemodynamic data. Ventricular arrhythmias were induced by atrial and right and left ventricular stimulation with a maximum of two extrastimuli in 18 patients. Induced arrhythmias were repetitive ventricular response in six patients, nonsustained ventricular tachycardia in four, sustained ventricular tachycardia in five, and ventricular fibrillation in three patients. With one exception, ventricular tachycardia was always rapid (cycle lengths ranged from 180 to 250 ms); it was polymorphic in six patients and monomorphic in three. Atrial stimulation induced rapid monomorphic ventricular tachycardia in one group A patient. The type and incidence of induced ventricular arrhythmias did not differ among the three groups. It is concluded that programmed electrical stimulation induces the same type of ventricular arrhythmia (rapid polymorphic ventricular tachycardia or ventricular fibrillation) in 'symptomatic' and 'asymptomatic' patients with hypertrophic cardiomyopathy, the incidence in the latter group being 19%. Induction by atrial stimulation of a rapid ventricular tachycardia may be a specific finding to identify patients with hypertrophic cardiomyopathy at risk for exercise-induced ventricular fibrillation.

Kuck KH et al. Eur Heart J. 1988 Feb;9(2):177-85.

Role of EPS in HCM with syncope

Recommendations	Class[a]	Level[b]	Ref.[c]
Invasive electrophysiological study is recommended in patients with documented persistent or recurrent supraventricular tachycardia (atrial flutter, atrial tachycardia, atrioventricular nodal re-entry tachycardia, accessory atrioventricular pathway mediated tachycardias) and in patients with ventricular pre-excitation, in order to identify and treat an ablatable substrate.	I	C	249,254 255
Invasive electrophysiological study may be considered in selected patients with documented, symptomatic, monomorphic, sustained (>30 s) ventricular tachycardia in order to identify and treat an ablatable arrhythmia substrate.	IIb	C	256,257
Invasive electrophysiological study with programmed ventricular stimulation is not recommended for sudden cardiac death risk stratification.	III	C	

- The routine use of electrophysiological studies (EPS) in <u>patients with syncope</u> or symptoms suggestive of arrhythmia <u>is not recommended</u>.

2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy

Mechanisms for syncope in HCM

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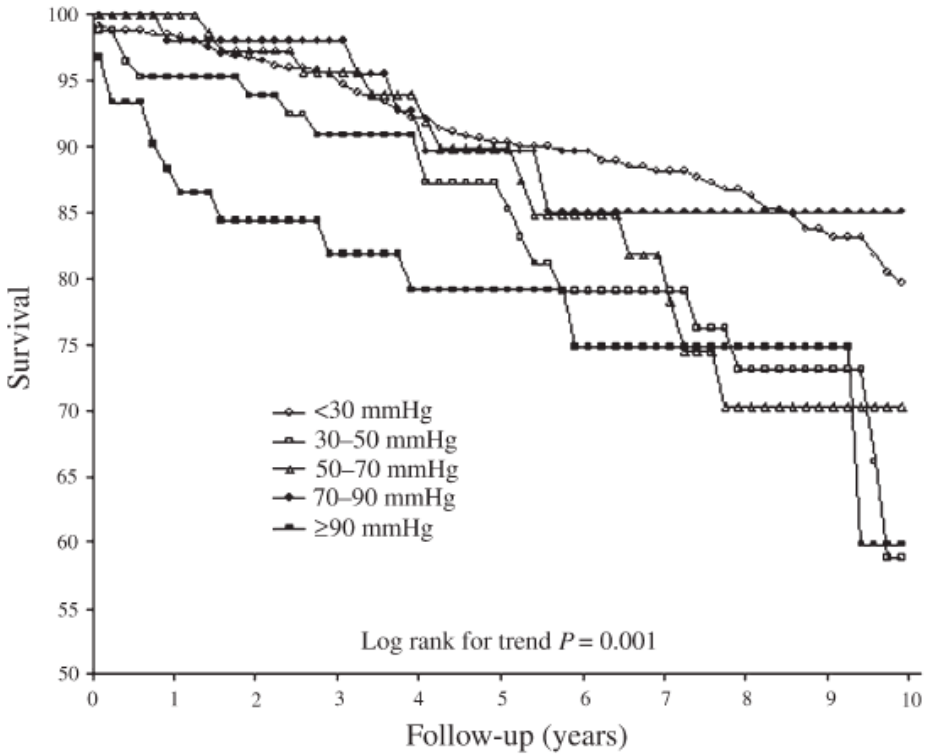
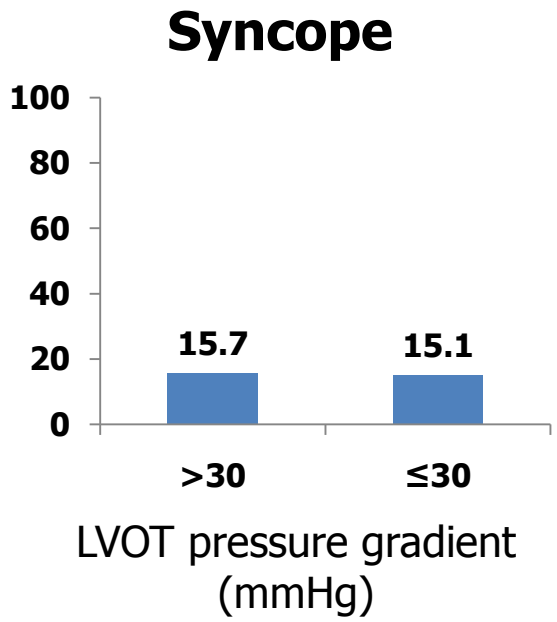
Williams L et al. Europace 2007;9:817-22

Left ventricular outflow tract obstruction and sudden death risk in patients with hypertrophic cardiomyopathy

- 917 patients with HCM (554 males, 43+15 years)
- During follow-up 61 months, 54 (5.9%) patients died suddenly

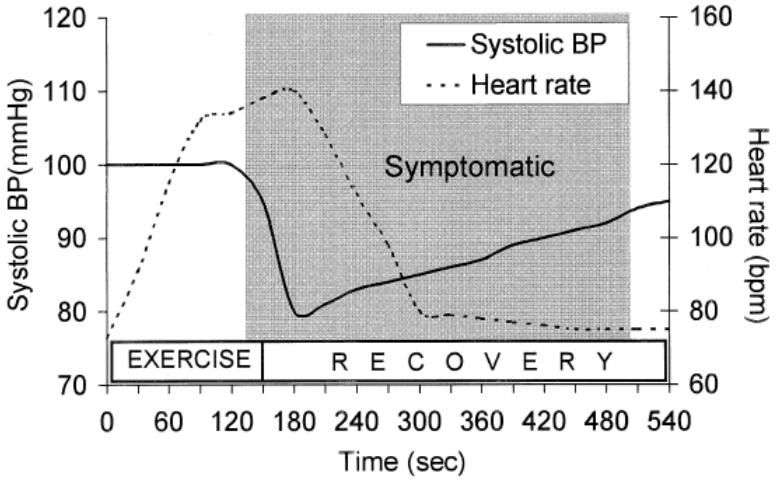




Elliott PM et al. Eur Heart J. 2006;27:1933– 41

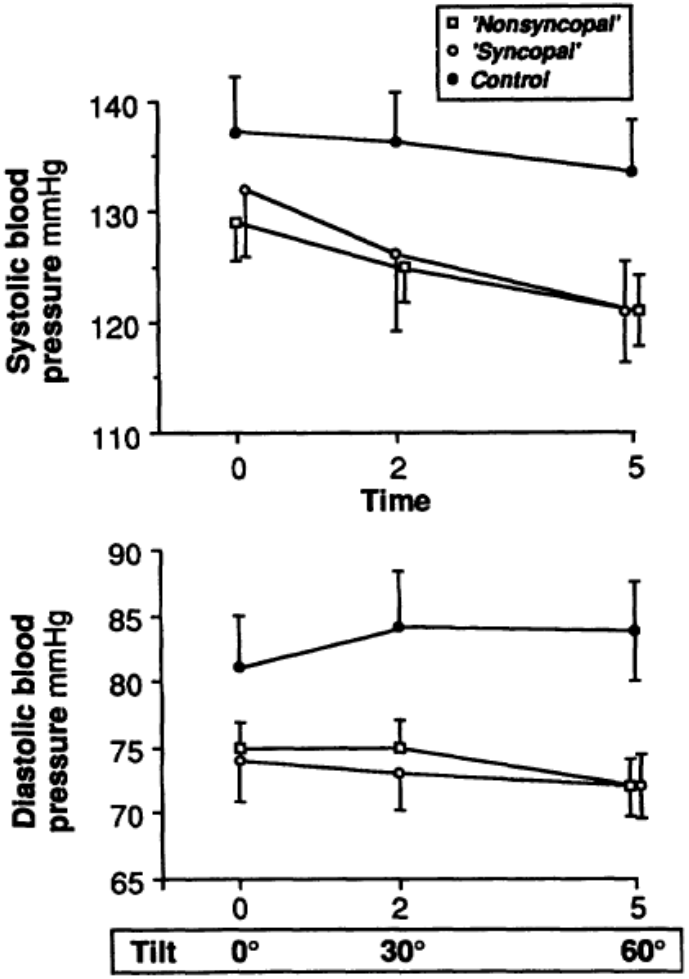
Abnormal BP responses during exercise

- ABPR is defined as
  - Failure of systolic BP to rise by at least 20 mmHg during maximal treadmill exercise
  - Fall of > 20 mmHg at peak exercise compared with preexercise levels
- Prevalence of ABPR : 22%*

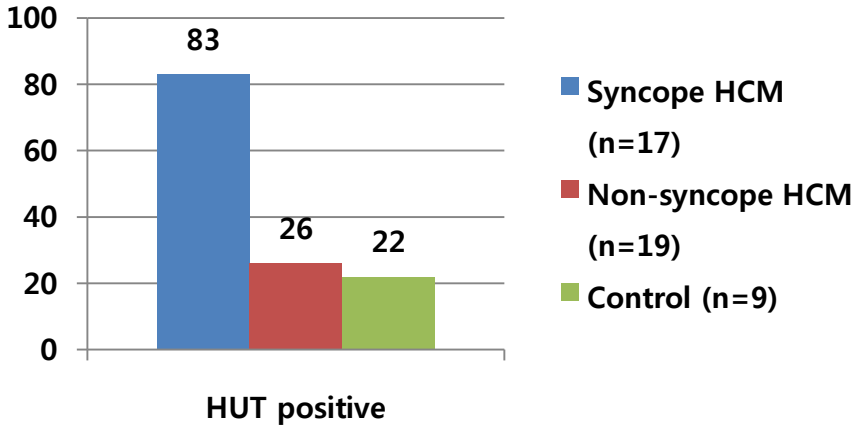


*Olivotto I et al. J Am Coll Cardiol 1999;33:2044–51

Head-up tilt testing in HCM



- Total prevalence of hypotension, i.e., positive cases and transient hypotension, was much higher in syncopal patients



Gilligan DM et al. Circulation. 1992;85:2140 –2148

Abnormal vascular control mechanisms

- **ABPR** may, in most cases, be at least in part due to an **exaggerated fall in systemic vascular resistance** related to inappropriate vasodilatation or a failure of vasoconstriction in non-exercising vascular beds

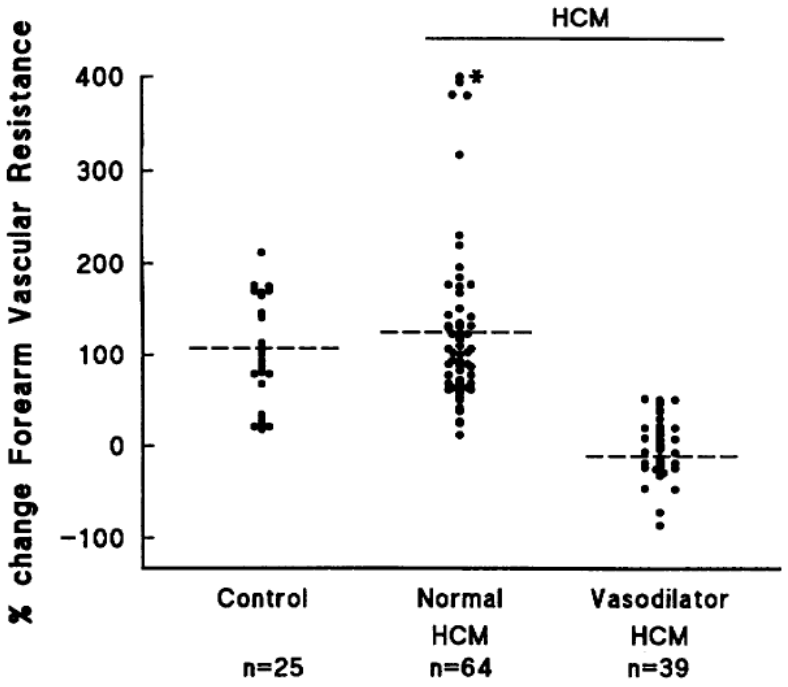


TABLE 3. Association of Exercise Hypotension and Vasodilator Responses in 103 Patients With Hypertrophic Cardiomyopathy

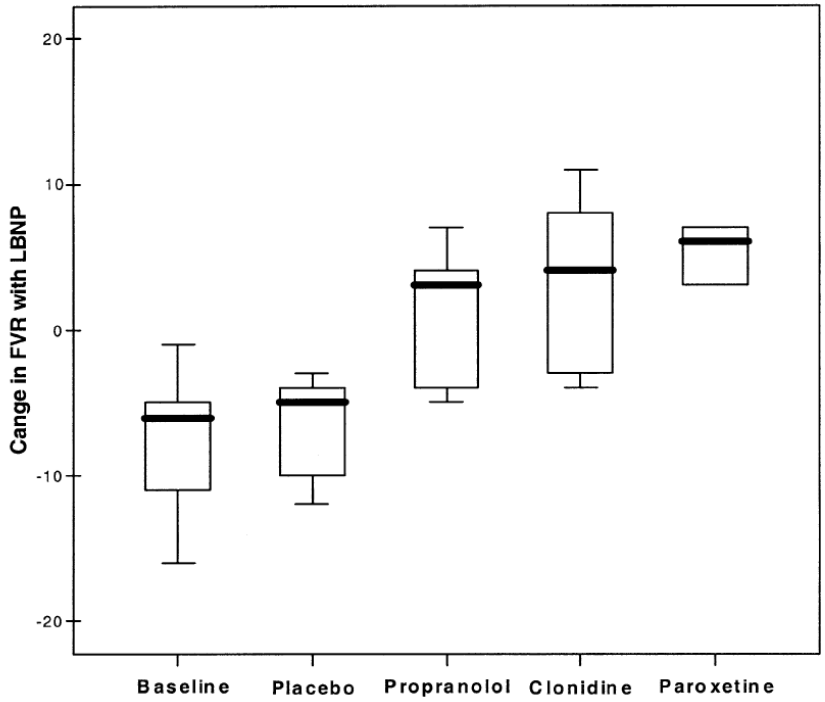
Blood pressure response	Plethysmography response	
	Normal (n=64)	Vasodilator (n=39)
Normal (n=65)	55	10
Exercise hypotension (n=38)	9	29

p=0.0001.

Counihan PJ et al. Circulation 1991;84:686–96

Reversal of Inappropriate Peripheral Vascular Responses in Hypertrophic Cardiomyopathy

- Paradoxical vasodilatation during LBNP occurs in 40% of patients with ABPR during exercise and is reversed by **propranolol, clonidine, and paroxetine**



Thaman R et al. J Am Coll Cardiol. 2005;46:883– 892

Approach in HCM with syncope

- **Need for individualized risk assessment**
  - Most patients who experience a syncopal episode do not die suddenly
  - more than one reason for syncope
- **Non-cardiovascular cause?**
  - Comorbidity? Diabetes, epilepsy
- **Cardiovascular cause, treatable?**
  - Atrial arrhythmia or bradycardia? drug, ablation, PM
  - Moderate to severe LVOTO? Drugs vs. invasive Tx
  - Abnormal vascular responses? Drugs
  - ICD

Case Follow-up

- 2015.10 NS-VT (10beats)
- 2016.2 syncope
  - 과음 다음날 고속버스 안에서 nausea/vomiting, dizziness, sweating후
  - No shockable rhythm on interrogation

Take Home Message

- Symptoms of impaired consciousness (syncope and presyncope) occur in 10–25% of patients with HCM
- Young patients with a history of recurrent syncope are associated with an increased risk of SCD
- Detailed investigations identify a probable mechanism in a minority of these, usually paroxysmal AF or VT
- In the majority of cases, however, no likely mechanism is found despite extensive investigation
- Syncope may be caused by mechanisms other than ventricular arrhythmia means that patients may remain at risk of recurrent syncope after ICD implantation

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Thank you for your attention