CARDIOMIOPATIE

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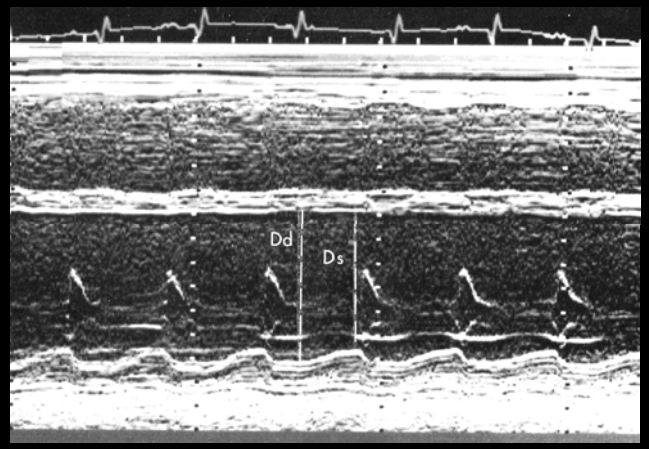
Cardiomyopathy WHO terminology and definitions: 1980 vs 1995

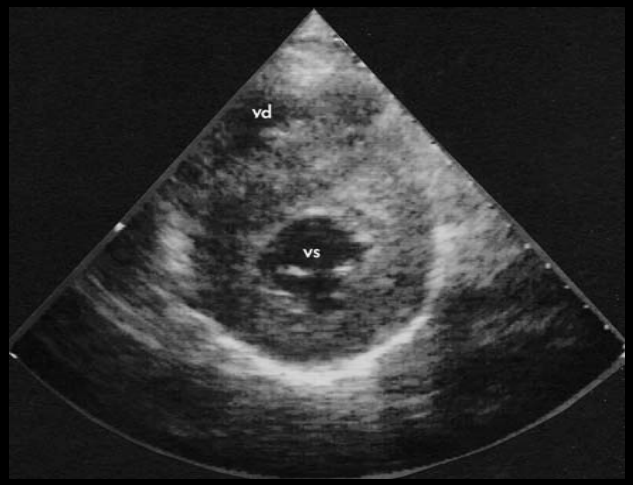
1980	1995
Cardiomyopathy: Heart muscle disease of unknown cause	**Cardiomyopathy:** Disease of the myocardium associated with cardiac dysfunction
Specific heart muscle disease: Heart muscle disease of known cause or associated with disorders of other system	**Specific (secondary) cardiomyopathy:** Heart muscle disease associated with specific cardiac or systemic disorders

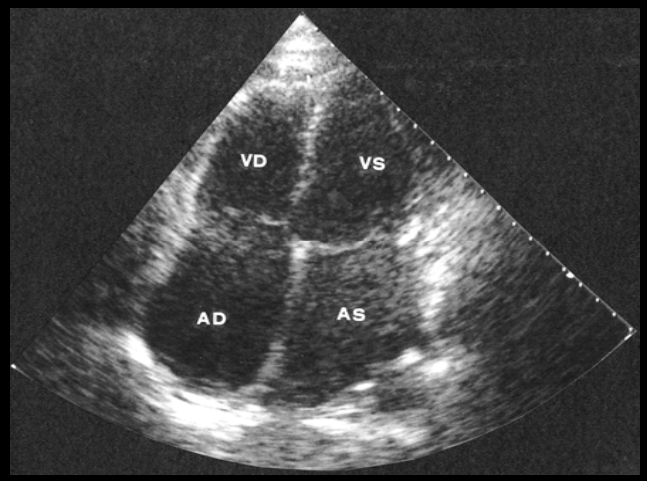
Cardiomyopathy WHO classifications: 1980 vs 1995

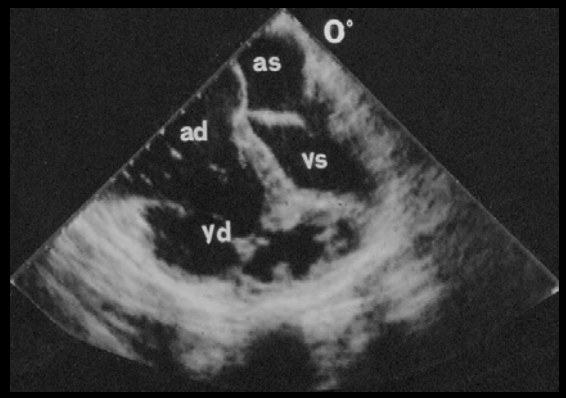
1980	1995
• Dilated	• Dilated
• Hypertrophic	• Hypertrophyc
• Restrictive	• Restrictive
	• Arrhythmogenic right ventricular

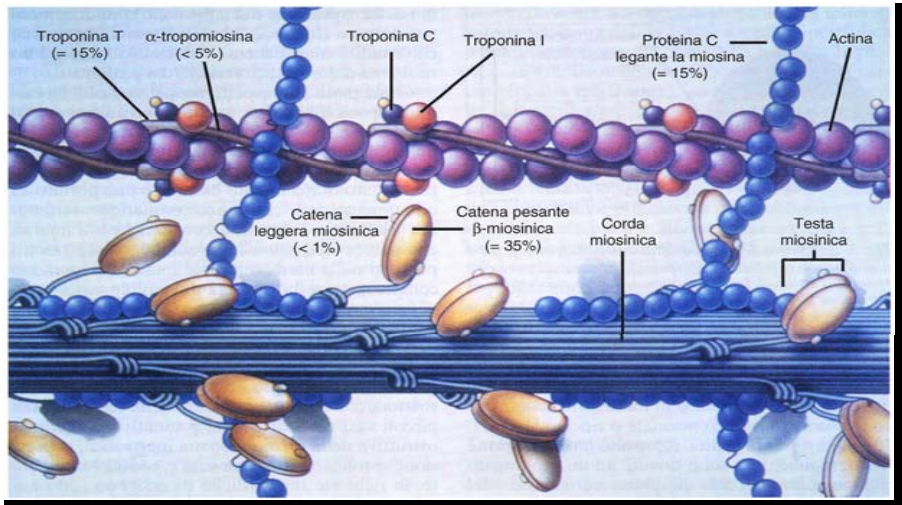
CARDIOMIOPATIE



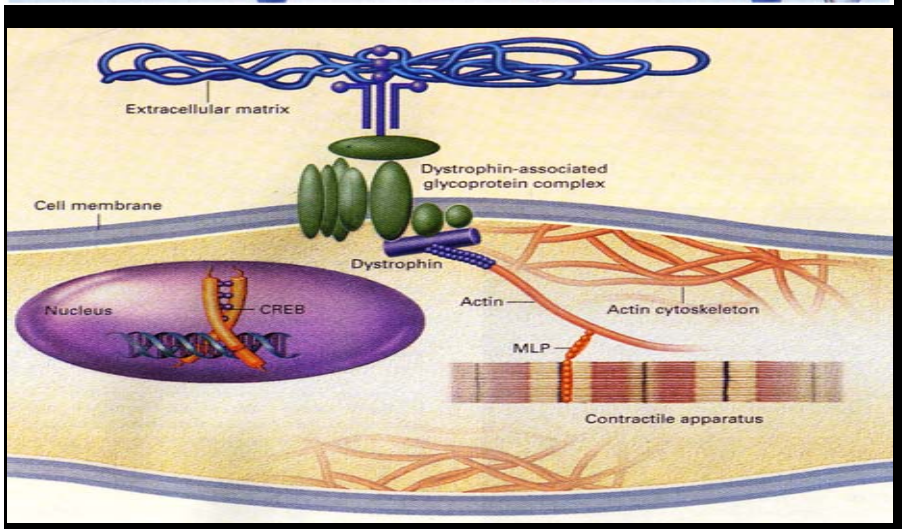




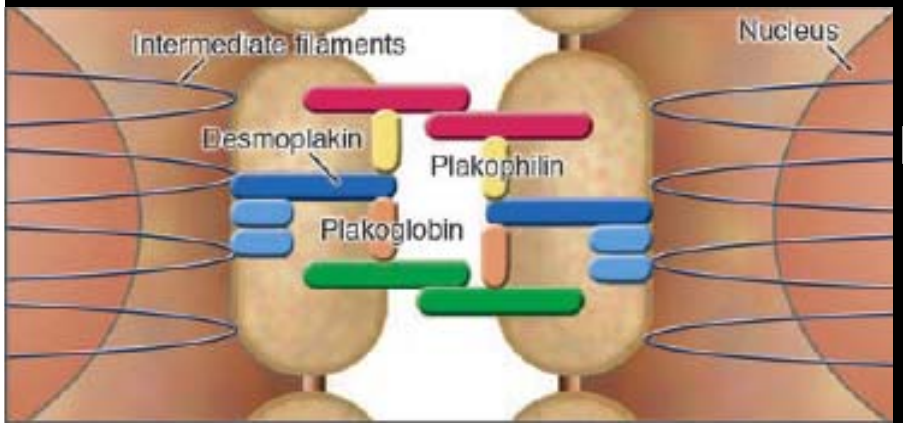




Mutazioni geni per le proteine DEL SARCOMERO → **CMPI**

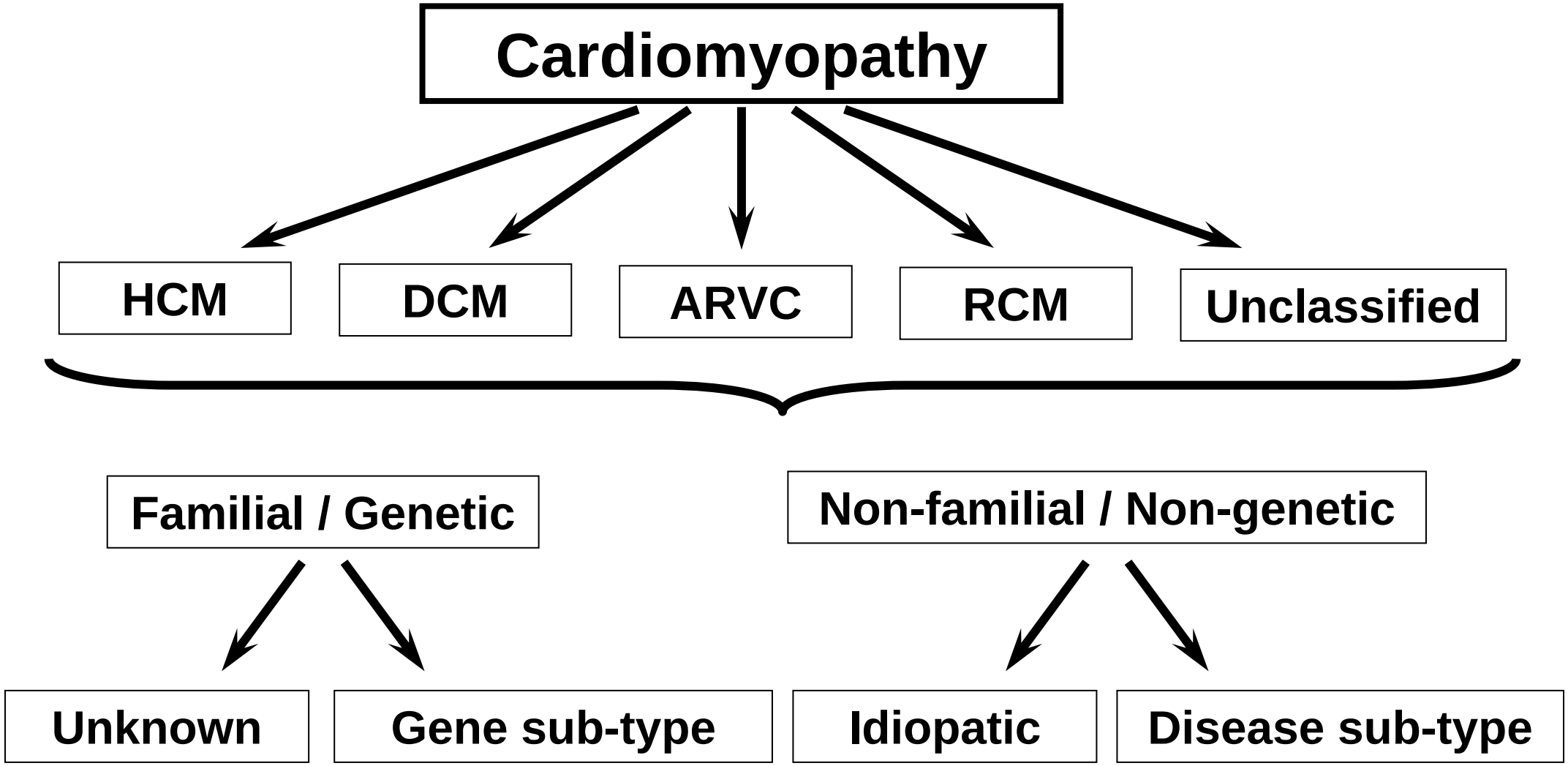


Mutazioni geni per le proteine DEL CITOSCHELETRO → **CMPD**

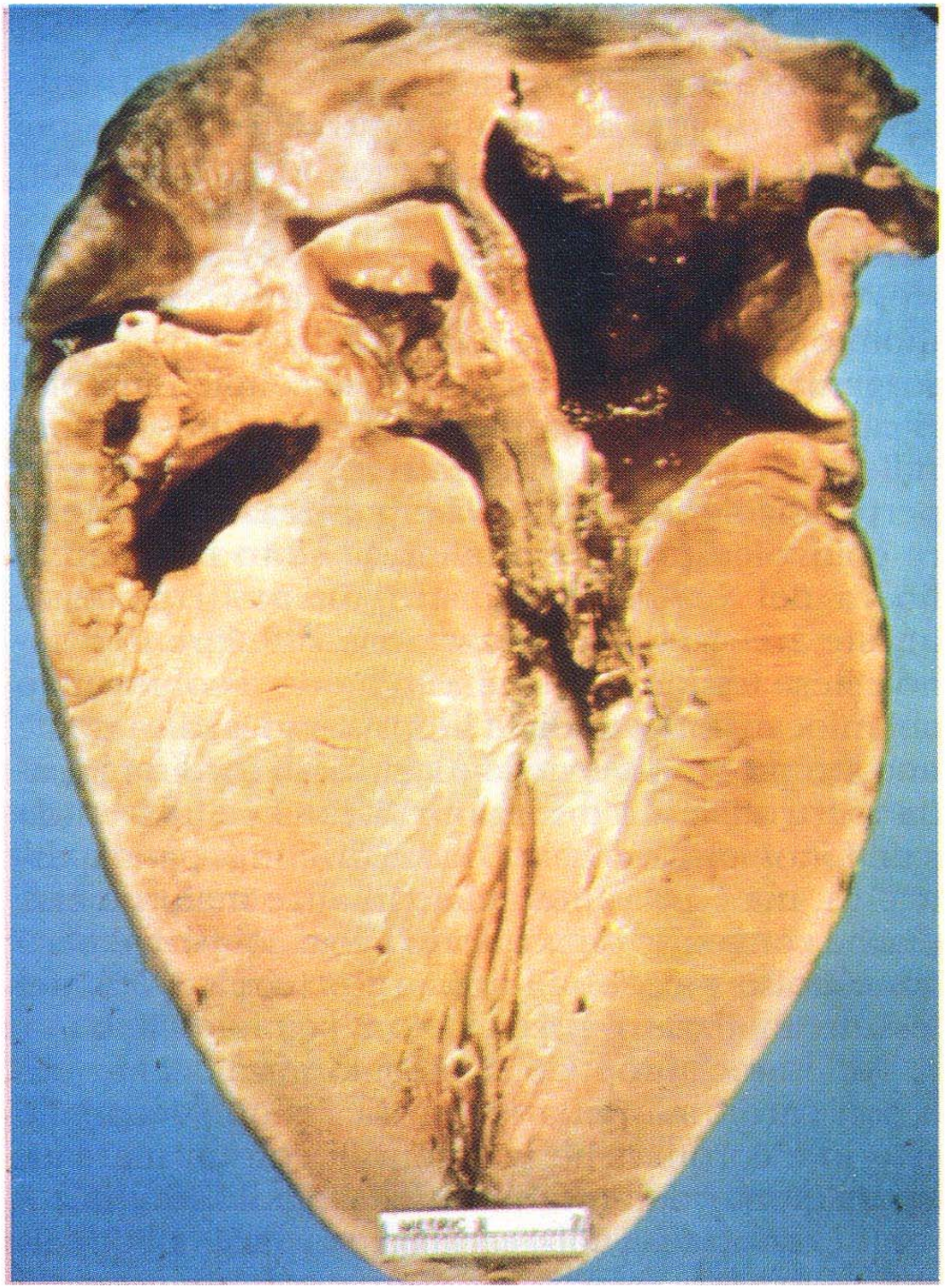


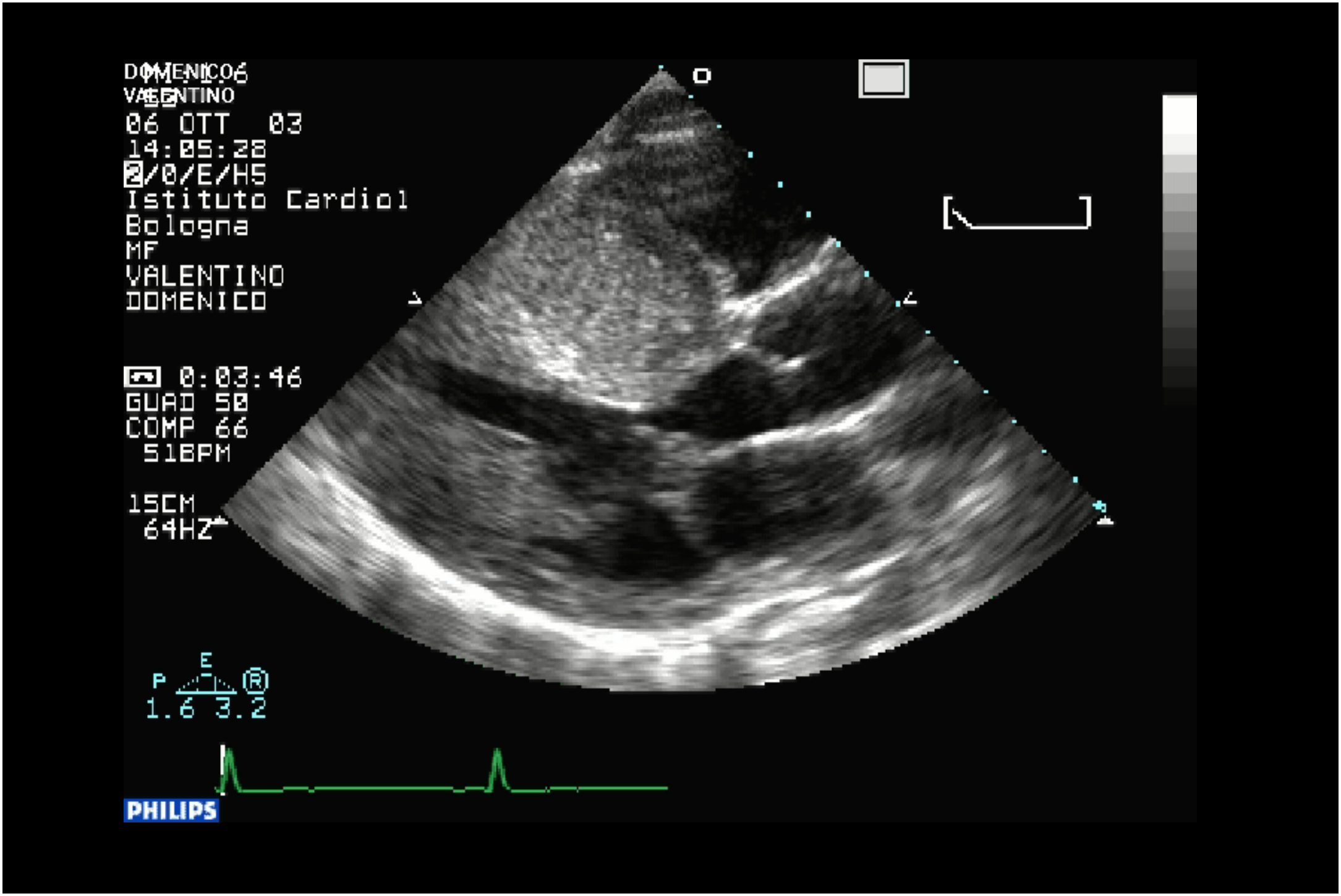
Mutazioni geni per le proteine DEI DESMOSOMI → **CMP VDx**

Summary of classification ESC WG 2007



CARDIOMIOPATIA IPERTROFICA

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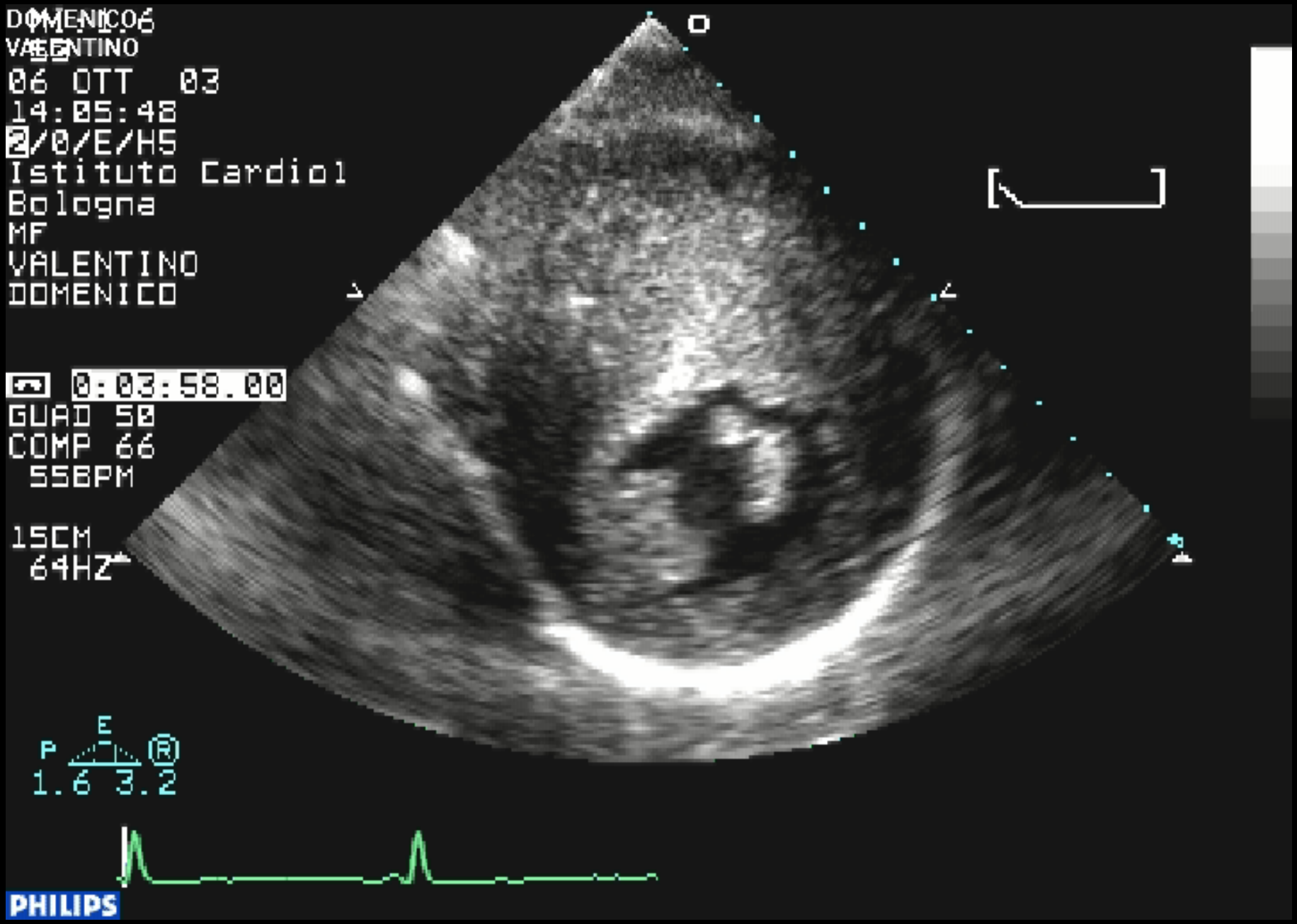
06 OTT 03
14:05:28
2/0/E/H5
Istituto Cardiol
Bologna
MF
VALENTINO
DOMENICO
0:03:46
GUAD 50
COMP 66
51BPM
15CM
64HZ
E
P
R
1.6 3.2
PHILIPS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Bologna
MF
VALENTINO
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E
P
R
1.6 3.2
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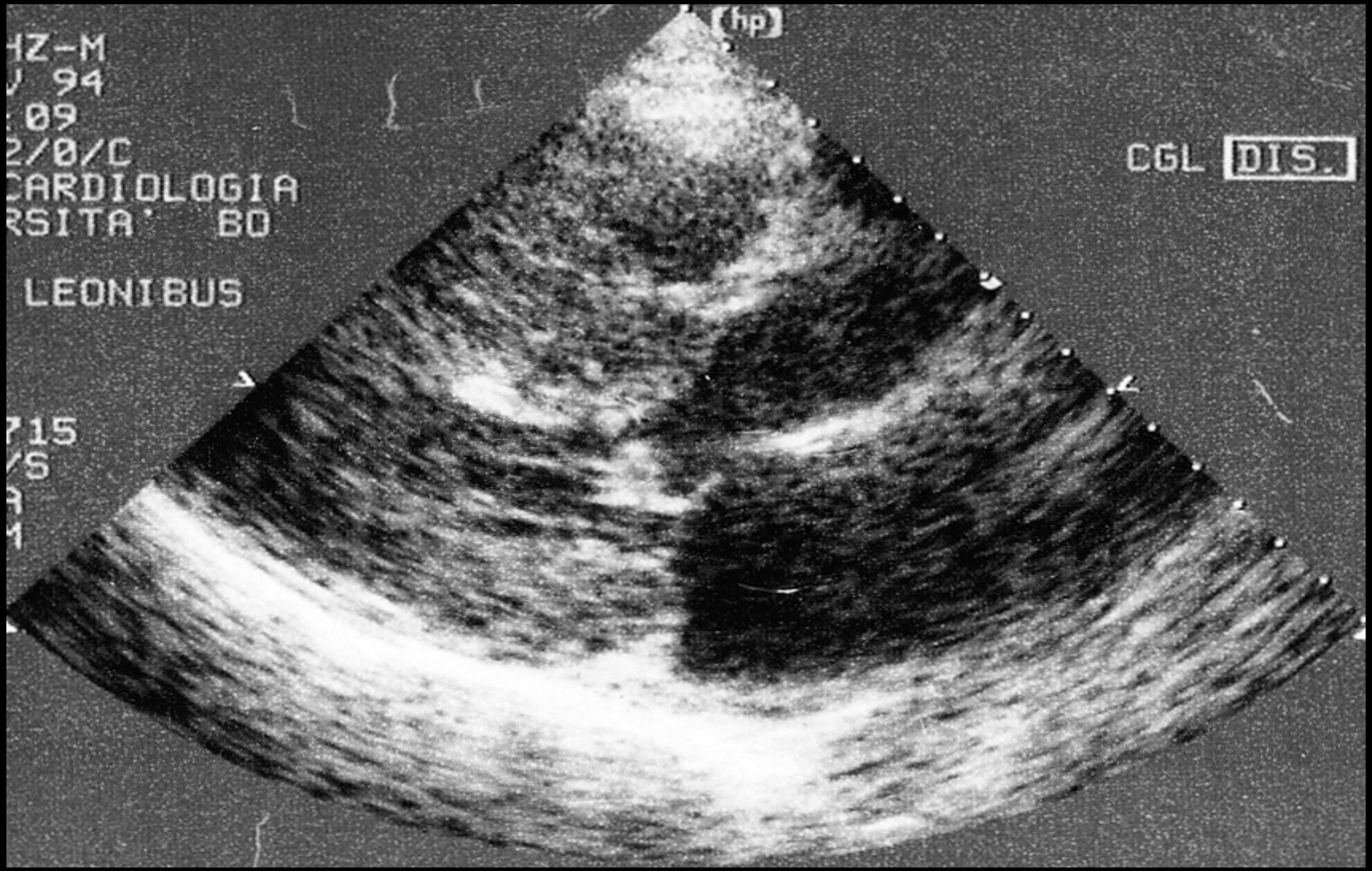
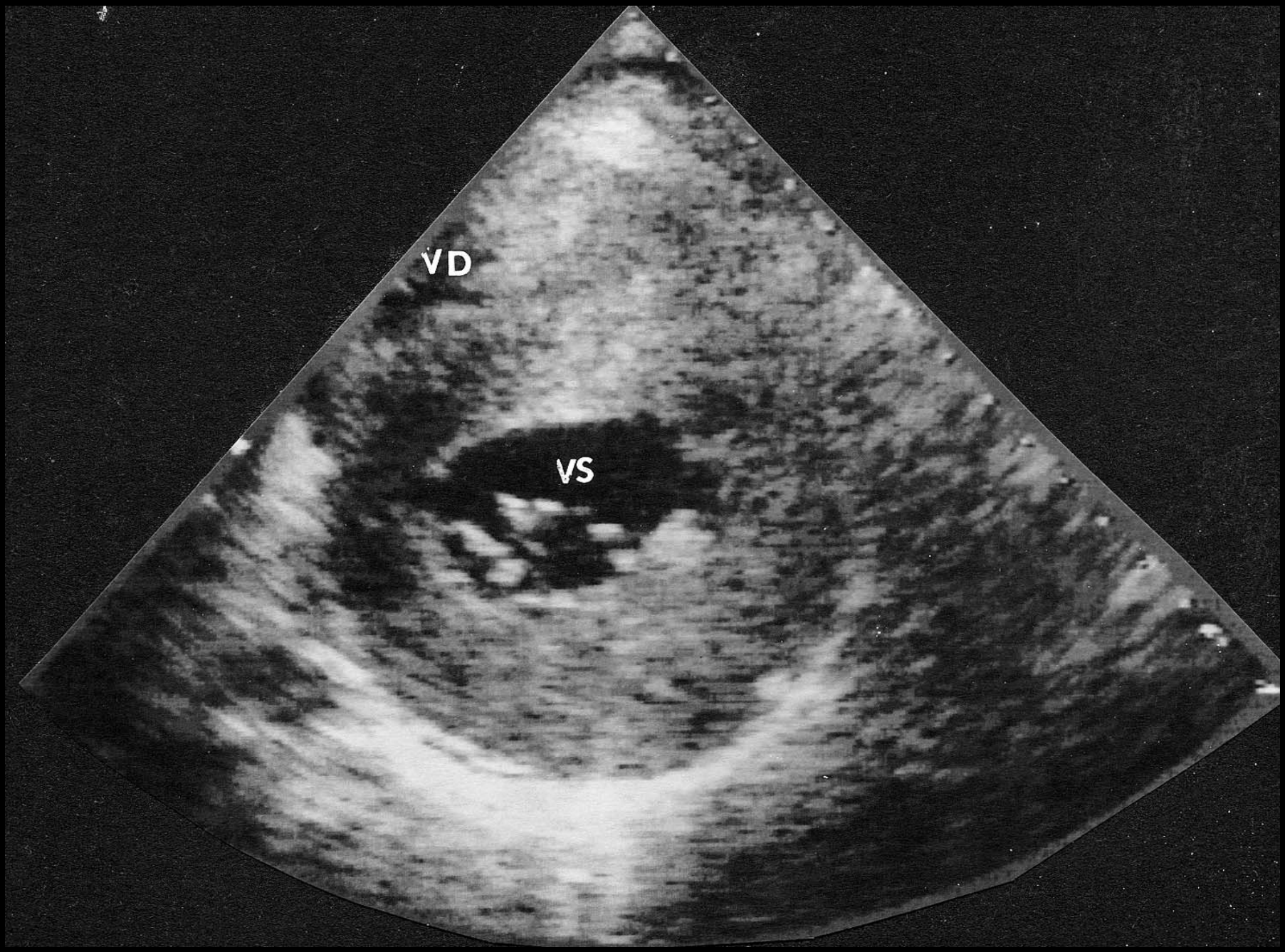
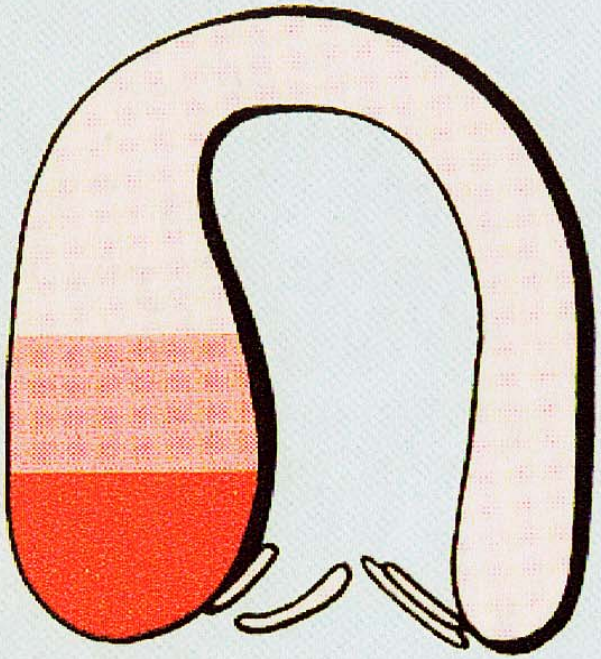
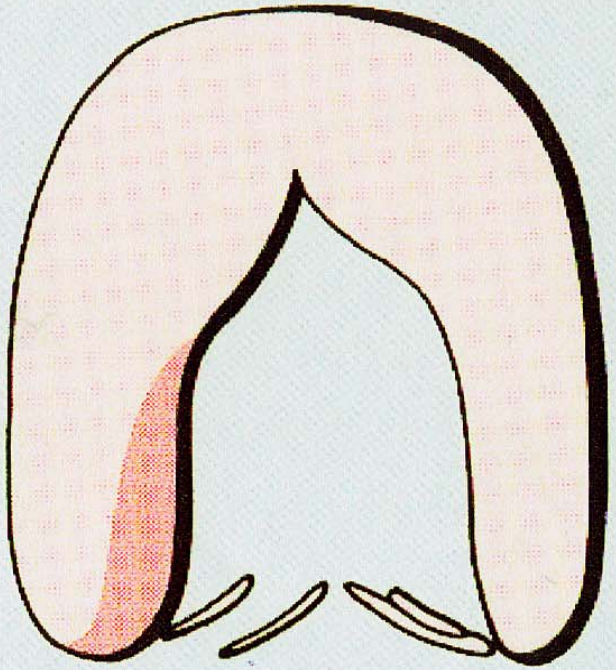

HZ-M
J 94
.09
2/0/C
CARDIOLOGIA
RSITA' BO
LEONIBUS
715
/S
hp
CGL
DIS.


VD
VS



Ipertrofia
settale



Ipertrofia
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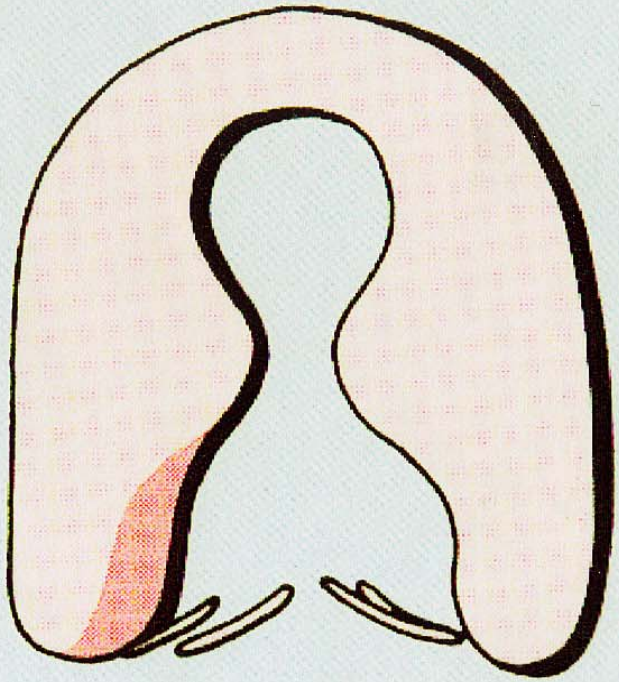

Ipertrofia
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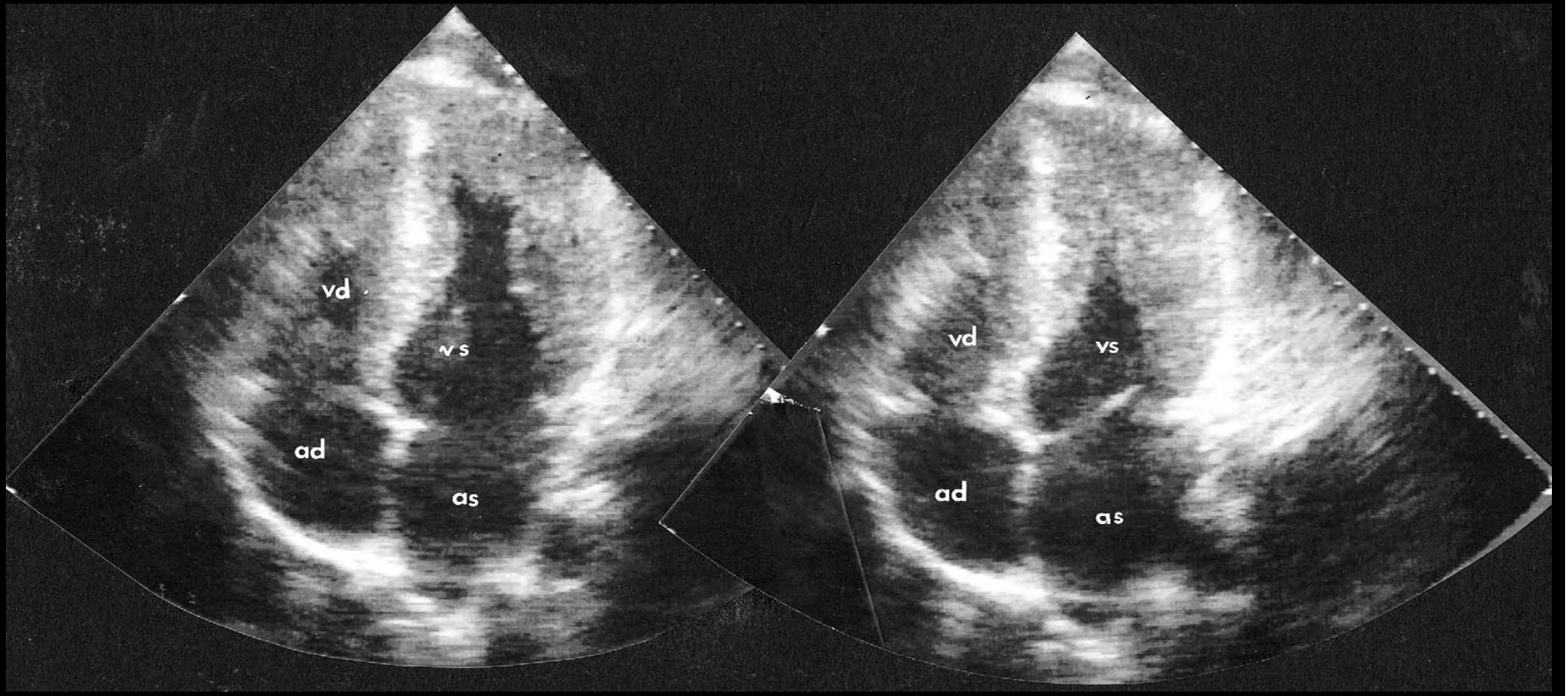
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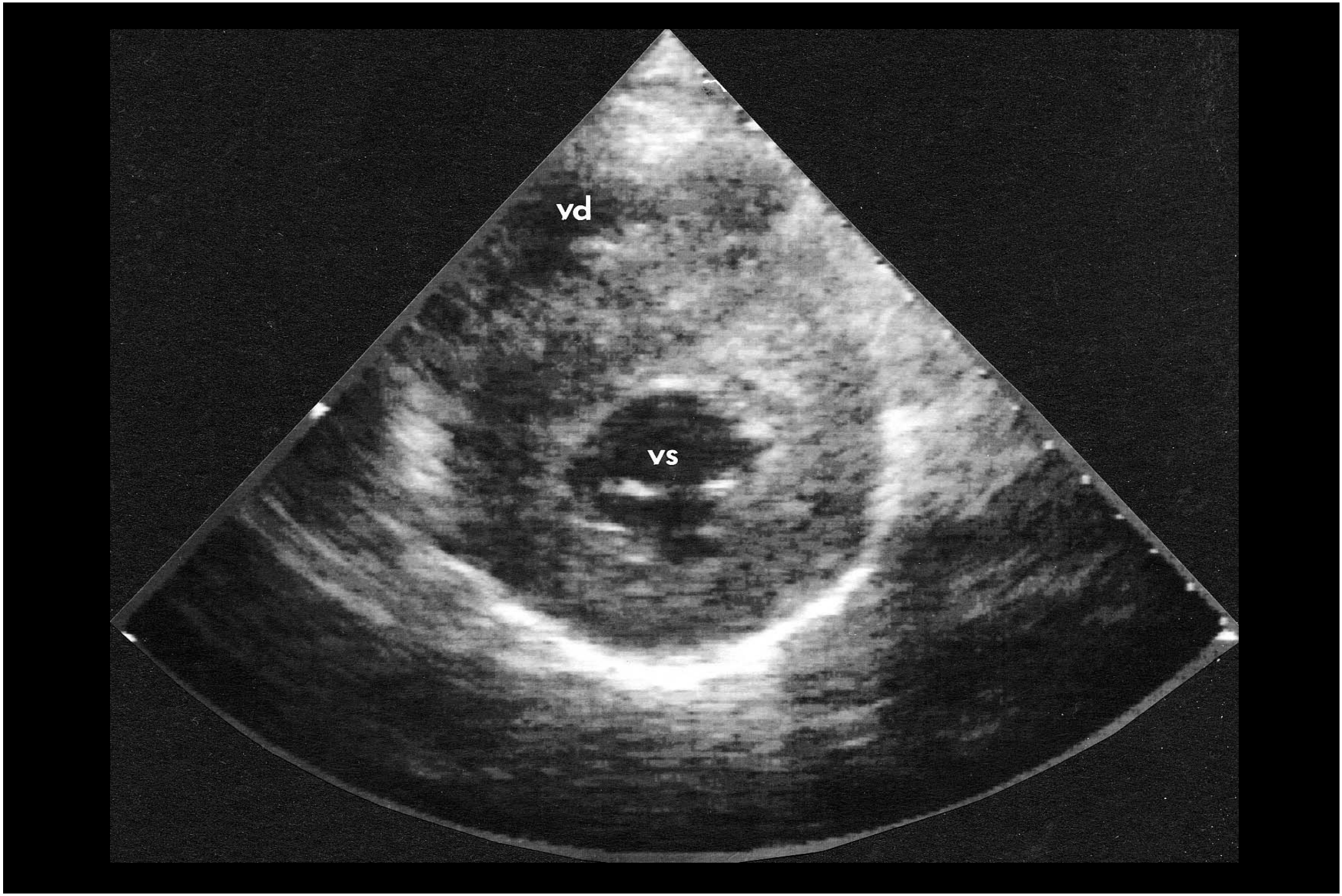
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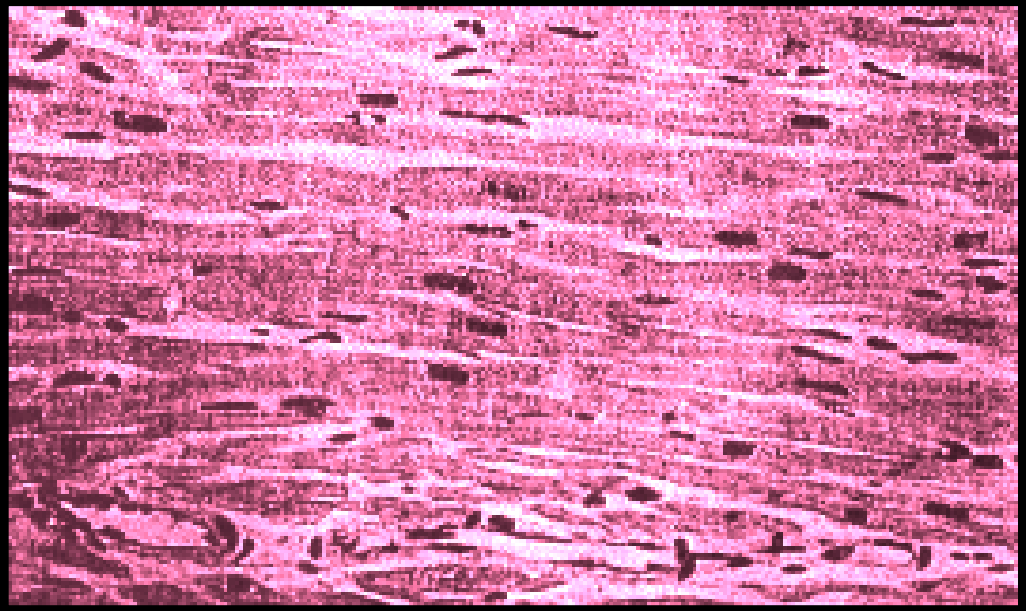
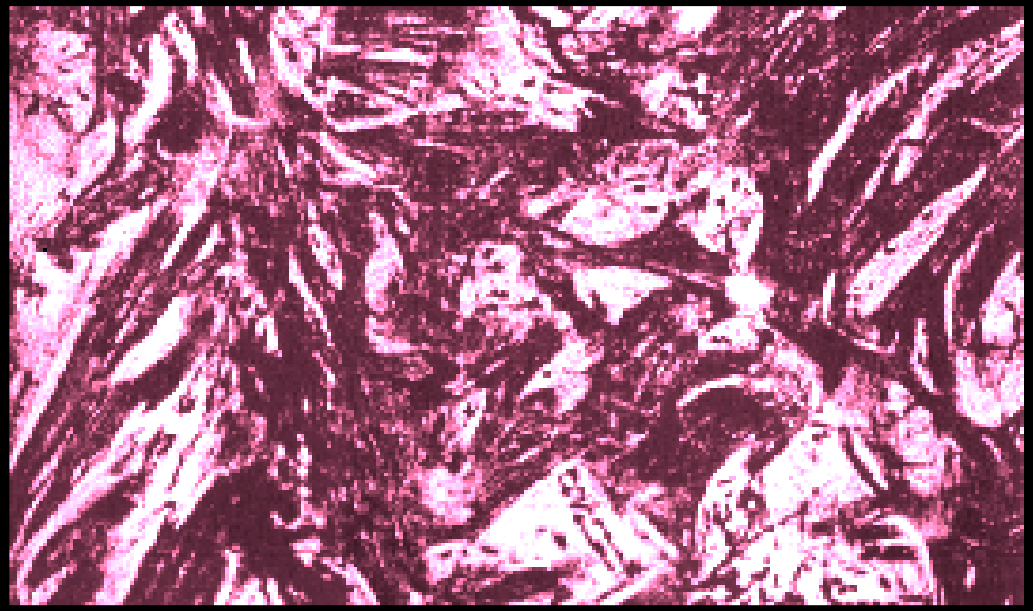
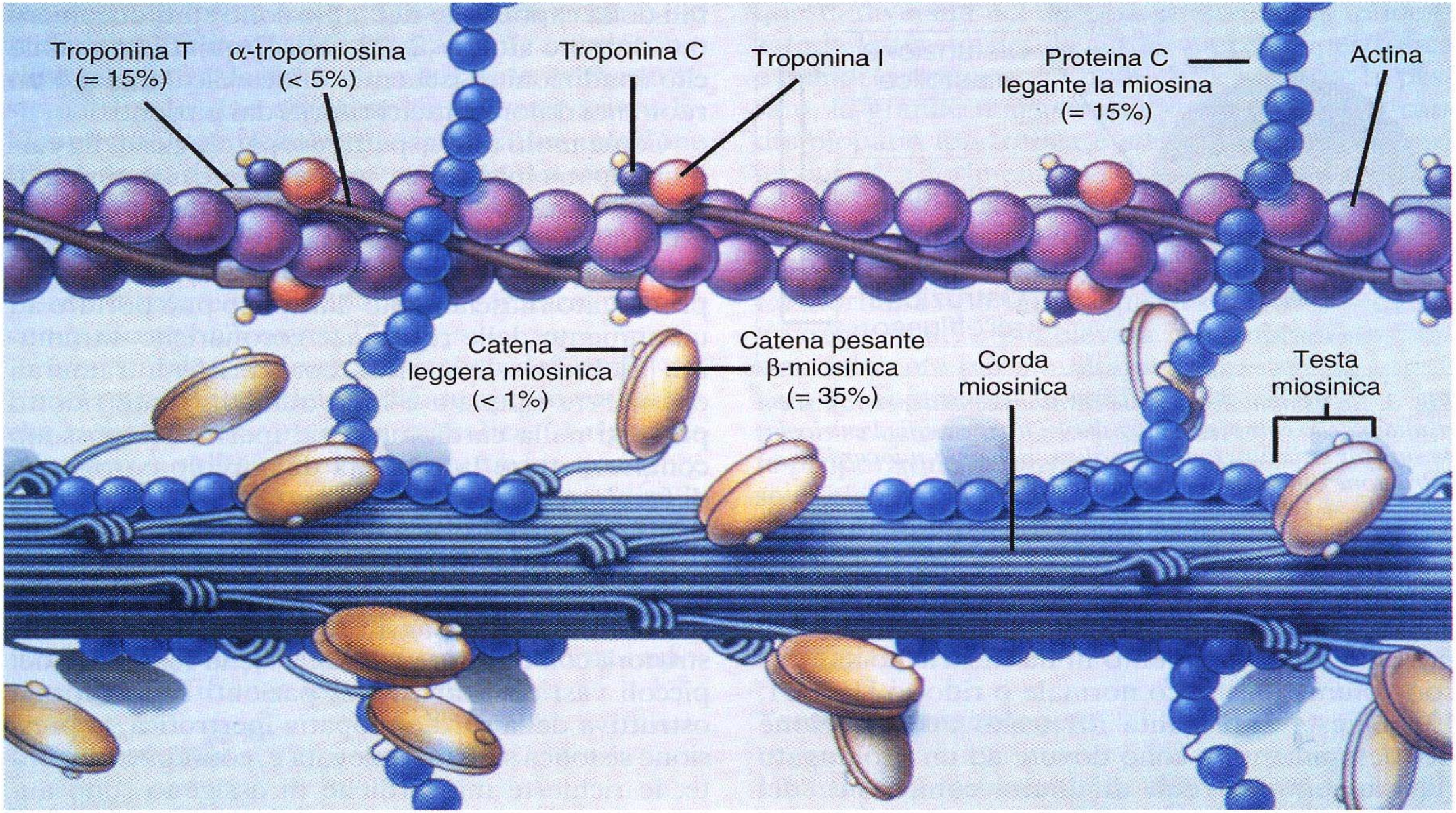
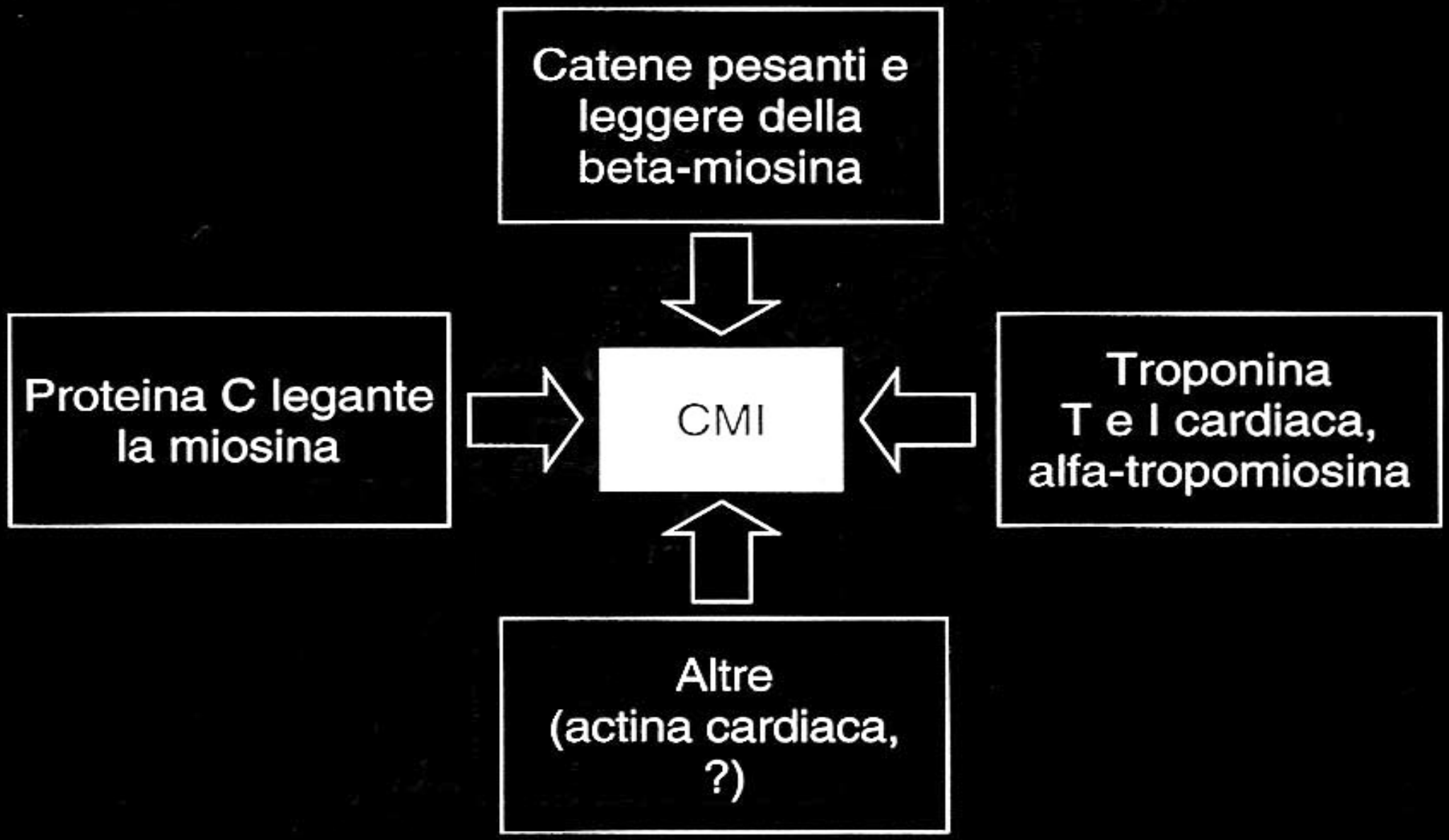


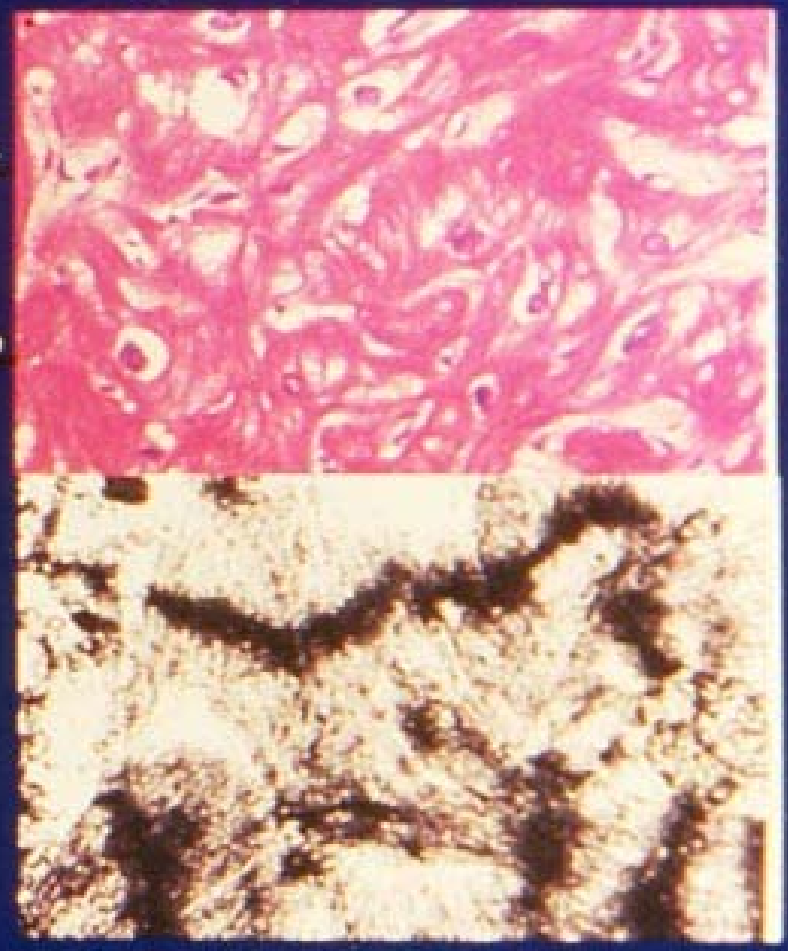


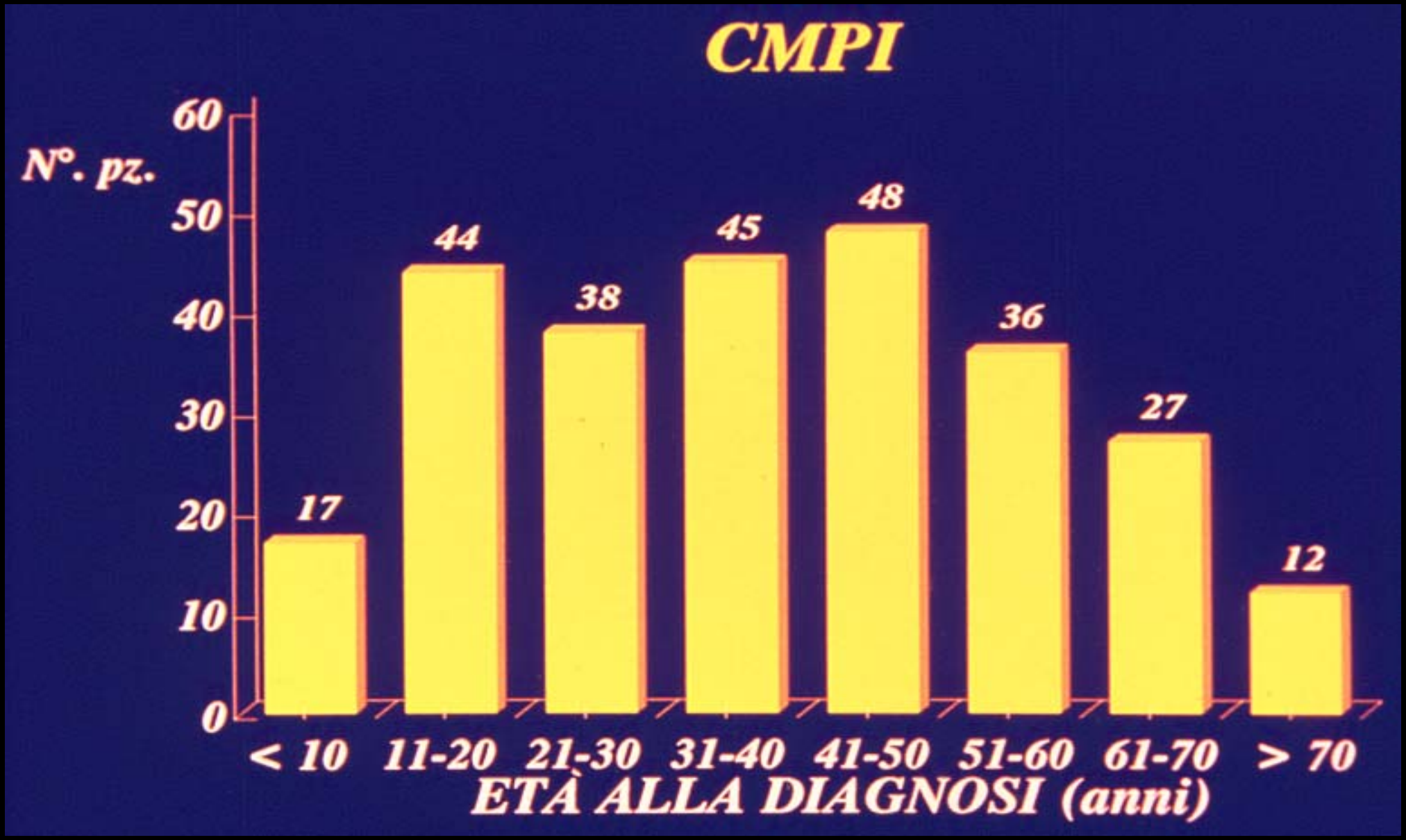

Troponina T
(= 15%)
α-tropomiosina
(< 5%)
Troponina C
Troponina I
Proteina C
legante la miosina
(= 15%)
Actina
Catena
leggera miosinica
(< 1%)
Catena pesante
β-miosinica
(= 35%)
Corda
miosinica
Testa
miosinica

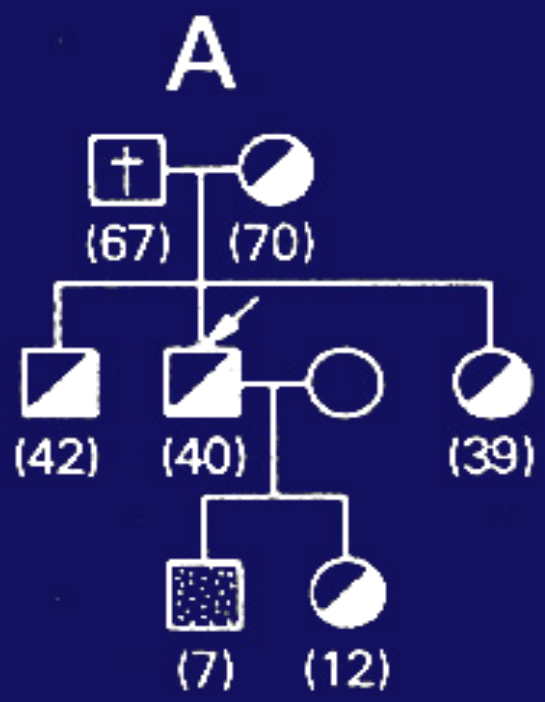
Cardiomiopatia ipertrofica

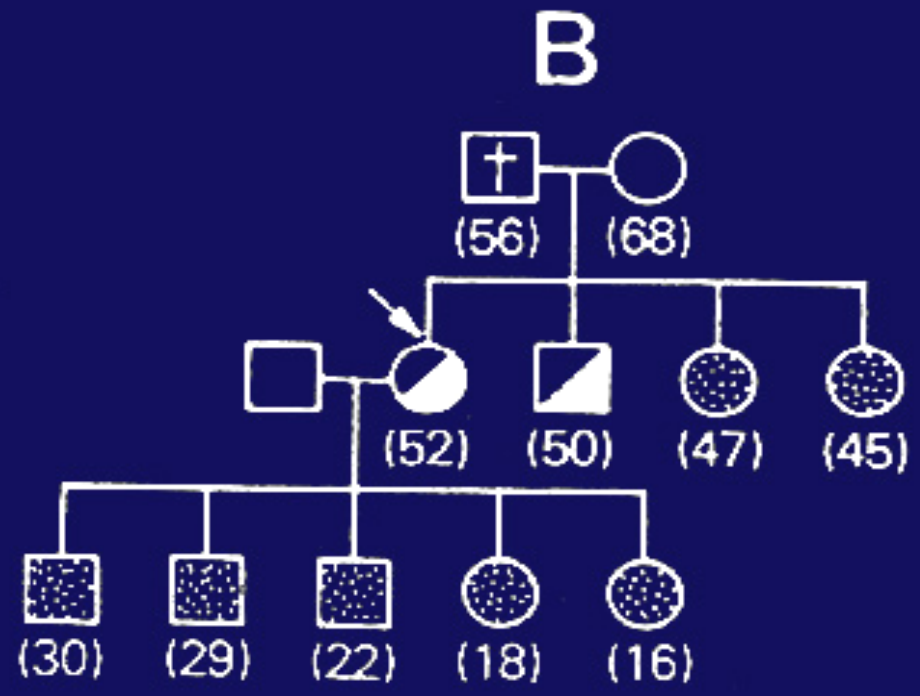


MUTAZIONE GENICA




CMPI
N°. pz.
60
50
40
30
20
10
0
17
44
38
45
48
36
27
12
< 10
11-20
21-30
31-40
41-50
51-60
61-70
> 70
ETÀ ALLA DIAGNOSI (anni)


A
(67)
(70)
(42)
(40)
(39)
(7)
(12)


B
(56)
(68)
(52)
(50)
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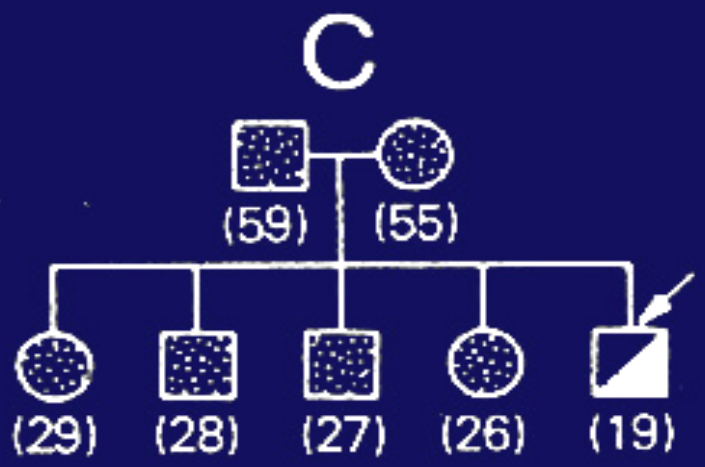
(30)
(29)
(22)
(18)
(16)


C
(59)
(55)
(29)
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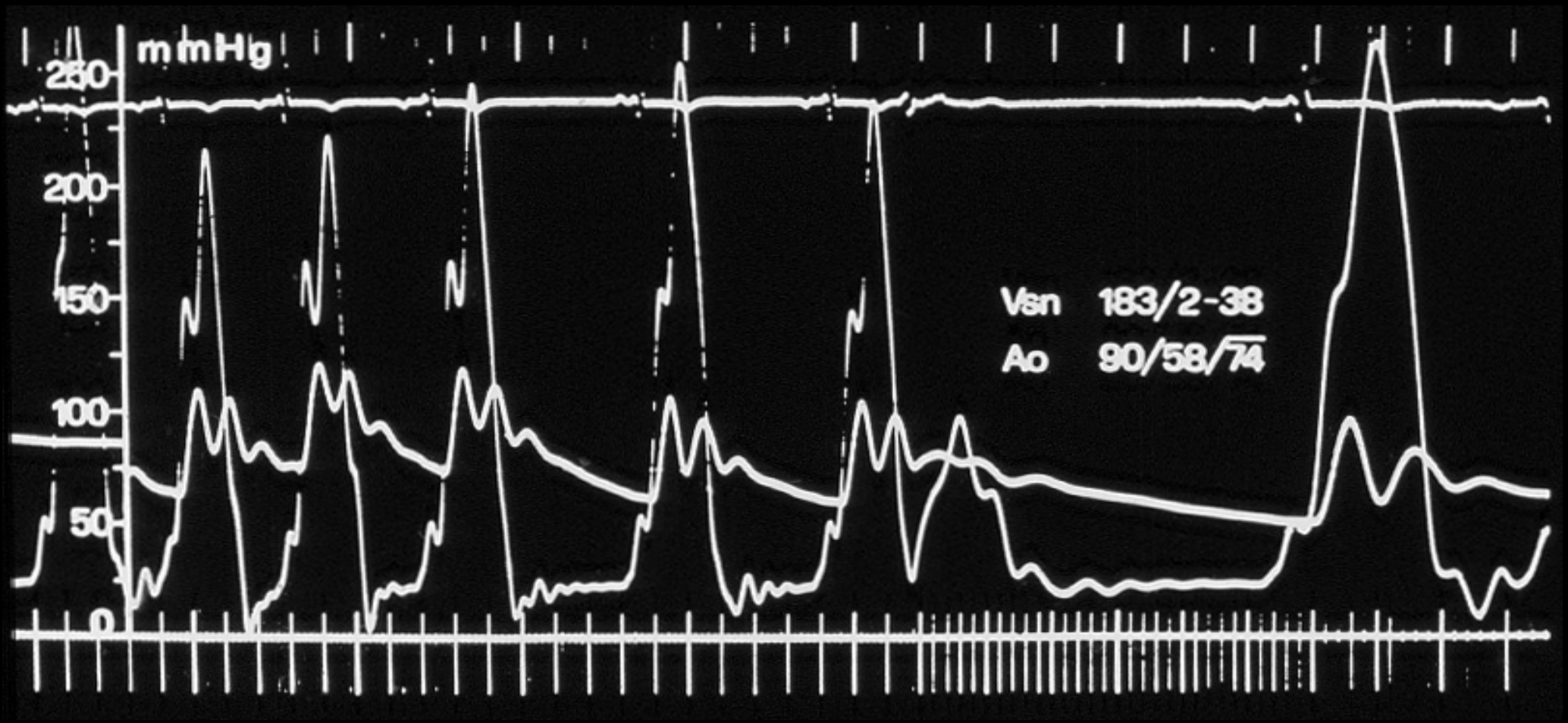
(27)
(26)
(19)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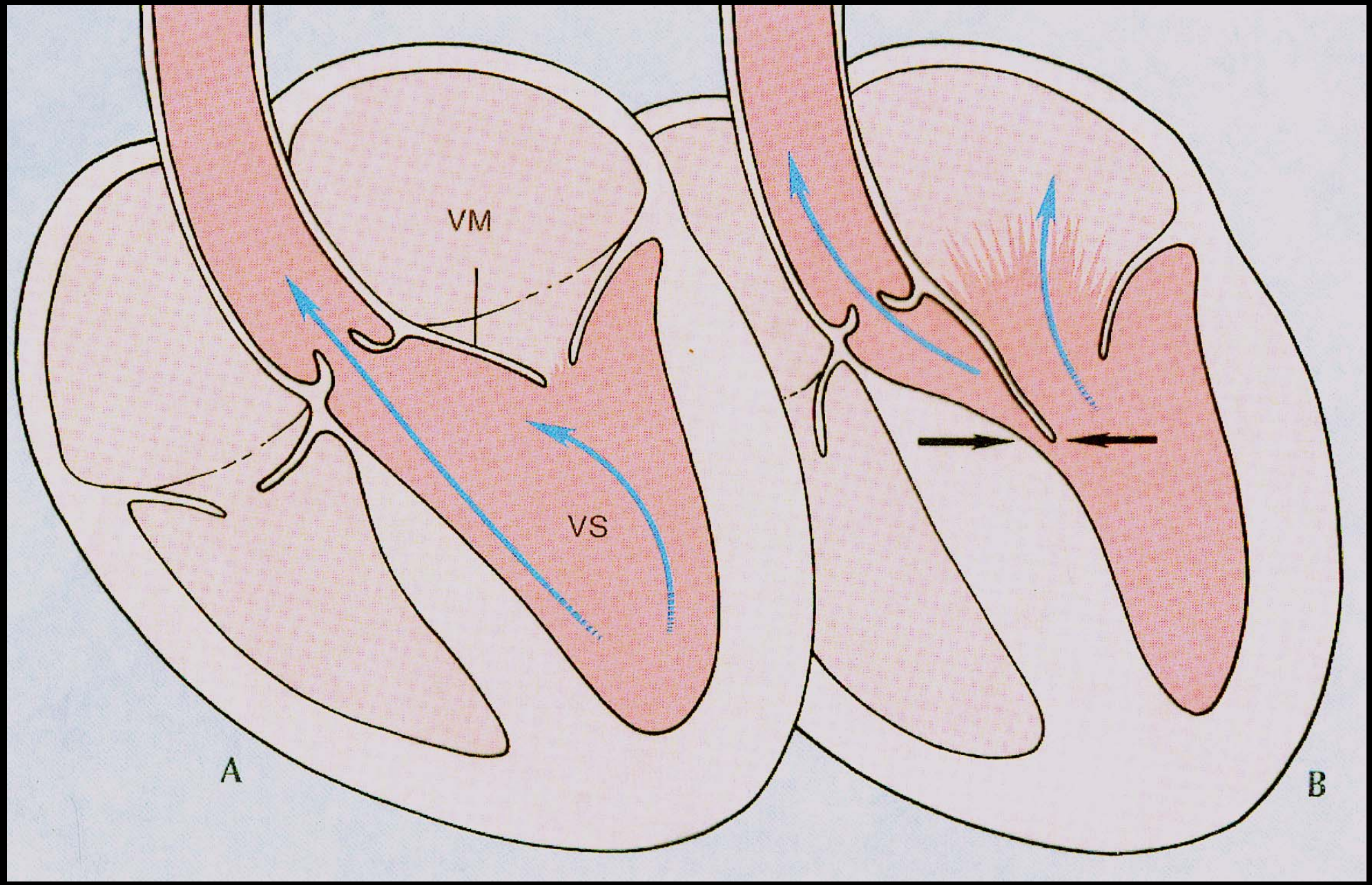
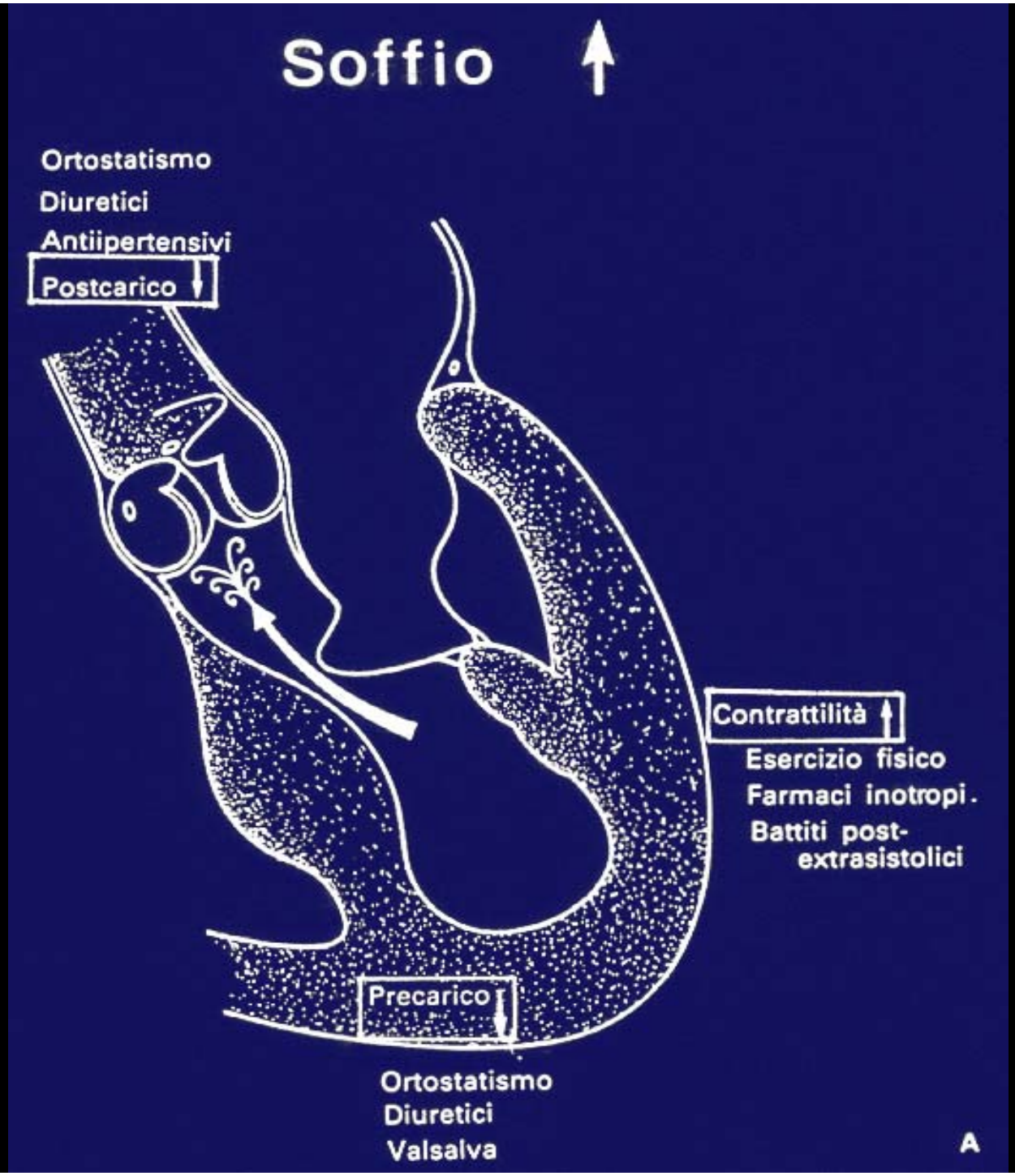
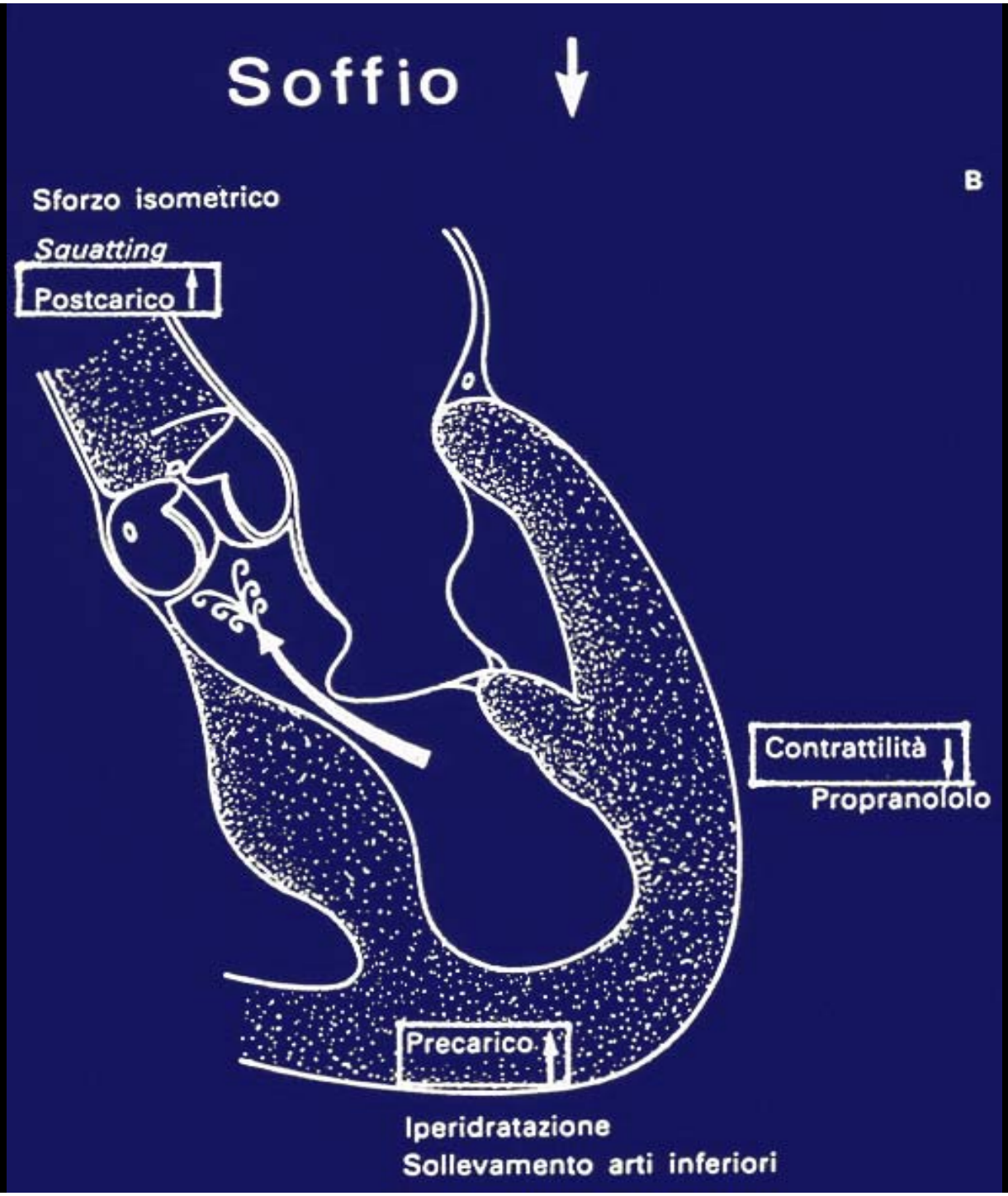
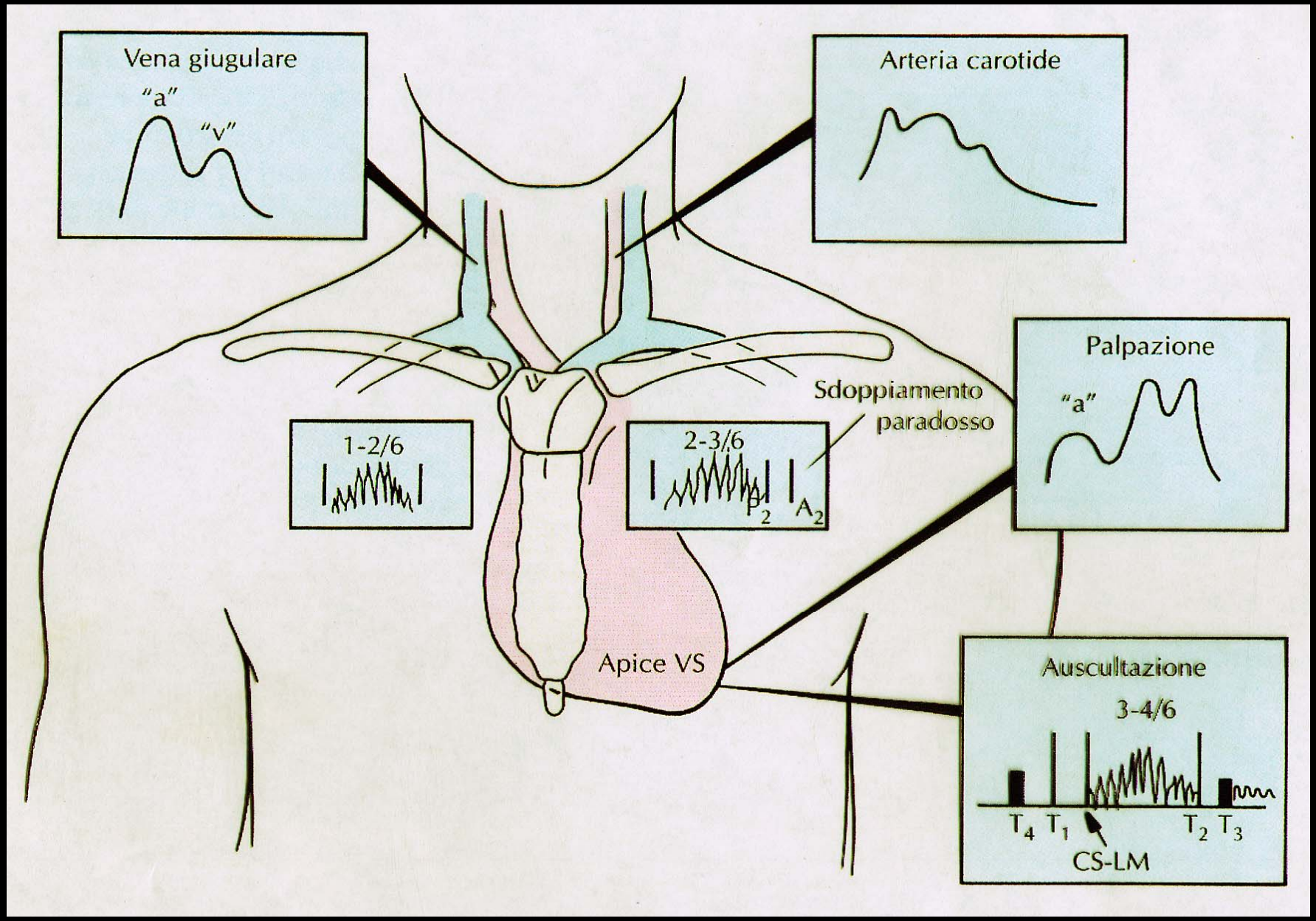
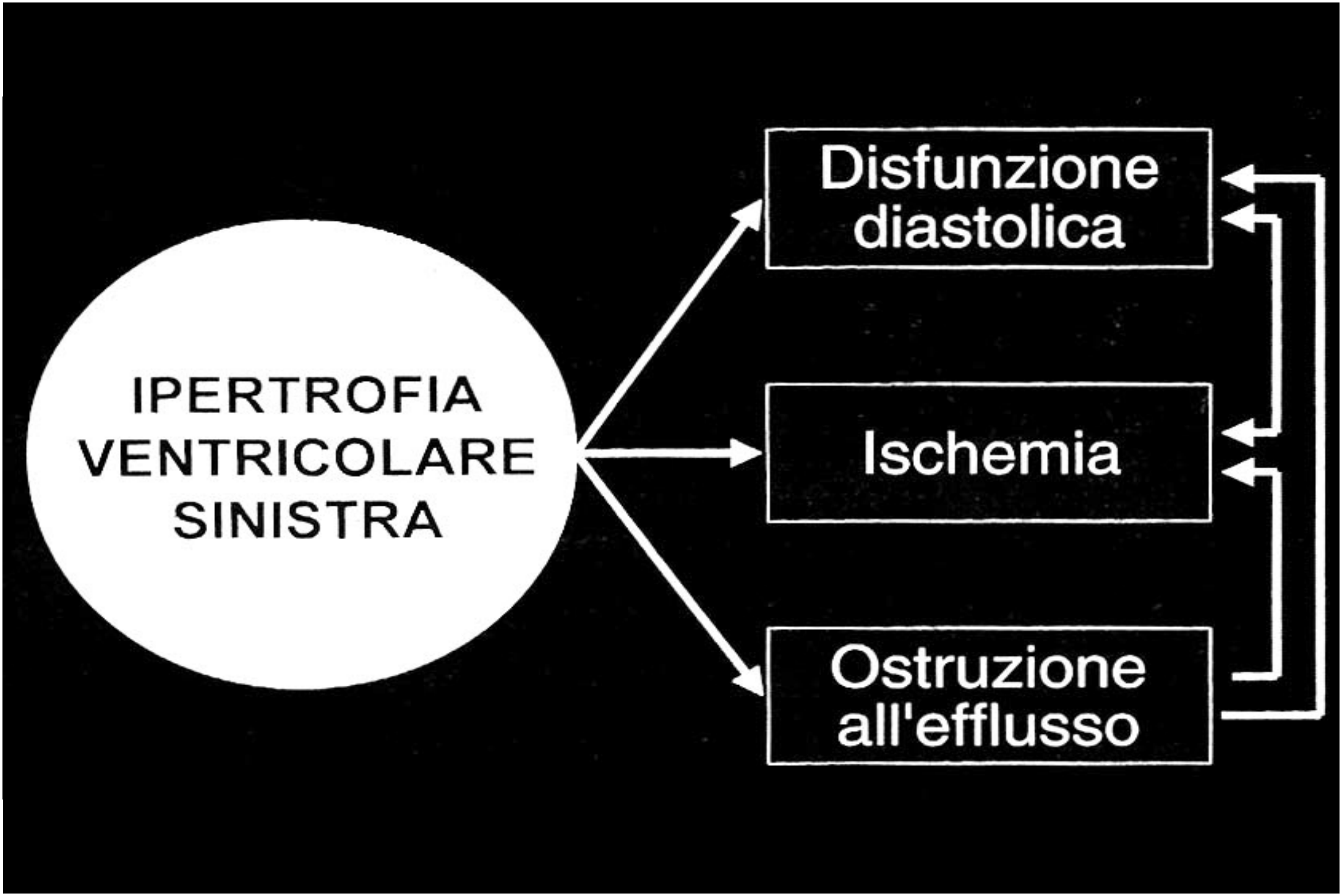
250
200
150
100
50
0
Vsn 183/2-38
Ao 90/58/74

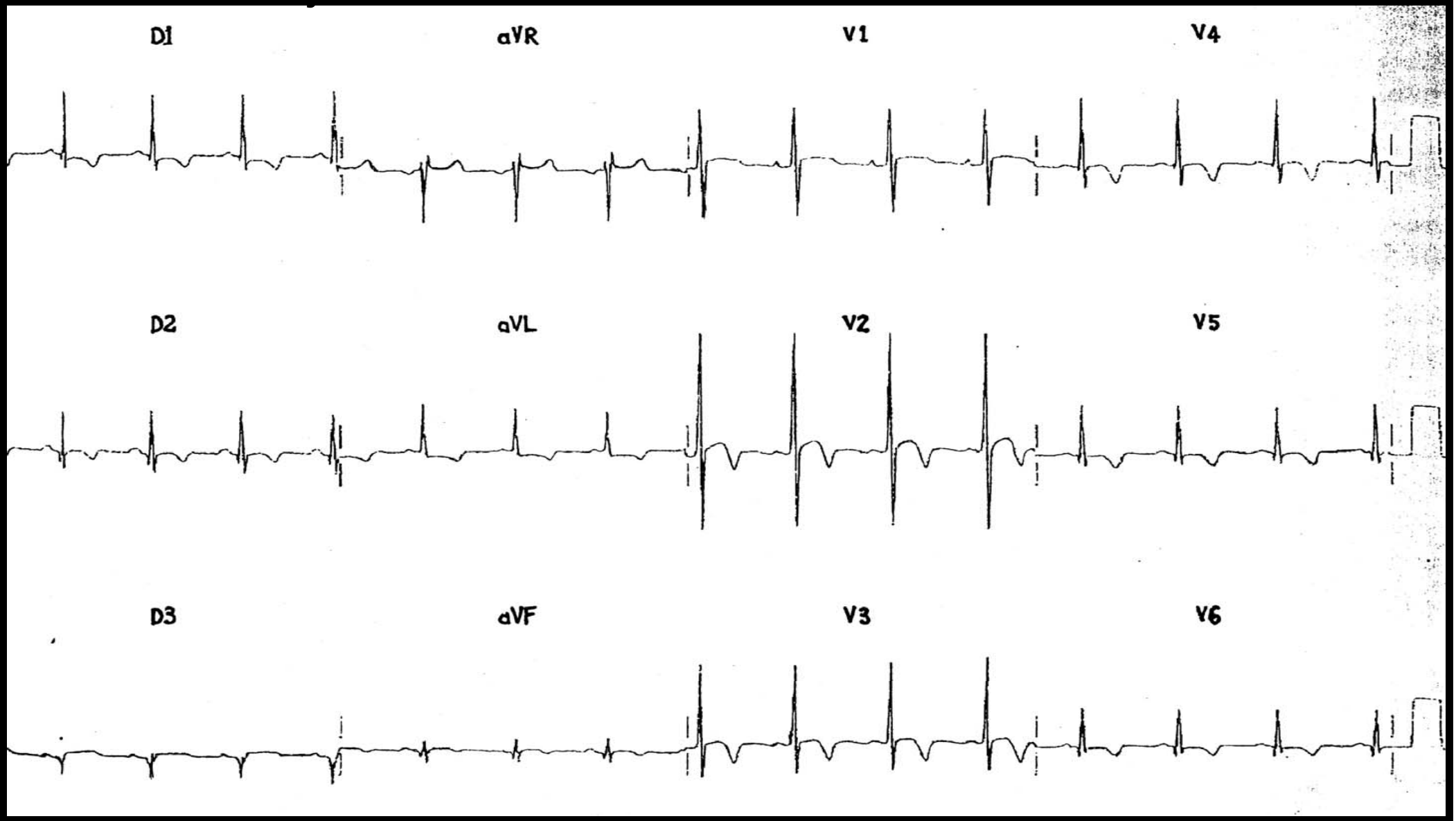

VM
VS
A
B

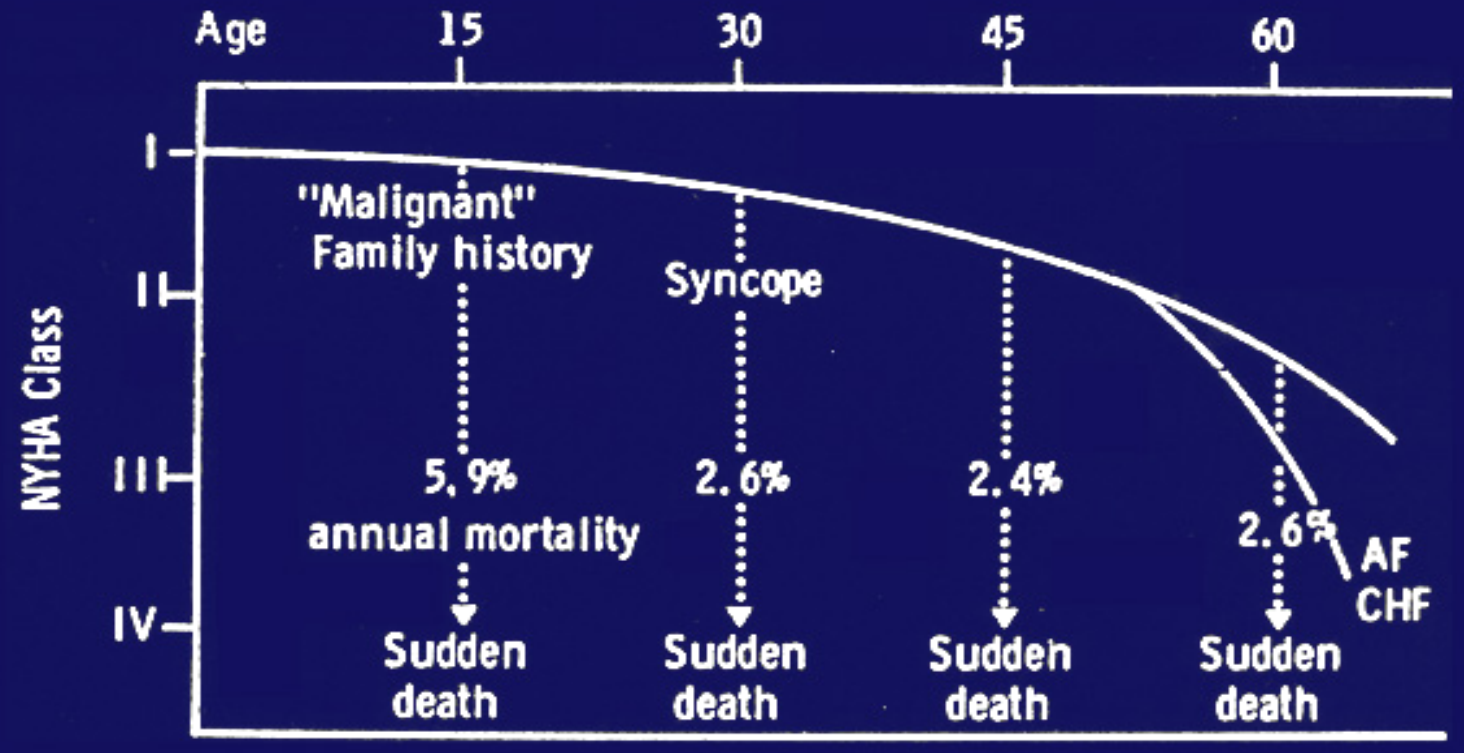

Soffio
Ortostatismo
Diuretici
Antiipertensivi
Postcarico
Contrattilità
Esercizio fisico
Farmaci inotropi.
Battiti post-
extrasistolici
Precarico
Ortostatismo
Diuretici
Valsalva
A


Soffio
B
Sforzo isometrico
Squatting
Postcarico
Contrattilità
Propranololo
Precarico
Iperidratazione
Sollevamento arti inferiori

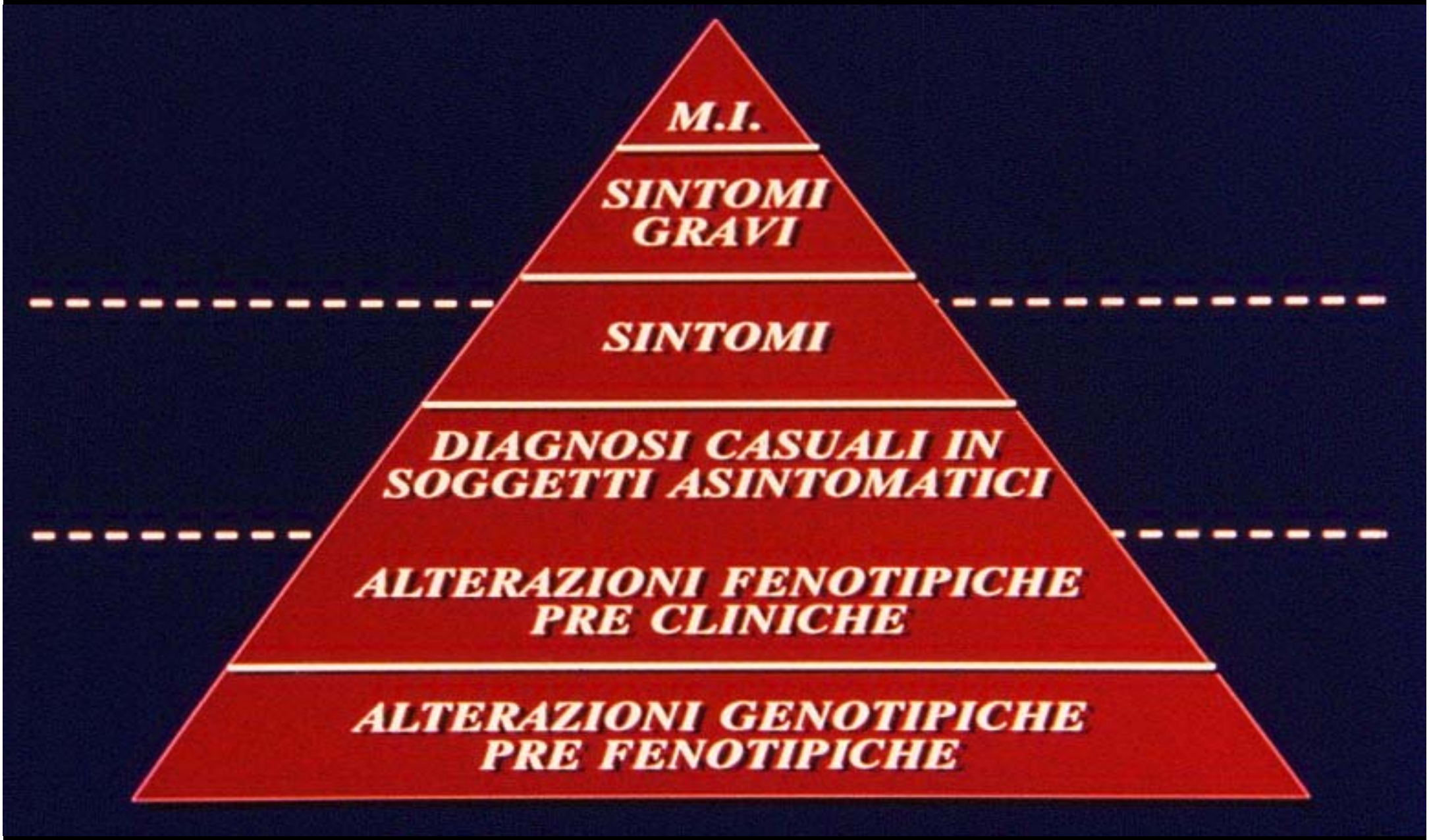

Vena giugulare
"a"
"v"
Arteria carotide
Palpazione
"a"
Sdoppiamento
paradosso
1-2/6
2-3/6
P_2
A_2
Apice VS
Auscultazione
3-4/6
T_4
T_1
T_2
T_3
CS-LM

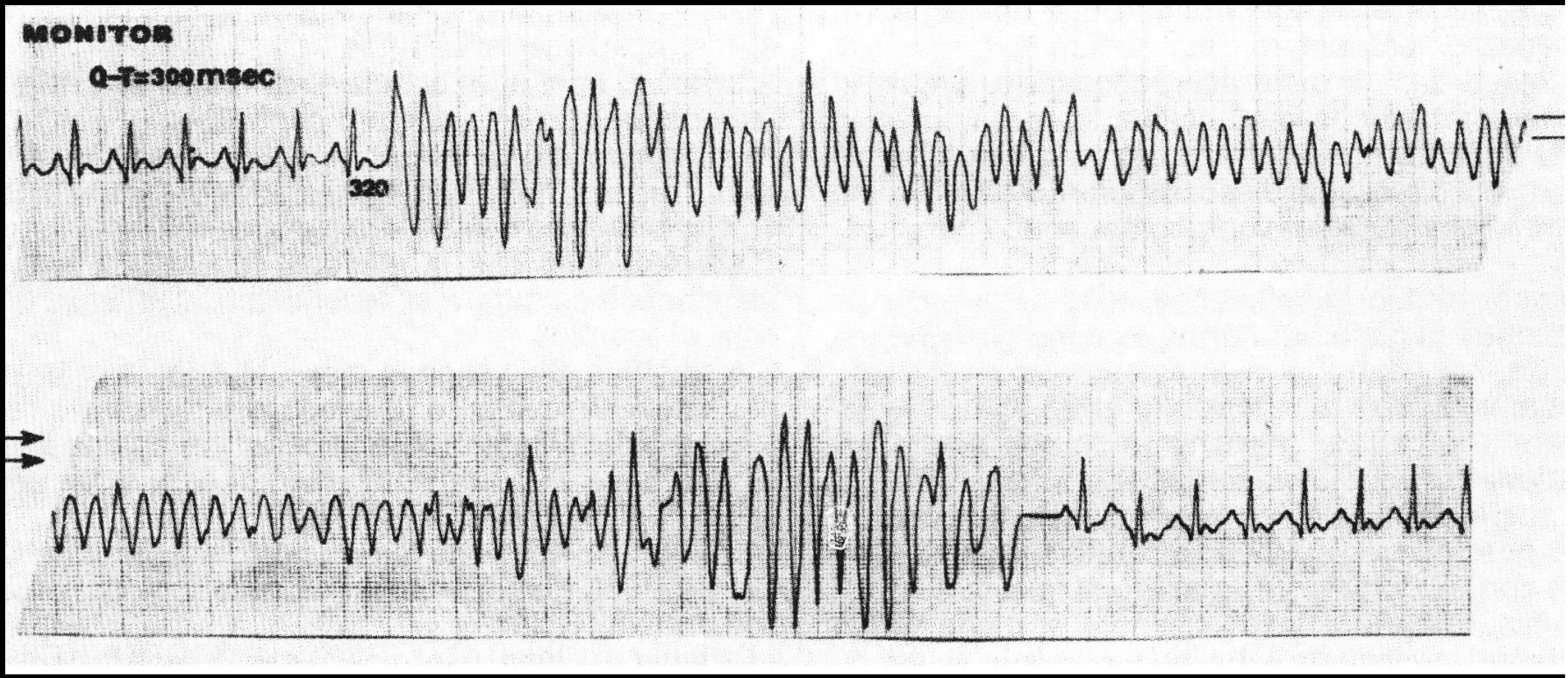

IPERTROFIA VENTRICOLARE SINISTRA
Disfunzione diastolica
Ischemia
Ostruzione all'efflusso


D1
aVR
V1
V4
D2
aVL
V2
V5
D3
aVF
V3
V6



A suggested natural history of hypertrophic cardiomyopathy. AF, atrial fibrillation; CHF, congestive heart failure; NYHA, New York Heart Association. (From McKenna and Goodwin, ref. 5, with permission.)


M.I.
SINTOMI GRAVI
SINTOMI
DIAGNOSI CASUALI IN SOGGETTI ASINTOMATICI
ALTERAZIONI FENOTIPICHE PRE CLINICHE
ALTERAZIONI GENOTIPICHE PRE FENOTIPICHE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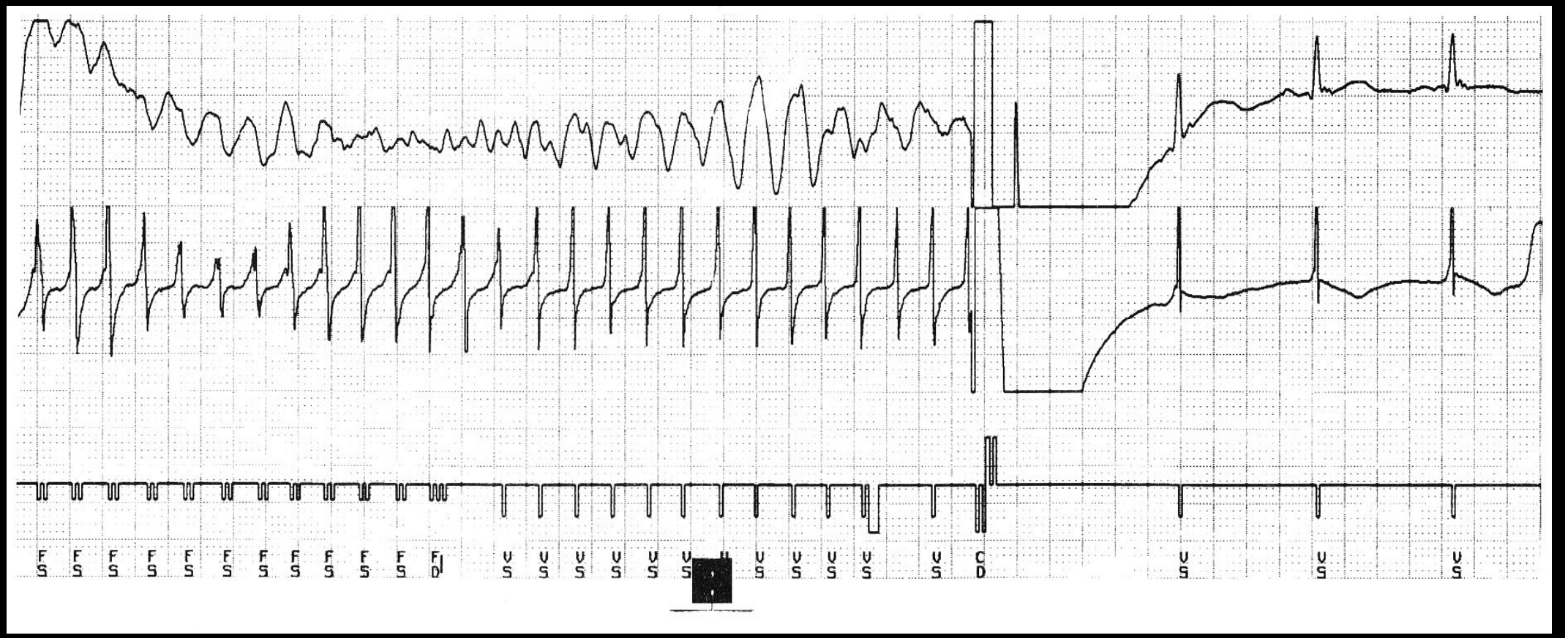
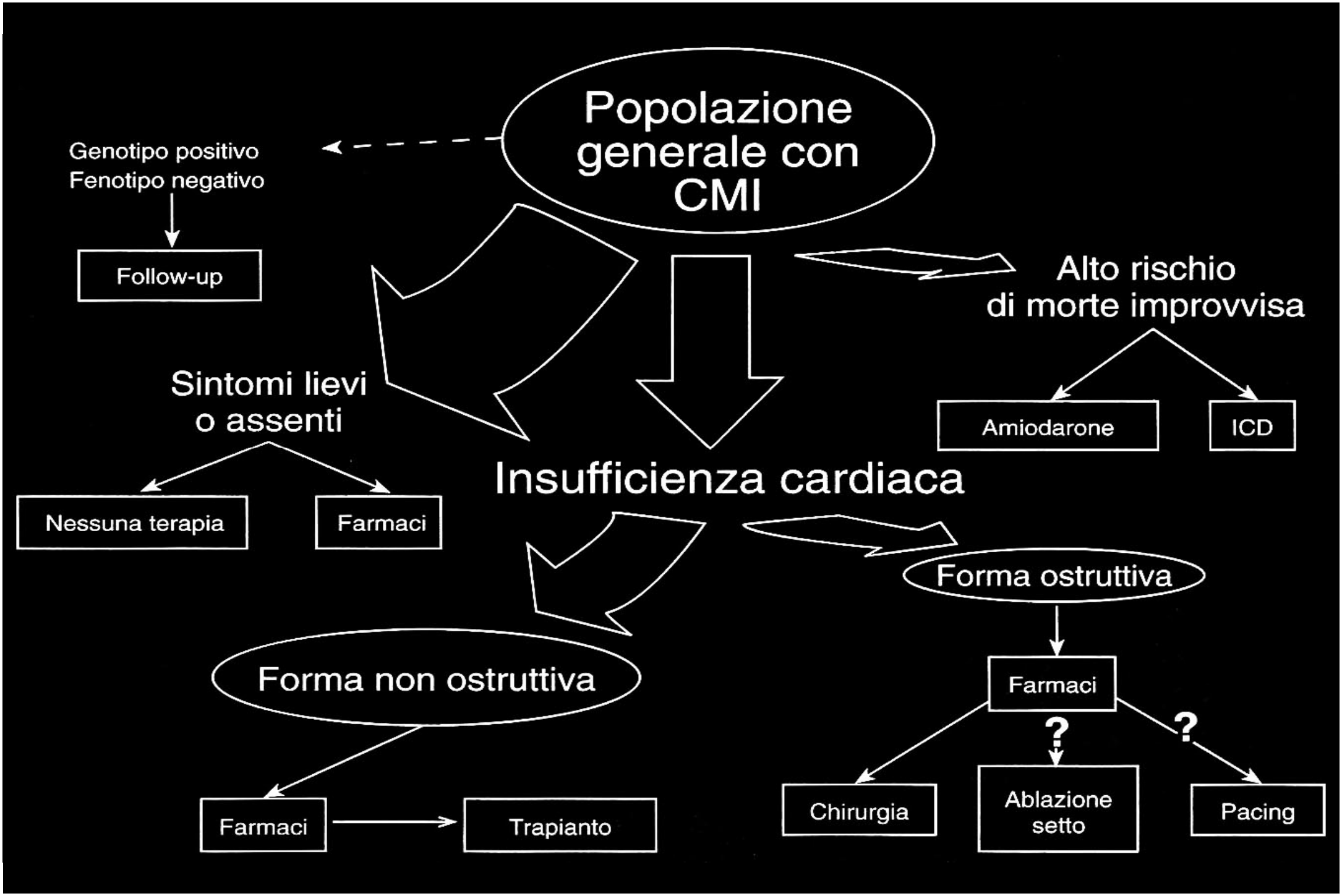
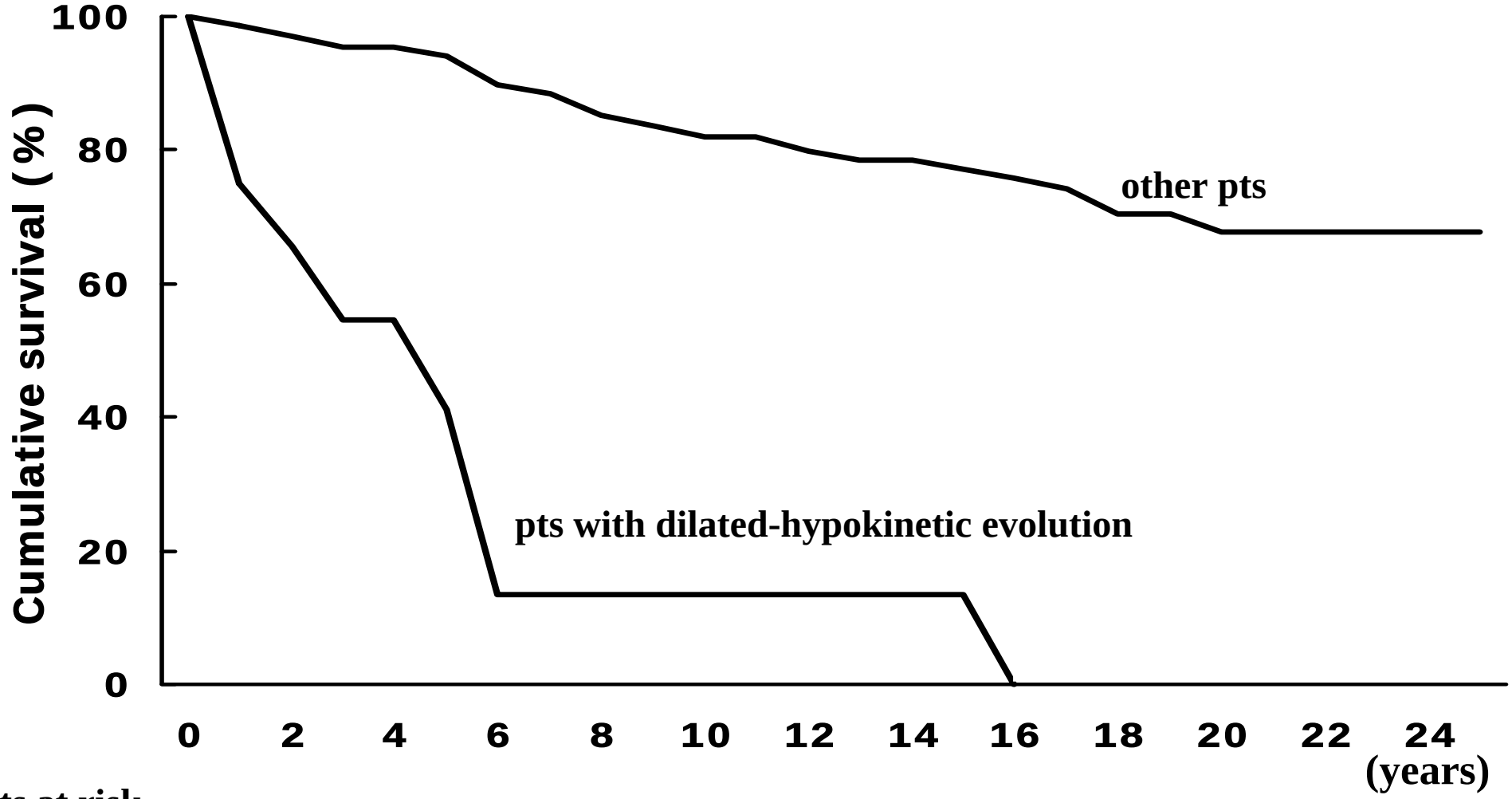

F S F S F S F S F S F S F S F S F S F S F D
V S V S V S V S V S V S V S V S V S V S V S
C D
V S
V S
V S


Popolazione generale con CMI
Genotipo positivo
Fenotipo negativo
Follow-up
Alto rischio di morte improvvisa
Amiodarone
ICD
Sintomi lievi o assenti
Nessuna terapia
Farmaci
Insufficienza cardiaca
Forma ostruttiva
Farmaci
?
?
Chirurgia
Ablazione setto
Pacing
Forma non ostruttiva
Farmaci
Trapianto

13 yrs

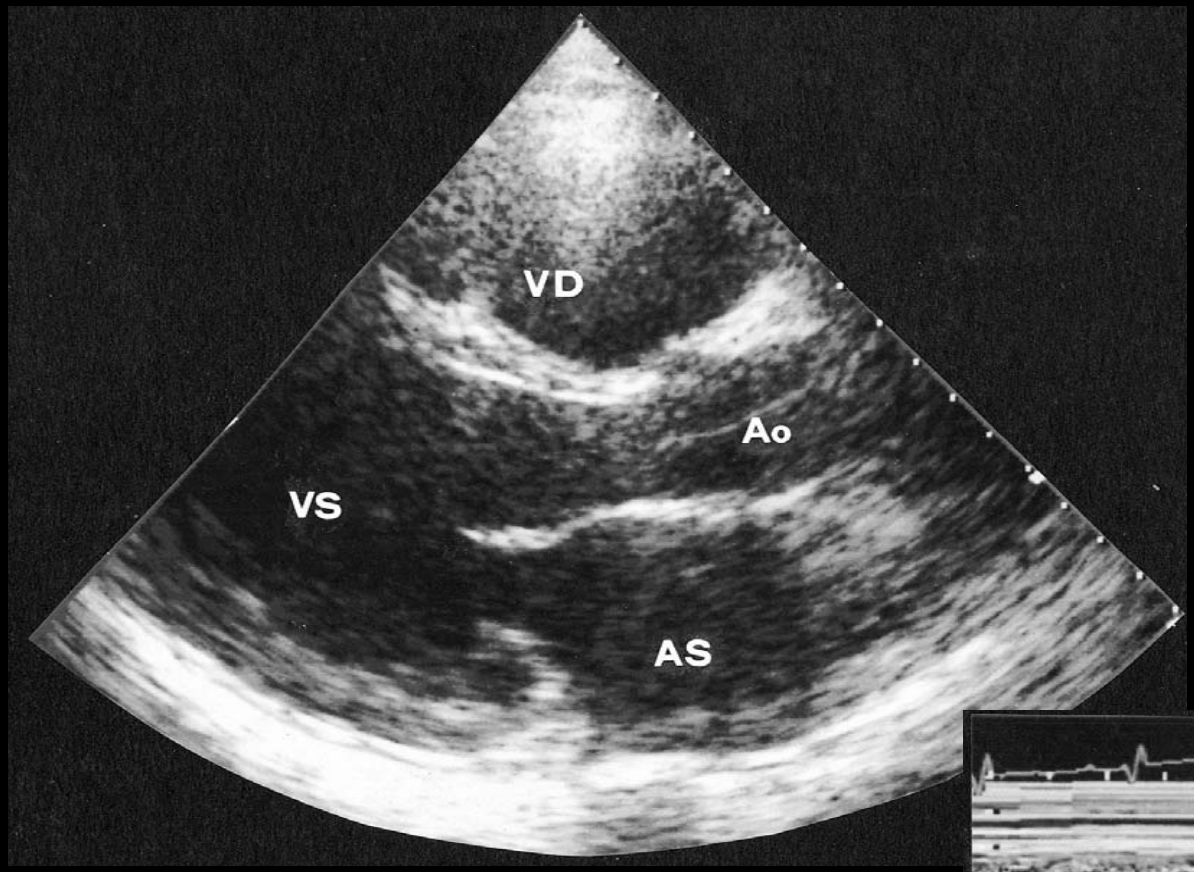
16 yrs

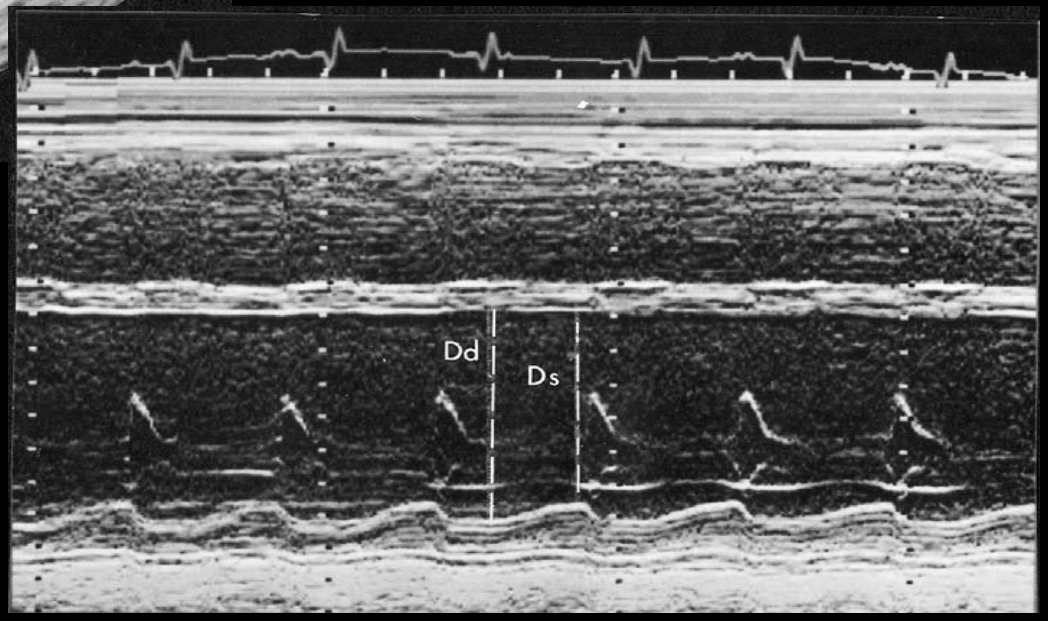
Heart-transplant free survival



Pts at risk

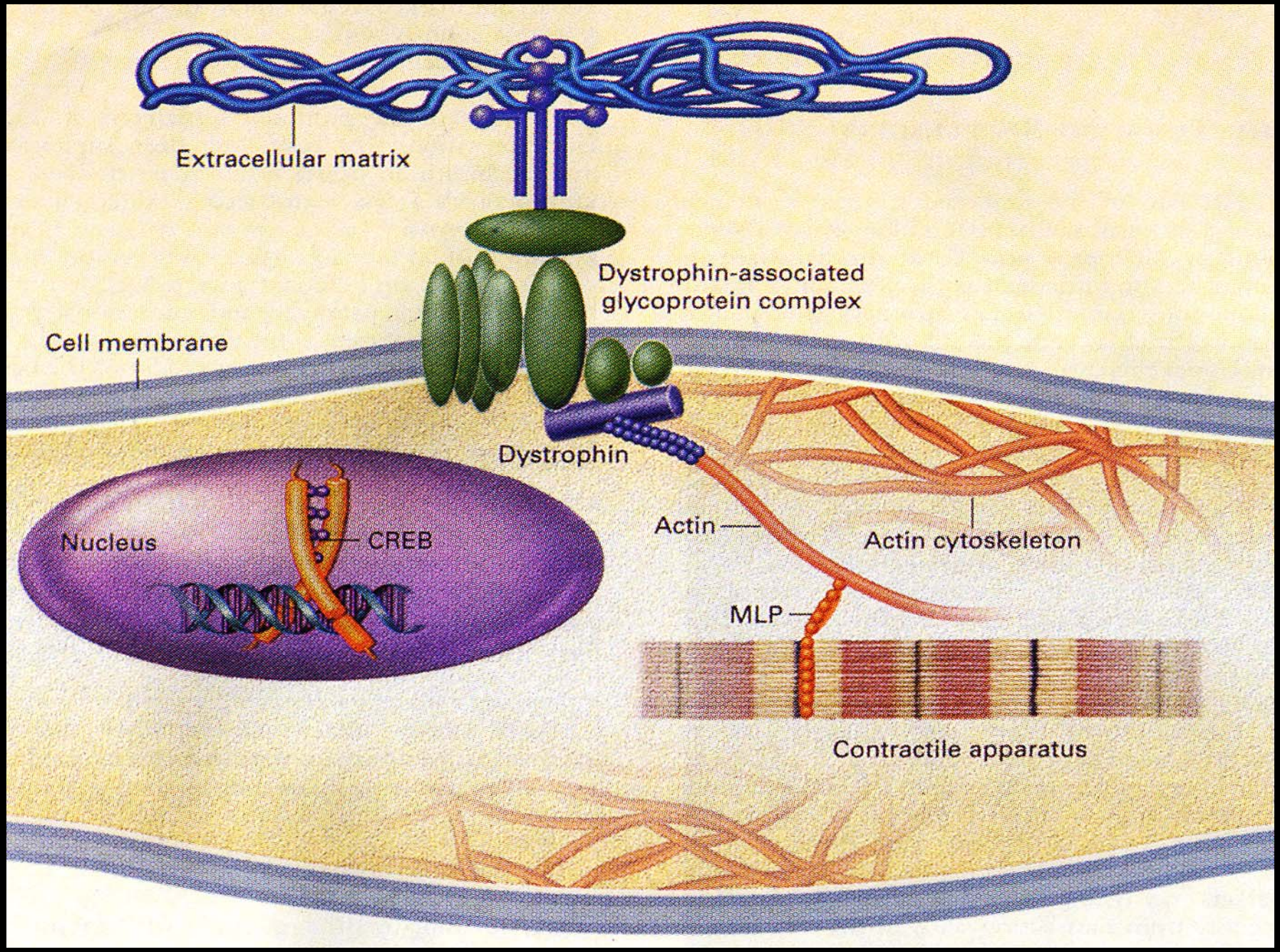
CARDIOMIOPATIA DILATATIVA

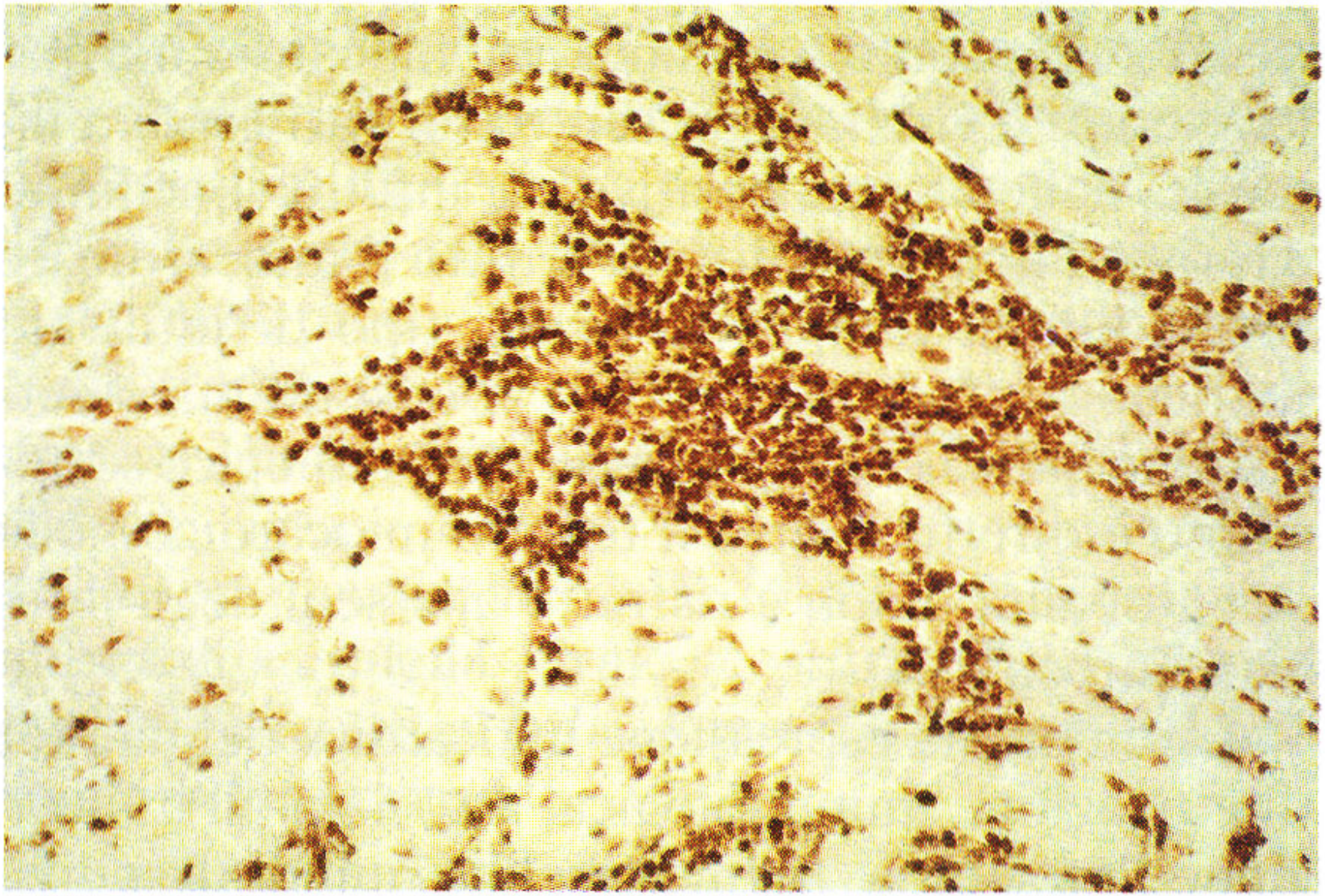

VD
Ao
VS
AS


Dd
Ds

Molecular Genetics of DCM

Chromosomal Locus	Mutant Protein
1q1-p1	Unknown
1q31-q32	Unknown
3p22-p25	Unknown
9q13-q22	Unknown
Xp21	Dystrophyn
15q14	Actin
Xq28	Emerin
17q12-21.33	α-Sarcoglycan (adhalin)
10q21-23	Metavinculin
1p11-q21 ; 1q11-23	Lamins A and C

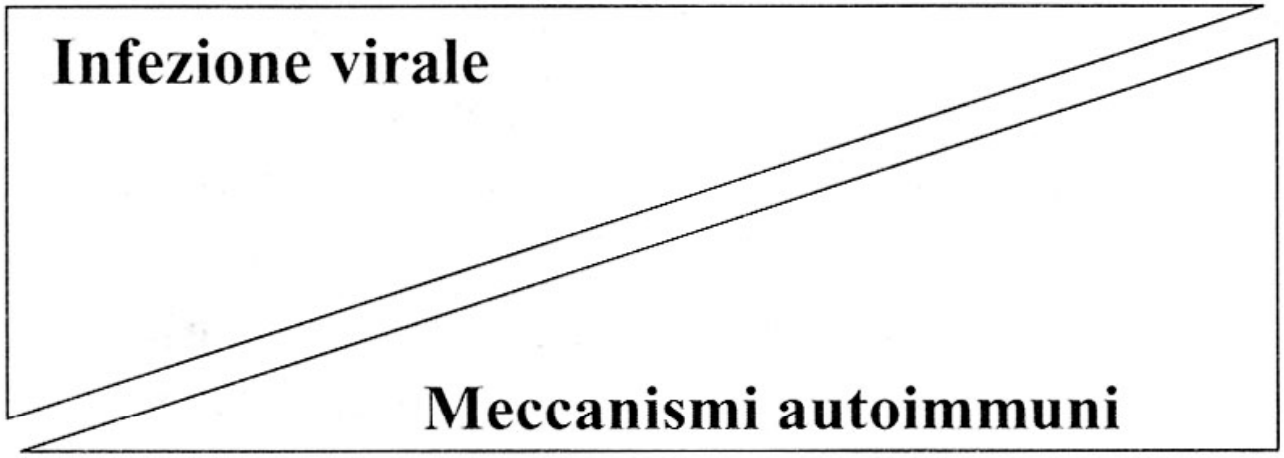

Extracellular matrix
Dystrophin-associated glycoprotein complex
Cell membrane
Dystrophin
Nucleus
CREB
Actin
Actin cytoskeleton
MLP
Contractile apparatus



Miocardite linfocitaria. Vasto agglomerato interstiziale di linfociti T memory (CD45RO, 50×).

MIOCARDITE VIRALE

Fasi patogenetiche e strategie terapeutiche specifiche



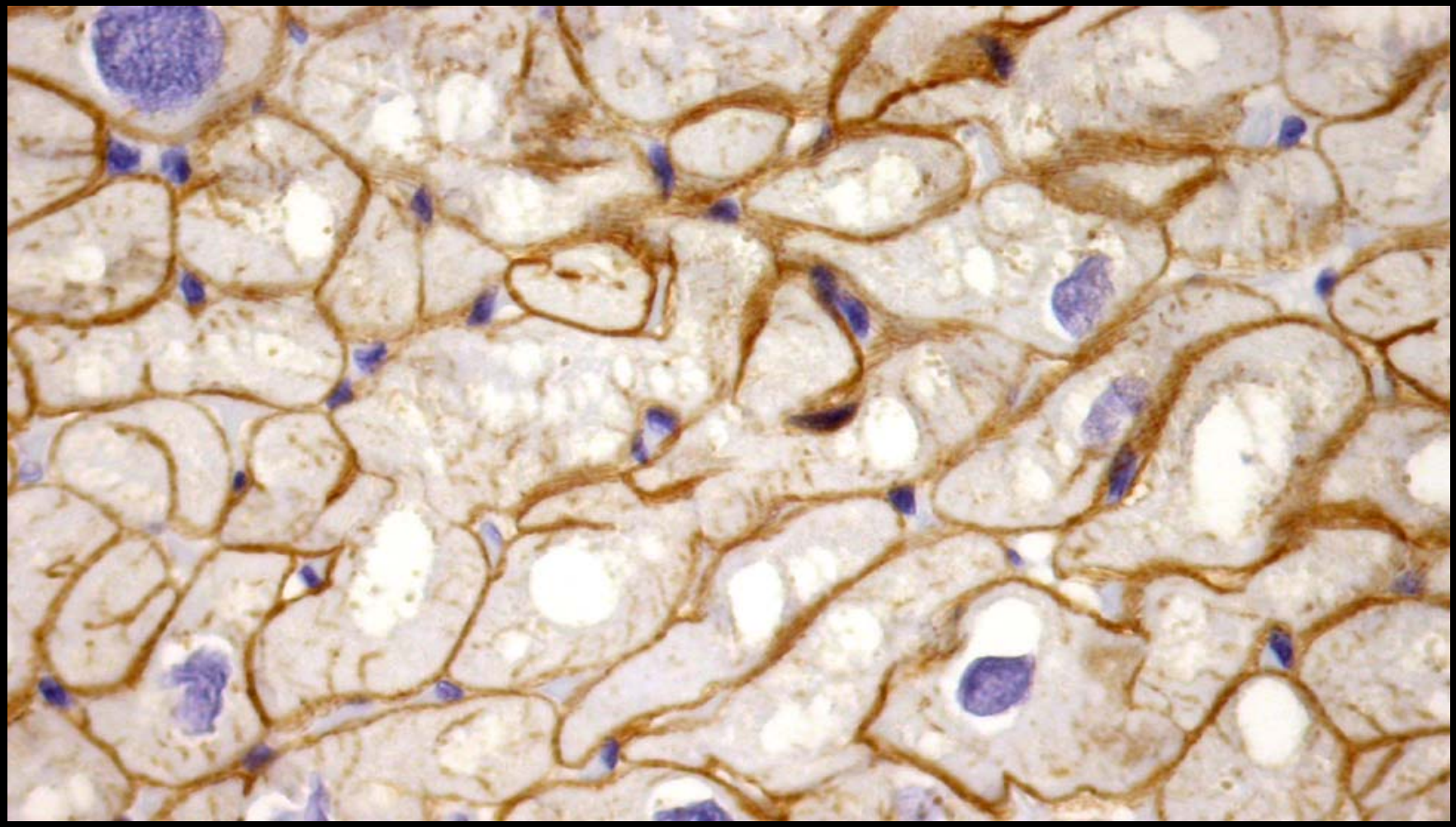
Miocardite acuta ⇢ *cronica*

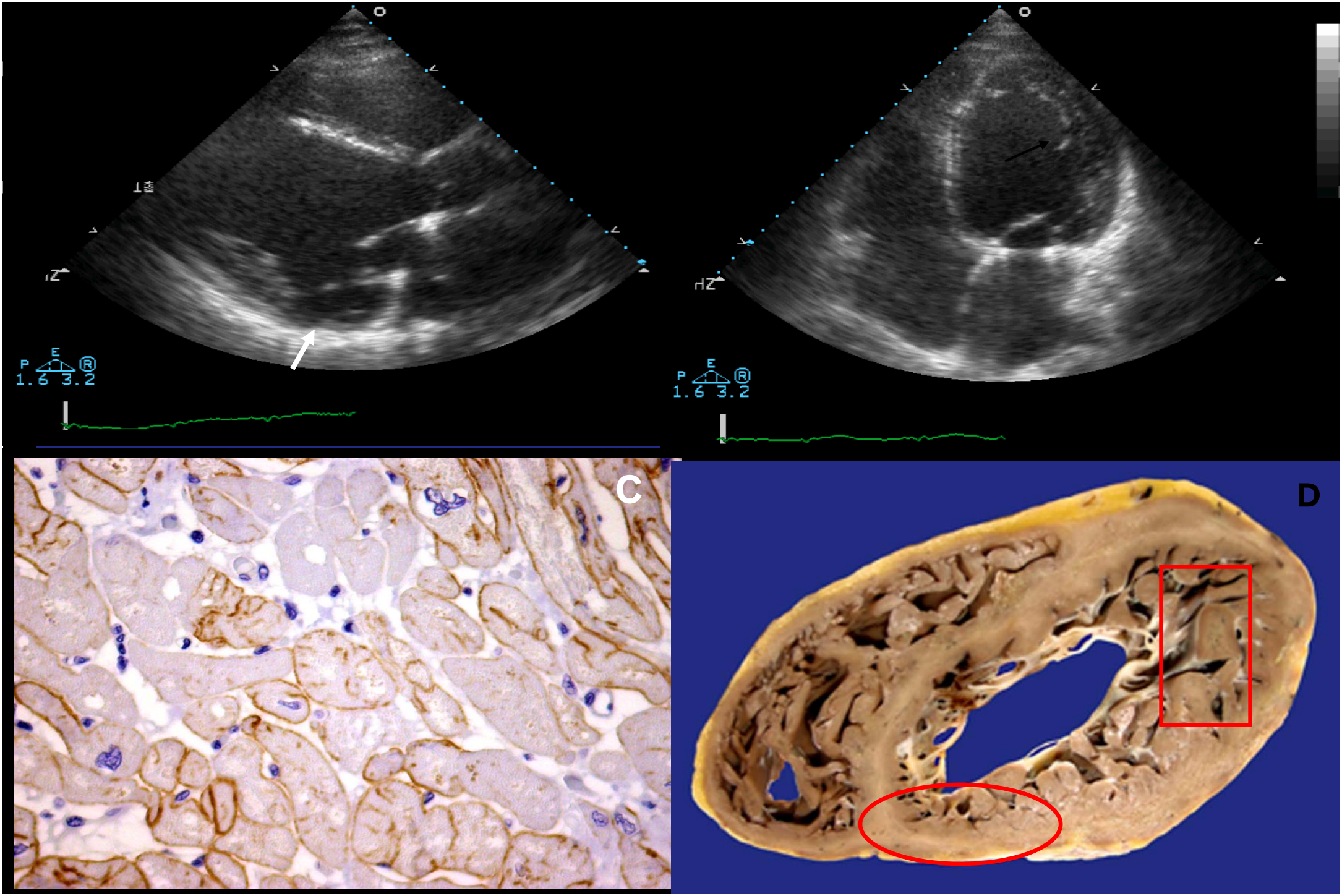
F. antivirali

Immunoglobuline ev

F. immunosoppressori

Normale colorazione istochimica per la distrofina




P
E
R
1.6 3.2
C
D

CMPD Terapia:

Terapia dell'insufficienza cardiaca

- *Beta-bloccanti (anche in soggetti asintomatici per prevenire il rimodellamento VSn)*
- *ACE-Inibitori*
- *Diuretici*

AICD in casi selezionati

Pace Maker biventricolare (terapia di resincronizzazione elettrica) nei casi sintomatici con BBSn

Trapianto cardiaco in casi selezionati

POTENZIALI CONTROINDICAZIONI AL TRAPIANTO CARDIACO

Età avanzata (>65 anni)

Ipertensione polmonare severa

Patologia renale o epatica irreversibile

Broncopneumopatia cronica ostruttiva

Infarto polmonare recente

Diabete mellito insulino-dipendente

Vasculopatia severa cerebrale o periferica

Ulcera peptica attiva

Cachessia severa o obesità

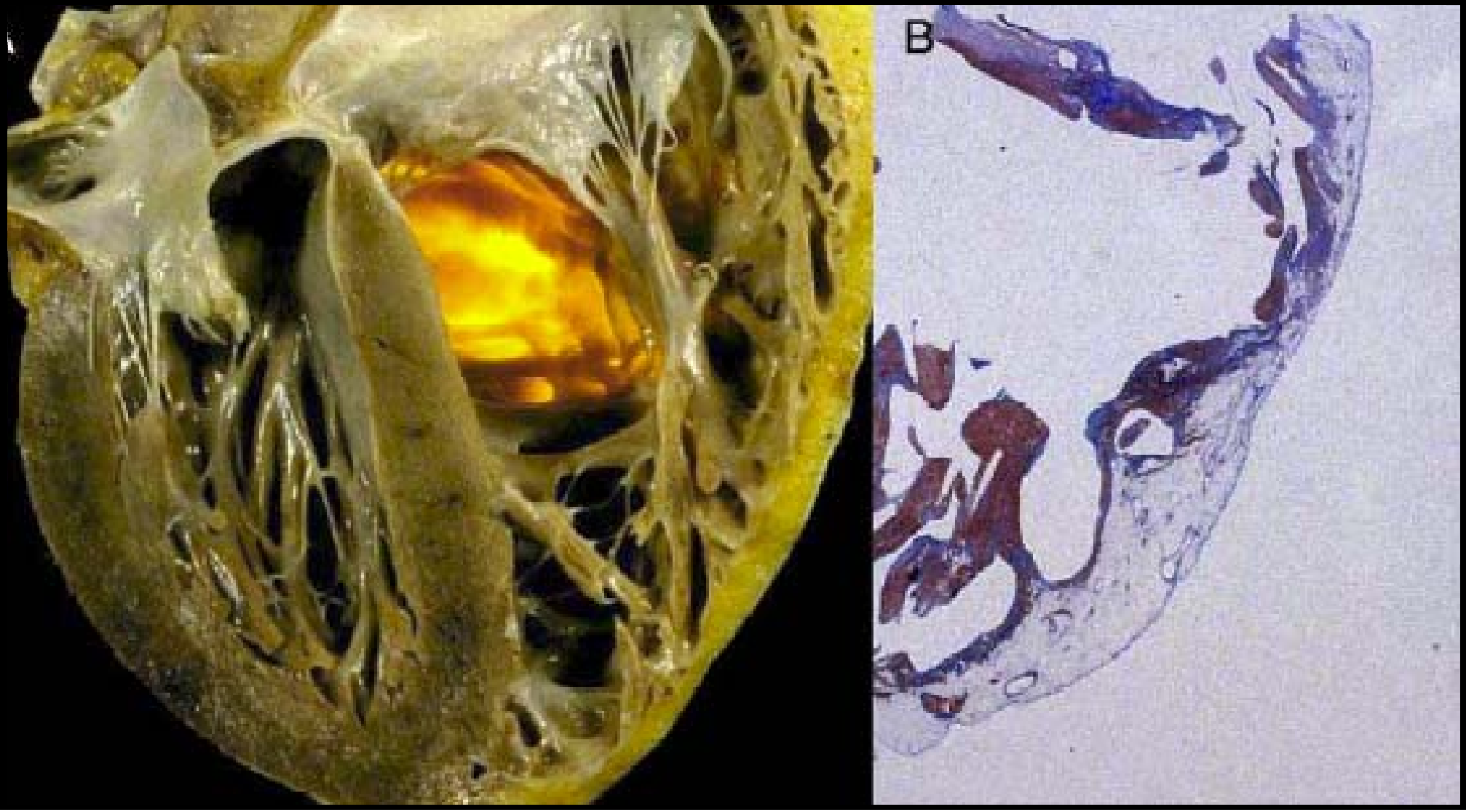
Altre patologie sistemiche con probabile limitazione della sopravvivenza o della riabilitazione

Supporto psicosociale esterno assente o inadeguato

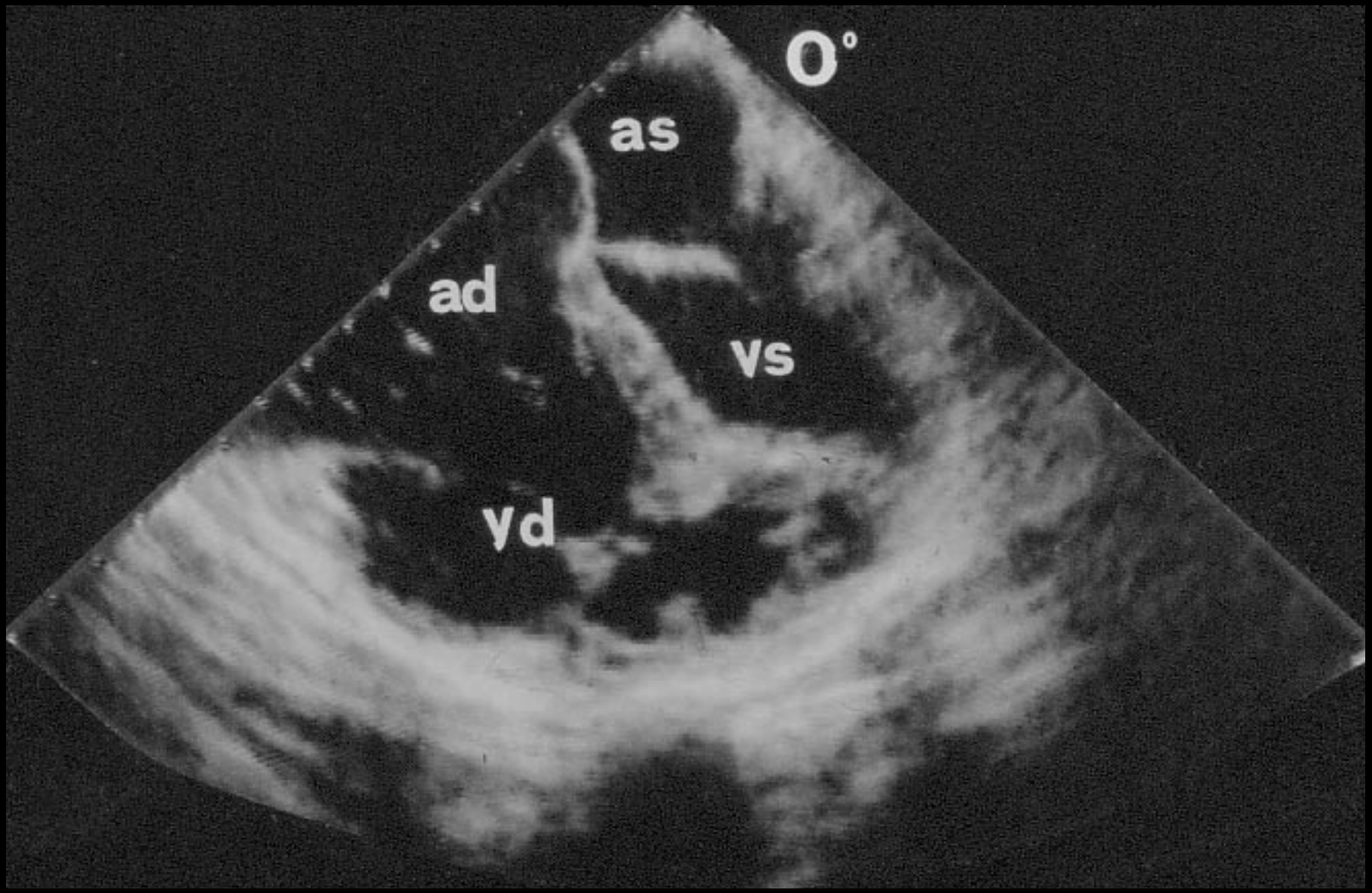
Precedente disturbo del comportamento o patologia psichiatrica che possano interferire significativamente con la collaborazione

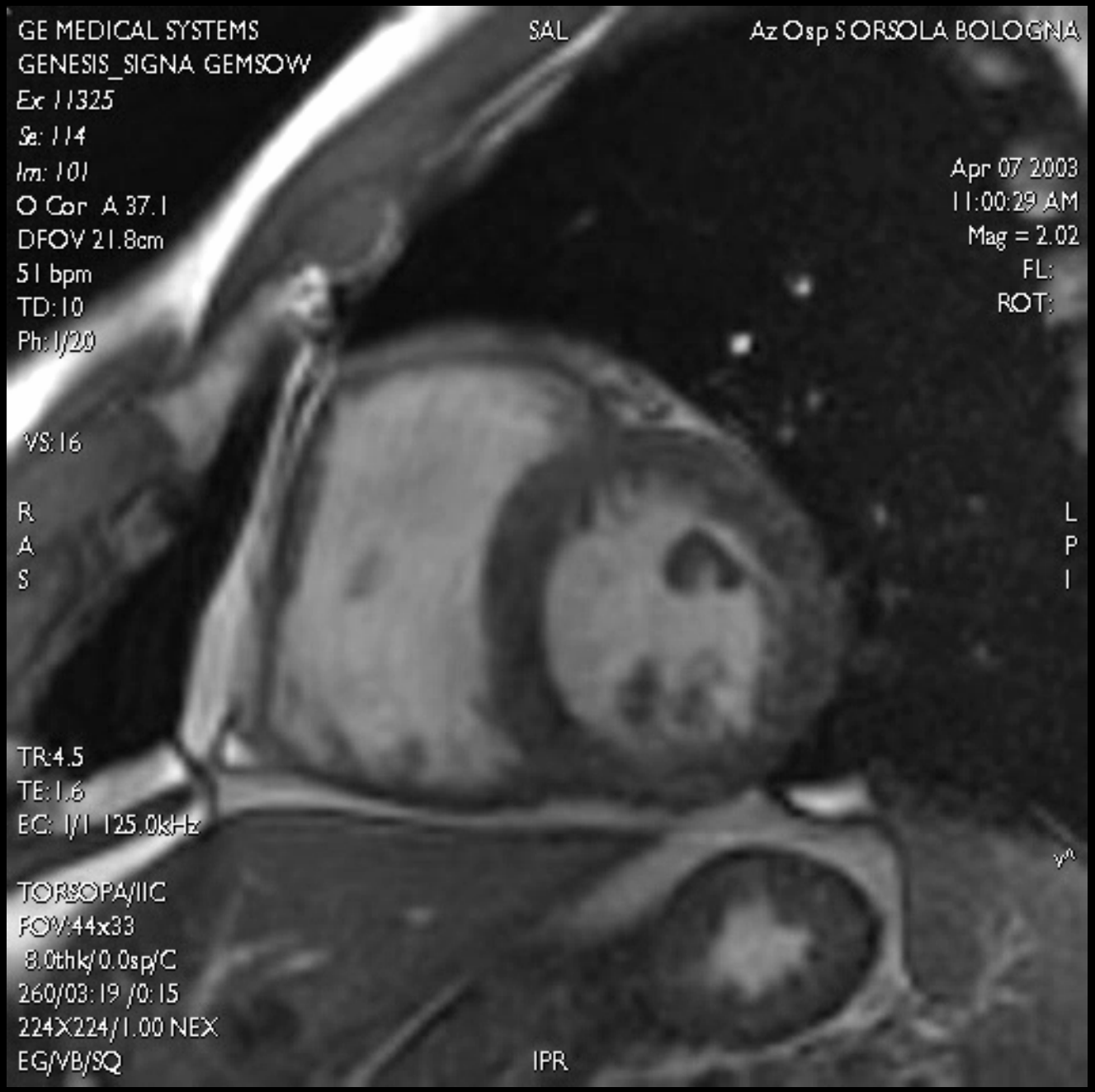
CARDIOMIOPATIA (o displasia) ARITMOGENA DEL VDx

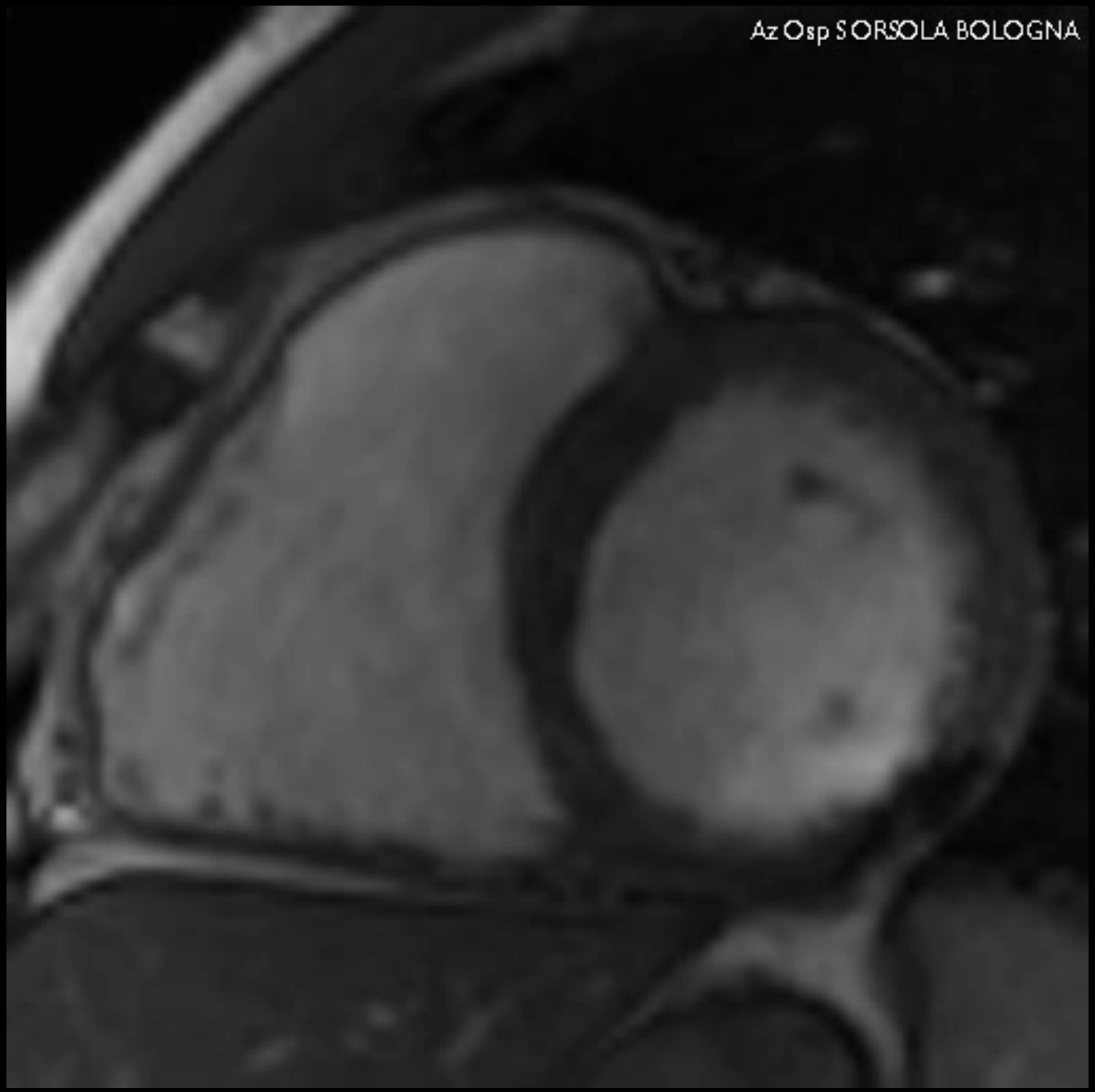
Cardiomiopatia aritmogena del VDx

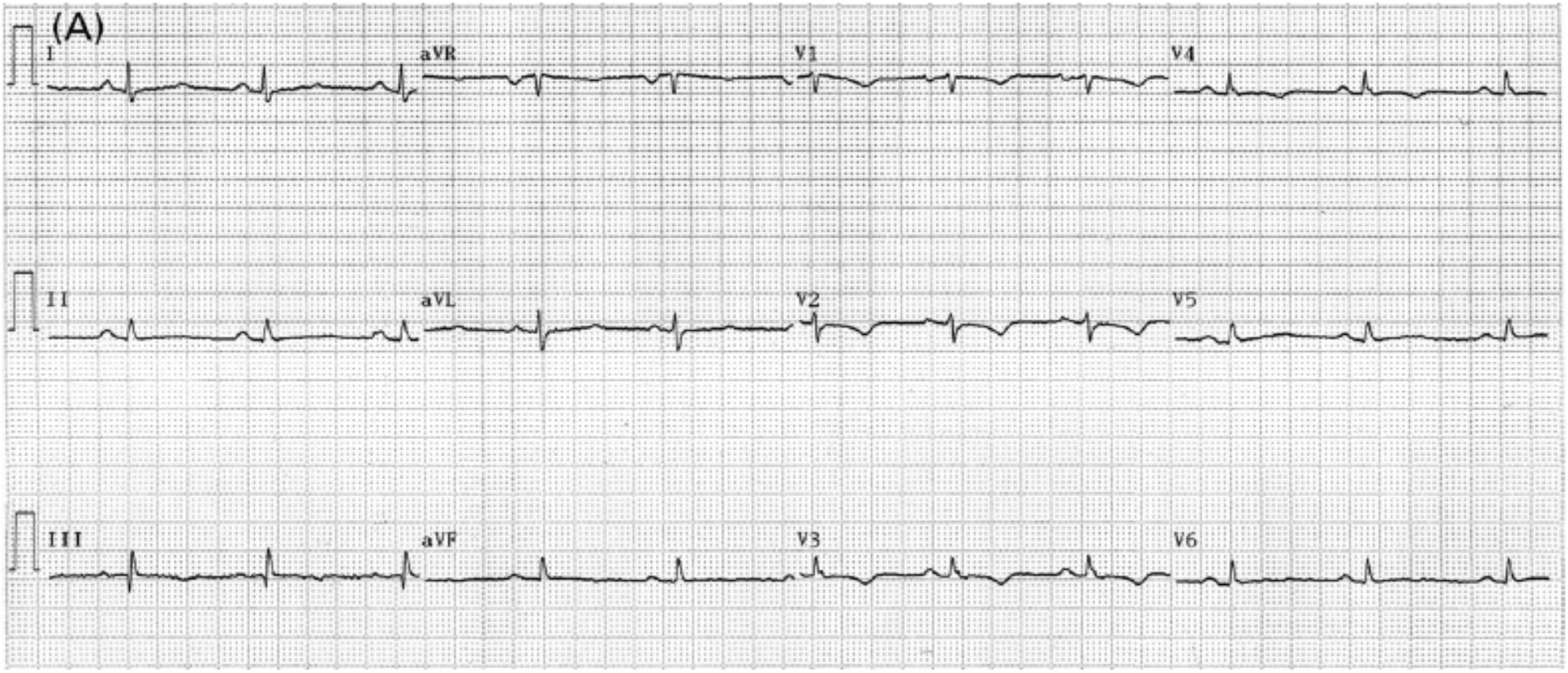


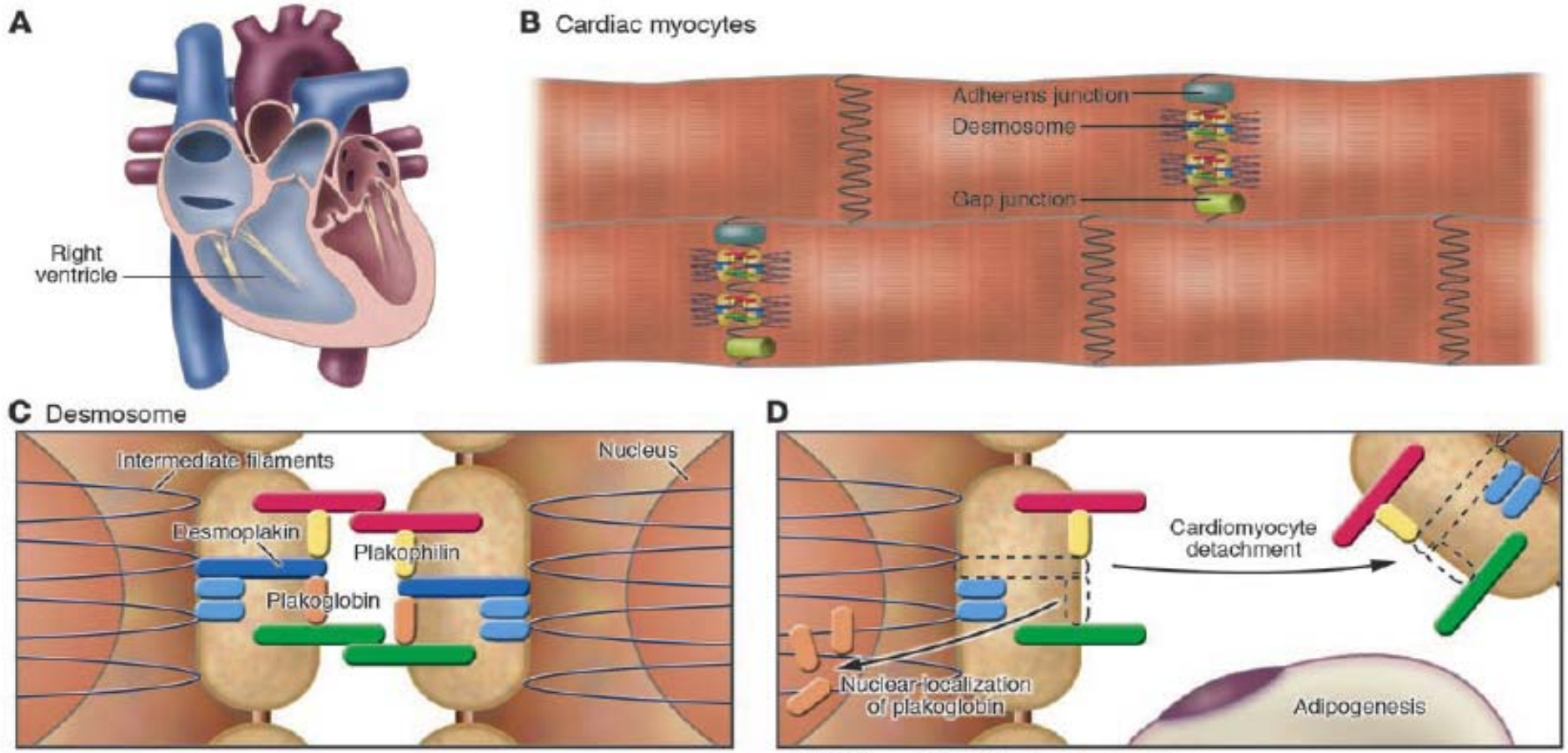
Cardiomiopatia aritmogena del VDx




GE MEDICAL SYSTEMS
GENESIS_SIGNA GEMSOW
Ex 11325
Se: 114
Im: 101
O Cor A 37.1
DFOV 21.8cm
51 bpm
TD:10
Ph: 1/20
VS:16
R
A
S
TR:4.5
TE:1.6
EC: 1/1 125.0kHz
TORSOPA/IIC
FOV:44x33
8.0thk/0.0sp/C
260/03:19 /0:15
224X224/1.00 NEX
EG/VB/SQ
SAL
IPR
Az Osp S ORSOLA BOLOGNA
Apr 07 2003
11:00:29 AM
Mag = 2.02
FL:
ROT:
L
P
I


Az Osp S ORSOLA BOLOGNA


(A)
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6



Inhibition of Wnt/β-catenin signaling
Increased number of adipocytes
Increased fibrosis and myocyte apoptosis
Ventricular arrhythmias and contractile dysfunction

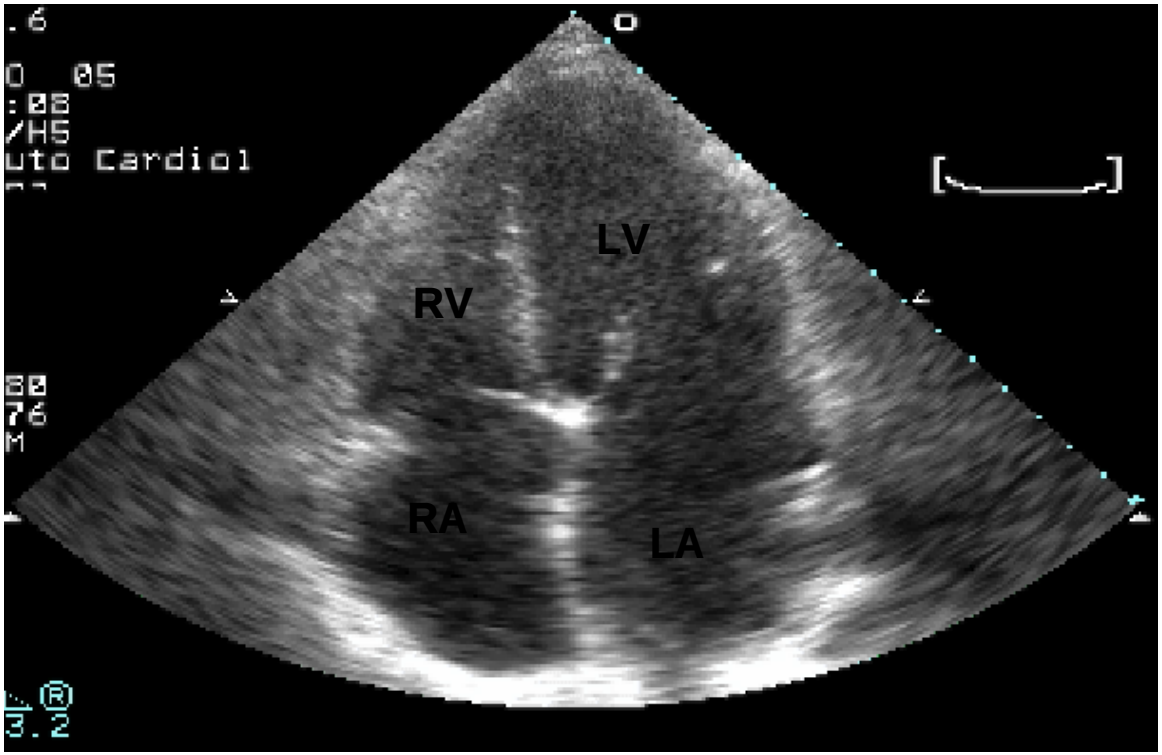
Table 1 Diagnostic criteria for arrhythmogenic right ventricular cardiomyopathy

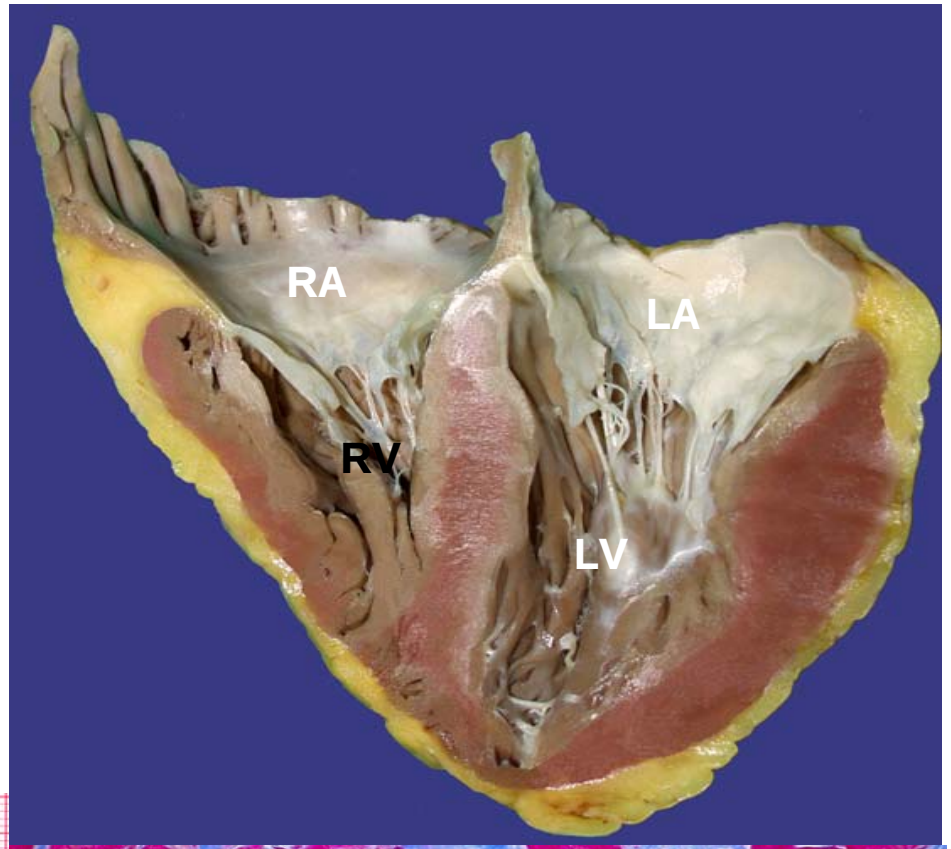
	Global and/or regional dysfunction and structural alterations	Tissue characterization of walls	Repolarization abnormalities	Depolarization abnormalities	Arrhythmias	Family history
Major	Severe dilatation and reduction of RV EF with no (or only mild) LV impairment. Localized RV aneurysms. Severe segmental RV dilatation.	Fibrofatty replacement of myocardium on endomyocardial biopsy		Epsilon waves or localized prolongation (>110 ms) of the QRS complex in right precordial leads.		Familial disease confirmed at necropsy or surgery.
Minor	Global RV dilatation and reduced EF with normal left ventricle. Regional right ventricular hypokinesis.		Inverted T waves in V2 and V3	Late potentials on SAECG	LBBB VT on ECG, Holter, or exercise testing. Frequent ventricular extrasystoles (>1000/24 hours) (Holter.)	Familial history of premature sudden death due to suspected ARVC. Familial history (clinical diagnosis based on present criteria.)

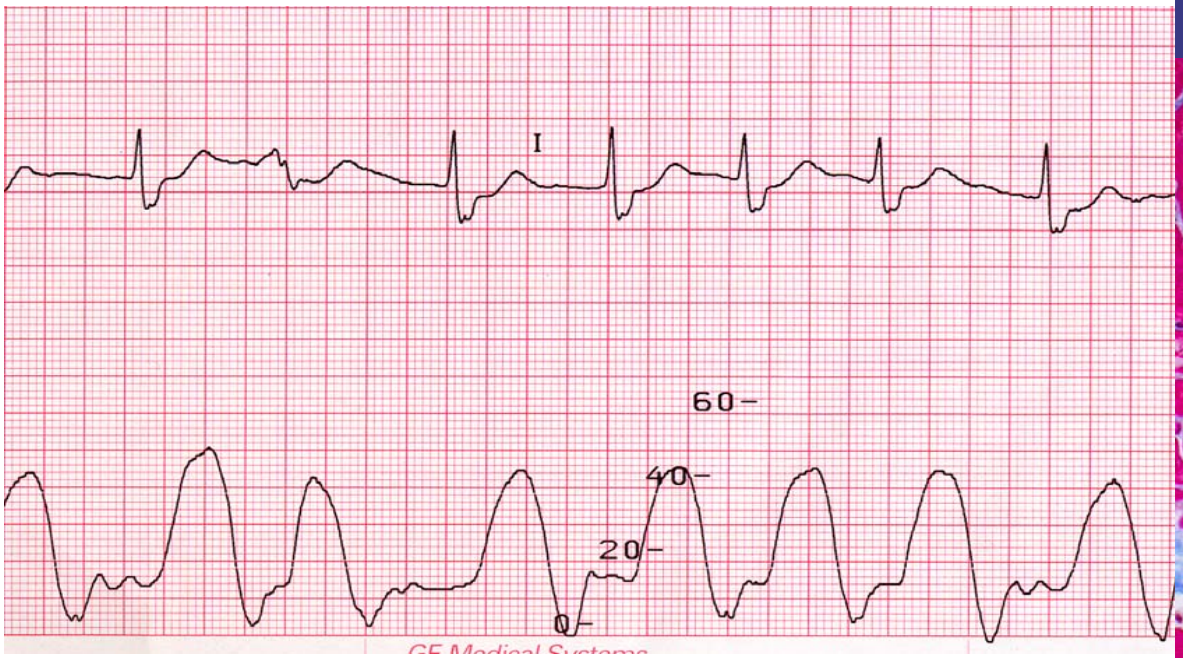
RV = right ventricle; EF = ejection fraction; LV = left ventricle; SAECG = signal-averaged electrocardiogram; LBBB = left bundle branch block; VT = ventricular tachycardia; ECG = electrocardiogram; ARVC = Arrhythmogenic right ventricular cardiomyopathy.

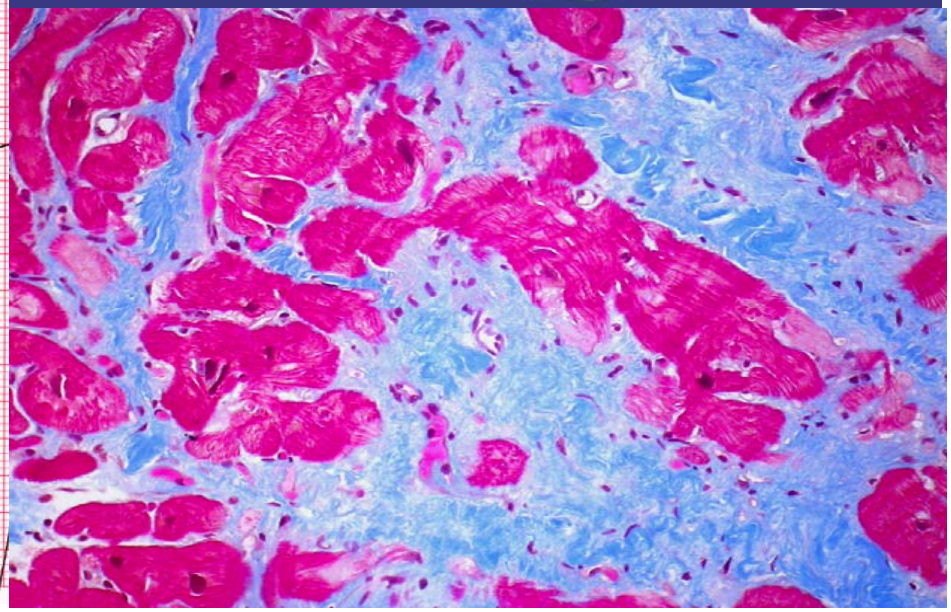
CARDIOMIOPATIE RESTRITTIVE

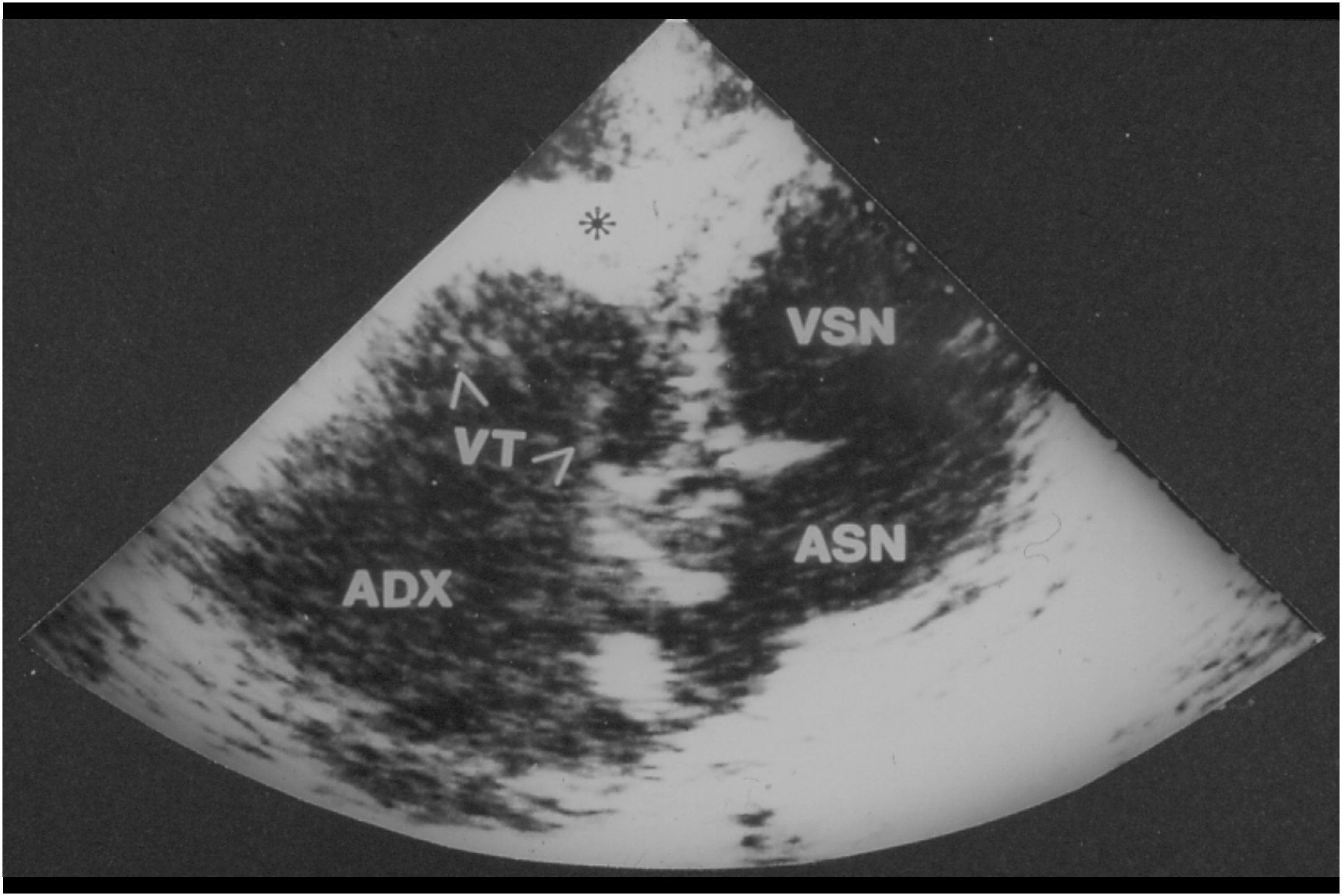
mm Hg
25
20
15
10
5
0
LV
RV


LV
RV
RA
LA

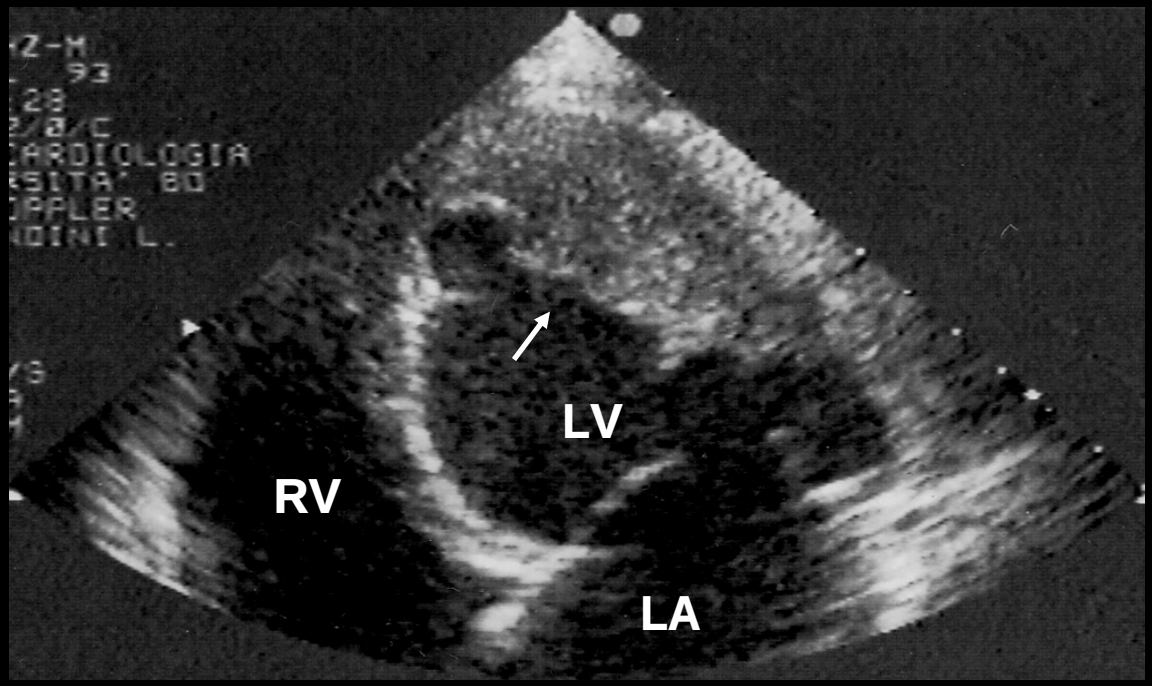

RA
LA
RV
LV

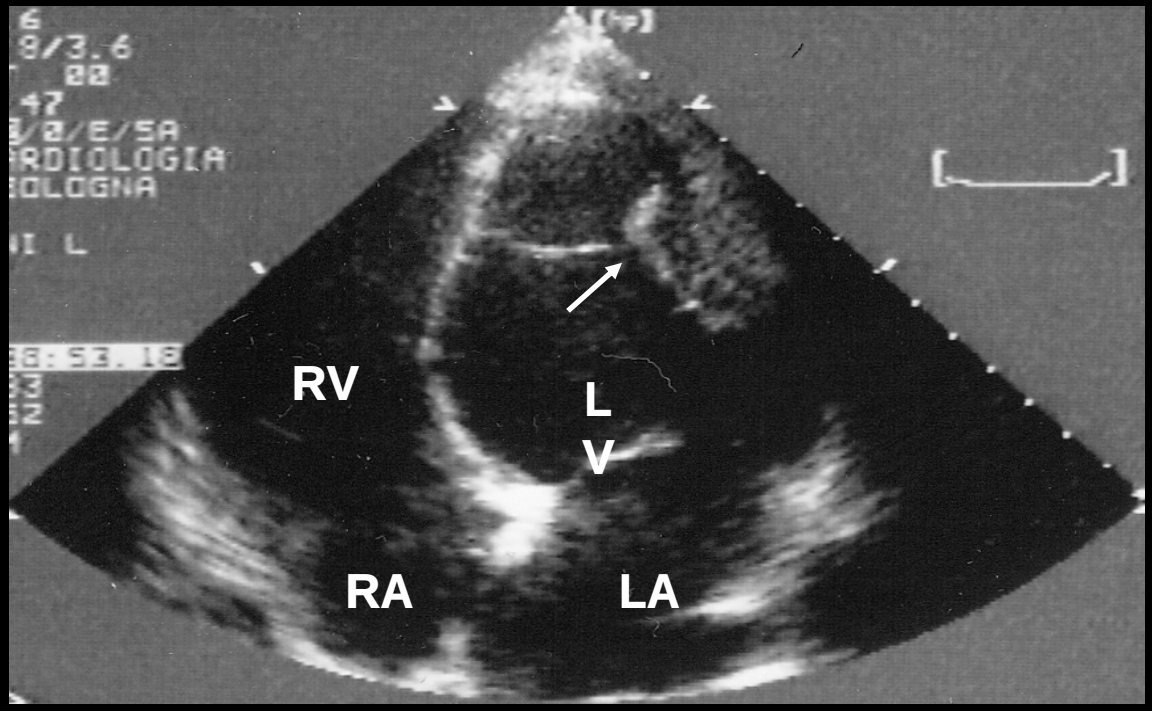

I
60
40
20
0




VSN
VT
ASN
ADX

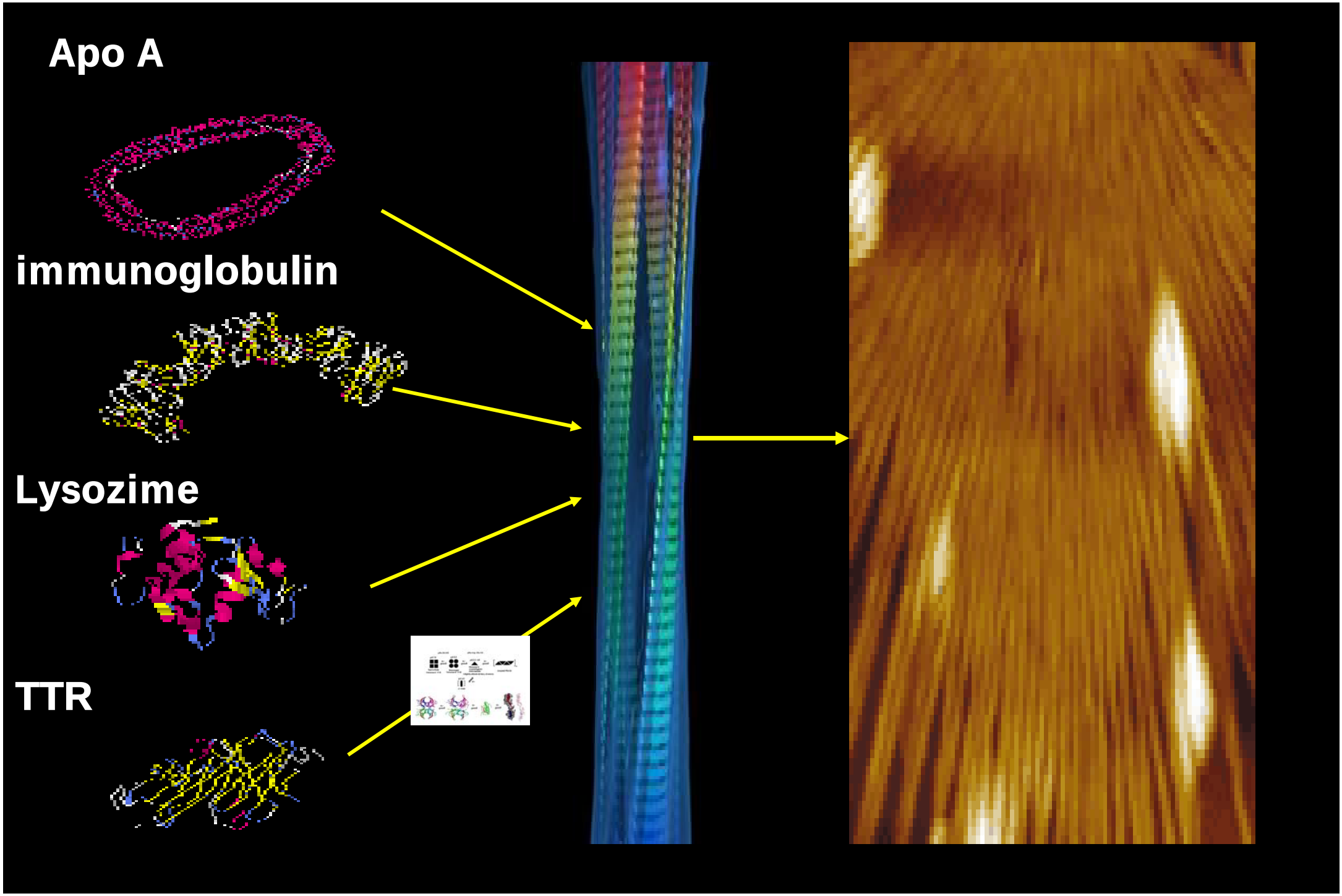
A

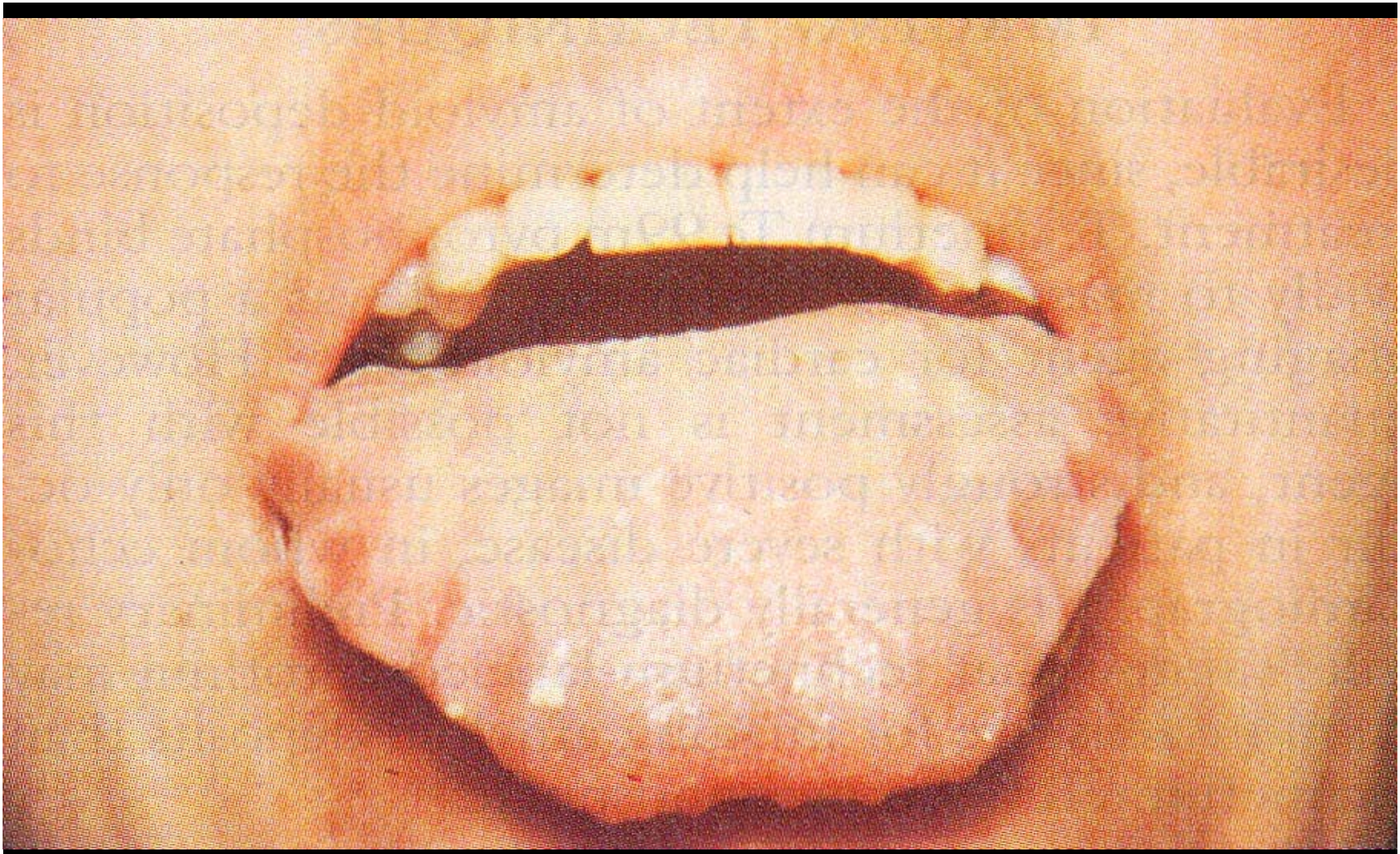




Terminology and Classification of Amyloidoses

Amyloid protein	Precursor	Syndrome or involved tissue
AL	immunoglobulin light chain	Primary / Myeloma associated
ATTR	Transthyretin	Familial (PAF) Senile (wilde type TTR)
AA	Serum AA	Secondary, reactive
A $ß_2$M	$ß_2$ microglobulin	Hemodyalisis associated
AApo AII	Apolipoprotein AII	Familial
AFib	Fibrinogen α chain	Familial
Alys	Lysozyme	Familial
....	....	....
Aß	Aß protein precursor	Alzheimer's desease, aging
APrP	Prion protein	Spongioform encephalopathies


Apo A
immunoglobulin
Lysozime
TTR

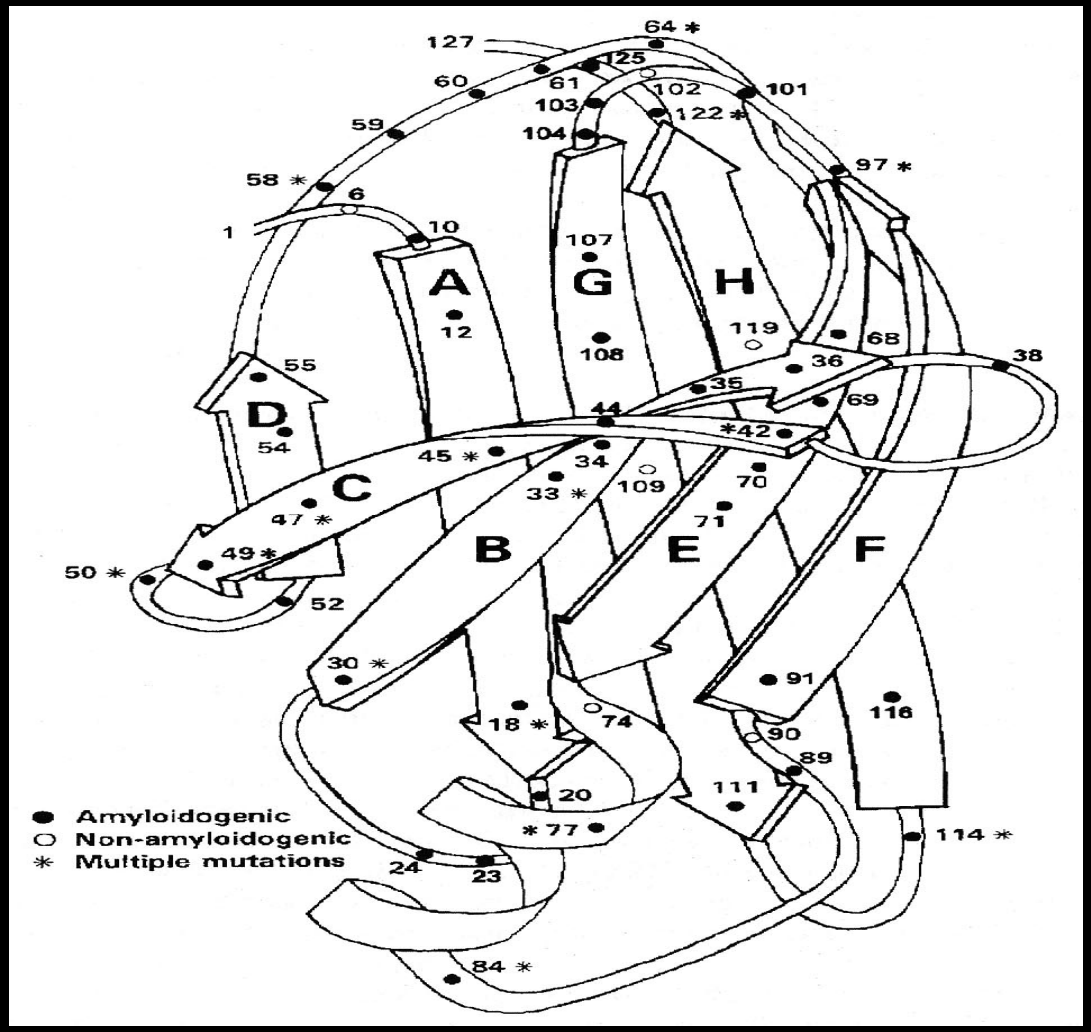


TRANSTHYRETIN (TTR)

- is costitutively expressed and synthesized by the liver with very small amounts made in the choroid plexus and retinal epitelium.
- Its functions include transport of saturated retinol binding protein and thyroxin

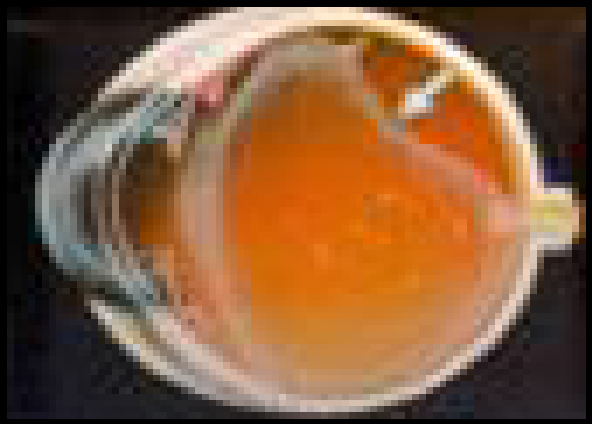
> 80 disease-related Mutations

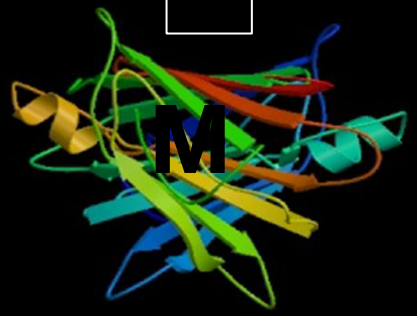
Most frequent: Val30Met

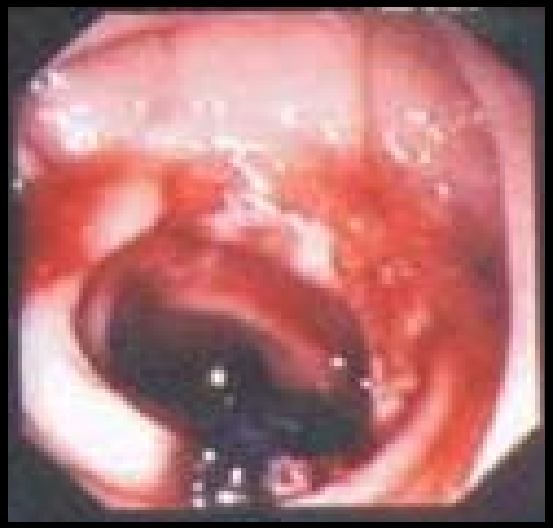


AS VIAGENS DE UM GENE
TRAVELS OF A GENE

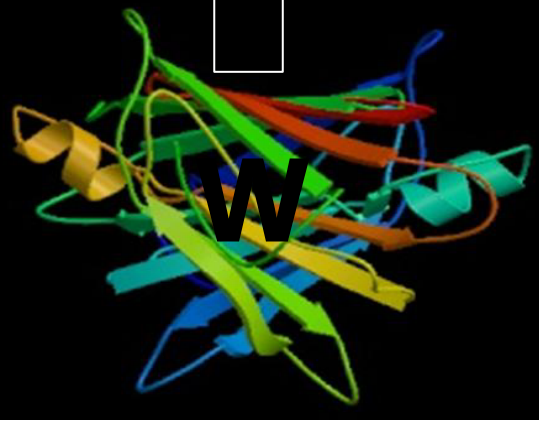
SPAGNA: I domini europei di Filippo II

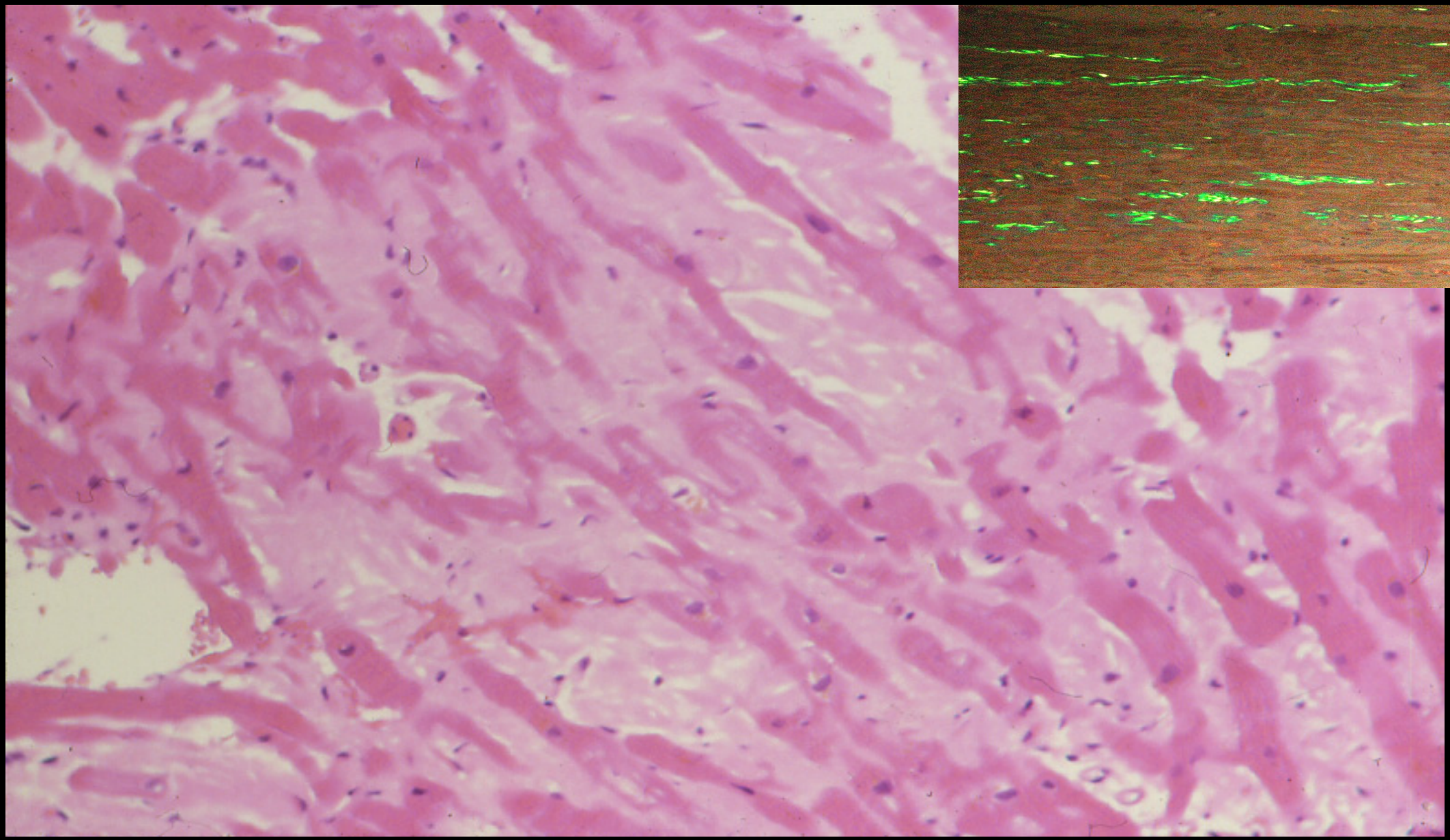


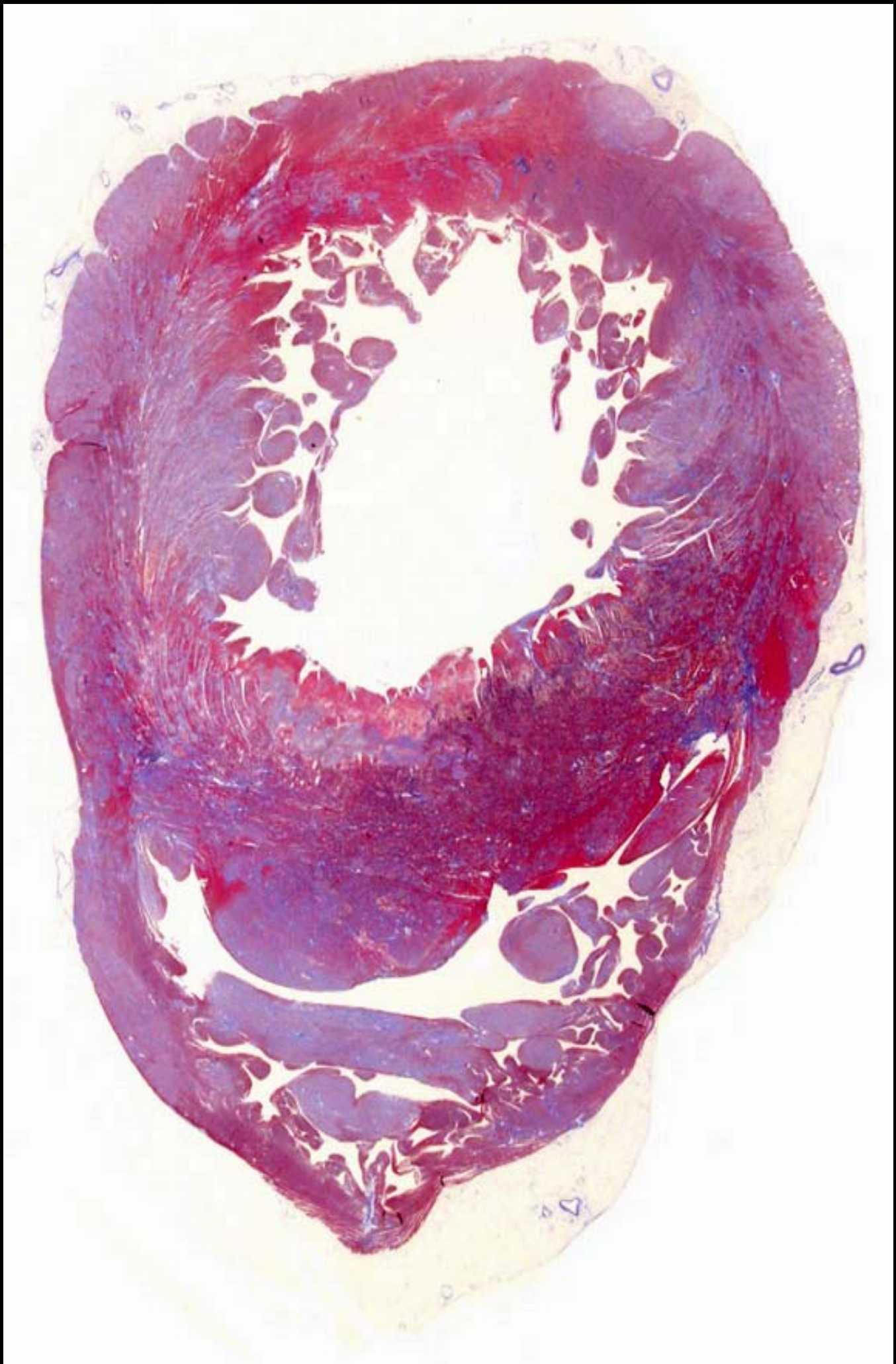

TM

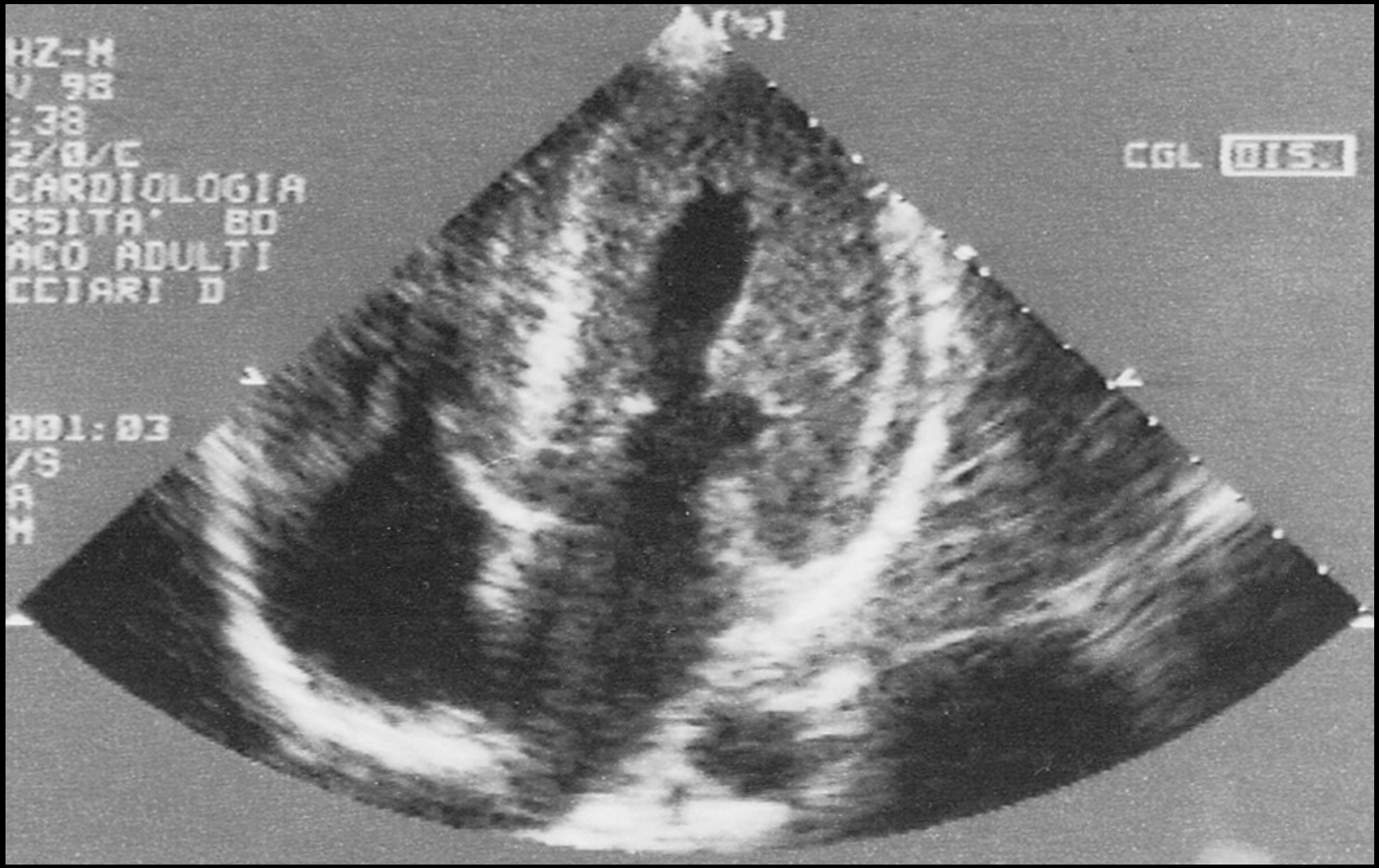


Wild type “senile” cardiac amyloidosis








HZ-M
V 98
:38
Z/0/C
CARDIOLOGIA
RSITA' BO
ACO ADULTI
CCIARI D
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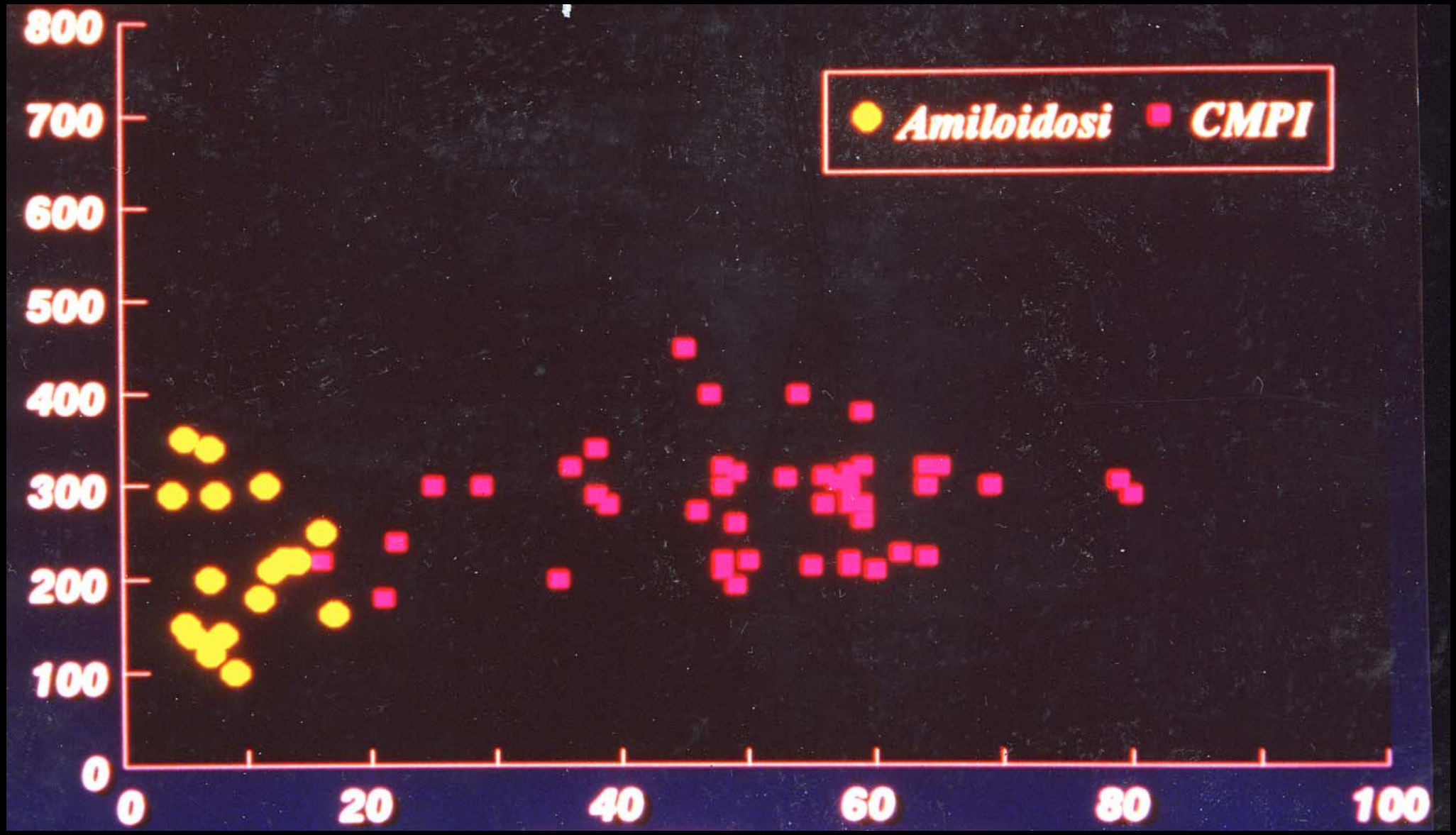
A
M
CGL 015.

4
3

Massa VSn (gr/m^2) ECO



"Total QRS score (mV)"

La terapia medica dello scompenso cardiaco da CMP amiloidotica

- Uso “giudizioso” dei diuretici
- Antialdosteronici
- ACE-Inibitori
- Ipersensibilità alla digitale
- Attenzione ai vasidilatatori “diretti”, in particolare nitrati e ca-antagonisti

Amyloidotic CMP:
therapeutic implications of etiologic diagnosis

AL

→ chemotherapy

- - → heart transplantation
↓
high dose chemotherapy
autologous stem cell transplantation

Hereditary ATTR

→ Liver transplantation

→ Heart-liver transplantation