Update on Hypertropic Cardiomyopathy

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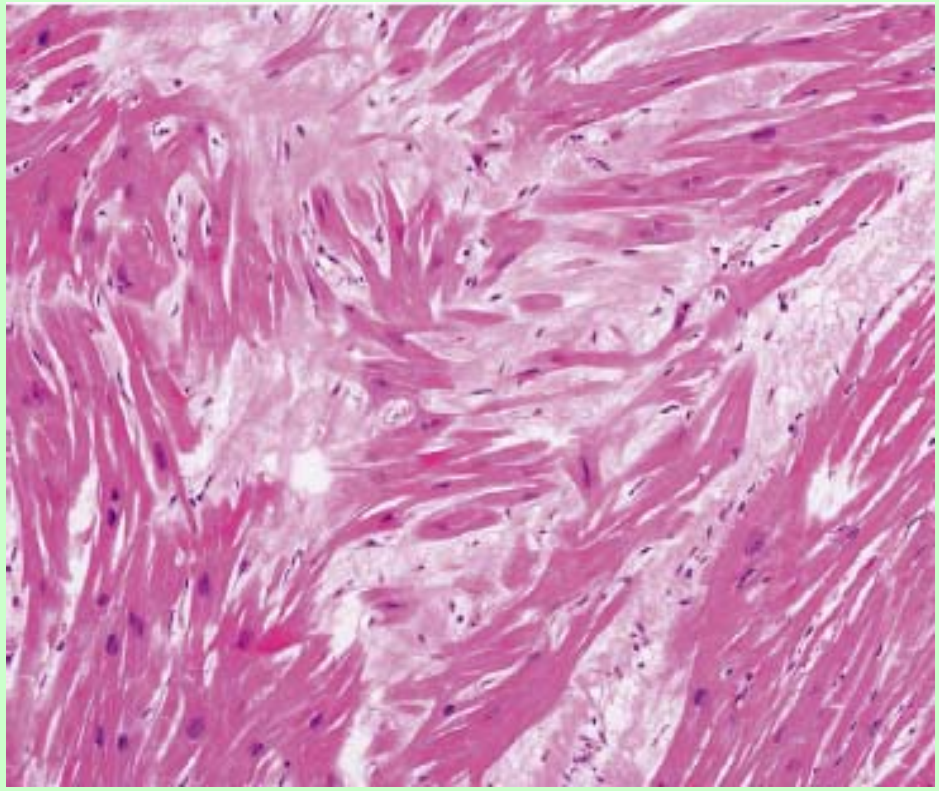
Introduction

- Myocardial hypertrophy without hemodynamic stress(e.g. HT)
- Myocyte disarray(pathology)
- Mutations in sarcometric genes: 0.2%, most common genetic heart disease
- Various phenotype(apHCM,DCMP) and genetic transmission (¼ of family, even old ages)

Normal parallel arrangement of myocyte with myocyte disarray and increased CT



Other characteristics:
Hypertrophy
Small vessel disease

Echocardiographic characteristics

1. Left ventricular Hypertrophy: > 15mm

   Asymmetric septal Hypertrophy

   (spared posterior wall)

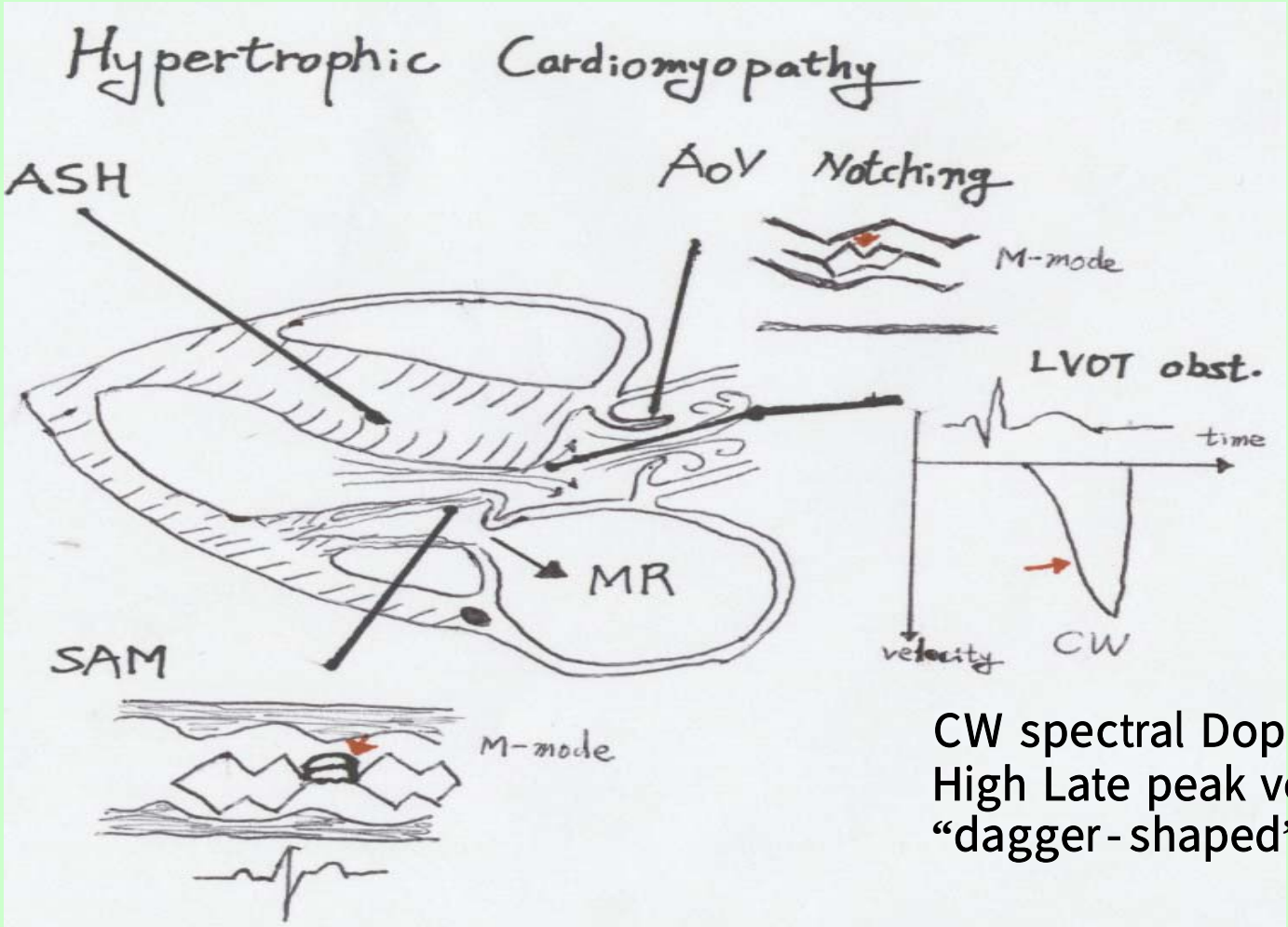
2. Subaortic dynamic obstruction: ¼

   "IHSS" or "HOCM"

3. Systolic anterior motion of mitral valve

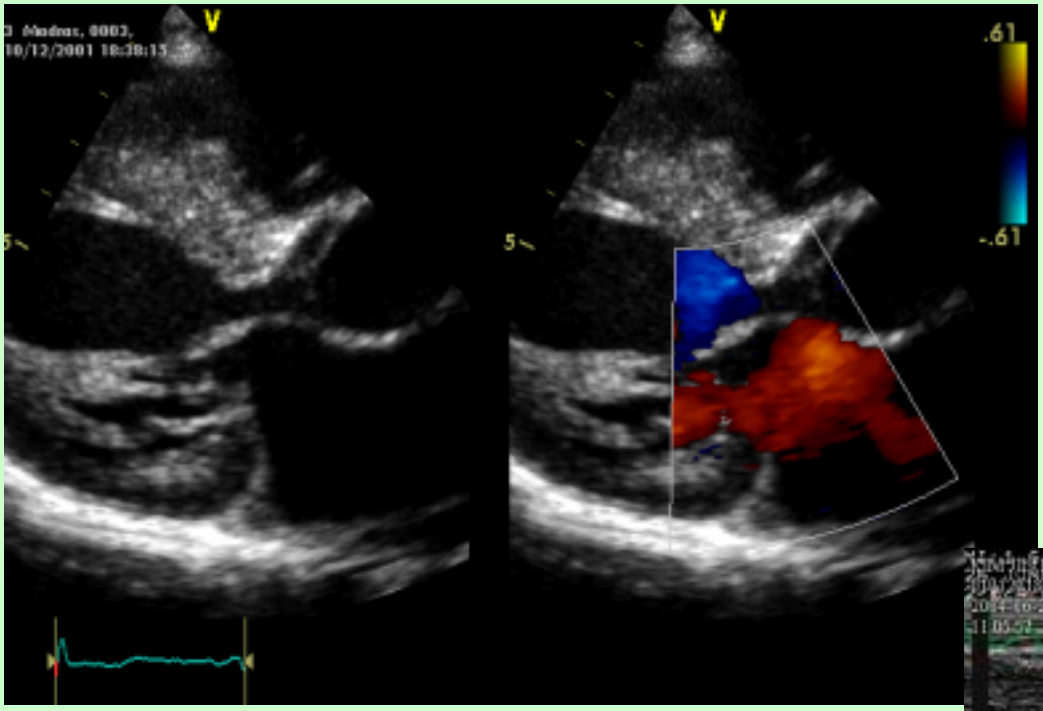
4. Diastolic dysfunction (usu, nl sys)

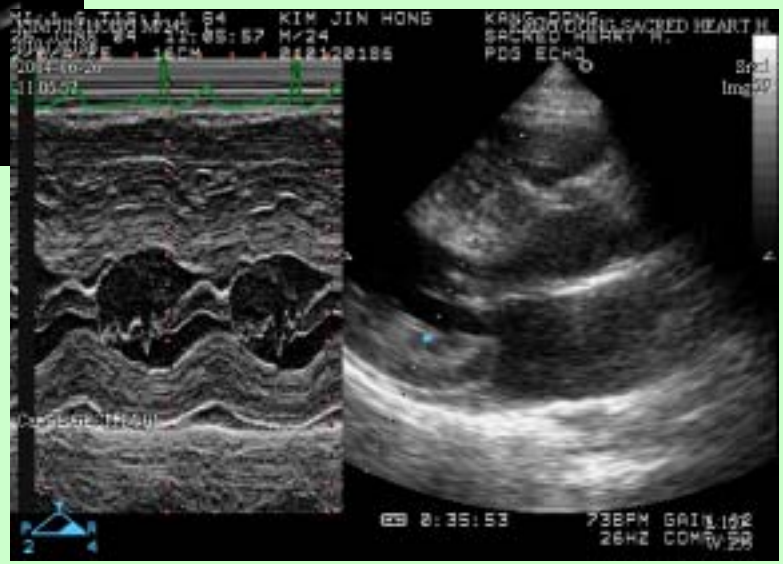
Diagram of HOCM



CW spectral Doppler
High Late peak velocity
"dagger-shaped"

Parasternal long axis view

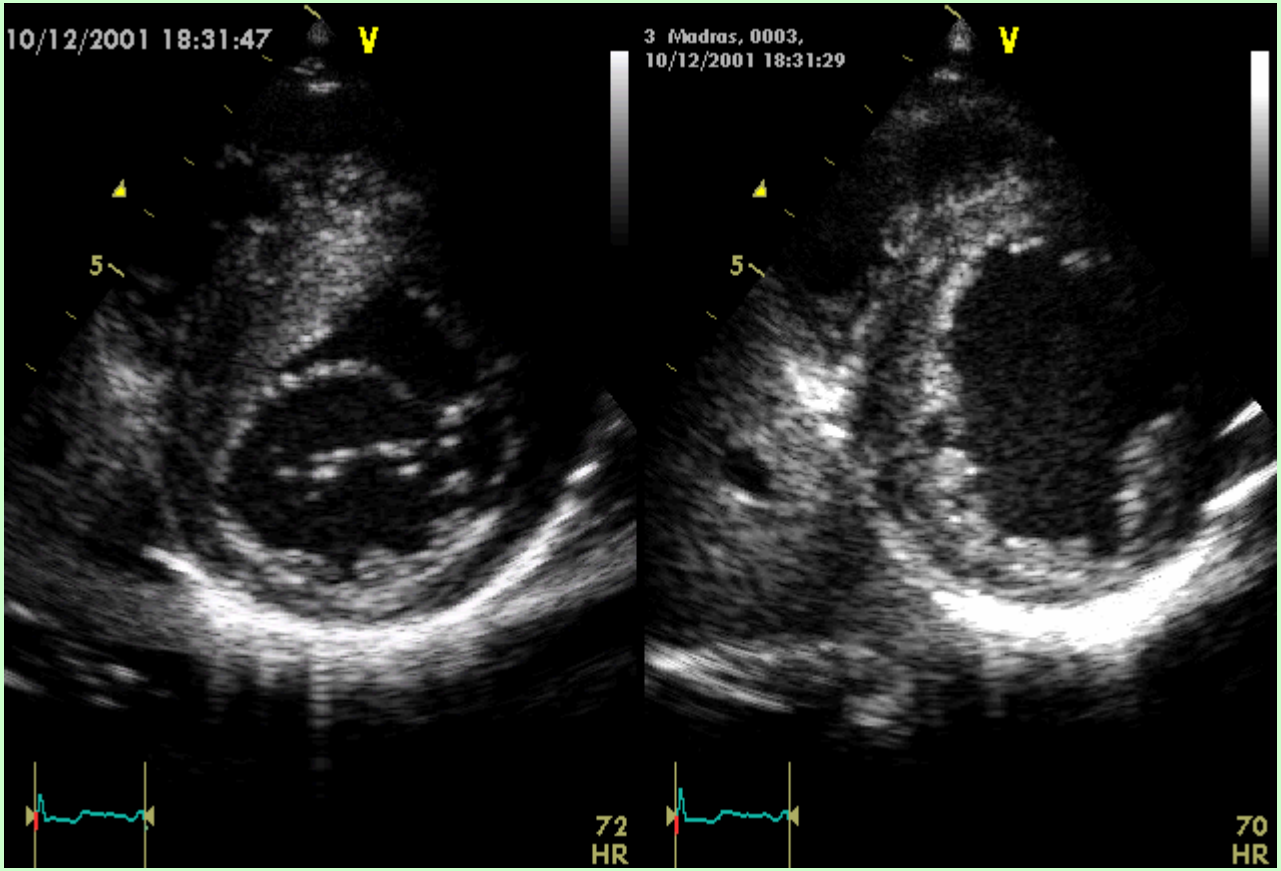




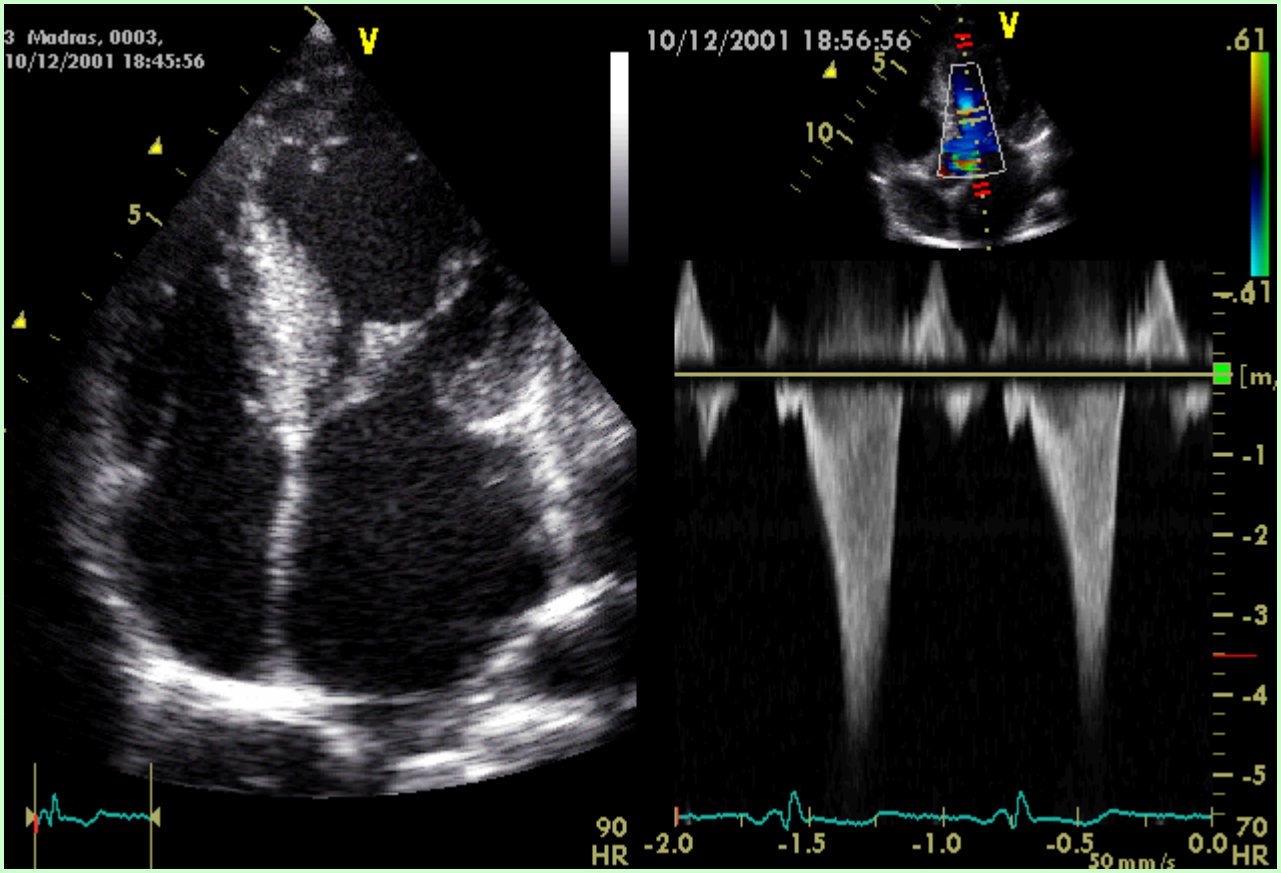
Parasternal short axis view

Base

midventricle



Apical 4C view with CW



Diagnostic Dilemma based on echo

1. LVH: “Sigmoid” septum(tourtuous aorta)

   Hypertensive heart

   Athletic heart

2. Subaortic Dynamic Obstruction

   Hypertensive heart with hypovolemia

CASE 1 : 69/ F

C.C: chest pain on exertion (3 Month ago)

duration: 5 min

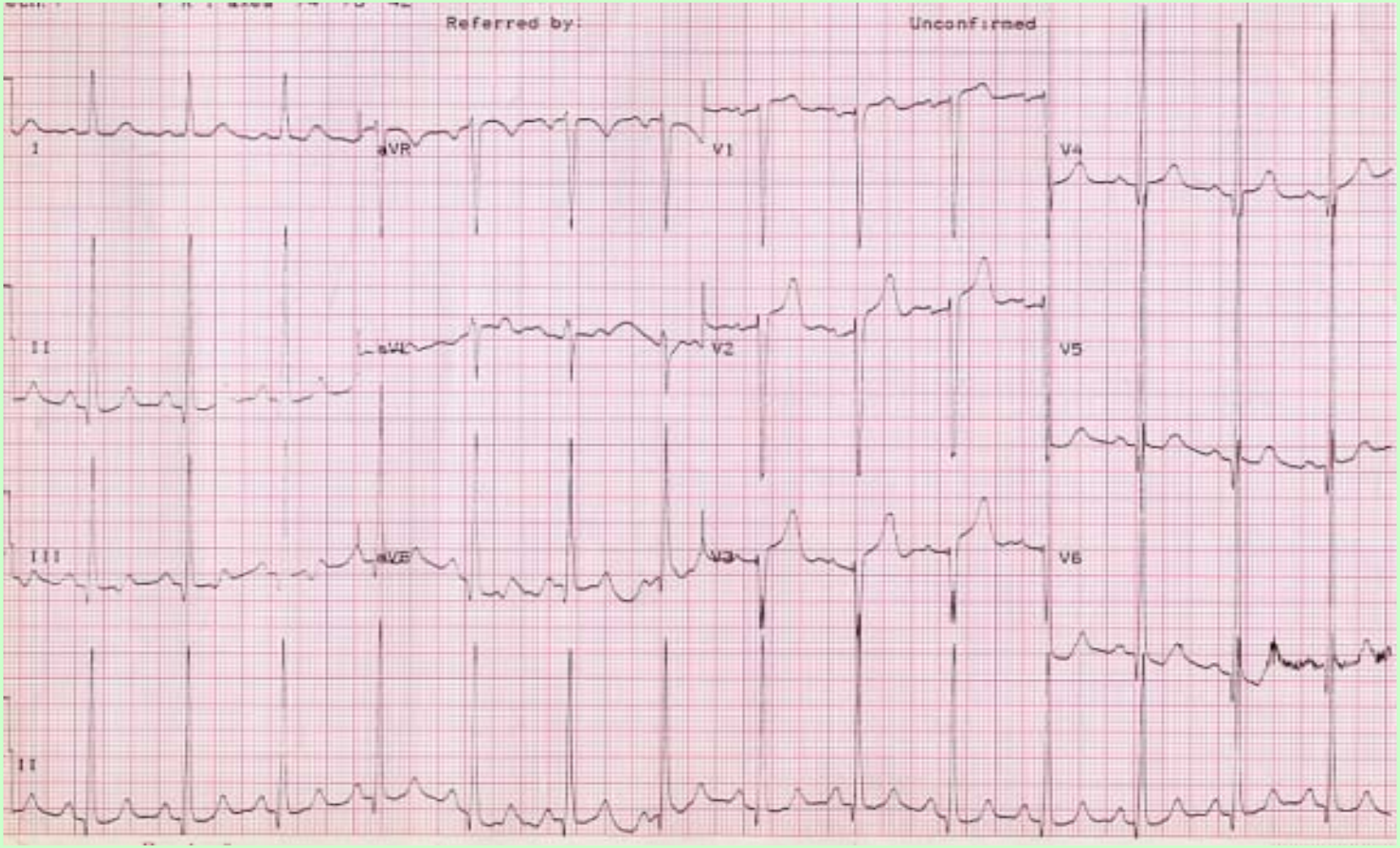
no sweating

P/E: BP 130/70, systolic murmur at apex

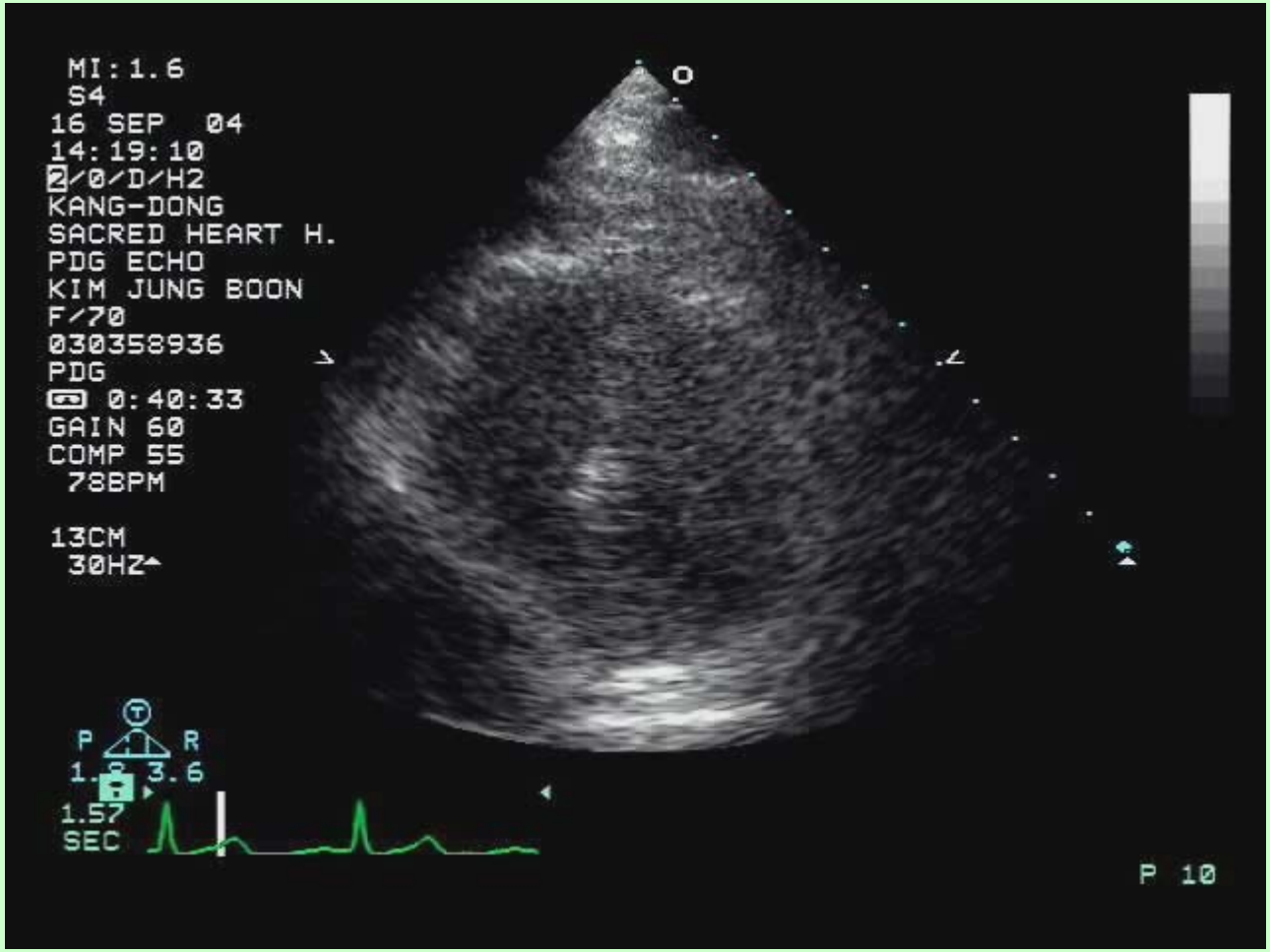
Lab: cholesterol 184mg/dl, Hb 10g/dl

Iron/TIBC 43/368, ferritin:20

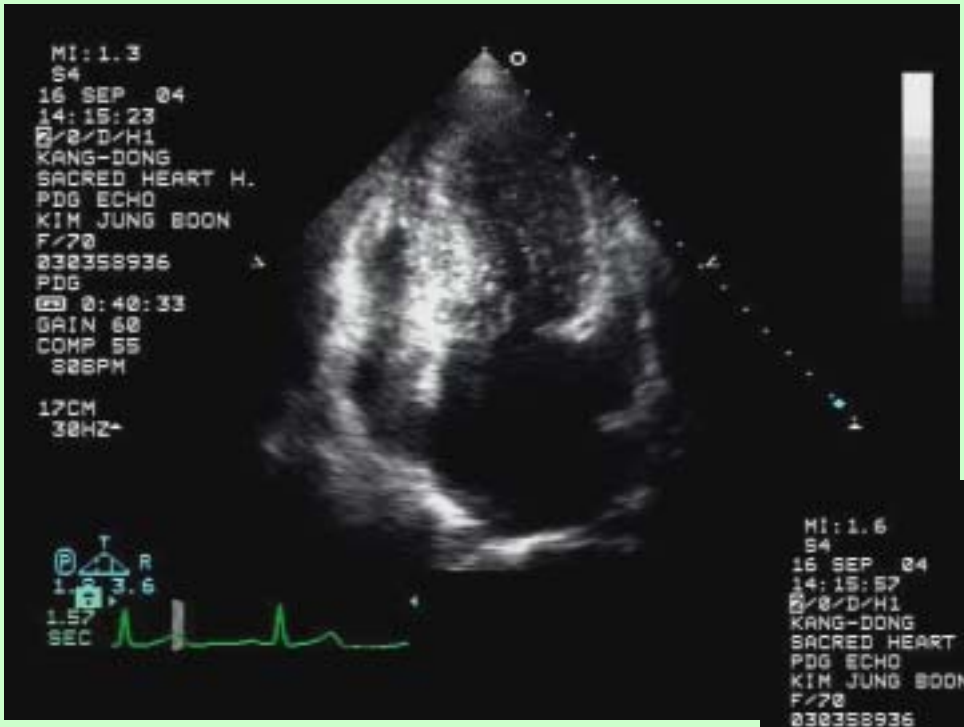
ECG


Referred by:
Unconfirmed
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

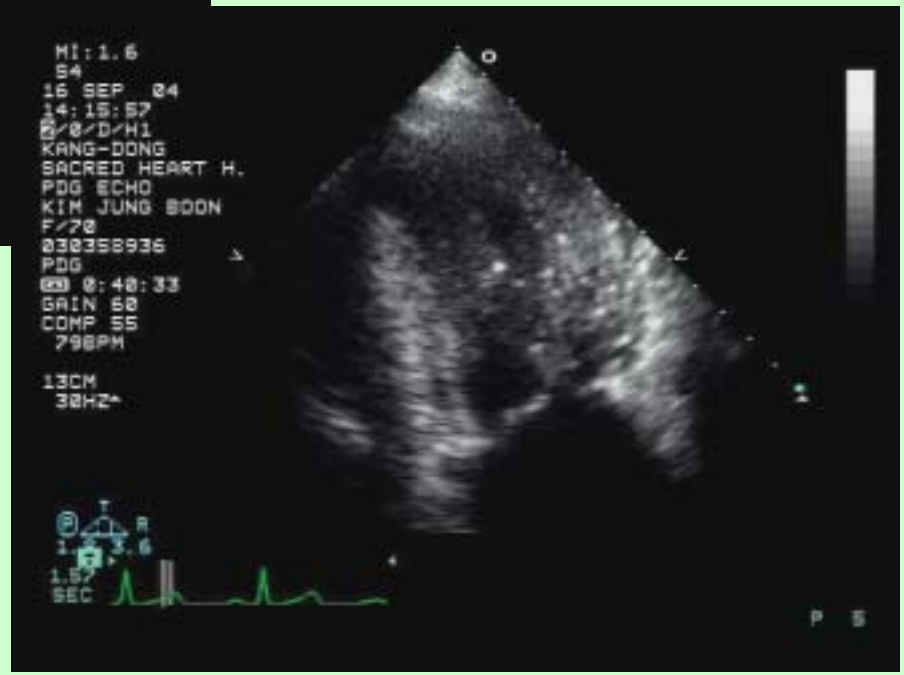
Parasternal short axis view
(poor PLAX image(sigmoid septum?)

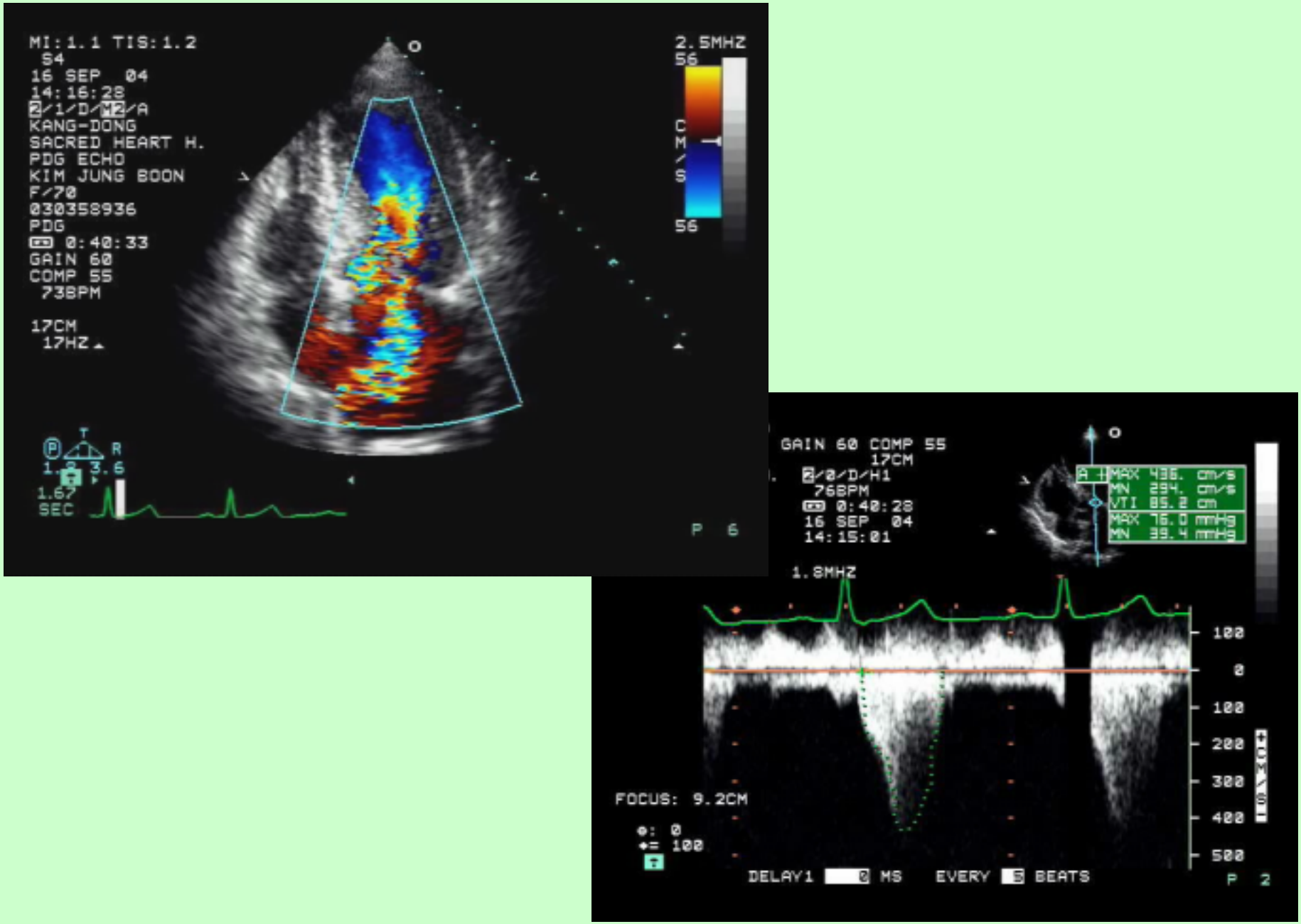


Apical 4C



Apical 2C

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S4
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14:16:28
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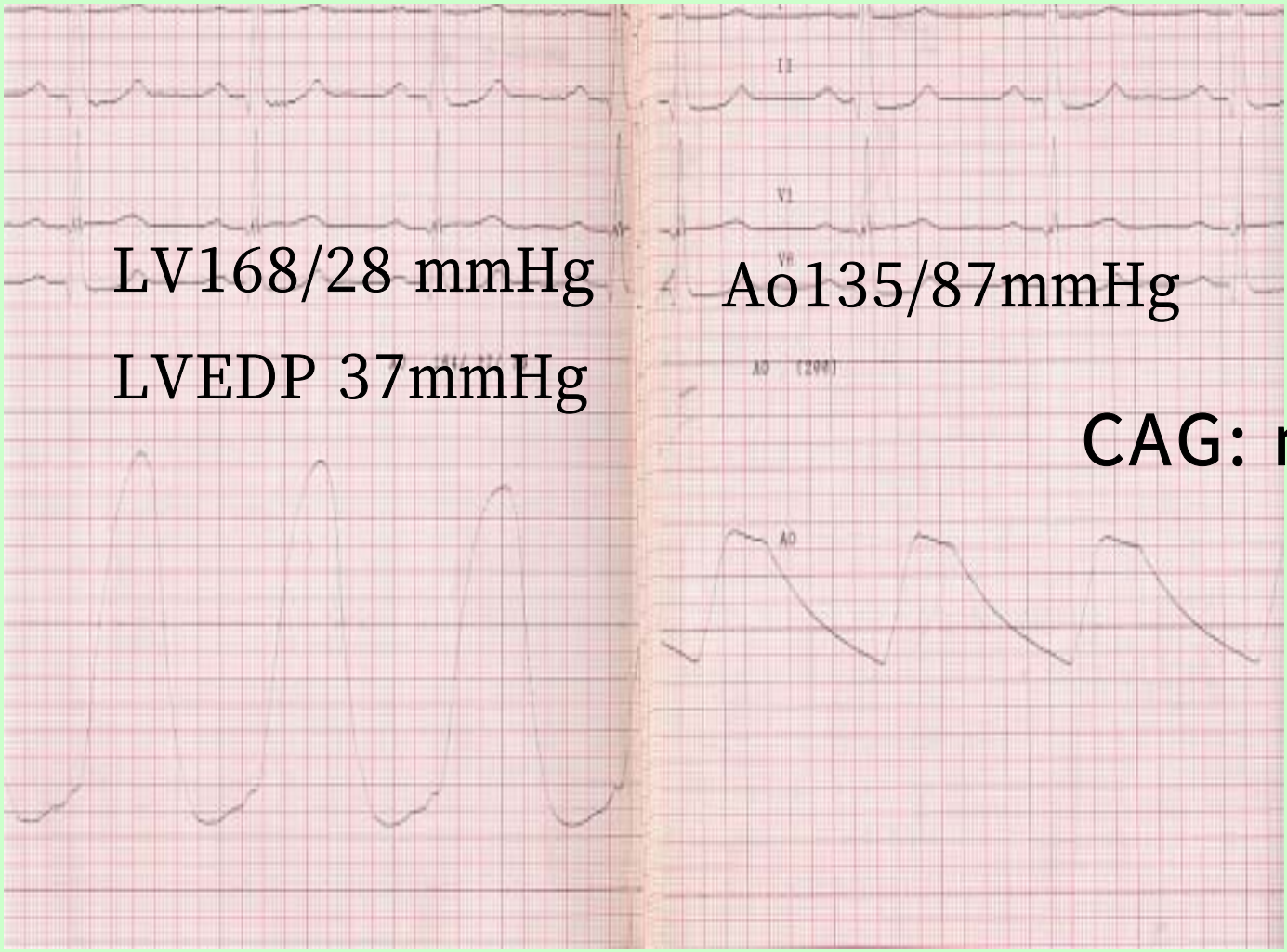
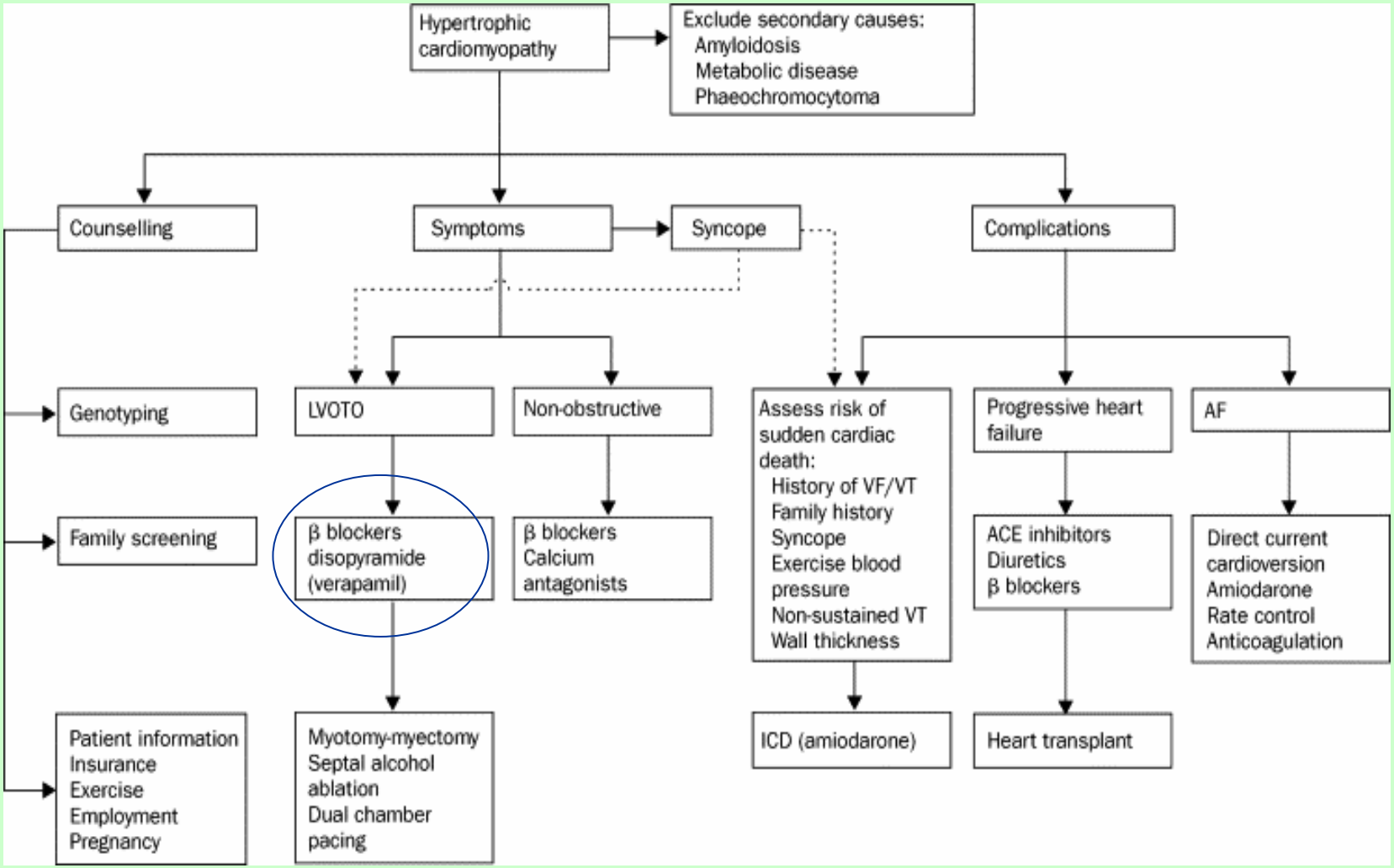
KANG-DONG
SACRED HEART H.
PDG ECHO
KIM JUNG BOON
F/70
030358936
PDG
0:40:33
GAIN 60
COMP 55
73BPM
17CM
17HZ
2.5MHZ
56
CM/S
56
1.67
SEC
P 6
GAIN 60 COMP 55
17CM
2/0/D/H1
76BPM
0:40:28
16 SEP 04
14:15:01
1.8MHZ
A MAX 436. cm/s
MN 294. cm/s
VTI 85.2 cm
MAX 76.0 mmHg
MN 39.4 mmHg
100
0
100
200
300
400
500
FOCUS: 9.2CM
0
100
DELAY1 0 MS EVERY 5 BEATS
P 2

Cardiac Cath after Transfusion



CAG: normal

Management Algorithm for HCM



CASE 1: 69/ F

OPD F/U: CCB and BB with Iron supplement

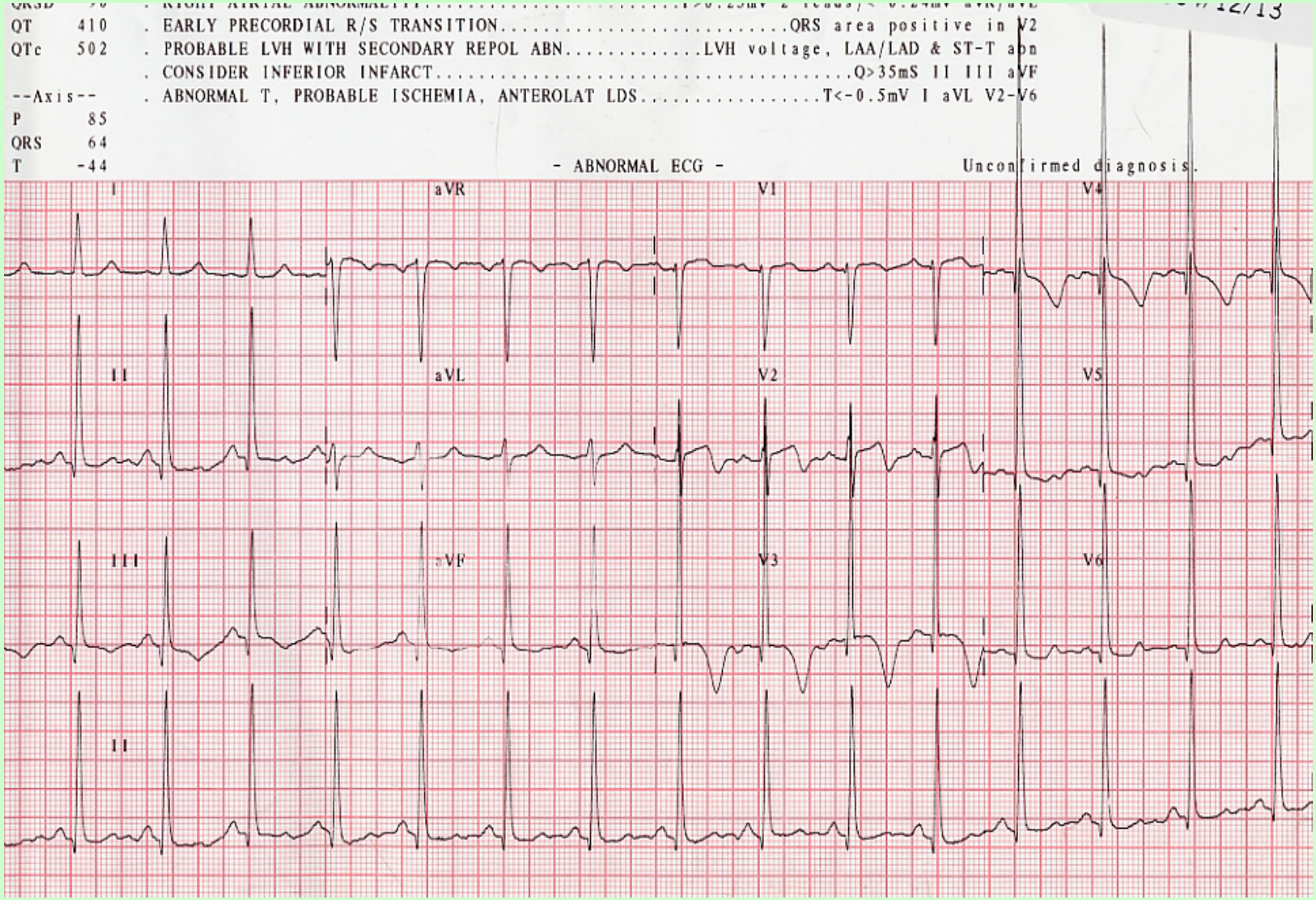
Recently, Postprandial discomfort (2 weeks ago)

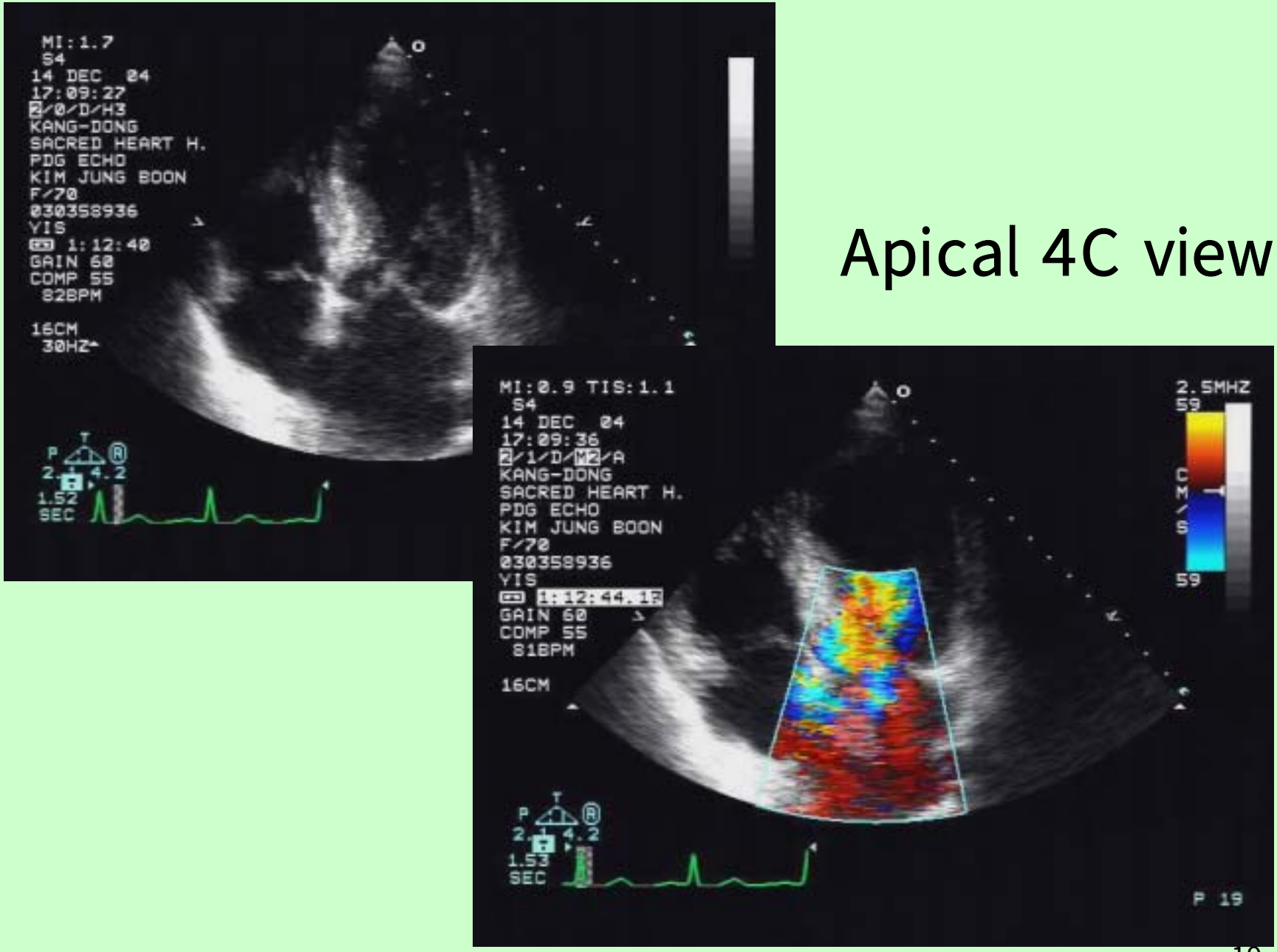
Admission due to melena with hematochezia

Lab: Hb 8.4 g/dl

EGD: Duodenal ulcer with gastric ulcer

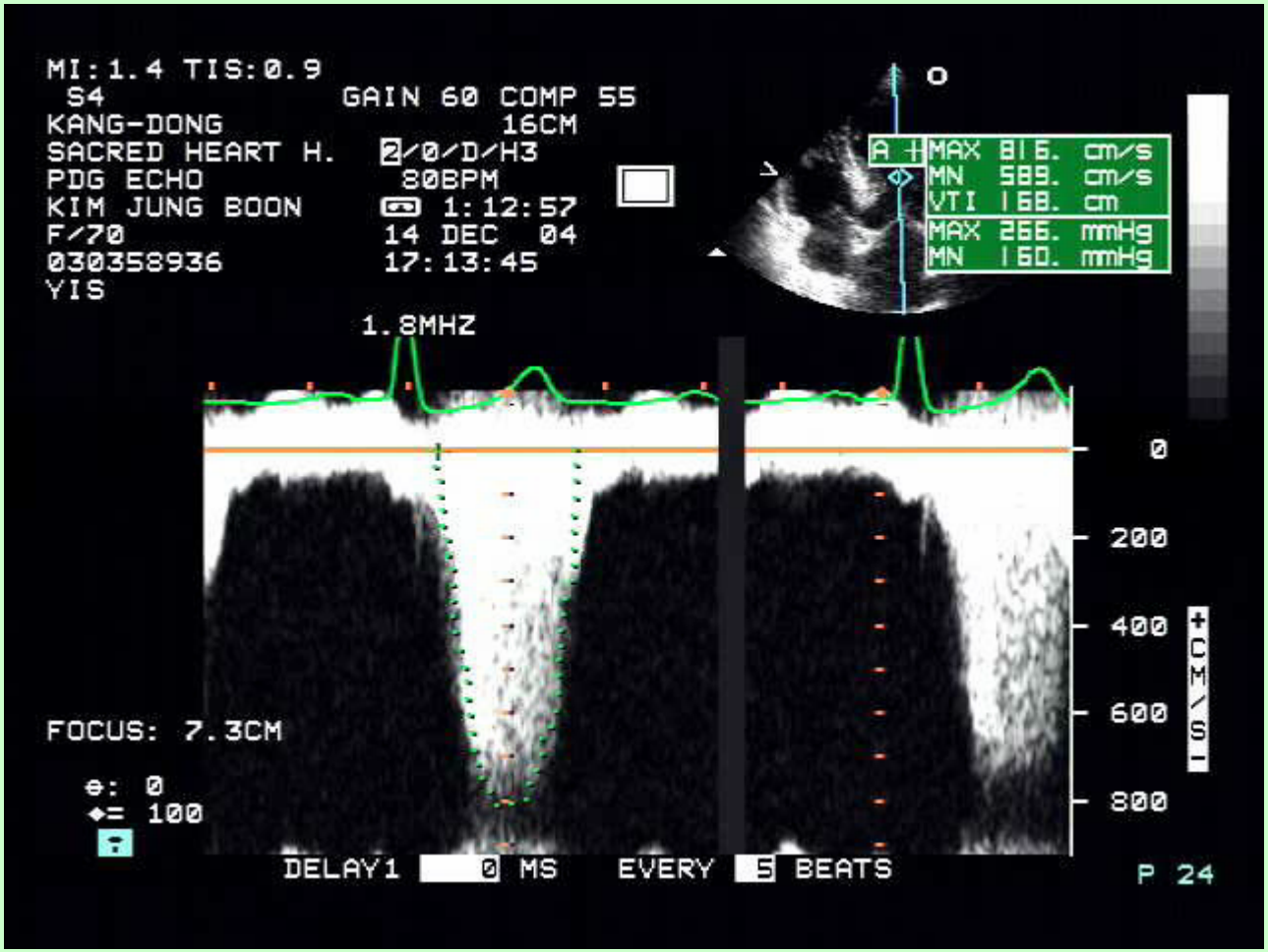
ECG at 2nd Admission





Apical 4C view

Apical 4C view with CW Doppler



Provocation of LVOT obstruction

- Valsalva maneuver:

  reduction of preload

- Post-PVC: increase of contractility

- Amyl nitrate inhalation:

  reduction of prelaod and afterload

CASE2: F/78

C.C: Palpitation and dyspnea

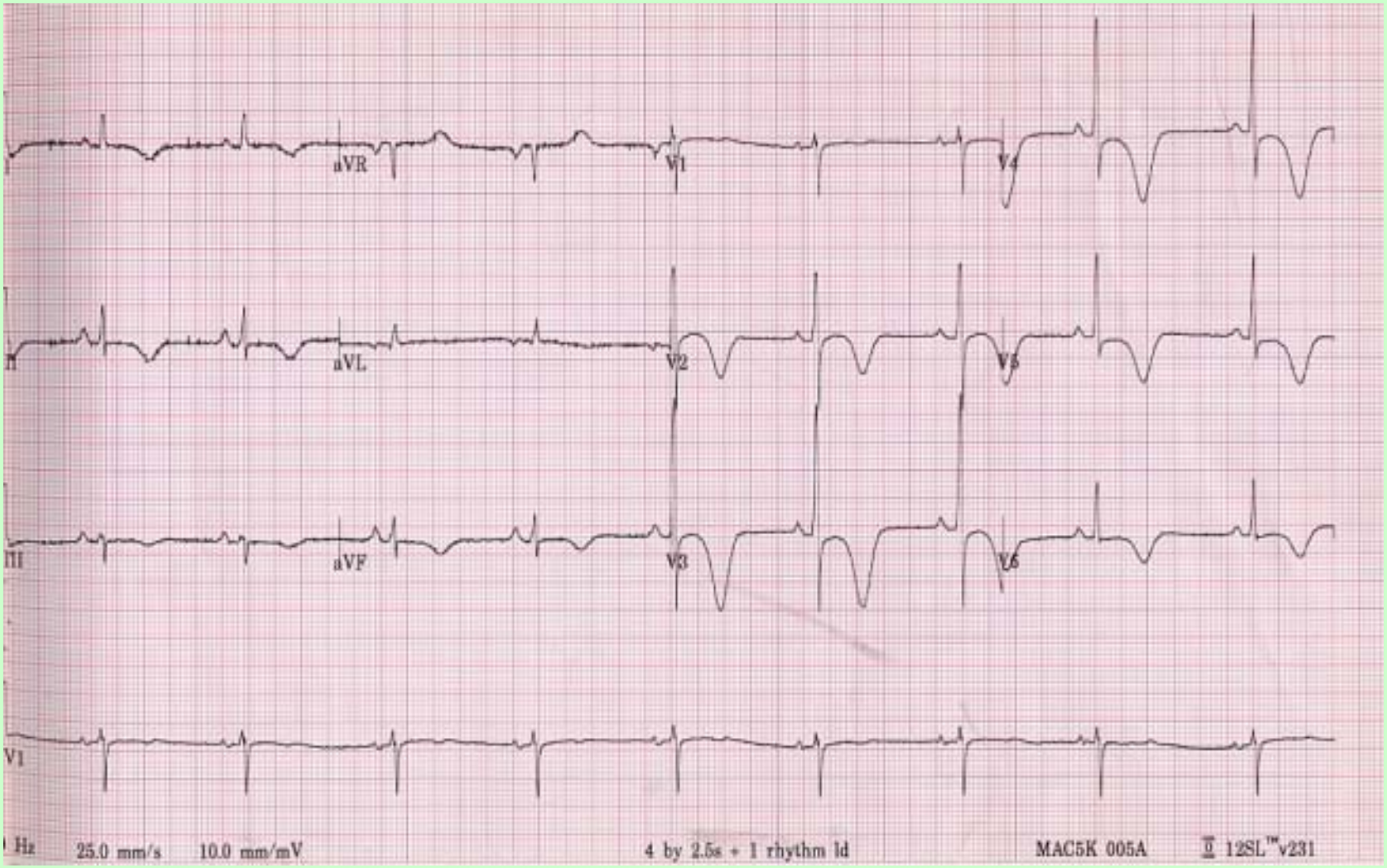
BHx: 타병원에서 울혈성 심부전 및 고혈압으로 치료중인 환자로 심계항진 및 호흡 곤란증이 동반되어 응급실방문. PSVT확인되었고 adenosine 정주 후에 종료되었음. 심부전 및 PSVT치료위해 전원됨.

타병원 echo: normal

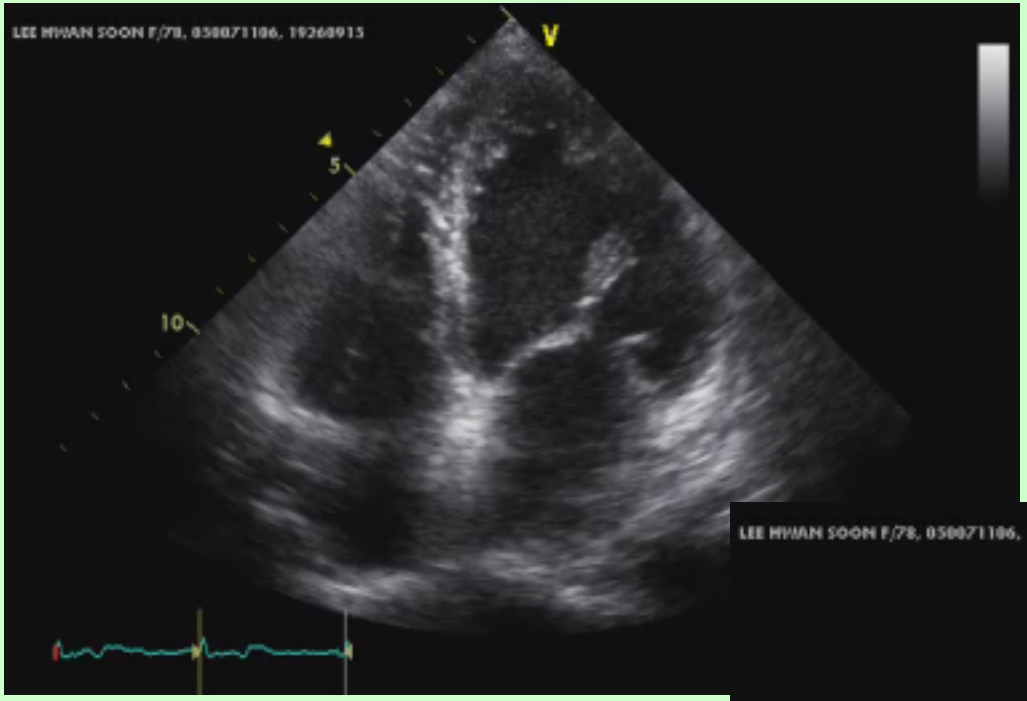
본원 CAG: normal

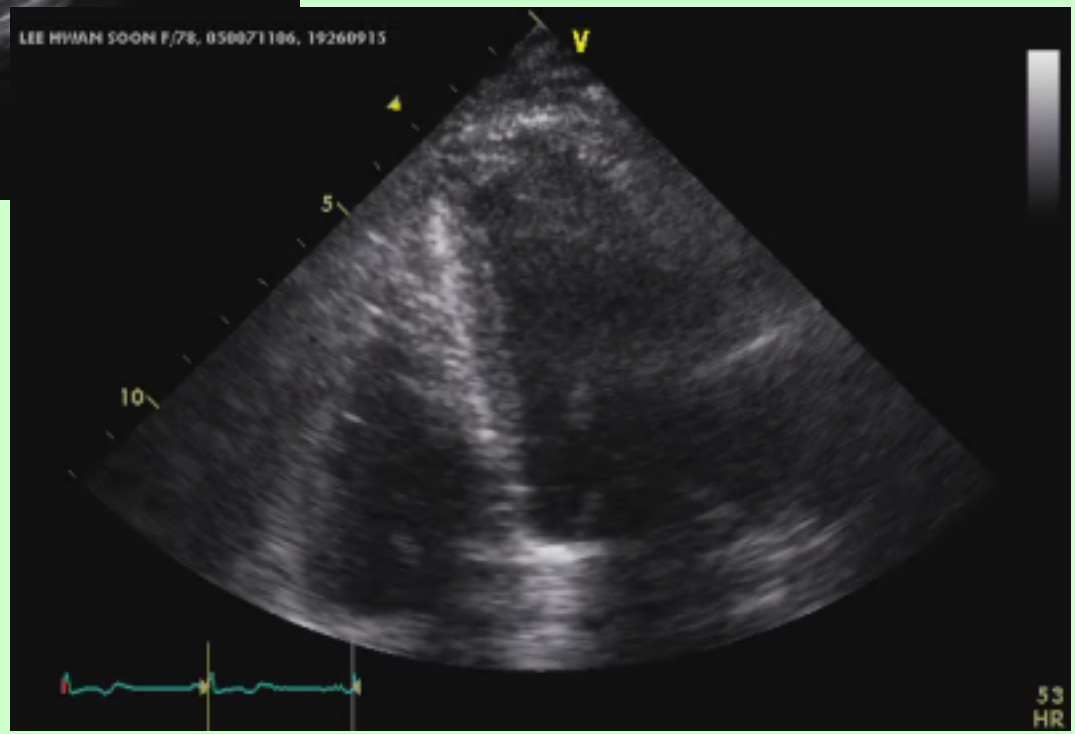
Mx: RFCM for AVNRT at EPS

ECG after RFCM



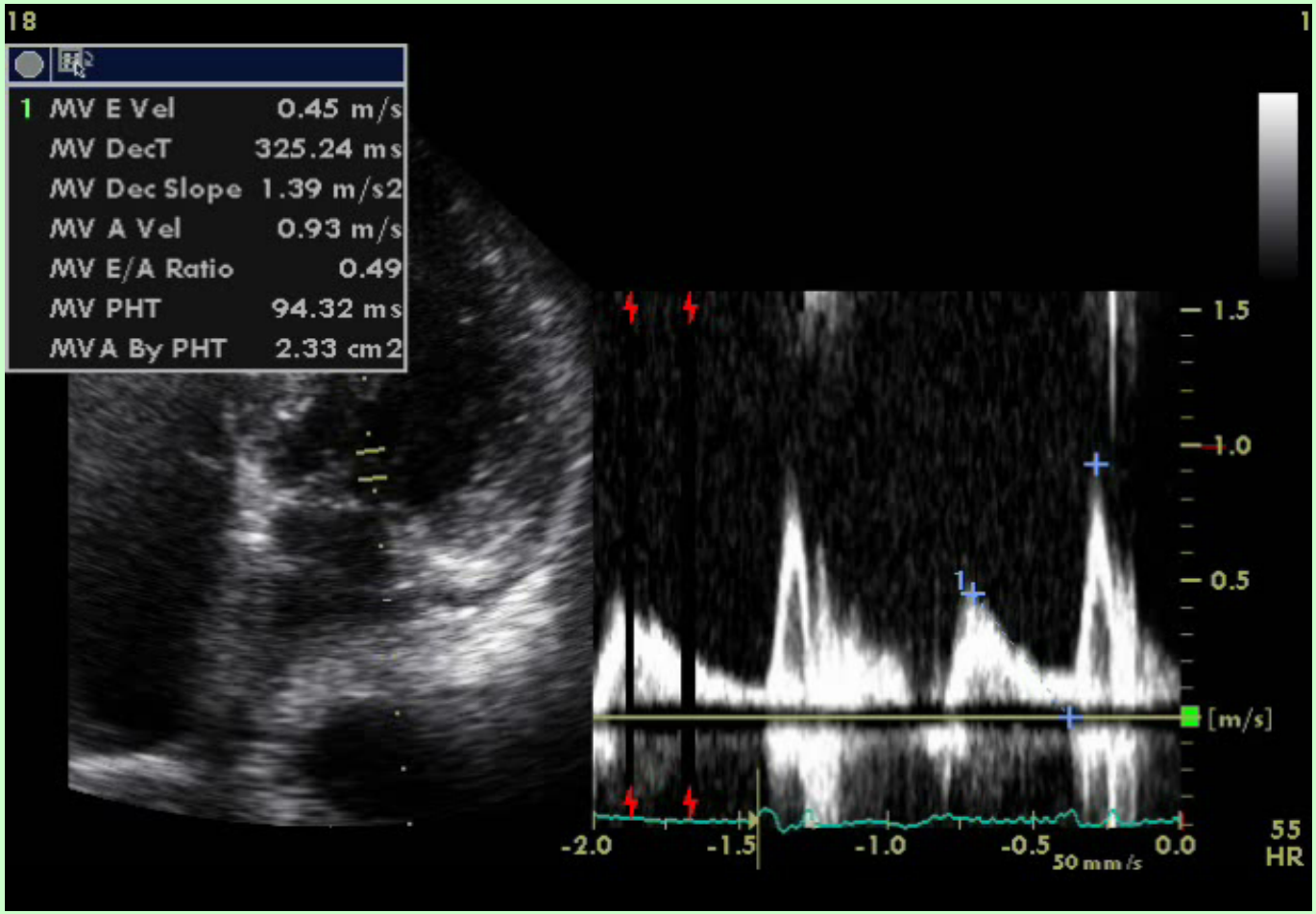
Apical 4C





True apex ?

Transmitral flow by PW



Apical HCM

1/4 of Japan, < 10% in western

Longterm outcome:

by Eriksson MJ, JACC 2002

Benign prognosis

Not associated with SCD

1/3: MI, arrhythmia

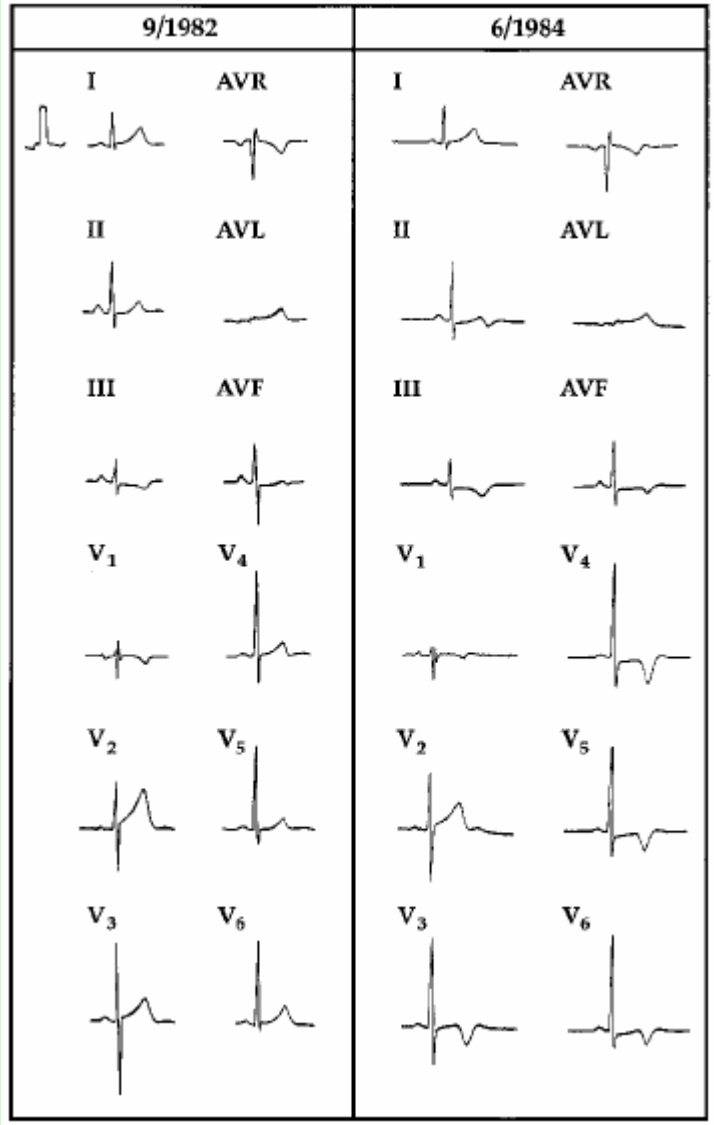
56 year/M
Routine exam for pilot license
In 1984

Circulation 2001 by BarryJ.Maron et al.

Extensive W/U due to ECG change:

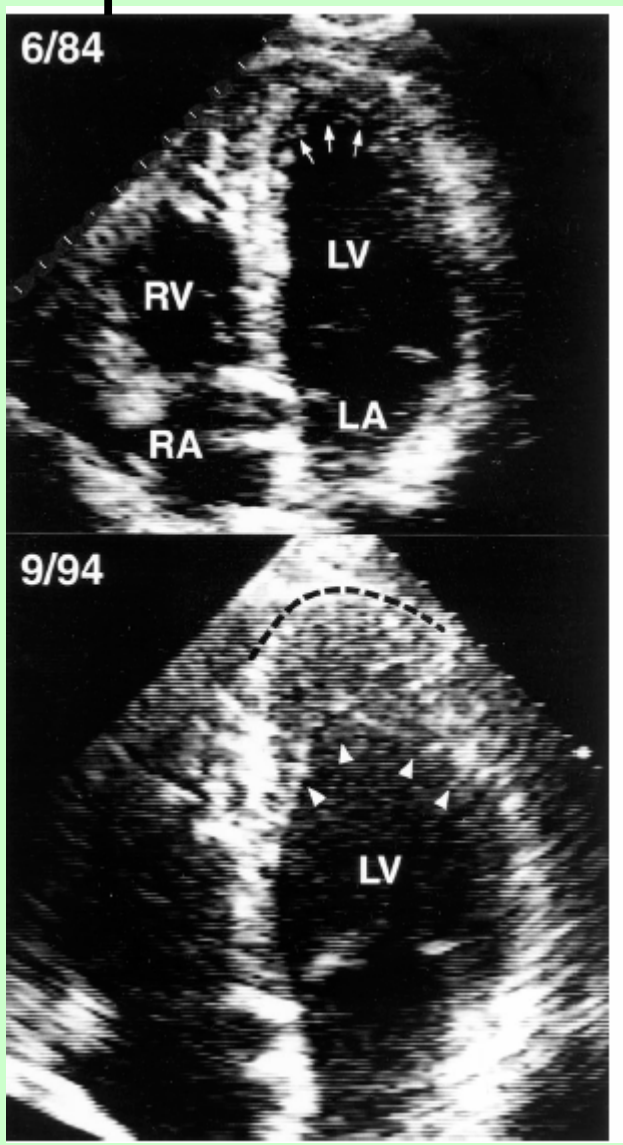
Stress test and CAG: normal

Echo:normal



10 years later
De novo development of Apical HCM at a advanced age

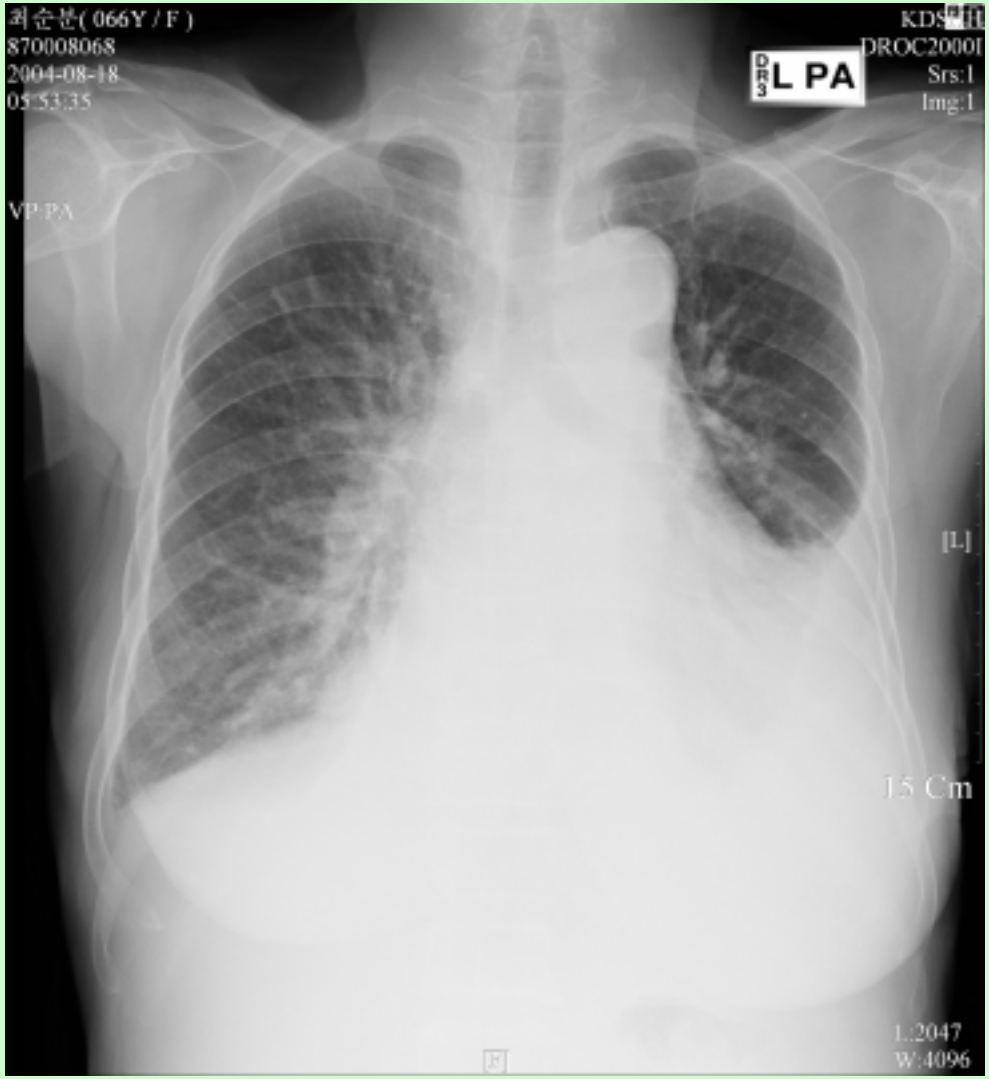
Apical 4C view



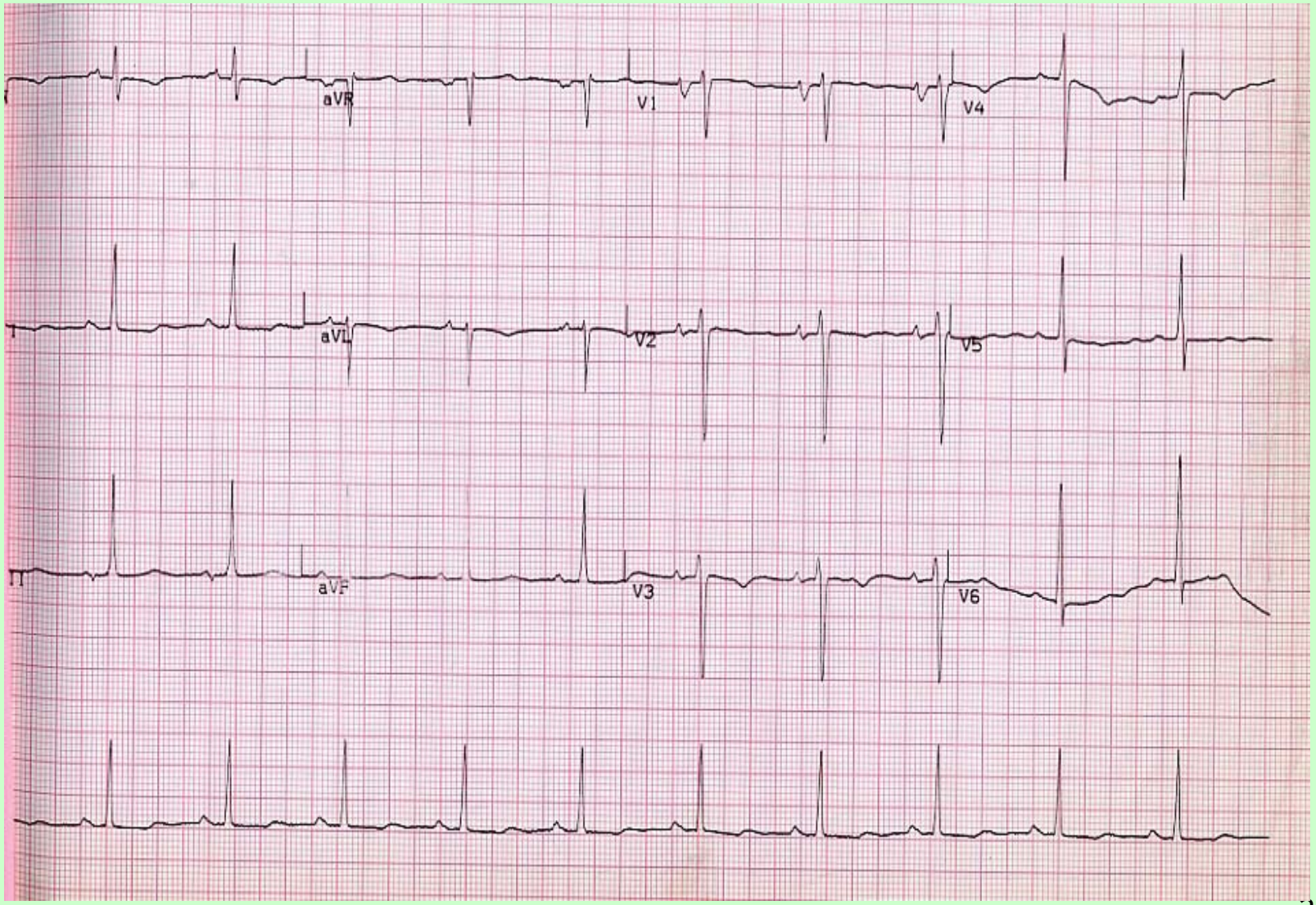
CASE 3: 67/F

CC: dypnea

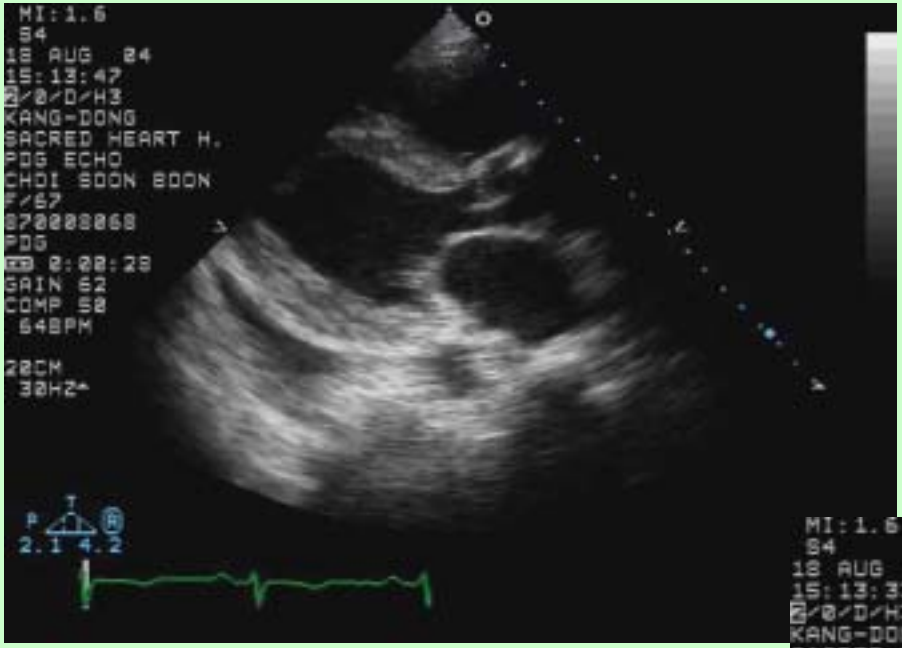
Chest PA at Admission



ECG at Admission



PLAX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18 AUG 04
15:13:47
2/0/D/H3
KANG-DONG
SACRED HEART H.
PDG ECHO
CHOI SOON BOON
F/67
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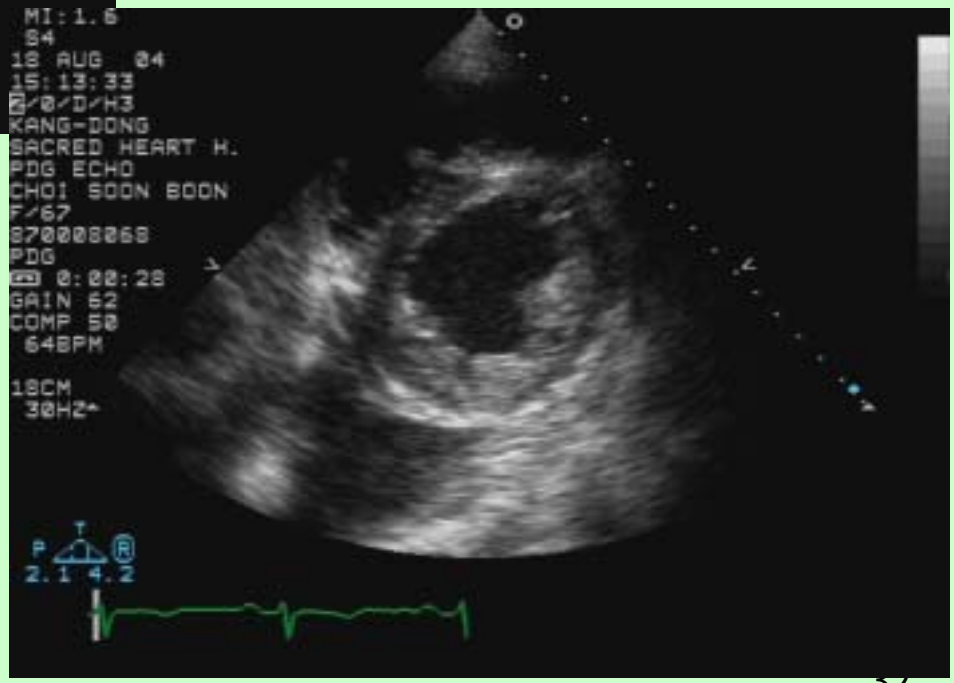
PDG
0:00:28
GAIN 62
COMP 50
64BPM
20CM
30HZ
2.1 4.2

PSAX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18 AUG 04
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SACRED HEART H.
PDG ECHO
CHOI SOON BOON
F/67
870008868
PDG
0:00:28
GAIN 62
COMP 50
64BPM
18CM
30HZ
2.1 4.2

Diagnostic Dilemma for nonobstructive HCM

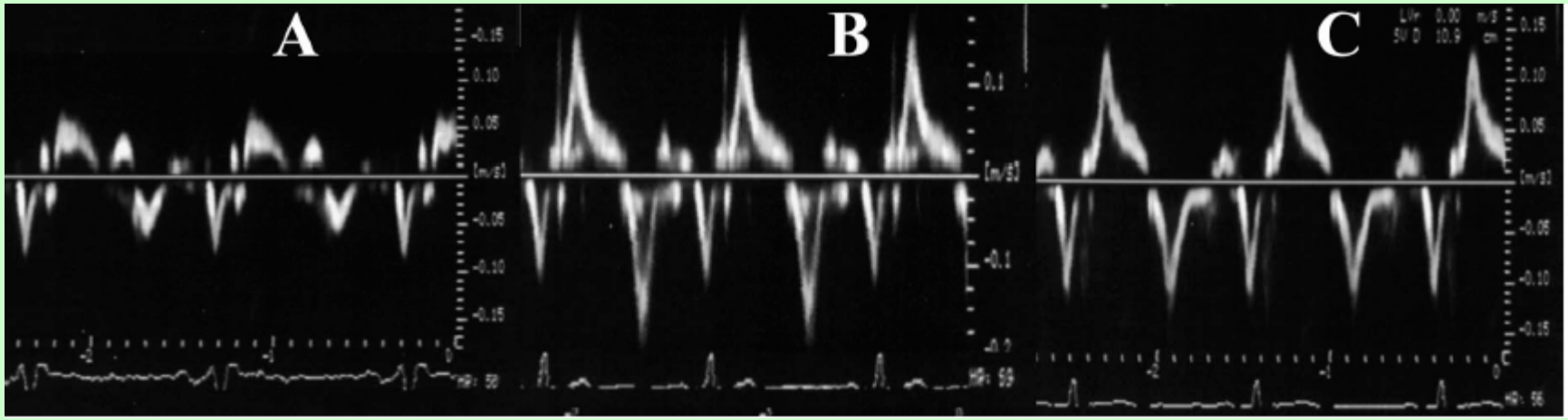
(esp, no ASH, WT <15mm)

Hypertensive LVH: concentric, WT<15mm

Athletic heart: enlarged, <15mm

New methodology: TDI(tissue Doppler image), SRI(strain rate image)

Tissue Doppler Image
(long axis from apical window)



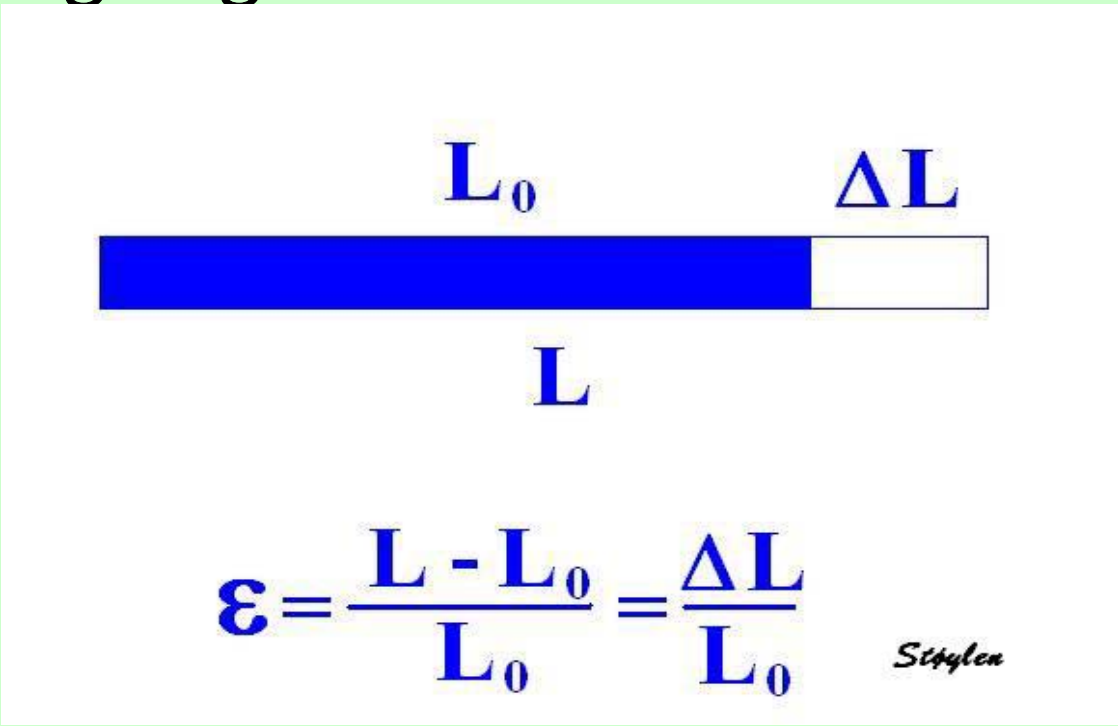
HCM (normal EF)

Athlete with LVH

control

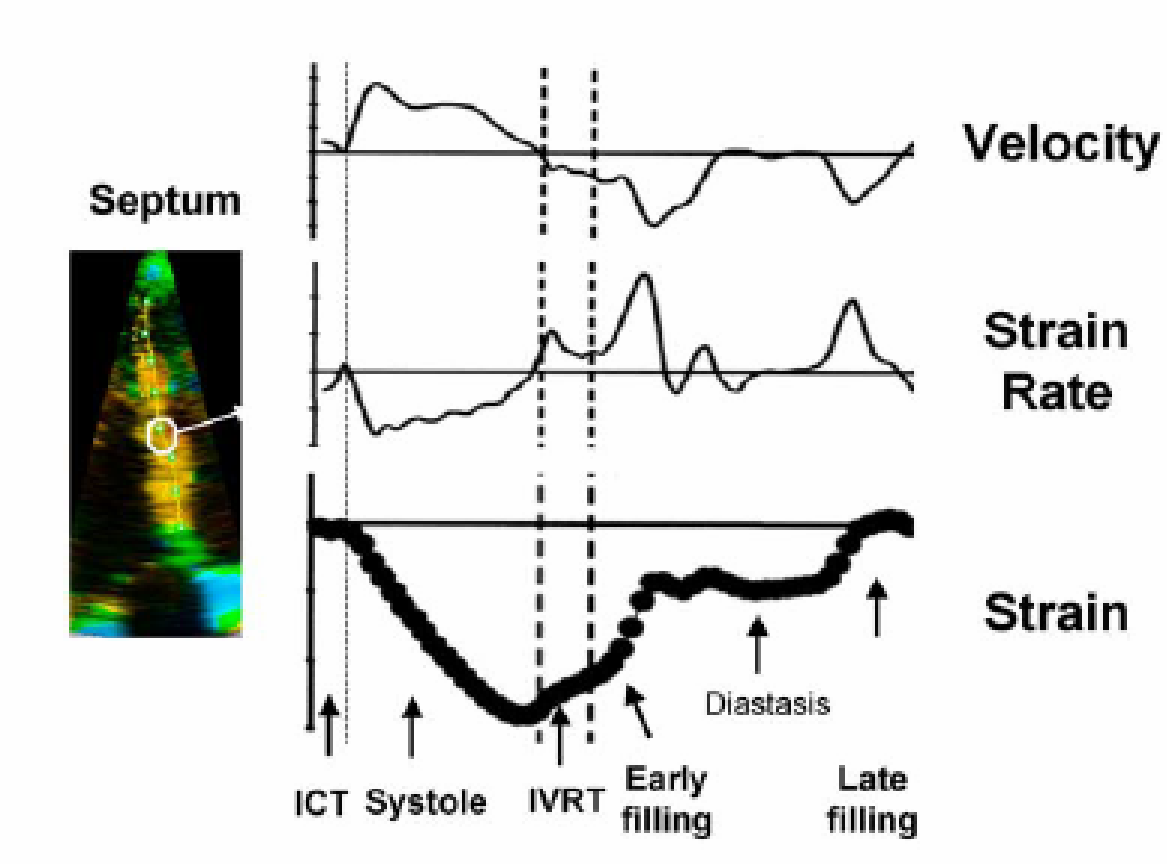
Strain

"stretching". In scientific usage, "deformation". linear strain can be defined by the Lagrangian formula:



Where ε is strain, L_0 = baseline length and L is the instantaneous length at the time of measurement

Data on timing of global events is implanted into normal regional velocity, strain (ε) rate, and strain rate (SR)curves to subdivide cardiac cycle into mechanical components.



ICT, Isovolumic contraction time; *IVRT*, isovolumic relaxation time.

Discrimination of Nonobstructive Hypertrophic Cardiomyopathy From Hypertensive Left Ventricular Hypertrophy on the Basis of Strain Rate Imaging by Tissue Doppler Ultrasonography

Tomoko S. Kato, et al.

(*Circulation*. 2004;110:3808-3814.)

Diagnosis based on echo and endocardial Bx

IVST/PWT ratio and Systolic Strain(ε_{sys})

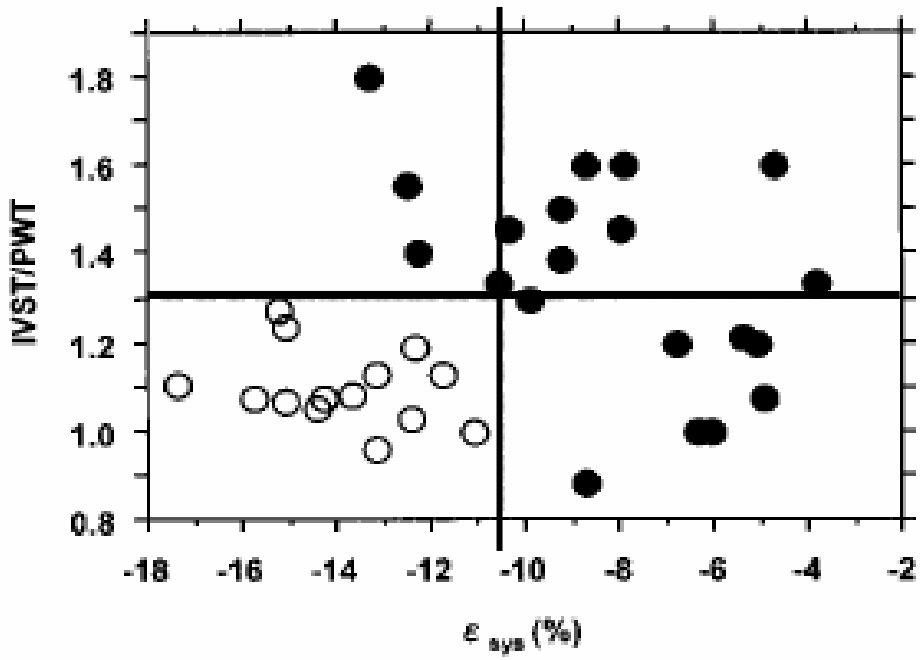
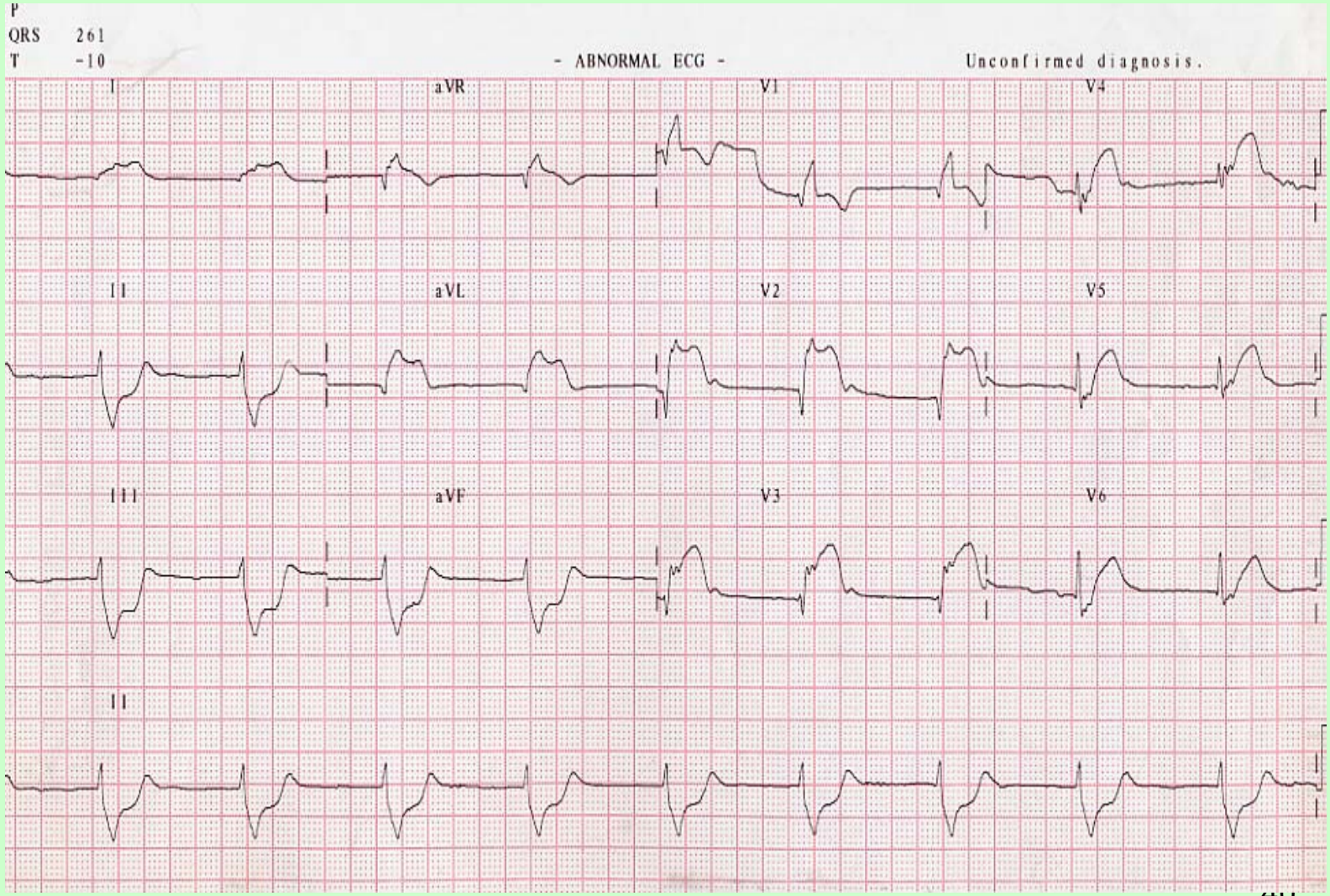


Figure 3. Relation between IVST/PWT ratio and ϵ_{sys} in patients with HCM (●) and those with H-LVH (○). Optimal cutoff values for discrimination between the 2 groups of patients are indicated.

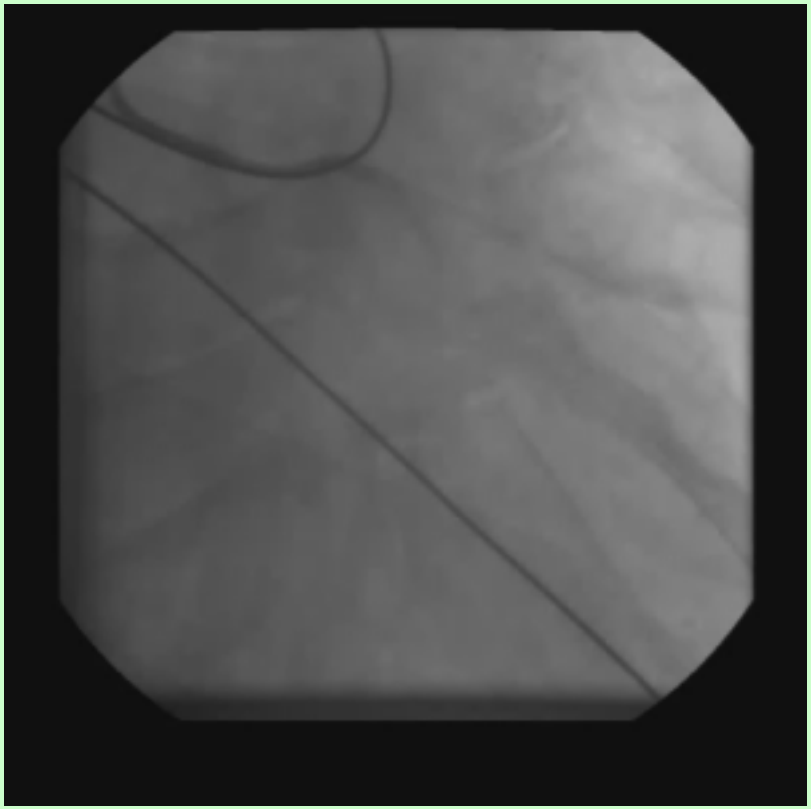
Case 4 : 67/M

- 2~3년전 고혈압을 진단받고 항고혈압약제 복용하던 분으로 내원일 가구 옮기던 중 갑자기 시작된 흉통과 cold sweating을 주소로 흉통 발생 30분 후에 본원 응급실 내원함.
- Smoking/alcohol (-/-)

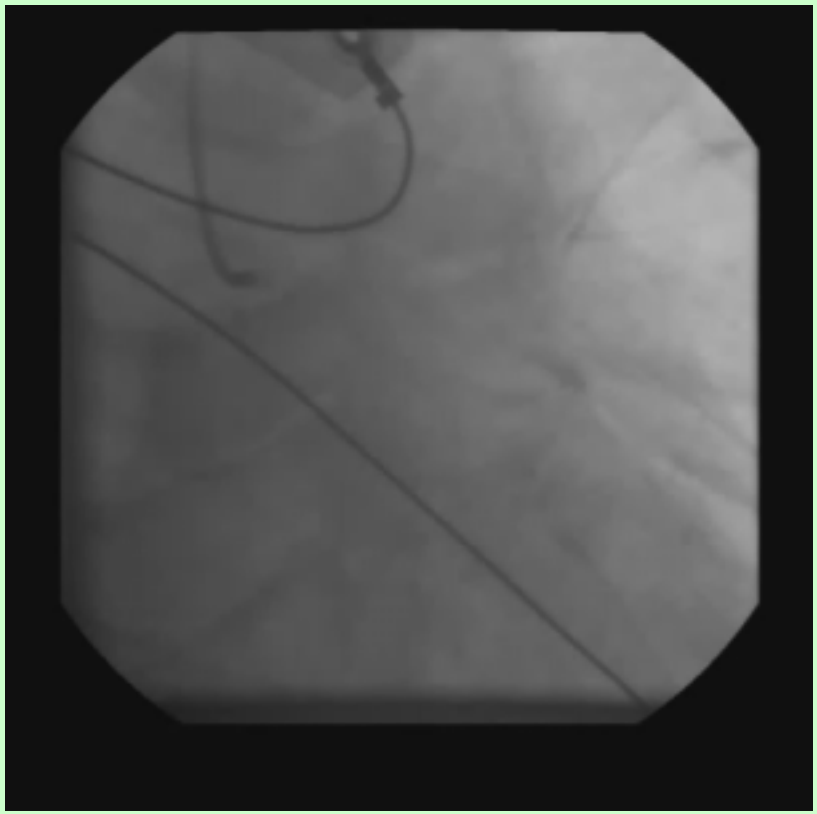
ECG at ER -> Cath room for prim. PCI



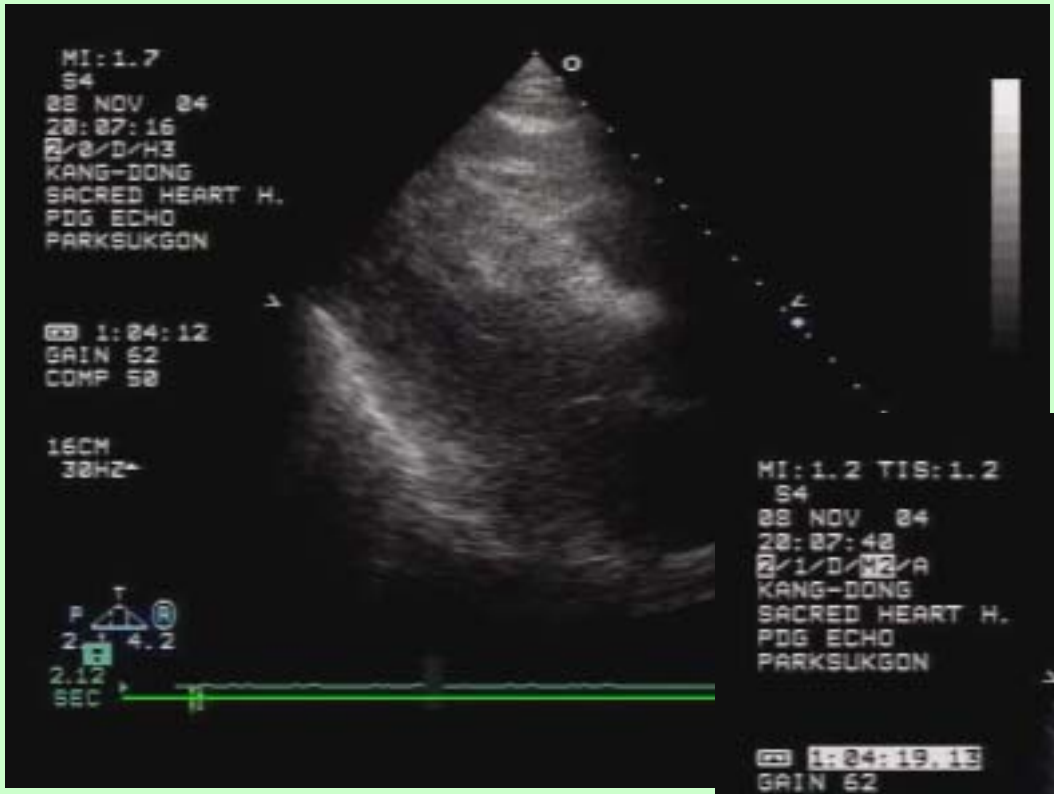
Left Coronary Artery

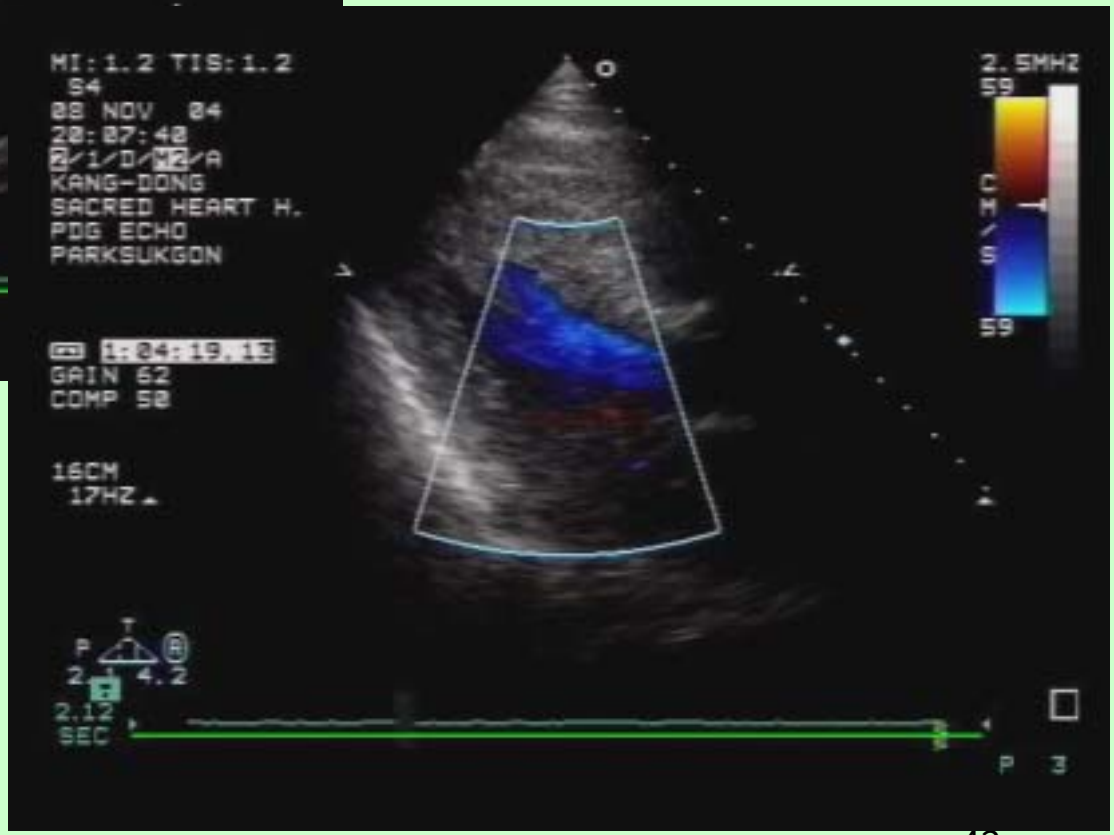


LCA (near orifice)



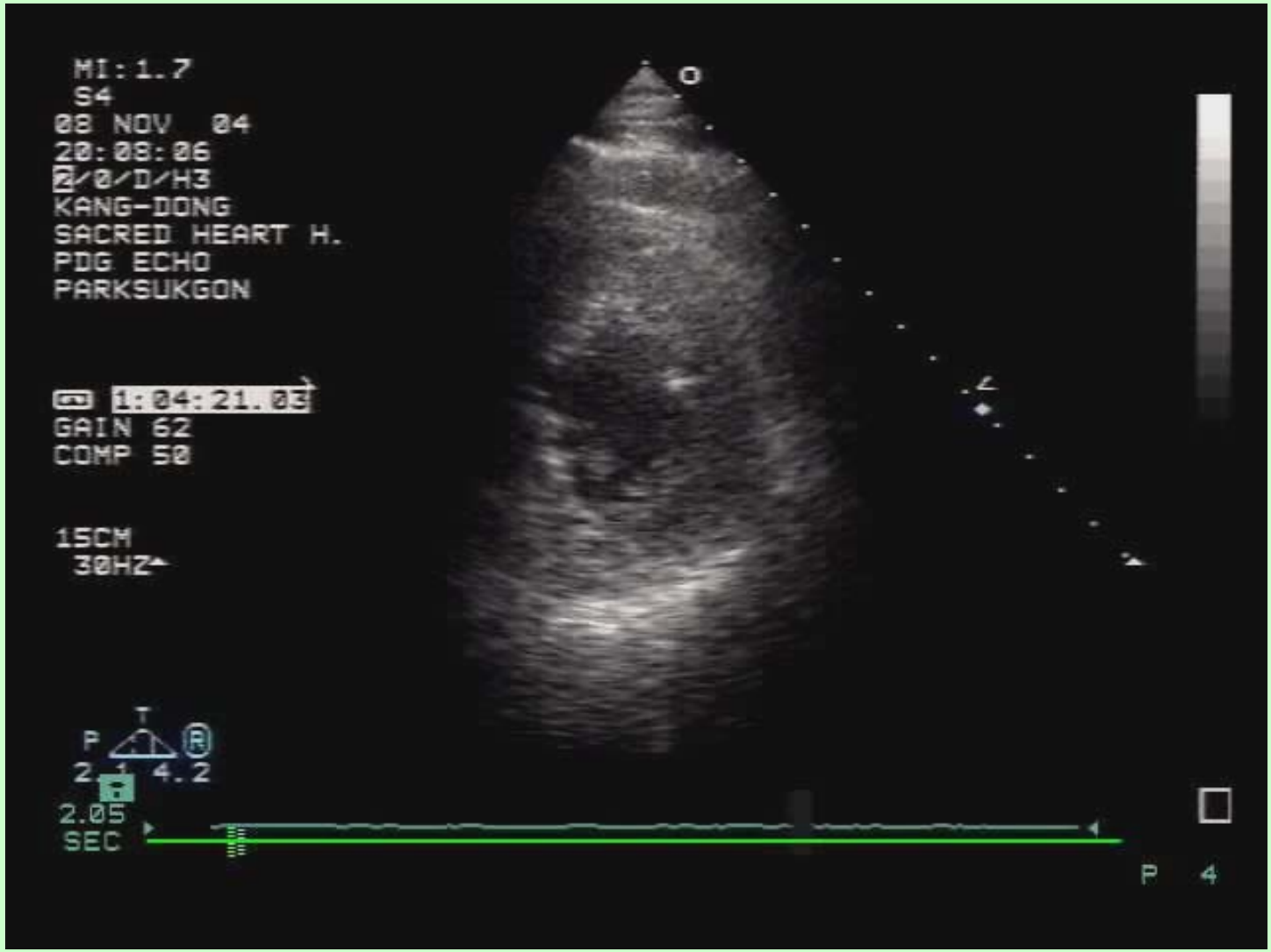
Shock during CAG
Intubation and IABP



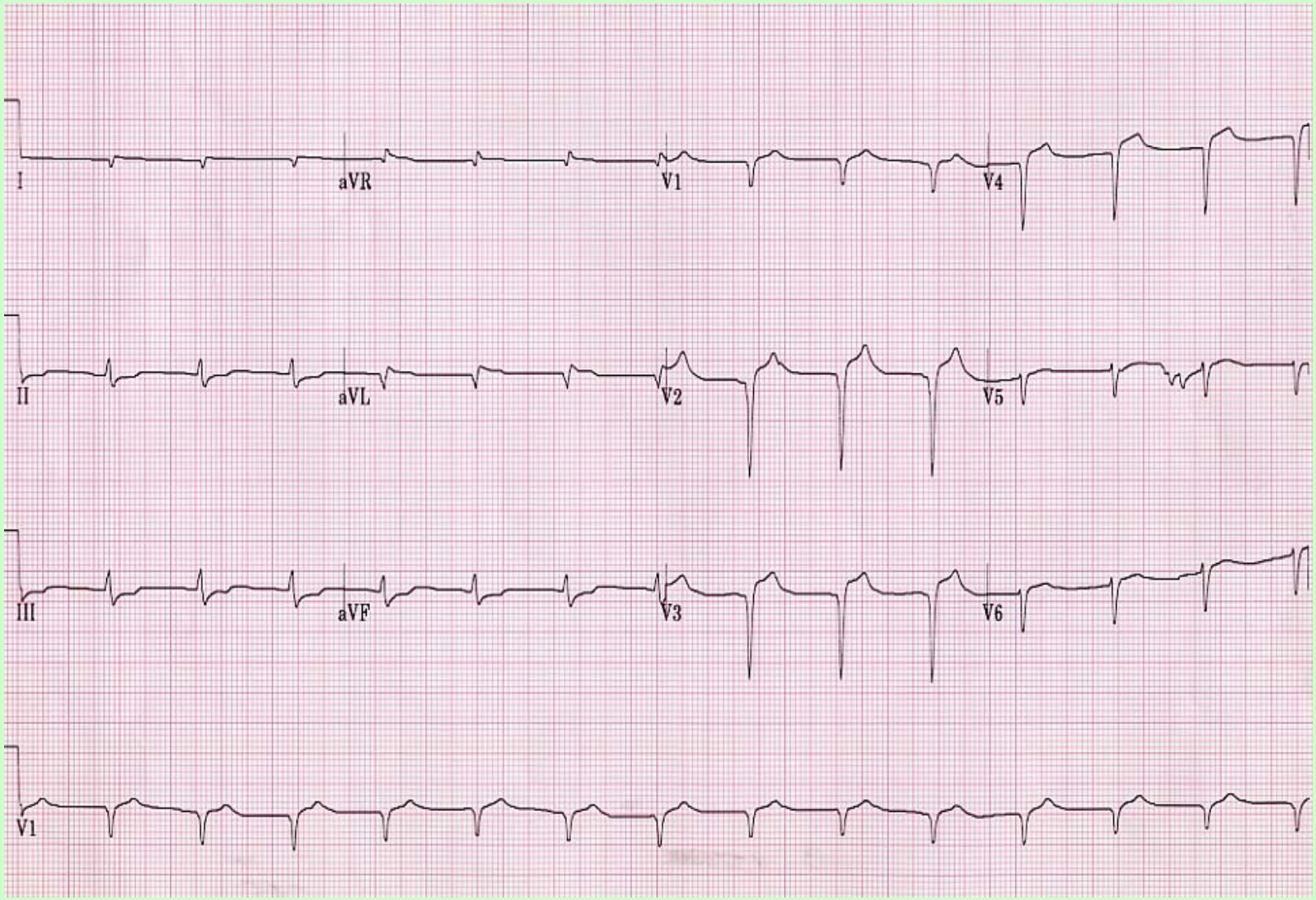


Parasternal
long-axis view

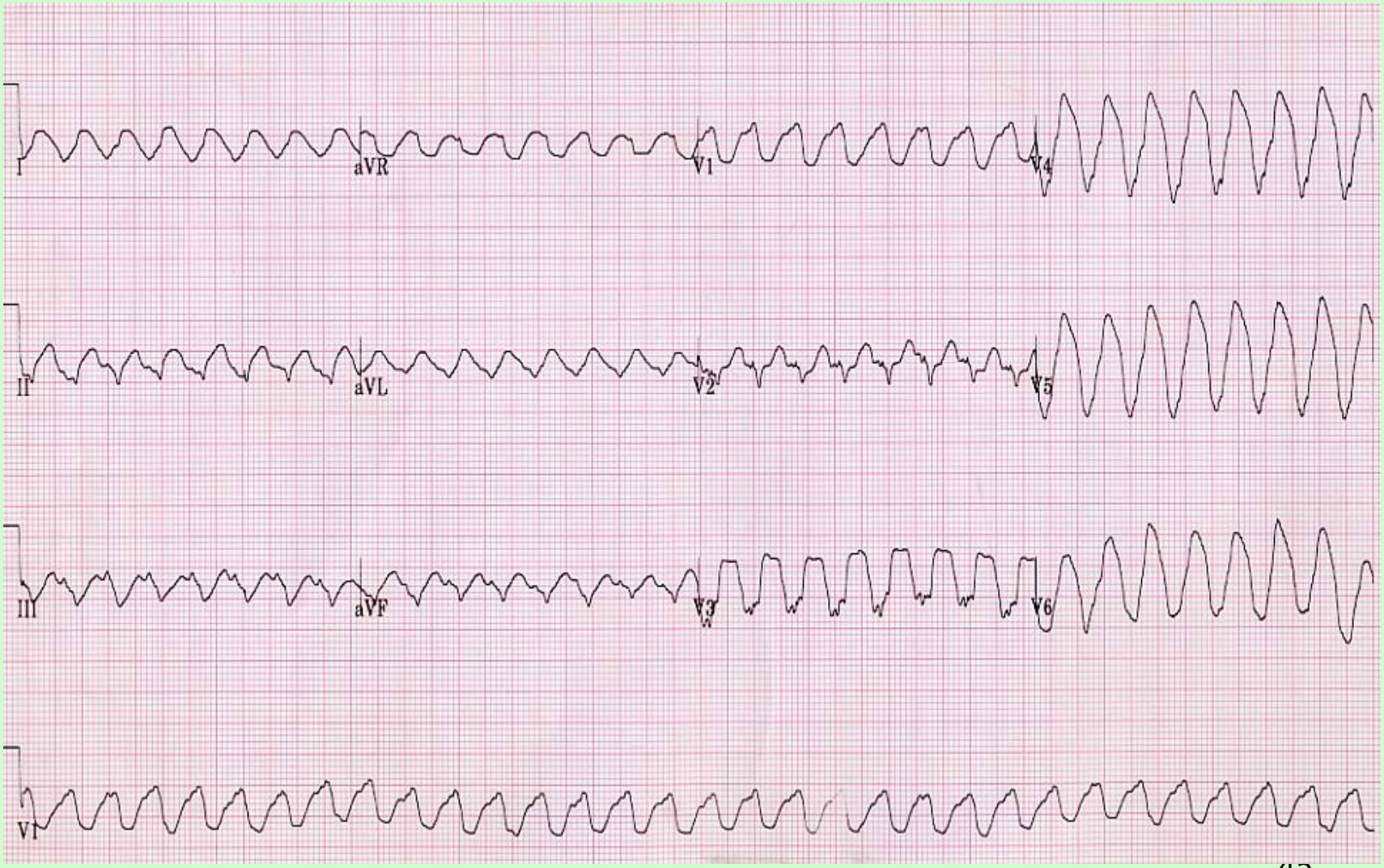
Parasternal short-axis view



ECG at CCU



ECG at CCU: later, repeated VT and VF



Possible mechanisms for myocardial ischemia in HCM

Increased myocardial oxygen demand
Myocardial Hypertrophy
Diastolic dysfunction
Myocyte disarray
LV outflow obstruction
Arrhythmia

Reduced myocardial perfusion
Small vessel disease
Abnormal vascular response
Myocardial bridges
Increased coronary vascular resistance

Etiology of Myocardial Necrosis and Evolution of Congestive Heart Failure in Patients with HCM

- Atherosclerotic coronary artery disease
- Intramural coronary arteries ("small vessel disease")
- Impaired vasodilator reserve of coronary artery
- Elevated left ventricular filling pressure
- Compression of septal perforator
- Myocardial bridging
- Spasm of coronary artery
- Mismatching of supply/demand in oxygen consumption
- Anomalous coronary arteries
- Septal myectomy
- Embolism to a major coronary artery branch
- Intraventricular pressure gradient
- Myocarditis

Case 5:호흡곤란을 주소로 내원한 32세 남자환자

- DM

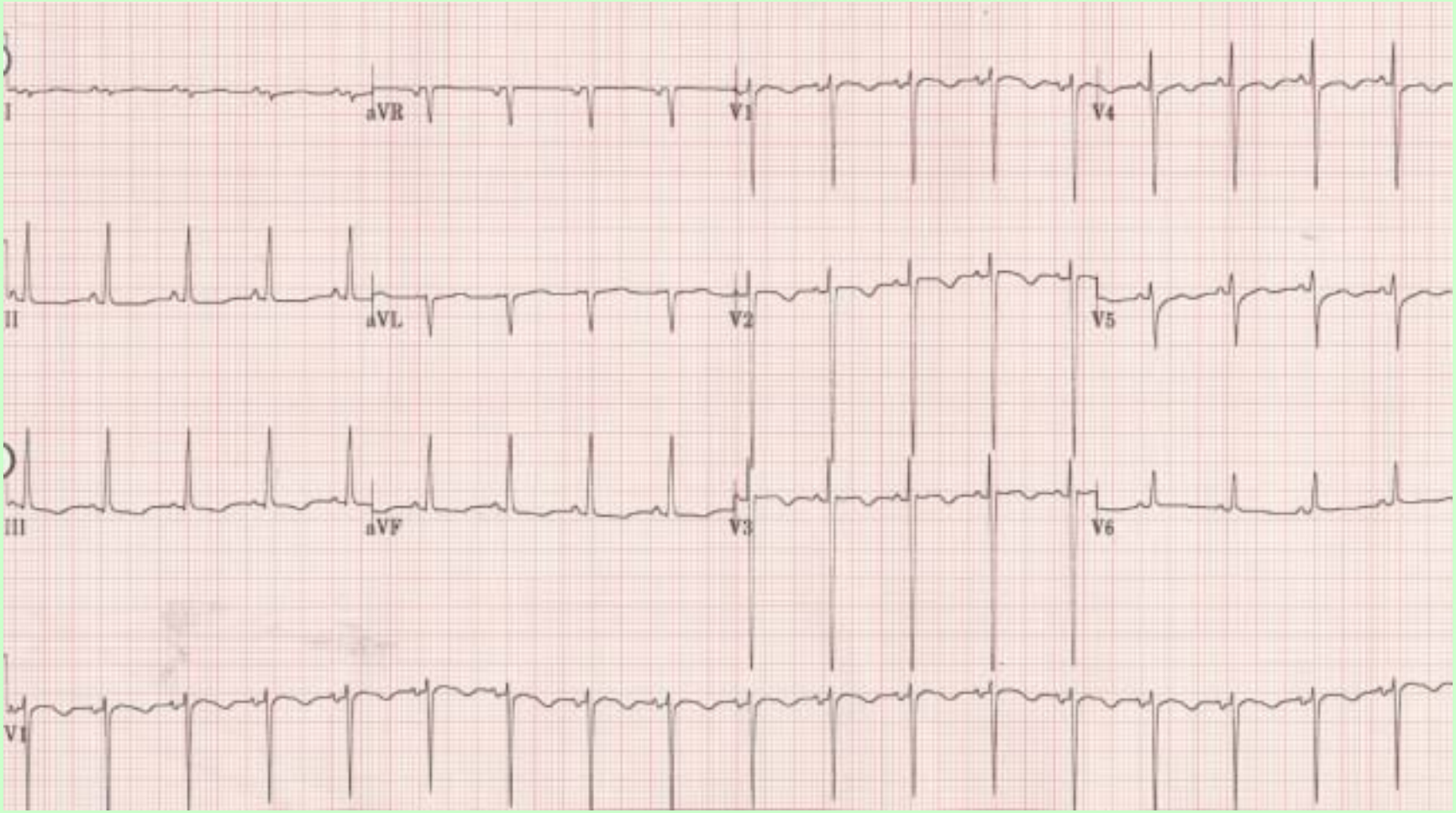
  1999년 local clinic에서 진단 후 OHA 복용

  2002년 3월 본원 내분비내과 입원, Type I DM으로 진단 후 Insulin치료 시작

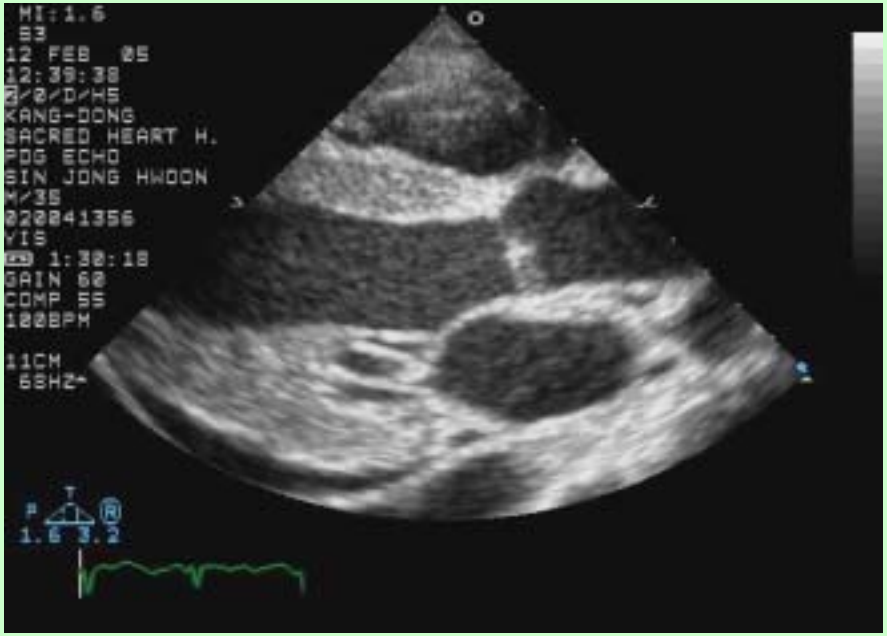
- Sensory neural hearing loss

  어렸을 때부터 왼쪽 청력이 좋지 않았고 2002년 입원 당시 오른쪽 청력도 나빠짐을 호소하여 이비인후과에 의뢰, 진단

Electrocardiography at admission



PLAX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12:39:38
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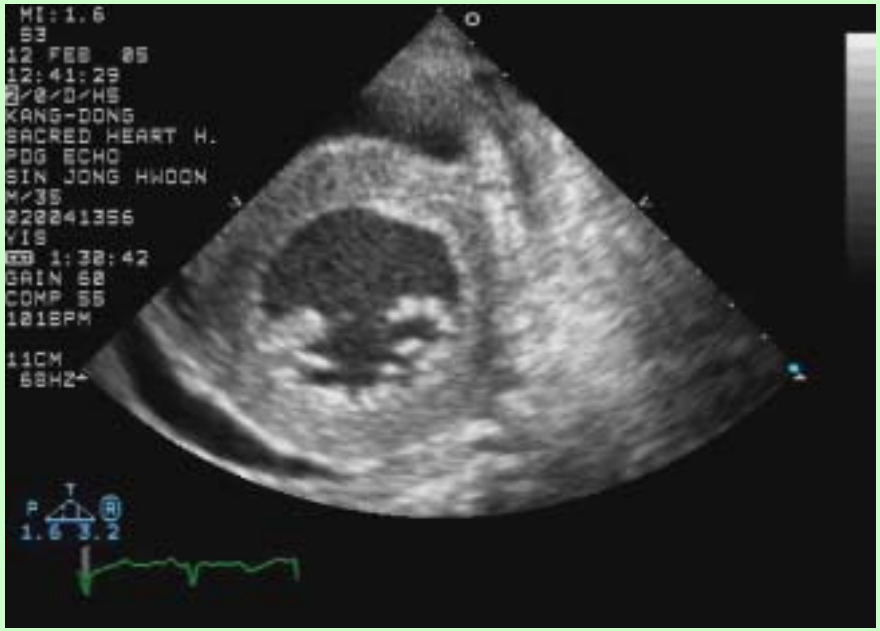
PDG ECHO
SIN JONG HWOON
M/35
0220841356
VIS
1:38:18
GAIN 60
COMP 55
1008PM
11CM
68HZ
1.6 3.2

PSAX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53
12 FEB 05
12:41:29
2/0/D/HS
KANG-DONG
SACRED HEART H.
PDG ECHO
SIN JONG HWOON
M/35
0220841356
VIS
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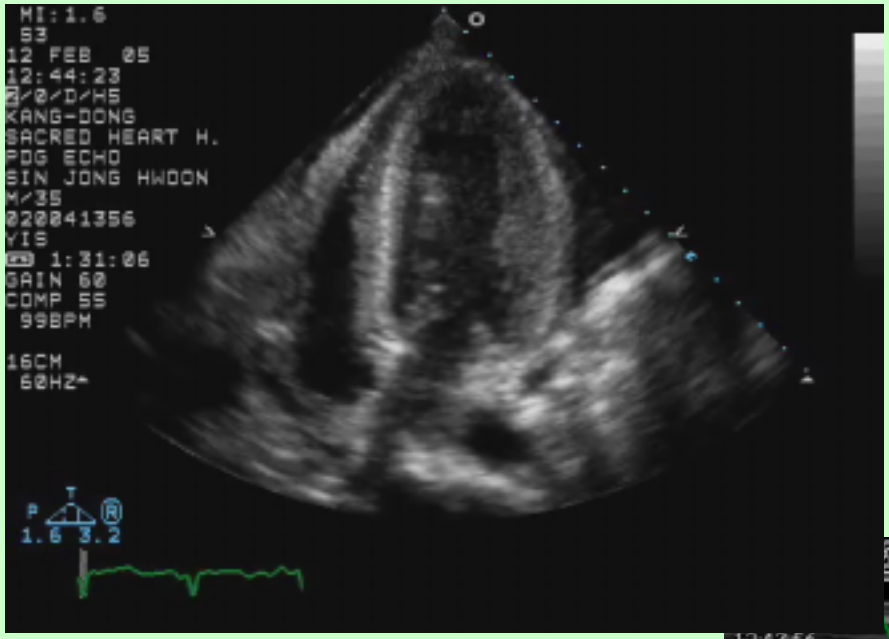
GAIN 60
COMP 55
1018PM
11CM
68HZ
1.6 3.2

A4C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53
12 FEB 05
12:44:23
2/0/D/H5
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M/35
220041356
YIS
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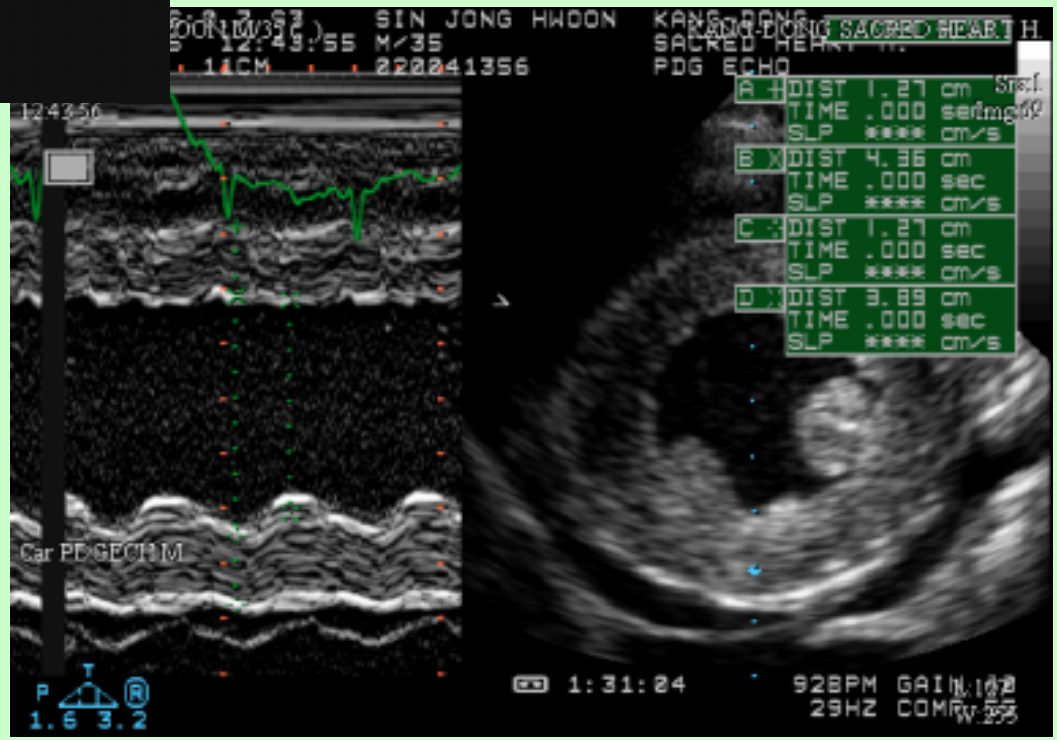
GAIN 60
COMP 55
99BPM
16CM
60HZ
1.6 3.2


SIN JONG HWOON
M/35
220041356
PDG ECHO
SACRED HEART H.
DIST 1.27 cm
TIME .000 sec
SLP **** cm/s
DIST 4.36 cm
TIME .000 sec
SLP **** cm/s
DIST 1.27 cm
TIME .000 sec
SLP **** cm/s
DIST 3.89 cm
TIME .000 sec
SLP **** cm/s
Car PD ECHO M
1:31:24
92BPM
29HZ
1.6 3.2

normal BP

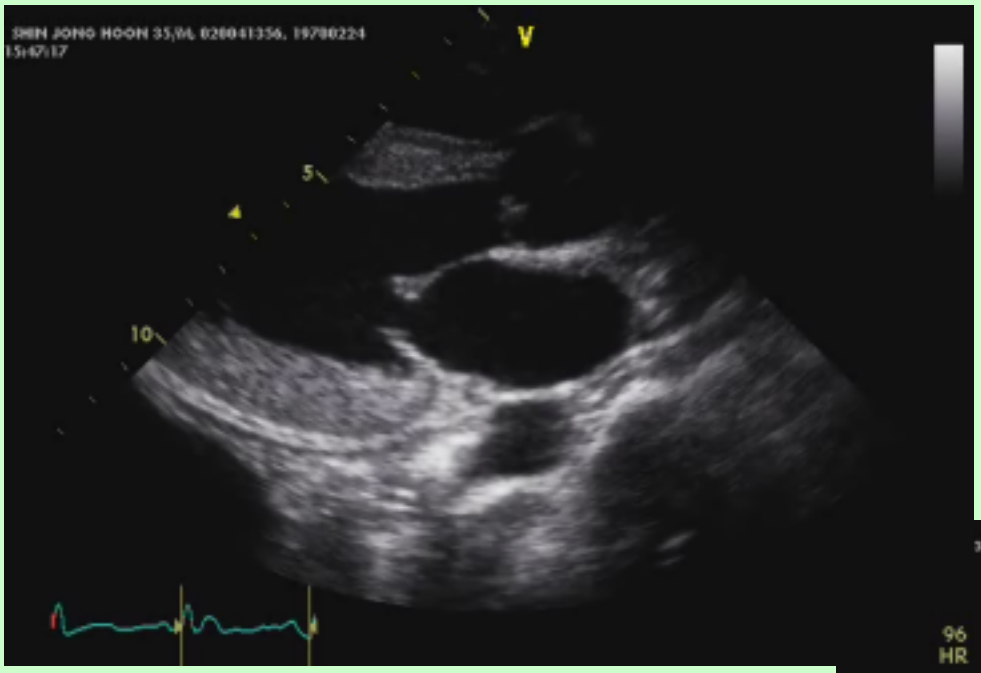
CAG: normal

Lab: no azotemia

First impression?

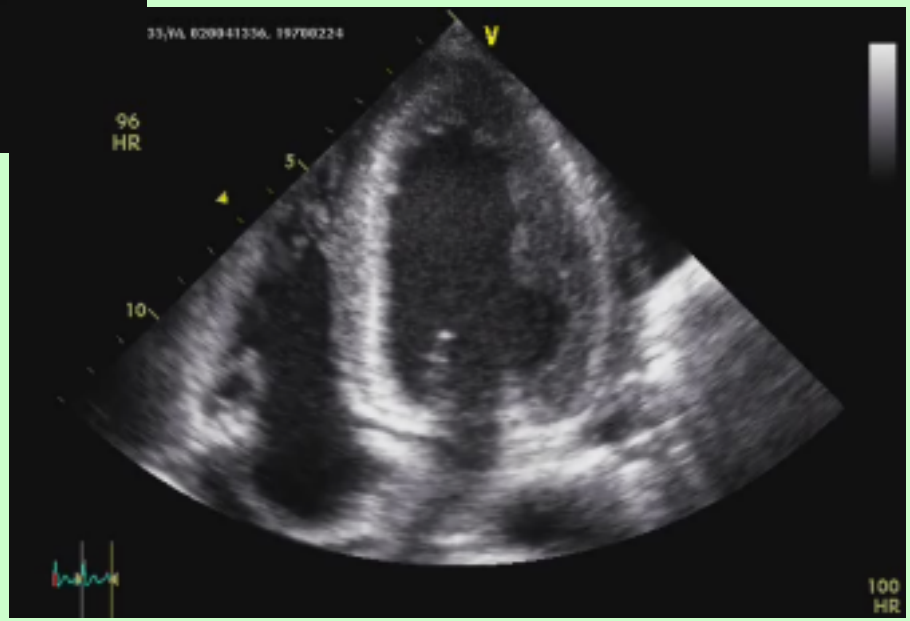
Medication: ACEI and diuretics for CHF

PLAX

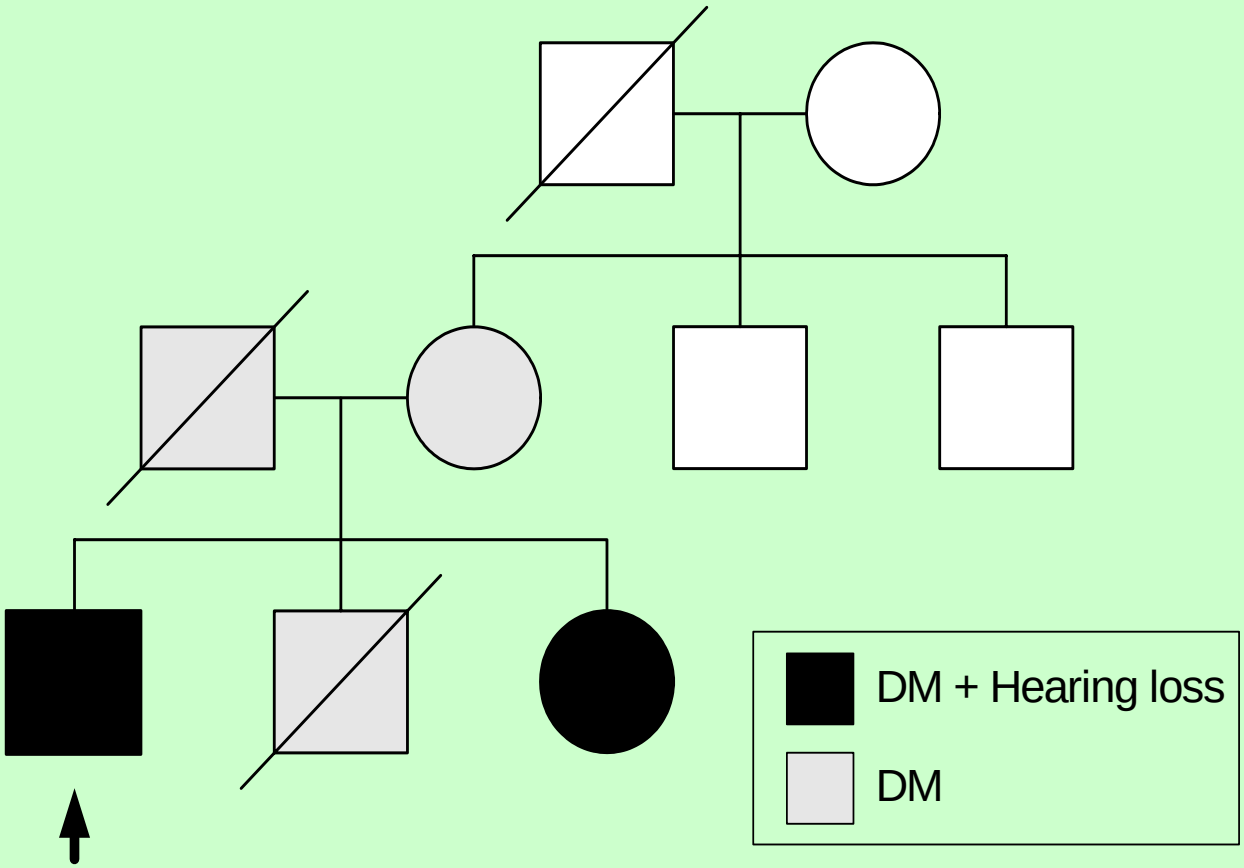


After medication

A4C



Pedigree

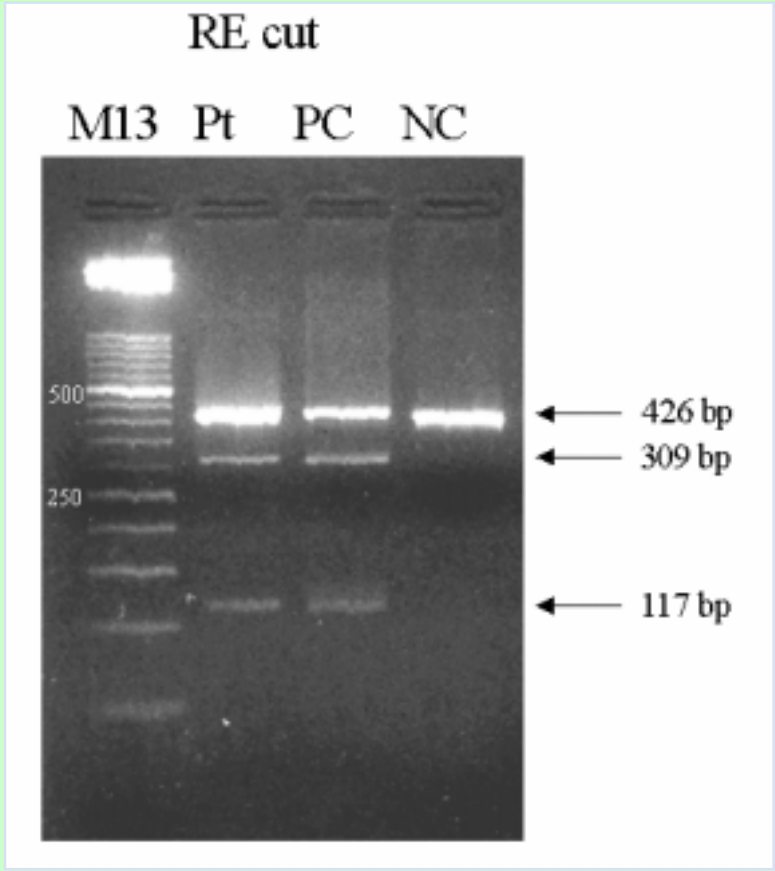


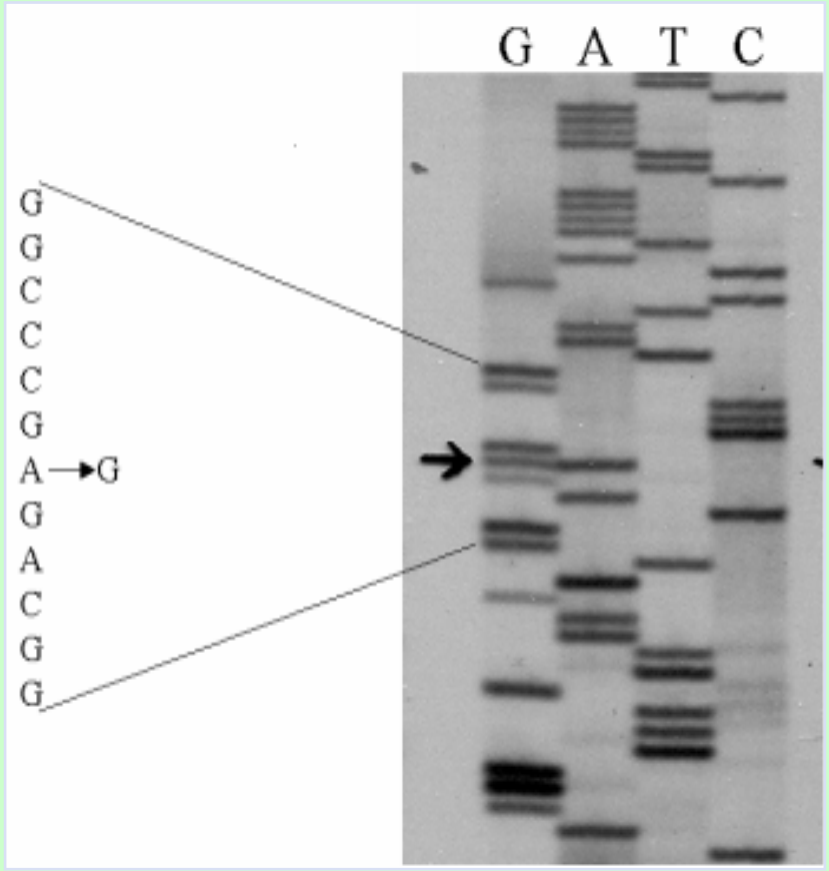
A3243G mitochondrial tRNA mutation

- MELAS : Mitochondrial encephalopathy, lactic acidosis, stroke-like episodes
- 1981 Human mitochondrial DNA 염기서열 밝혀짐
- MIDD : Maternally Inherited Diabetes and Deafness

  = Mitochondrial diabetes, 1992

Genetic analysis : PCR-RFLP & Sequencing





Cardiac involvement in mitochondrial disease

- Circulation. 1995;91:955-961
- Kagoshima Univ. Japan, Rhuichiro Anan et al.
- Mitochondrial DNA defect가 확인된 환자 17명

- Kearns-Sayre syndrome (Deletion of mtDNA)
- Ocular myopathy (Deletion of mtDNA)
- MERRF ; myoclonus epilepsy with ragged red fibers (Point mutation of mtDNA, 8344 A to G)
- MELAS (Point mutation of mtDNA, 3243 A to G)

Table 1. Results of Cardiac and Genetic Analyses in Patients With Mitochondrial Diseases

Patient	Age, y	Sex	Diagnosis	ECG	Chest Radiograph	Echocardiogram	Deletion of mtDNA, kbp	Point Mutation of mtDNA	
								8344 A→G	3243 A→G
1	15	M	KSS	Complete AV block resulting from HV block	Normal	MR (mild), TR (mild)	+, 5	−	−
2	22	M	KSS	CRBBB, inverted T	Normal	Mitral valve prolapse	+, 5	−	−
3	43	F	KSS (probable)	LAD (−60°), prolonged HV (60 msec)	Normal	Normal	+, 5	−	−
4	17	M	Ocular myopathy	Normal	Normal	ND	+, 5	−	−
5	18	M	Ocular myopathy	RAD (+120°)	Normal	Normal	+, 9.5	−	−
6	21	F	Ocular myopathy	Normal	Normal	ND	+, 5	−	−
7	35	F	Ocular myopathy	Normal	Normal	ND	+, 5.5	−	−
8	39	M	Ocular myopathy	Normal	Normal	ND	+, 3.8	−	−
9	52	M	Ocular myopathy	ST dep, inverted T, VPC	Normal	Diffuse hypokinesis of LV	+, 2.8	−	−
10	36	M	MERRF	ST dep, inverted T, VPC	Cardiomegaly	LVH (ASH) Diffuse hypokinesis of LV	−	+	−
11	37	F	MERRF	ST dep, inverted T, LAD (−50°), QS pattern	Cardiomegaly Congestion	LVH (ASH) Diffuse hypokinesis of LV	−	+	−
12	45	M	MERRF	Normal	Normal	Normal	−	+	−
13	12	M	MELAS	Normal	Normal	Normal	−	−	+
14	15	M	MELAS	VPC	Normal	Normal	−	−	+
15	15	M	MELAS	WPW syndrome	Cardiomegaly	LVH (symmetrical)	−	−	+
16	48	F	MELAS	ST dep, inverted T	Normal	Normal	−	−	+
17	54	F	MELAS	APC	Normal	LVH (symmetrical) Diffuse hypokinesis of LV	−	−	+

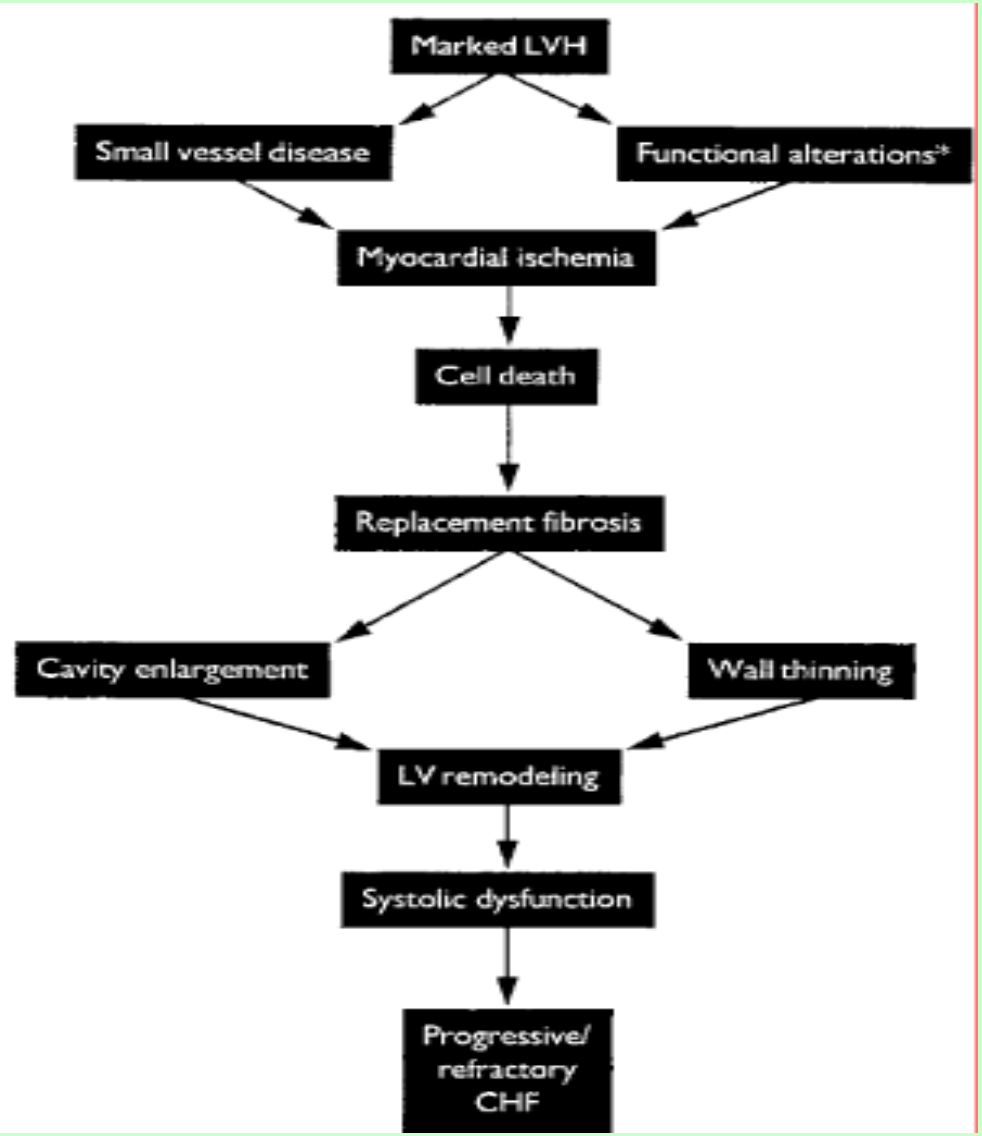
Cause of Death

1. Sudden cardiac death
2. CHF:
   - LVOT obstruction
   - DCMP

Conversion into DCMP:

- burned phase of HCM:10%
- LV remodeling

Pathogenesis of the end-stage phase of HCM



Potential Risk Factors for SCD in HCM

History of SCD
Family history of Premature death
"Malignant" causal mutations
"Malignant" modifier genes
History of syncope
Magnitude of LVH: 30 mm이상
Extent of myocyte disarray
Extent of interstitial fibrosis
Early onset of the disease
Myocardial ischemia on perfusion tomography
Abnormal BP response to exercise
Presence of nonsustained VT on Halter

Progressive Left Ventricular Remodeling in Patients With Hypertrophic Cardiomyopathy and Severe Left Ventricular Hypertrophy

Rajesh Thaman et al. J Am Coll Cardiol 2004;

Left ventricular remodeling is common in patients with severe LVH and contributes to the low prevalence of severe LVH seen in middle age and beyond.

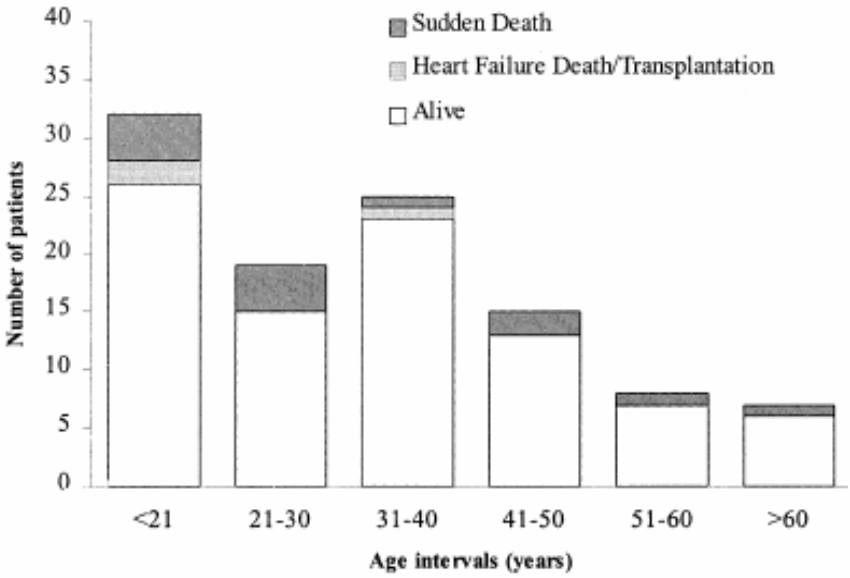


Table 2. Changes in Echocardiographic Measurements During Follow-Up

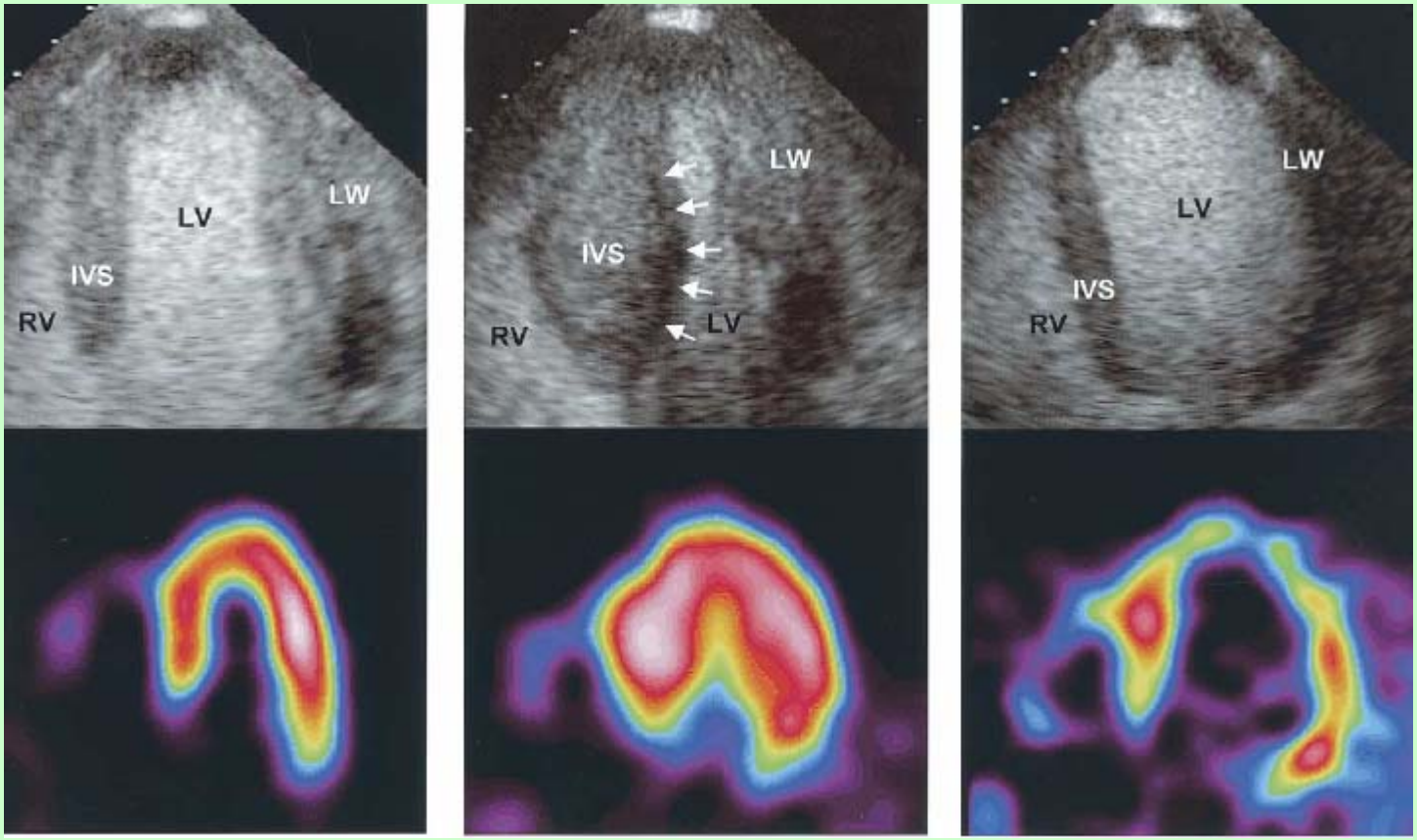
	Mean ± SD	95% CI Lower	95% CI Upper	p Value*
LVEDD (mm)	5.5 ± 6.6	7.1	4.0	<0.00001
LVESD (mm)	5.0 ± 6.8	6.6	3.4	<0.00001
FS (%)	−3.9 ± 11.9	−1.1	−6.7	0.008
LAD (mm)	4.3 ± 6.5	5.8	2.7	<0.00001
MLVWT (mm)	−5.2 ± 4.4	−4.1	−6.2	<0.00001
Mitral valve				
Anterior septum	−3.8 ± 4.5	−2.7	−4.8	<0.00001
Posterior septum	−2.6 ± 4.6	−1.5	−3.7	0.00002
Posterior wall	−0.5 ± 2.8	0.2	−1.2	0.1
Lateral wall	−1.2 ± 2.8	−0.5	−2.0	0.002
Papillary muscle				
Anterior septum	−4.4 ± 4.5	−3.3	−5.5	<0.00001
Posterior septum	−2.9 ± 4.3	−1.8	−4.0	<0.00001
Posterior wall	−0.2 ± 2.7	0.5	−0.8	0.6
Lateral wall	−1.1 ± 3.2	−0.3	−2.0	0.01
Apex				
Anterior wall	−1.5 ± 3.8	−0.5	−2.6	0.005
Posterior wall	−0.4 ± 2.1	0.2	−1.0	0.2

*Two-tailed.

CI = confidence interval; other abbreviations as in Table 1.

Microvascular function by MCE: small vessel disease

Intravenous MCE and Horizontal perfusion images using thallium-201 scintigraphy: Inoue K, AJC 2004



control subject nonobstructive HCM HCM-HF

Coronary flow: CFR, CVR

Coronary Hemodynamics in Patients With Symptomatic Hypertrophic Cardiomyopathy

Eric H. Yang et al

Am J Cardiol 2004;94:685–687

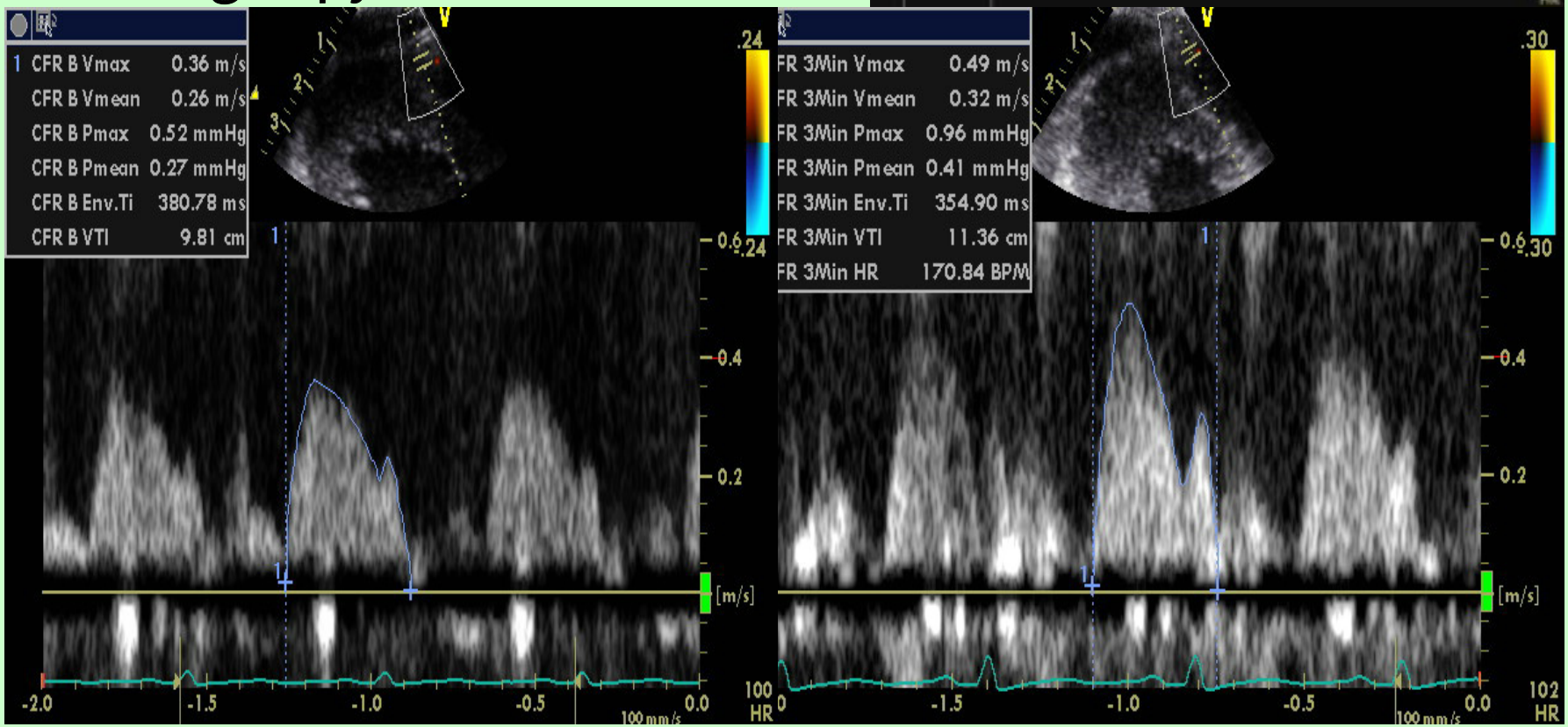
Using Doppler guidewire
CFR: IC adenosine and Ach

TABLE 2 Coronary Flow Velocity Recordings in Patients With Symptomatic Hypertrophic Cardiomyopathy and in Controls

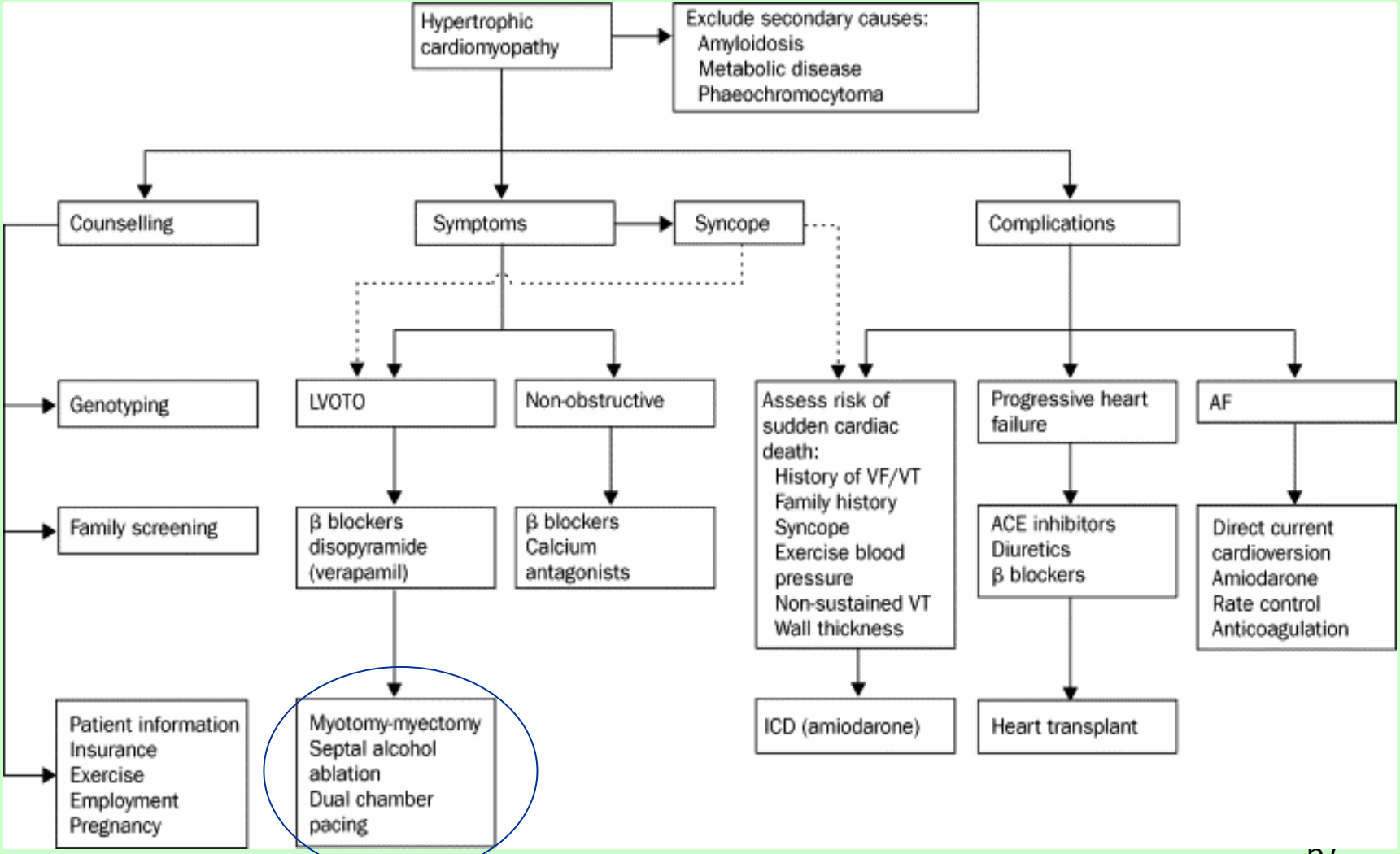
	Patients	Controls	p Value
Age (yrs)	53 ± 17	53 ± 14	NS
Heart rate (beats/min)	63 ± 11	74 ± 9	NS
Mean aortic pressure (mm Hg)	96 ± 16	95 ± 12	NS
Average peak systolic velocity (cm/s)	6 ± 4	13 ± 5	0.03
Average peak diastolic velocity (cm/s)	34 ± 12	24 ± 5	NS
Diastolic to systolic velocity ratio	5.7 ± 3	1.8 ± 5	0.03
Systolic velocity time integral (cm)	−2.2 ± 5.3	4.0 ± 1.1	0.01
Diastolic velocity time integral (cm)	26.3 ± 14.8	12.2 ± 3.9	0.003
Total velocity time integral (cm)	24.1 ± 14.7	16.2 ± 4.0	NS
Coronary diameter (mm)	3.1 ± 0.4	2.6 ± 0.3	0.02
Coronary blood flow (ml/min)	52 ± 19	33 ± 11	0.03
Coronary resistance (mm Hg/ml/min)	2.12 ± 0.91	3.13 ± 0.93	0.05
Coronary flow reserve	2.1 ± 0.7	3.4 ± 1.0	0.02
Diastolic deceleration rate (cm/s^2)	40.7 ± 13.2	27.5 ± 8.5	0.03

Transthoracic Doppler of distal LAD

Coronary Flow Reserve Using Dipyridamole



Management for HCM



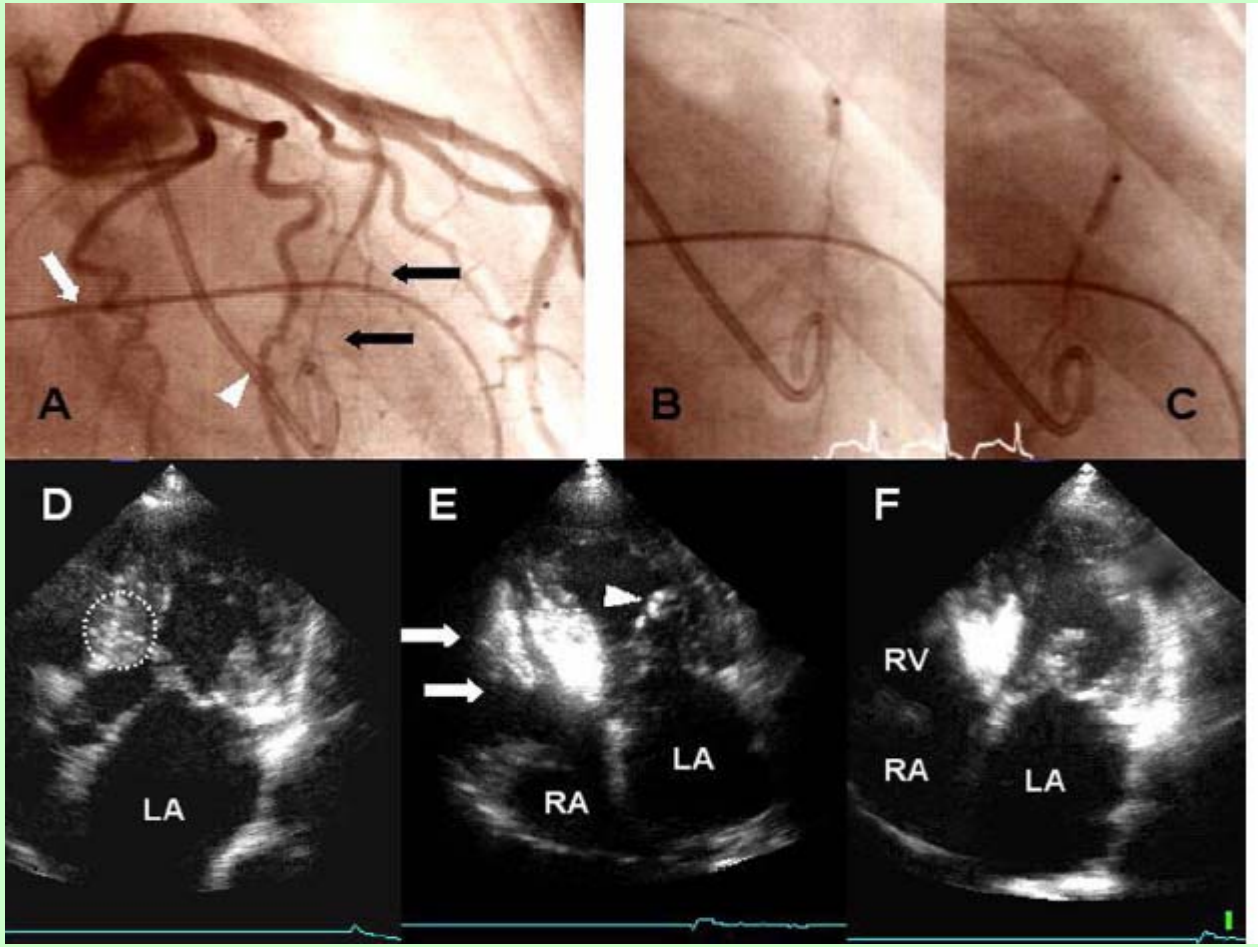
Echo-guided percutaneous septal ablation

Tx strategies

1. Medical therapy
2. Reduction of myocardial septum
   : Systolic PG at Rest ≥ 50mmHg
   after provocation≥ 100mmHg
3. Implantation of ICD

Test injection of echocontrast agents

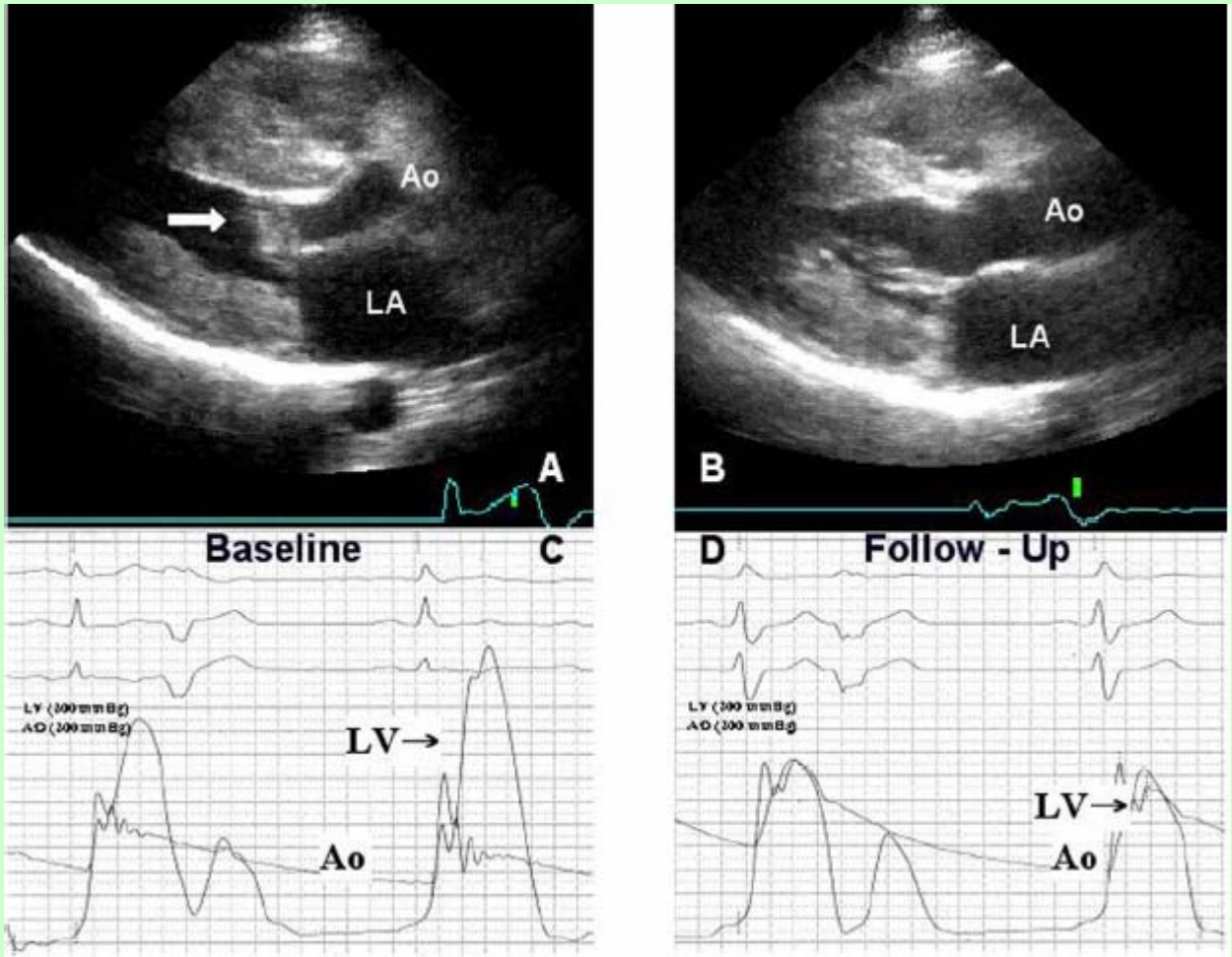
Before ethanol injection in septal branch



Septal perforator prox
Contrast injection

Septal perforator subdiv
Contrast injection

Optimal morphologic and hemodynamic results of PTSMA



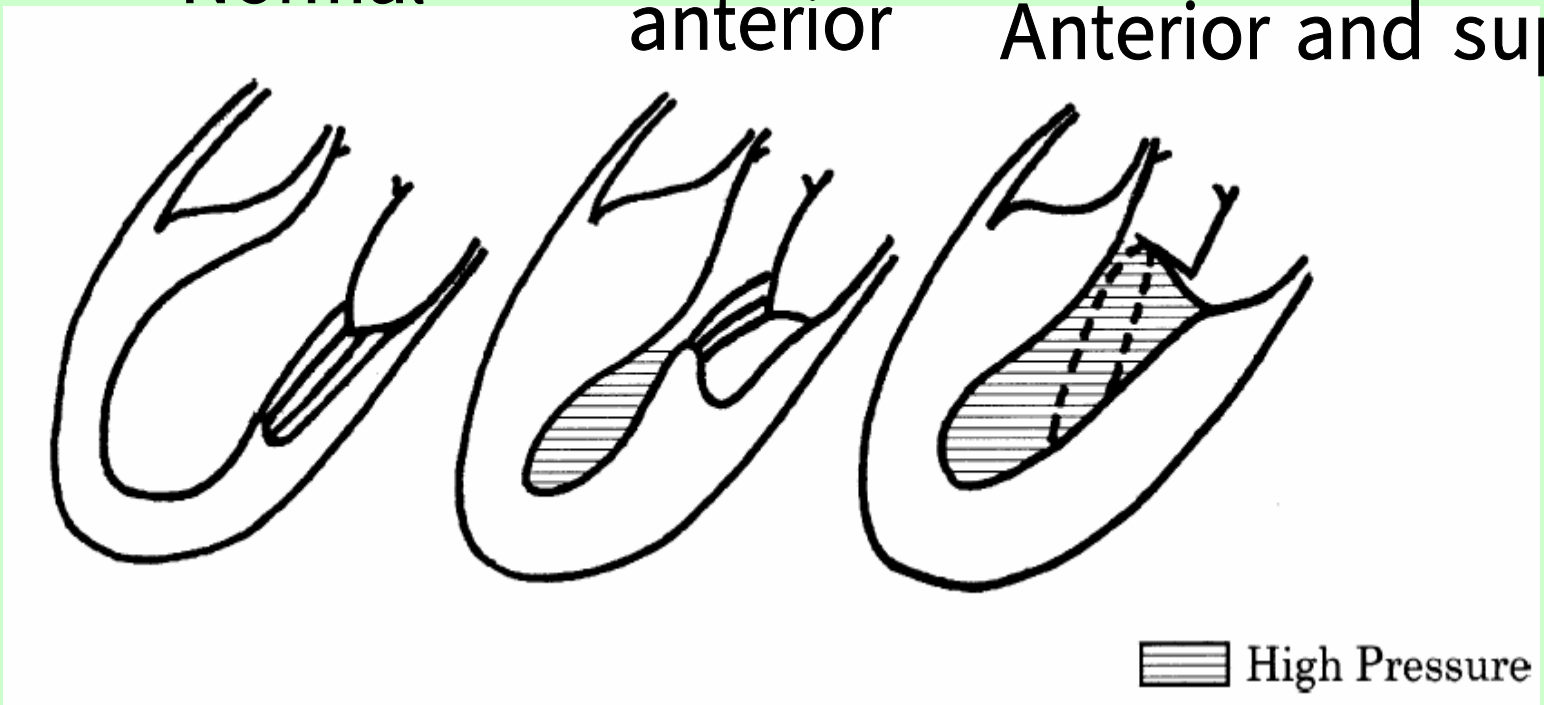
Classification of SAM

By Nagata S et al. Br Heart J 1983

Normal

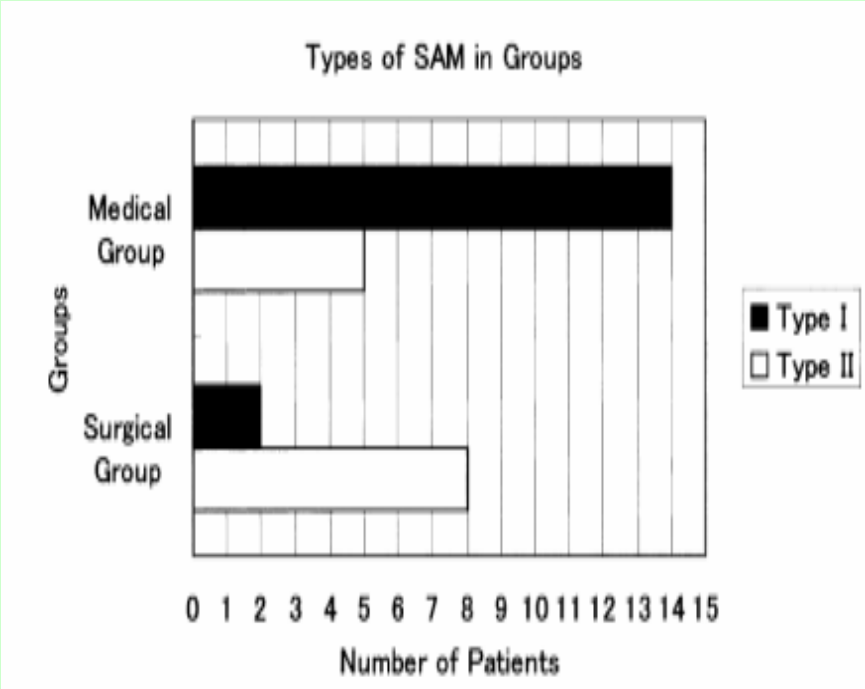
Type I: anterior

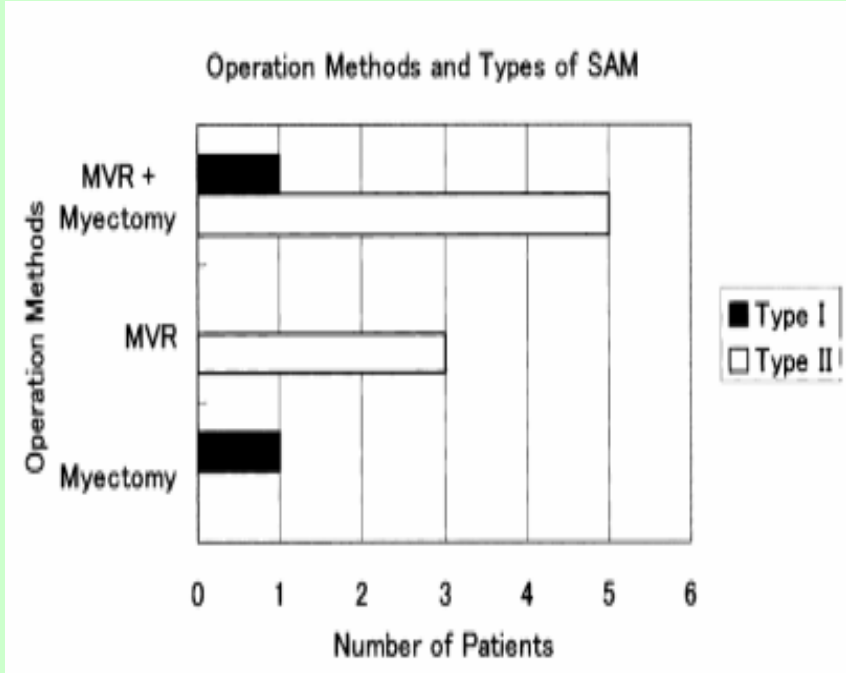
Type II: Anterior and superior



Characteristics of HOCM refractory to Medical treatment and Selection of Surgical Methods

By Hirasawa Y, J Card Surg 2005

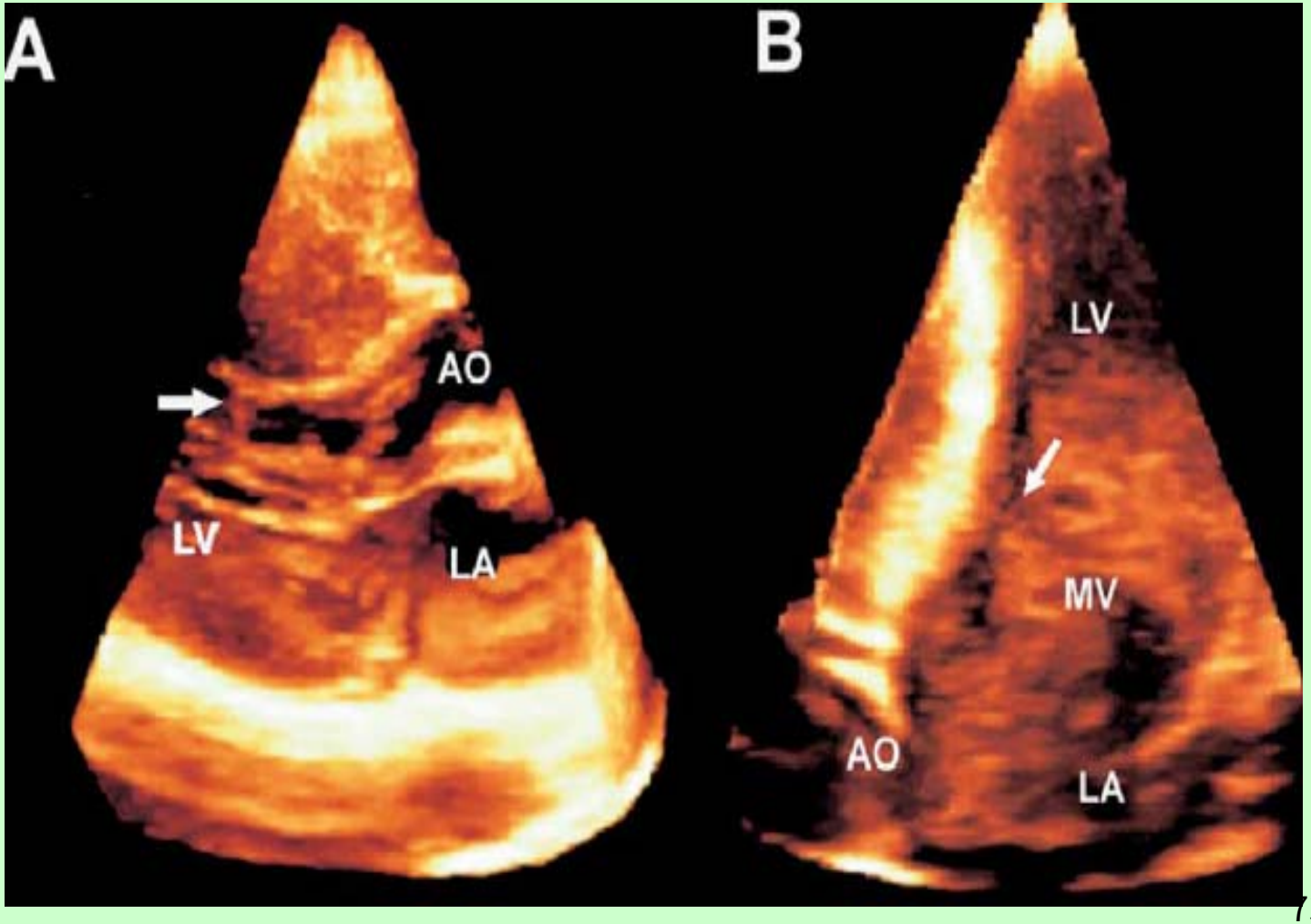




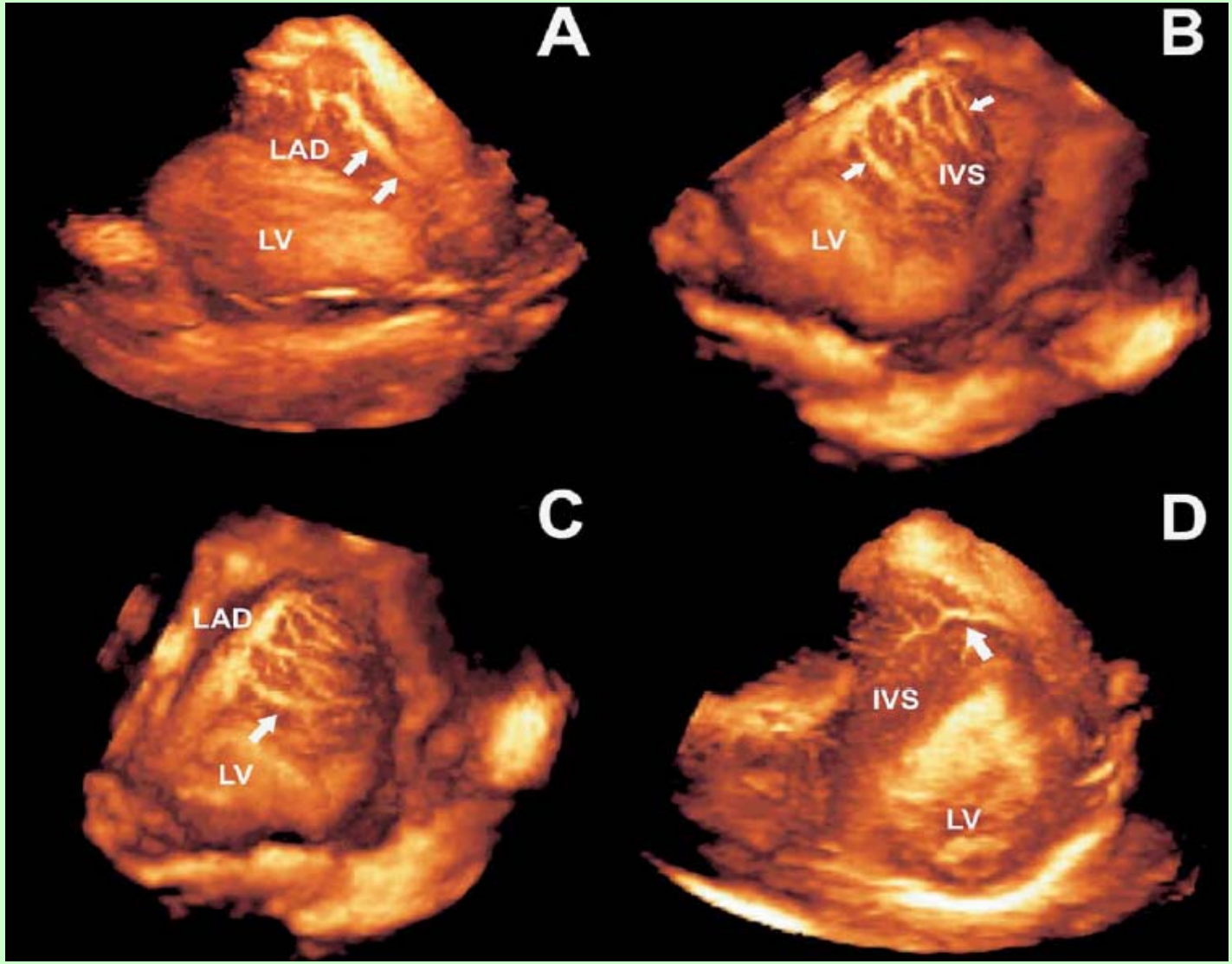
RT-3D with Contrast echo(perflurocarbon)

Parasternal

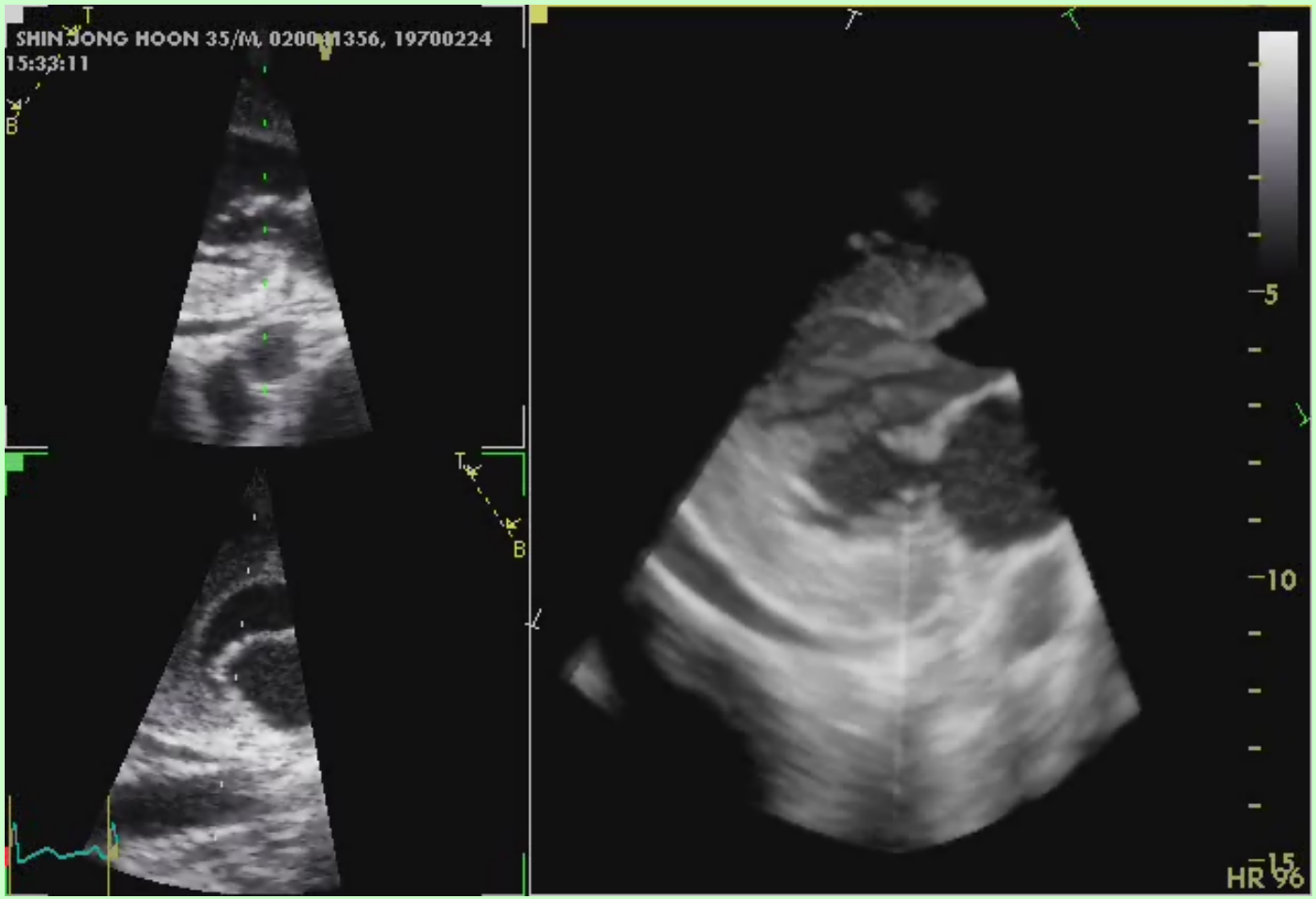
Apical



LAD and septal perforator



3D - RT: parasternal view



3D-RT: parasternal short axis view