UMBERTO I
POLICLINICO DI ROMA

Falls and Syncope in the Elderly

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SAPIENZA
UNIVERSITÀ DI ROMA

falls in geriatric age

PROBLEM'S PERCEPTION

- 30% of over 65 ys old subjects
- 40% of over 80 ys old subjects
- more than 60% of istutionalized old subjects experience at least one fall

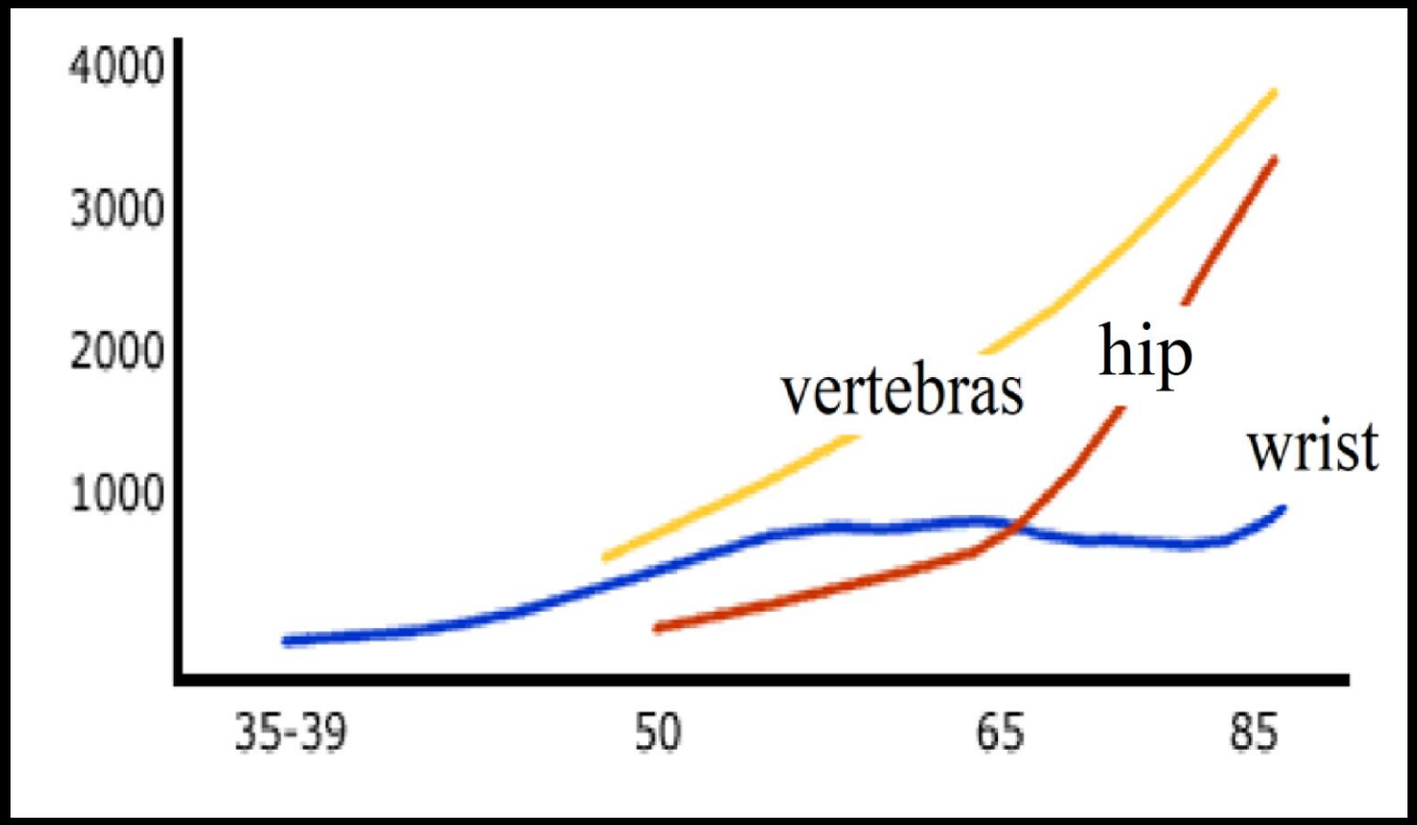
WHERE DO THEY FALL?

- 60% at the home
- 30% in the public area
- 10% residential facilities

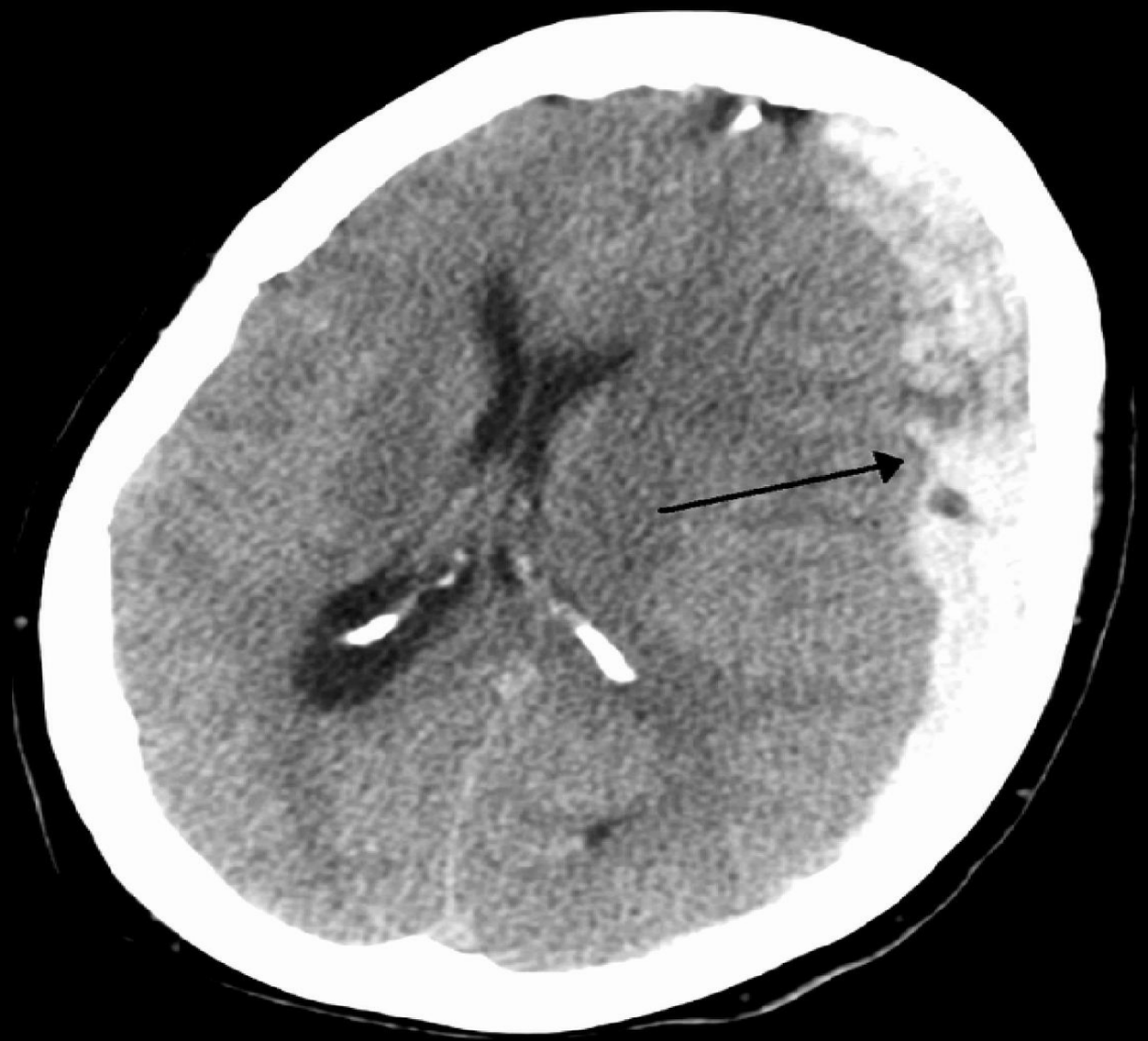
FALL CONSEQUENCES

- 65 % of 75 ys old subjects deceased after fall
- skeletric fracture is the likely outcome
- 75 % of the elderly patients with hip fracture dies within 1 year

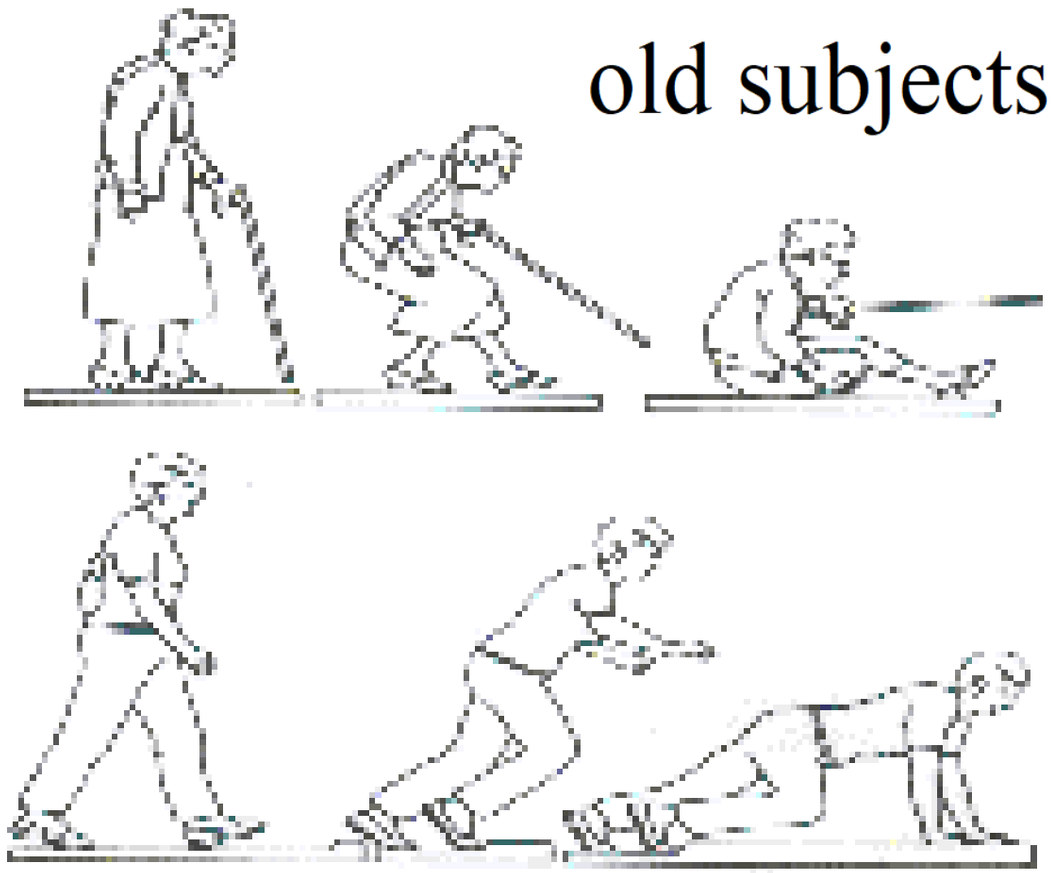
Age related incidence of fractures



IMPORTANT CONCOMITANT CAUSE OF ELDERLY FRACTURES IS OSTEOPOROSIS



old subjects

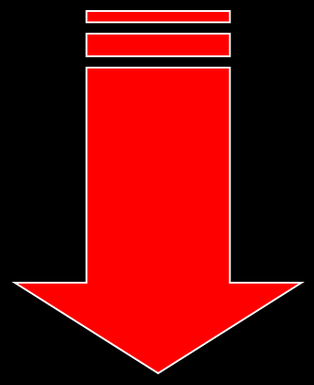


young subjects

PSYCOLOGICAL CONSEQUENCES

- post-trauma anxiety-depression
- loss of self-confidence
- loss of functional independence

PREVENTION OF ELDERLY FALLS



PREVENTION

MORBIDITY

MORTALITY

CAUSES OF FALLS IN THE ELDERLY

- Accidental falls
- Syncope or presyncope

CAUSES OF FALLS IN THE ELDERLY

Accidental fall

Syncope or presyncope

RISK FACTORS OF ACCIDENTAL FALLS IN THE ELDERLY

- Intrinsic factors
- Estrisic factors

Intrinsic Factors	RR
Muscle weakness	4,4
History of falls	3
Gait disturbances	2,9
Balance impairment	2,9
Use of mobility aids	2,6
Visual impairment	2,5
Joint diseases	2,4
ADL reduction	2,3
Depression	2,2
Cognitive impairment	1,8
Over 80 ys old	1,7

POSTURE AND AGING

- Postural stability perception
- Muscle strength (sarcopenia)
- Balance perception
- Latency times (reduction of nerve conduction velocity)
- Ability to adapt to changes in objectives and supports

FALLS

Estrinsic factors
Drug therepy (antihypertensive, sedative-hypnotic, hypoglycaemic drugs…)
Home (lighting, floors, carpets, tables, steps…)
Outdoor (sidewalks, curbs, holes, hollows…)
Clothes (shoes, slippers..)

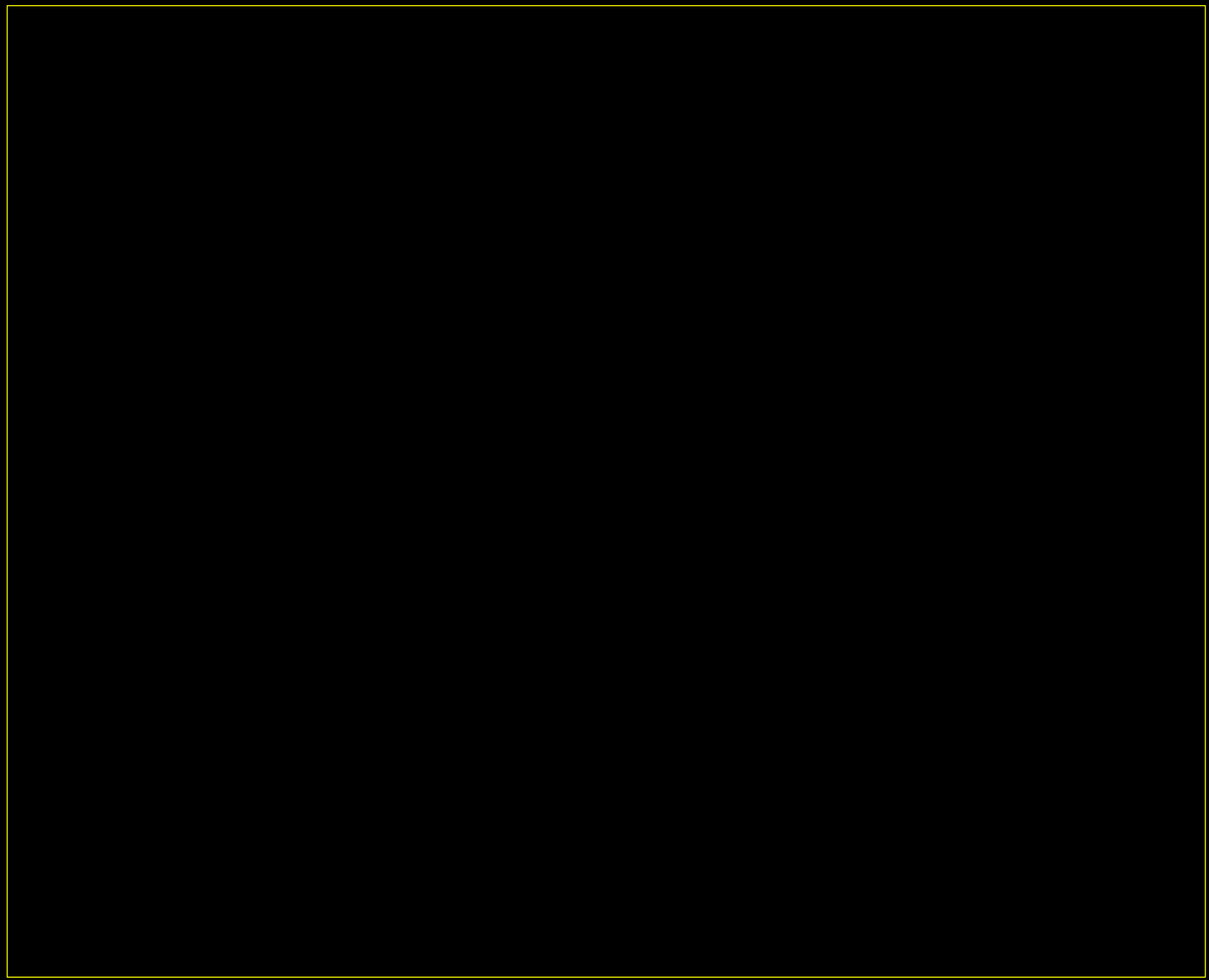
EVALUATION OF FALL RISK

- Chair standing test
- Standing Balance Test
- Timed Walking

Guralnik 1994

- Balance assessment
- Gait assessment

Tinetti 1987



CAUSES OF FALLS IN THE ELDERLY

Accidental falls

Syncope or presyncope

SYNCOPE DEFINITION

Syncope is a syndrome characterized by a transient self-limited episode of loss of consciousness (LOC) occurring as a result of a brief interruption of oxygen supply to the brain.

Pre-Syncopal Symptoms

Pre-syncopal symptoms are characterized by a sudden sense of generalized weakness with the patient feeling as if their legs woulden't carry them anymore, a black veil before the eyes or blurred vision, tinnitus, sometimes heart palpitations or sweating. Any or all of these symptoms appear suddenly concomitantly with an imminent fainting sensation but disappear spontaneously, usually in less than a minute.

CONDITIONS INCORRECTLY DIAGNOSED AS SYNCOPE

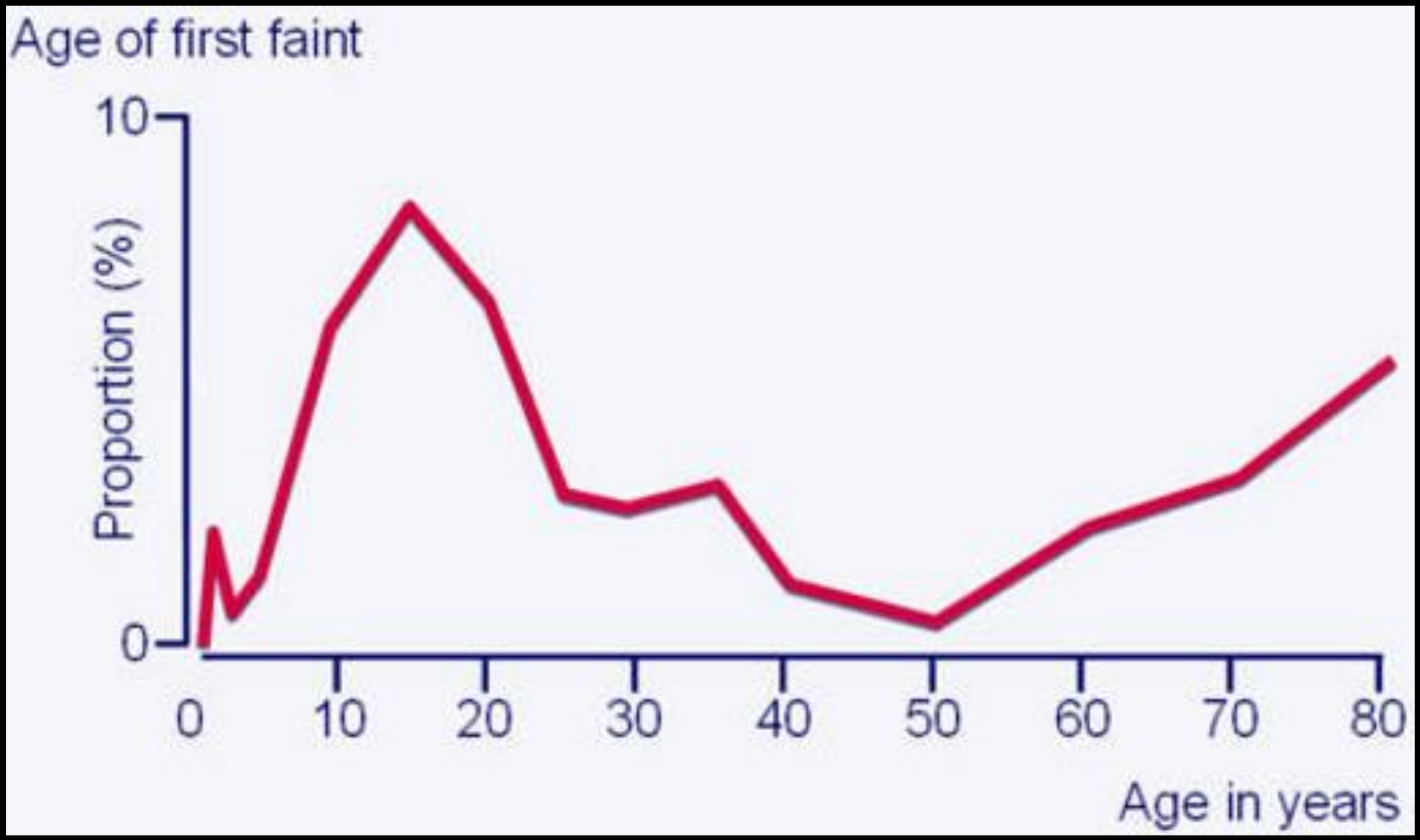
Disorders with partial or complete LOC but without global cerebral hypoperfusion

- Epilepsy
- Metabolic disorders including hypoglycemia, hypoxia, hyperventilation with hypocapnia
- Vertebrobasilar TIA

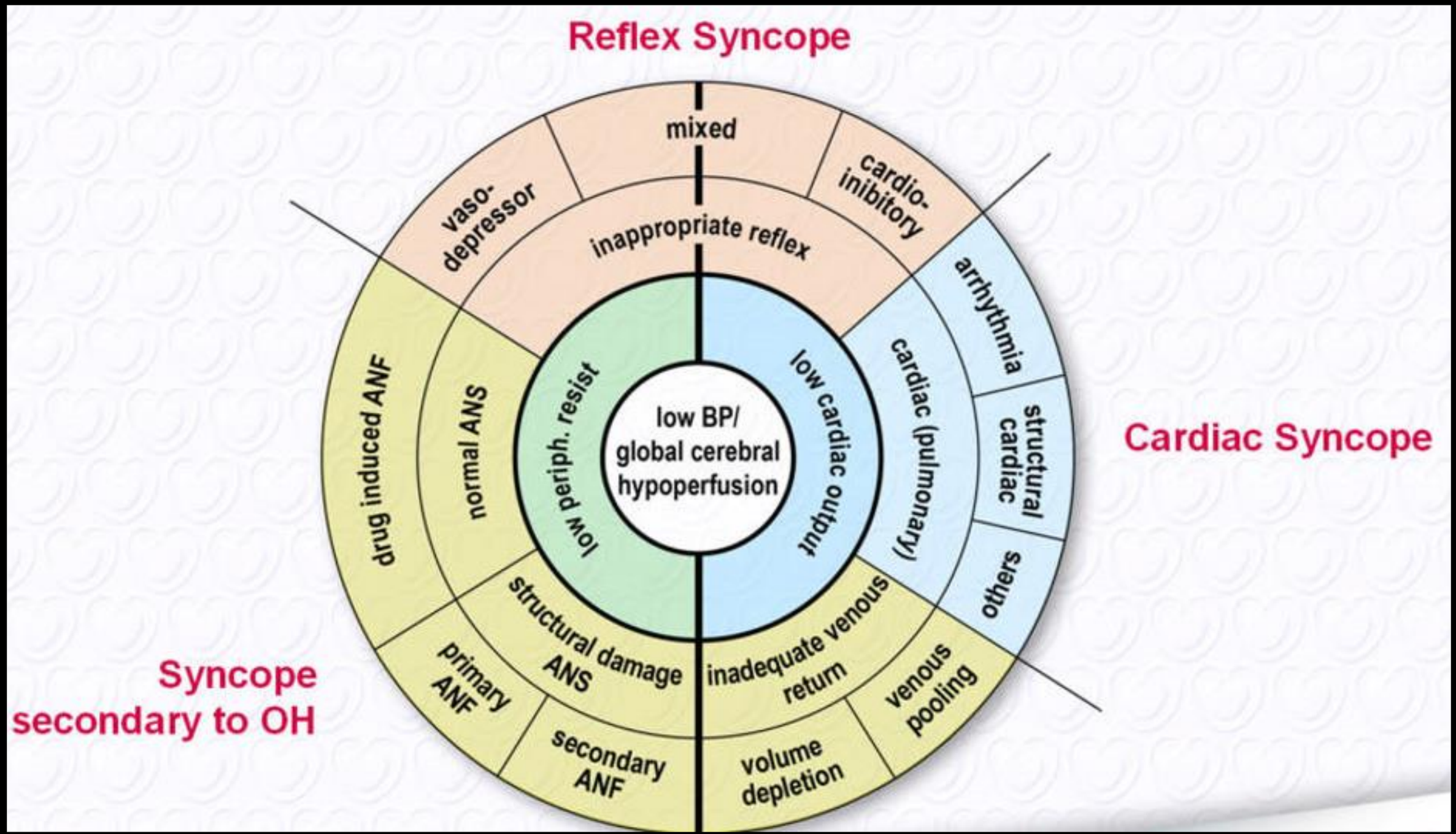
Disorders without impairment of consciousness

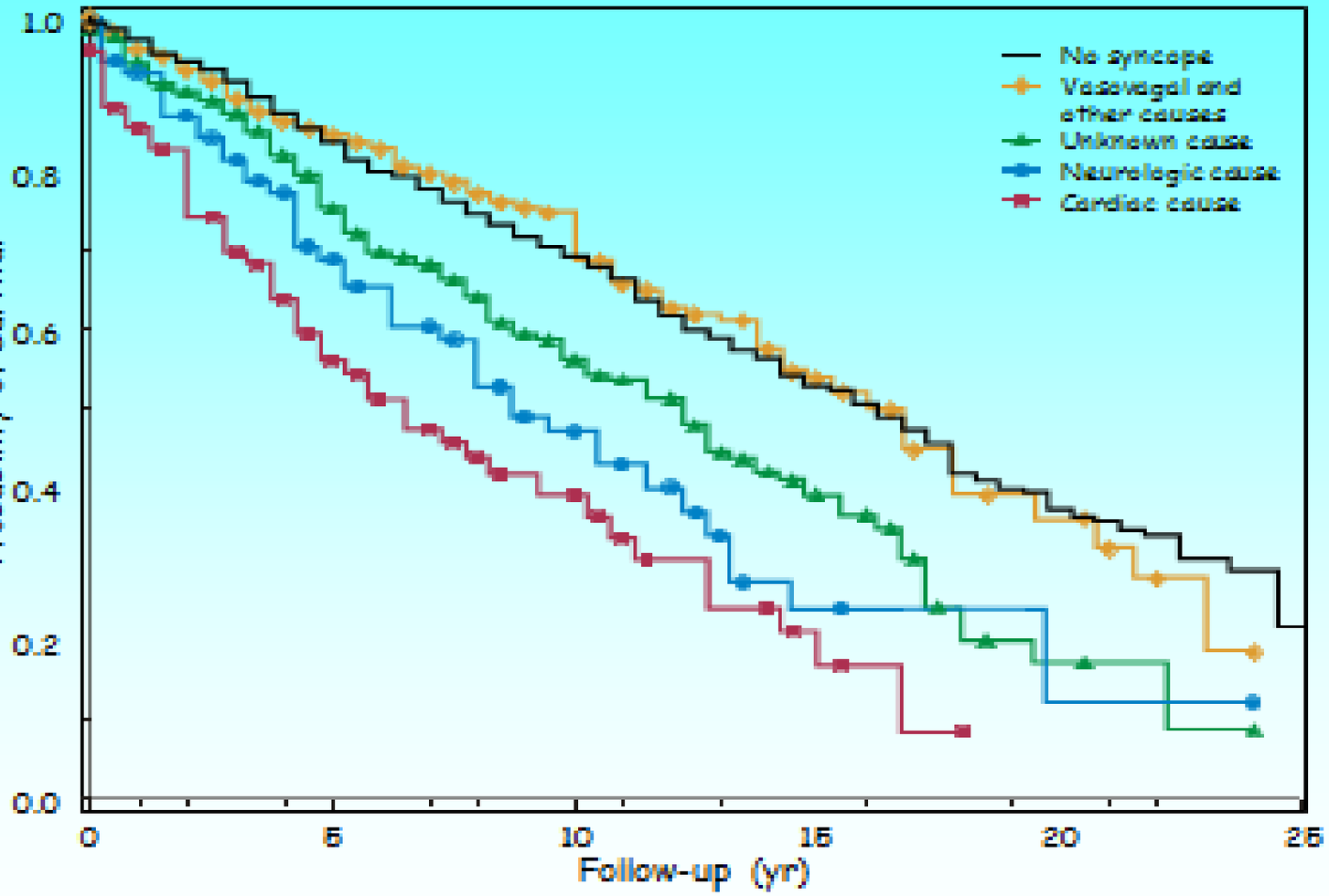
- Cataplexy
- Drop attacks
- Falls
- Functional (psychogenic psedosyncope
- TIA or carotid origin

Schematic presentation of the distribution of age and cumulative incidence of first episode of syncope in the general population from subjects up to 80 years



CLASSIFICATION AND PATHOPHYSIOLOGY





Soteriades ES, Evans JC, Larson MG, et al. NEJM. 2002;347:878-85.

INITIAL EVALUATION

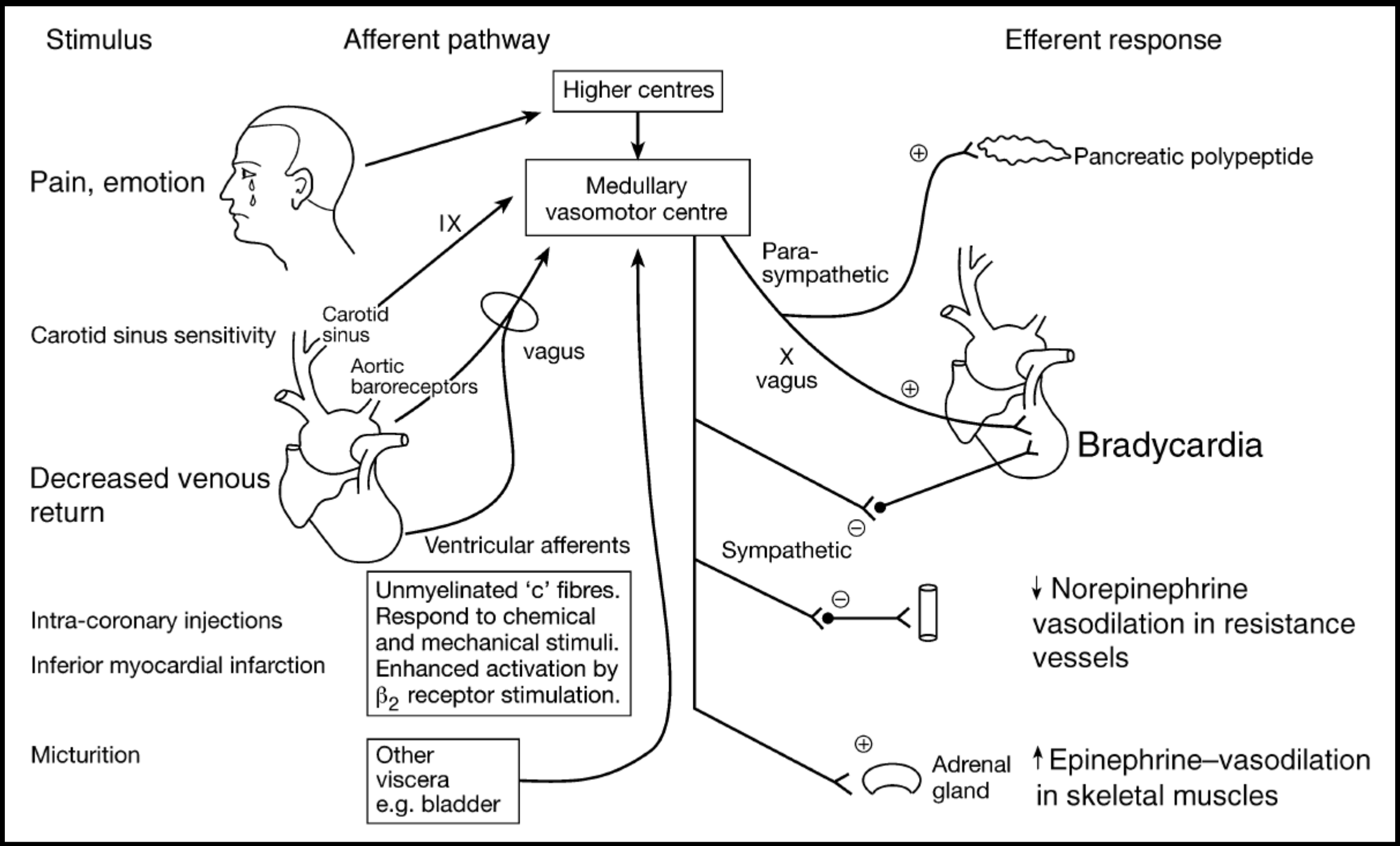
THE INITIAL EVALUATION OF A PATIENT PRESENTING WITH T-LOC CONSISTS OF:

- A CAREFUL HISTORY,
- PHYSICAL EXAMINATION,
- BP MEASUREMENT,
- ECG.

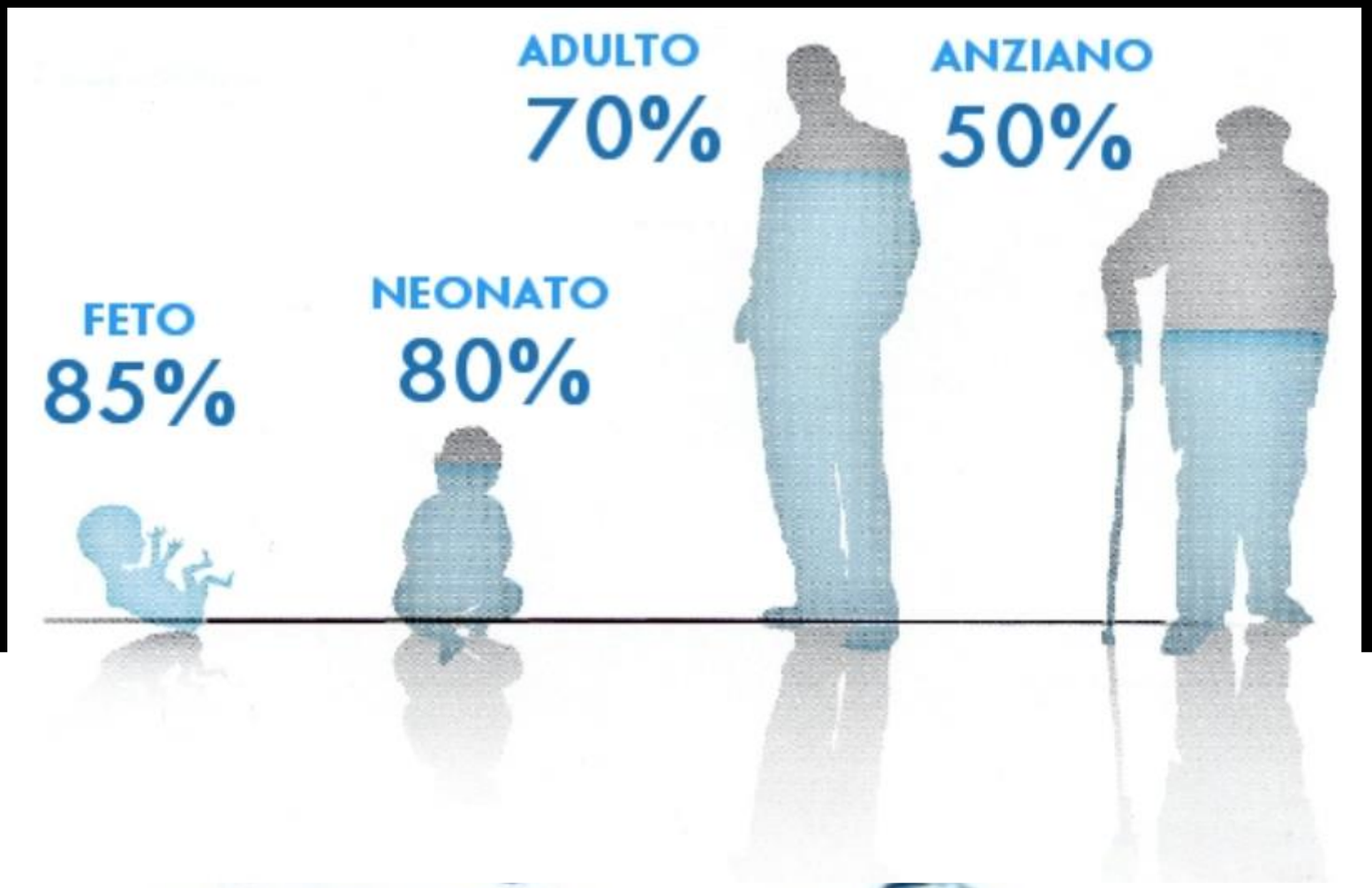
Neurally-mediated syncope	Orthostatic hypotension syncope	Arrhitmics syncope	Cardiopulmonary syncope	Neurological syncope
• Vasovagal • Carotid sinus hypersensitivity • Situational	• Pure autonomic failure (PAF, MSA, m. Parkinson, Lewy body dementia • Secondary autonomic failure(diabetes, kidney failure,…) • Drugs	• Bradycardia syndrome (sick sinus syndrome) • Tachicardia syndrome	• Aortic stenosis • AMI • Acute Cor Pulmonale • Pulmonary hypertension	• Vascular thievery • TIA • Ictal bradycardia
56%	2%	20%	3%	1%

18% unknown causes

JACC 2001; 37: 1921-1928



Kinsella SM Br J Anaesth. 2001;86(6):859-868



DISIDRATAZIONE

CAROTID SINUS SYNDROME (CSH)

Recurrent syncope due to excessive bradycardia and/or hypotension
in response to carotid sinus stimulation with no other apparent attributable cause of syncope.

In older people there is significant overlap between the symptoms of falls and syncope, this has been particularly demonstrated in CSH where older people with the reproducibly abnormal bradycardic response present with falls rather than syncope.

DIAGNOSTIC TESTS

Carotid sinus massage (CSM)

- Indications:

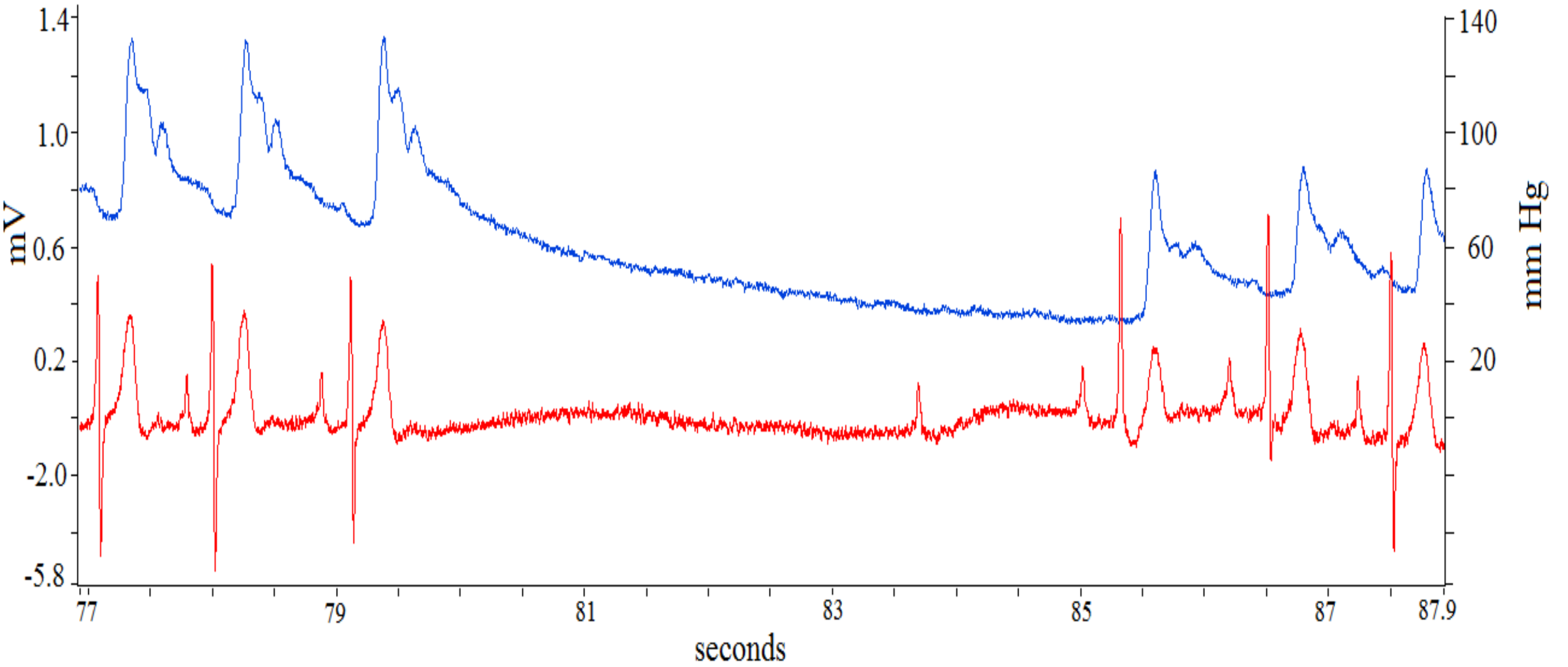
- >40 years with syncope of unknown etiology after initial evaluation.

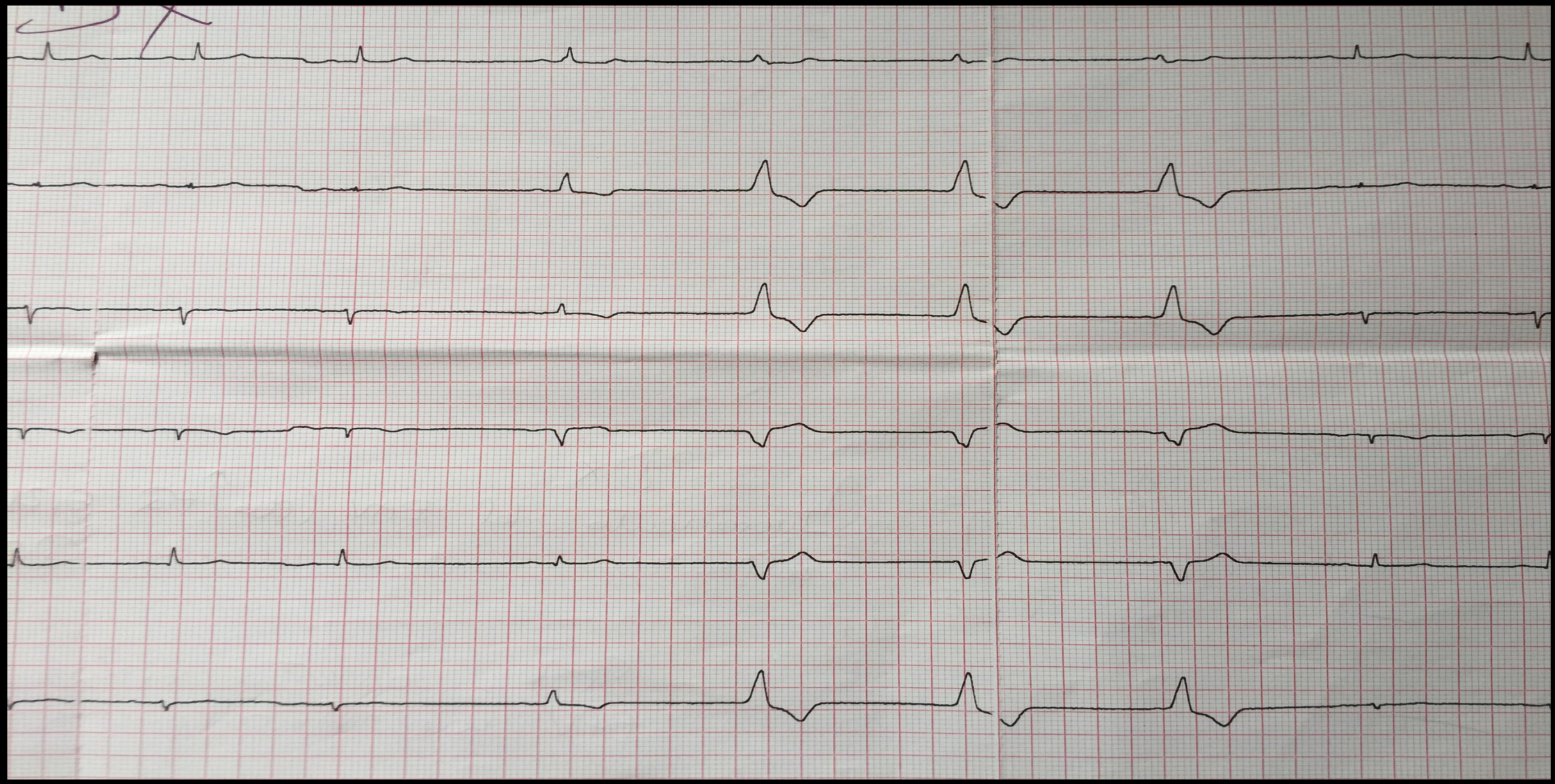
- Controindications:

- CSM should be avoided in patients with previous TIA or stroke within the past three months and in patients with carotid murmurs

- Diagnostic criteria:

CSM is diagnostic if syncope is reproduced in presence of asystole longer than 3s and/or fall in SBP >50 mmHg


1.4
1.0
0.6
0.2
-2.0
-5.8
mV
140
100
60
20
mm Hg
77
79
81
83
85
87
87.9
seconds



70 /min 5 mm/mV

I

II

III

aVR

aVL

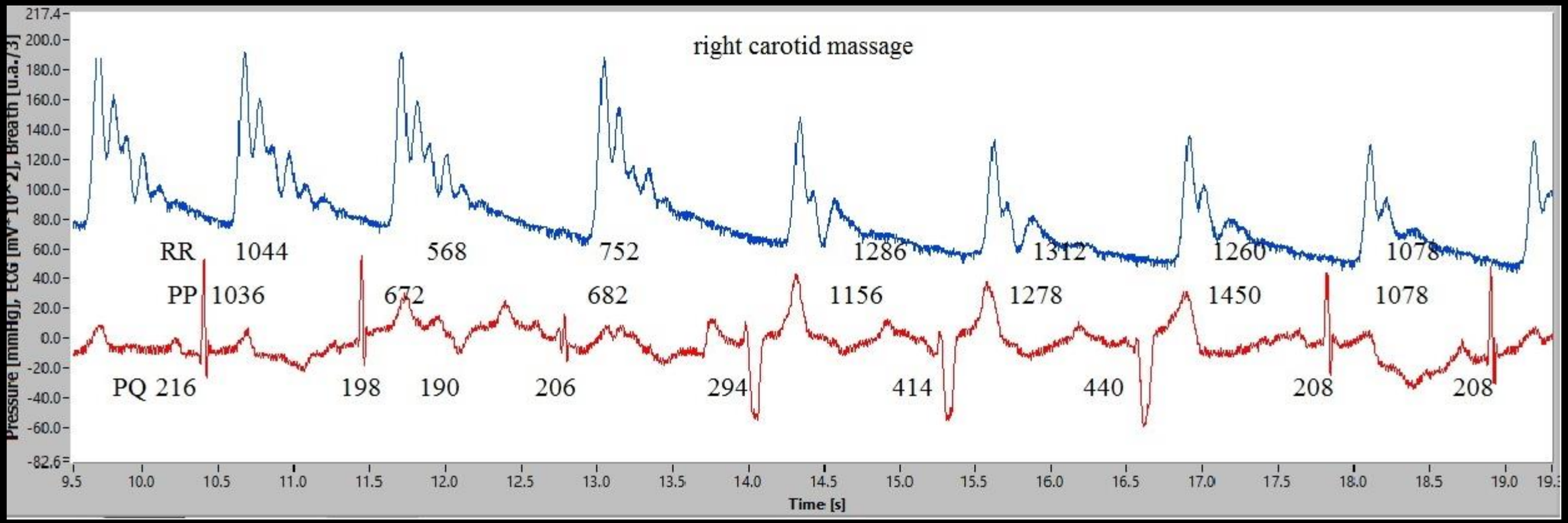
aVF

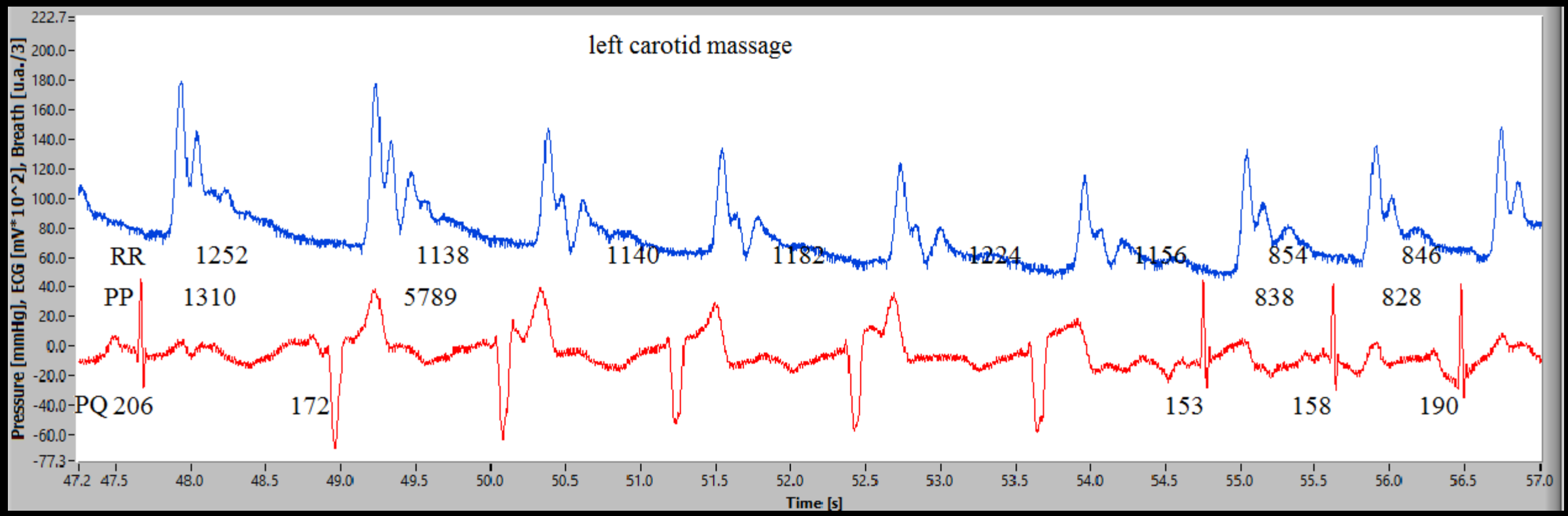
El. scolleg. C1

0.05 - 25 Hz F50

34.457

MyCardioPad XL V3e10 M 25 mm


right carotid massage
RR 1044 568 752 1286 1312 1260 1078
PP 1036 672 682 1156 1278 1450 1078
PQ 216 198 190 206 294 414 440 208 208
Pressure [mmHg], ECG [mV*10^2], Breath [u.a./3]
Time [s]


left carotid massage
RR 1252 1138 1140 1182 1224 1156 854 846
PP 1310 5789 838 828
PQ 206 172 153 158 190
Pressure [mmHg], ECG [mV*10^2], Breath [u.a./3]
222.7
200.0
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
-20.0
-40.0
-60.0
-77.3
47.2 47.5 48.0 48.5 49.0 49.5 50.0 50.5 51.0 51.5 52.0 52.5 53.0 53.5 54.0 54.5 55.0 55.5 56.0 56.5 57.0
Time [s]

Neurally-mediated syncope	Orthostatic hypotension syncope	Arrhitmics syncope	Cardiopulmonary syncope	Neurological syncope
• Vasovagal • Carotid sinus hypersensitivity • Situational	• Pure autonomic failure (PAF, MSA, m. Parkinson, Lewy body dementia • Secondary autonomic failure(diabetes, kidney failure,…) • Drugs	• Bradycardia syndrome (sick sinus syndrome) • Tachicardia syndrome	• Aortic stenosis • AMI • Acute Cor Pulmonale, • Pulmonary hypertension	• Vascular thievery • TIA • Ictal bradycardia

Vasovagal syncope

In older adults vagal tone is reduced.
Vasodepressor syncope is much more common without classical prodromal features such as nausea, pallor and diaphoresis.

DIAGNOSTIC TEST
Tilt testing

- <u>Indications:</u>

- In case of unexplained single syncopal episode in high-risk settings or recurrent episodes in the absence of organic heart disease, after cardiac causes of syncope have been excluded.
- When it is needed to demonstrate susceptibility to reflex syncope to the patient
- To discriminate reflex and OH syncope.
- For differentiating syncope with jerking movements from epilepsy
- For evaluating patients with recurrent unexplained falls
- For evaluating patients with frequent syncope and psychiatric disease

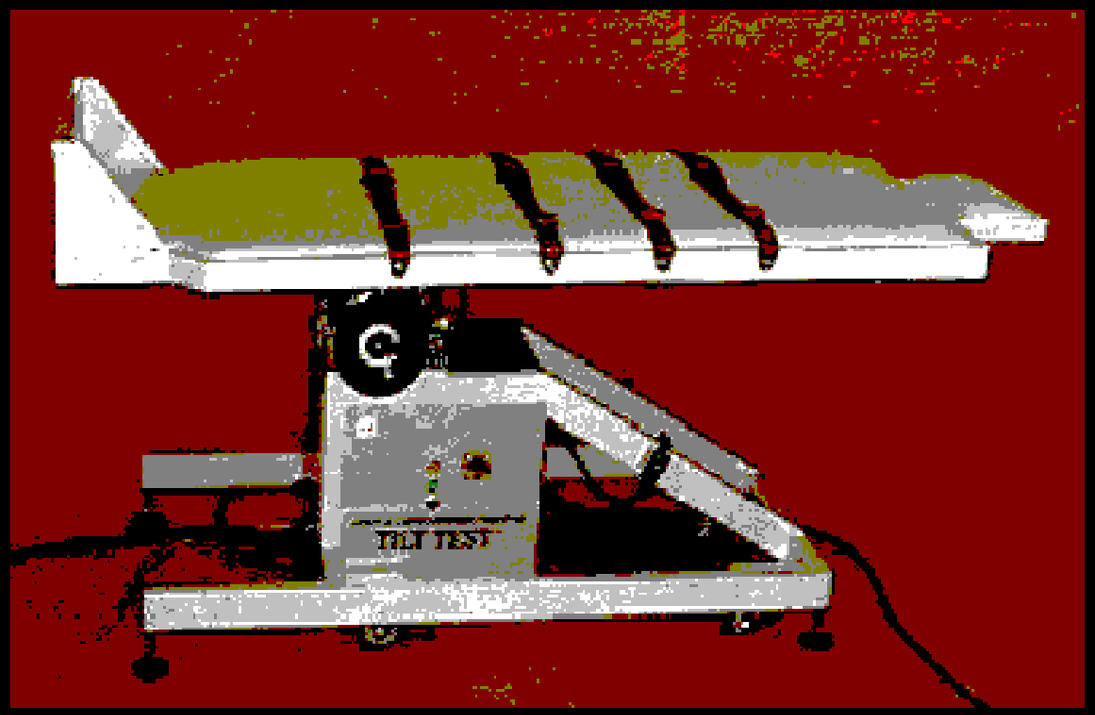
DIAGNOSTIC TEST

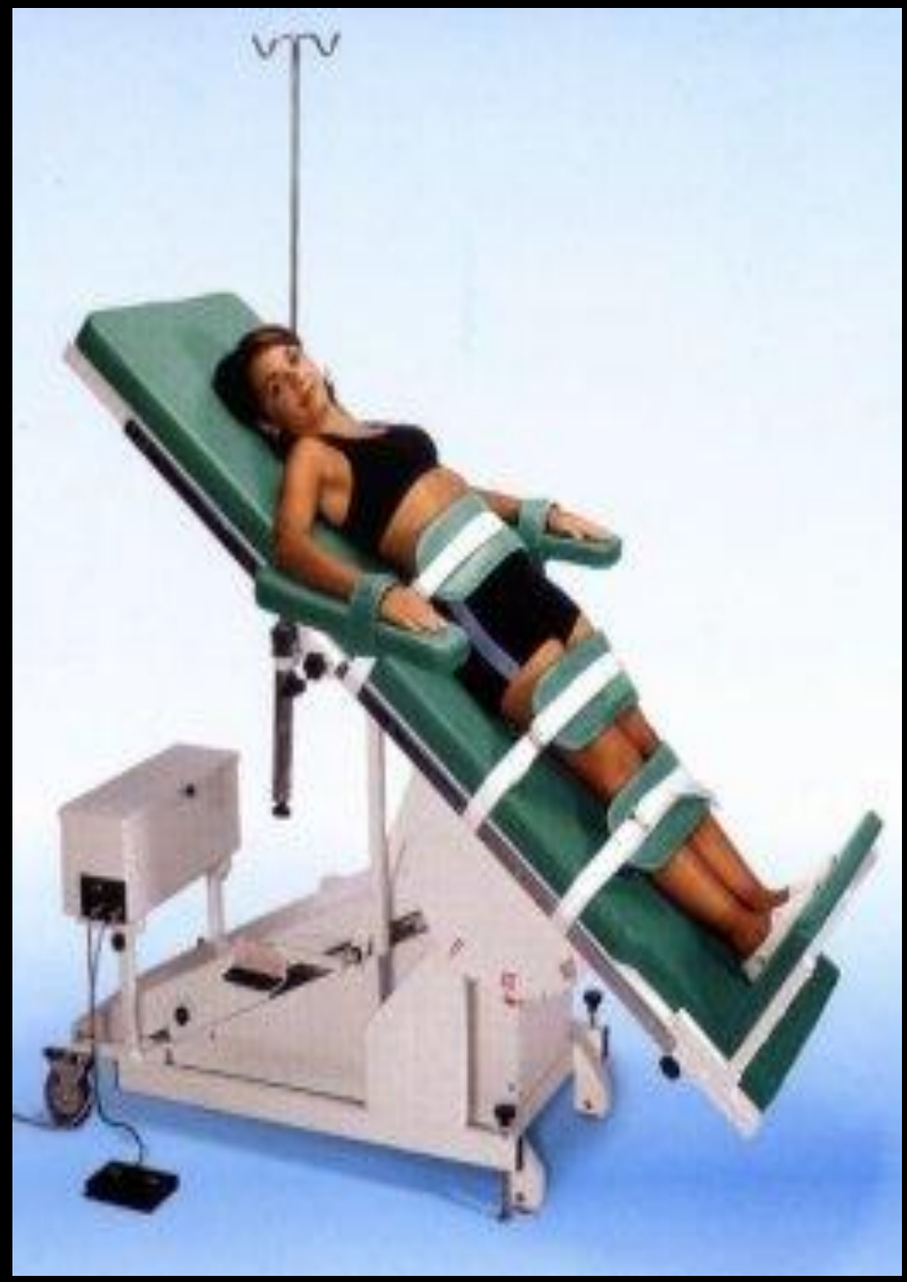
Tilt testing

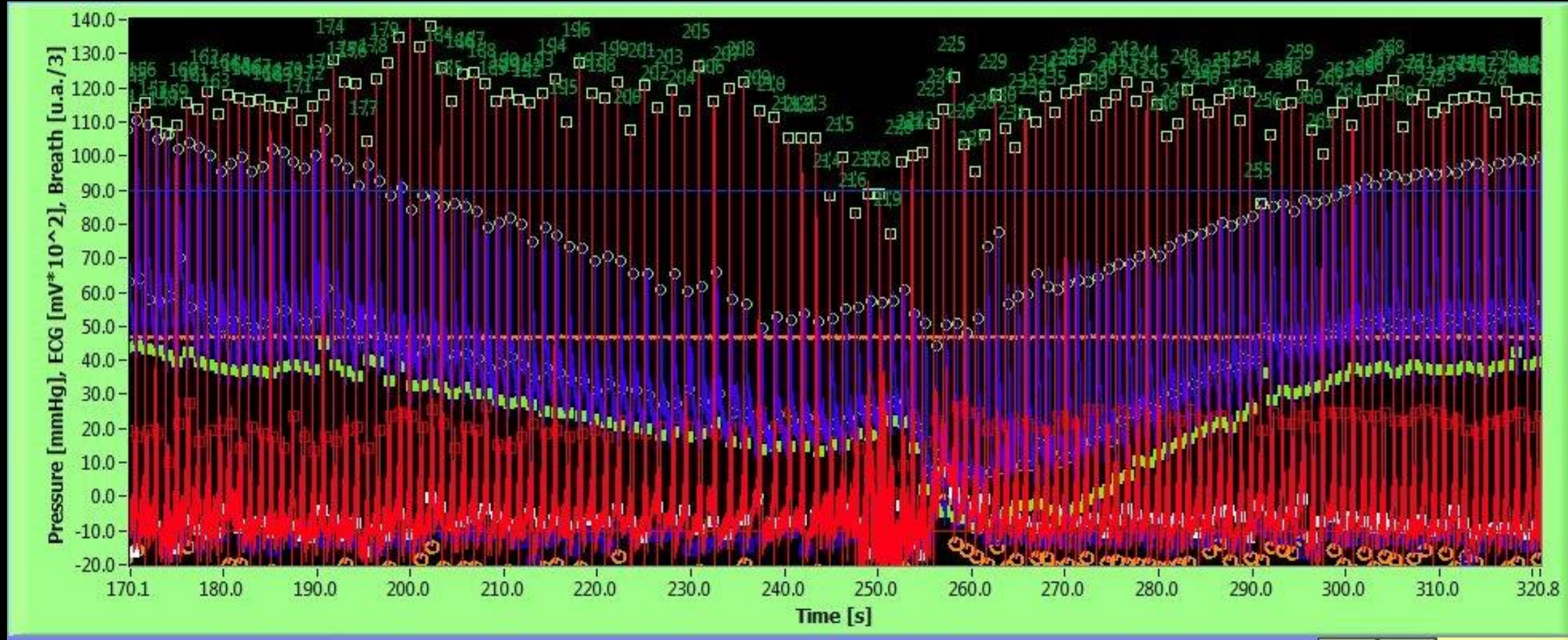
- Methodology

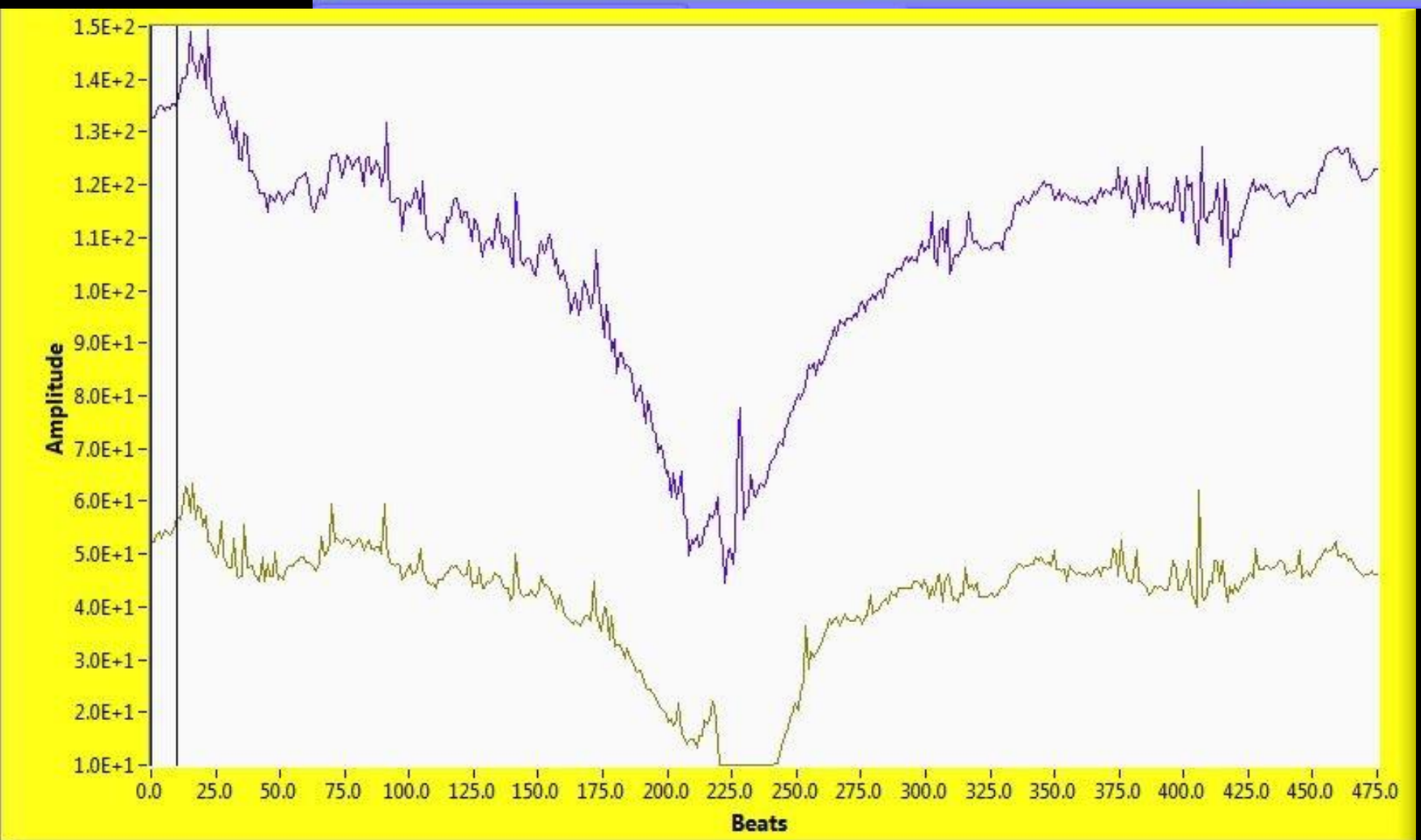
- Supine pre-tilt phase of at least 5 min
- Tilt angle between 60° to 70°, is recommended
- Passive phase of a minimum of 20 min and a maximum of 45min, is recommended
- For nitroglycerine, a fixed dose off 300/400 mcg sublingually administered in the upright position, is recommended

TILT-TABLE

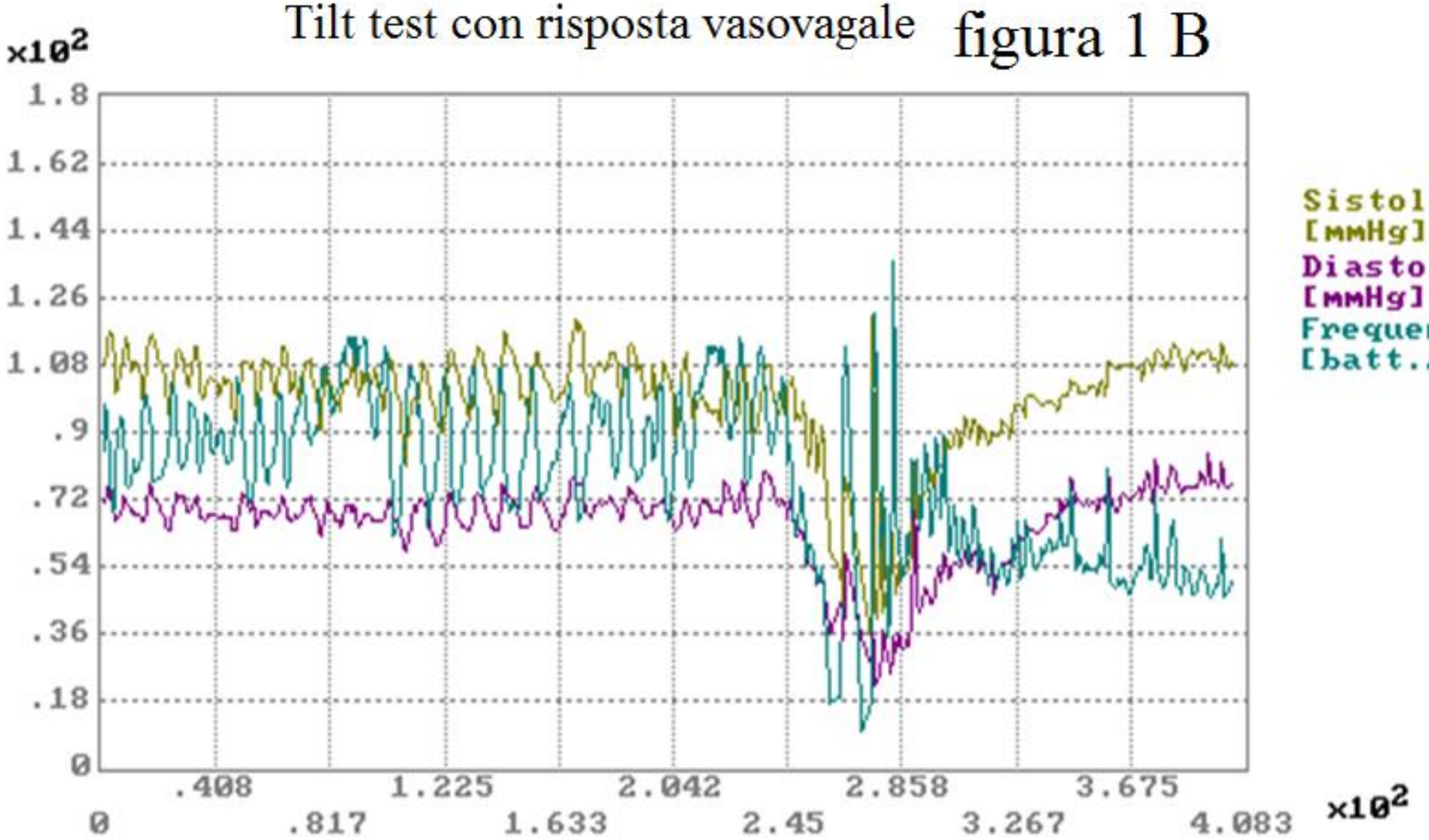





Pressure [mmHg], ECG [mV*10^2], Breath [u.a./3]
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
-20.0
170.1
180.0
190.0
200.0
210.0
220.0
230.0
240.0
250.0
260.0
270.0
280.0
290.0
300.0
310.0
320.8
Time [s]


Amplitude
1.5E+2
1.4E+2
1.3E+2
1.2E+2
1.1E+2
1.0E+2
9.0E+1
8.0E+1
7.0E+1
6.0E+1
5.0E+1
4.0E+1
3.0E+1
2.0E+1
1.0E+1
0.0
25.0
50.0
75.0
100.0
125.0
150.0
175.0
200.0
225.0
250.0
275.0
300.0
325.0
350.0
375.0
400.0
425.0
450.0
475.0
Beats

Tilt test con risposta vasovagale figura 1 B



Upright tilt → Peripheral venous pooling → ↓ Venous return → ↓ Left ventricular volume → ↓ Left ventricular contractility → ↓ Mechanoreceptor stimulation → ↓ Vasomotor center

Vasomotor center → ↓ Sympathetic tone → ↓ Peripheral vasodilatation → ↓ Hypotension → **Syncope**

Vasomotor center → ↑ Vagal tone → ↓ Bradycardia or asystole → **Syncope**

DIAGNOSTIC TEST
Tilt testing

- <u>Diagnostic criteria</u>

-In patient without structural heart disease:

- reflex syncope
- orthostatic hypotension

-LOC in absence of hypotension and or bradycardia:

- psychogenic pseudo syncope

Neurally-mediated syncope	Orthostatic hypotension syncope	Arrhitmics syncope	Cardiopulmonary syncope	Neurological syncope
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DIAGNOSTIC TEST

Active standing

- <u>Indications</u>:

- manual intermittent determination of BP supine and during active standing for 3 min

- <u>Diagnostic criteria:</u>

- The test is diagnostic when there is a *symptomatic or asymptomatic fall* in SBP from baseline value >20 mmHg or DBP > 10 mmHg or a decrease of SBP to <90 mmHg

(Totali 888 Secondi)

Sist. R-R int / Secondi
[mmHg] [msec/10] [sec.]

SYNDROMES OF ORTHOSTATIC INTOLERANCE ABLE TO CAUSE SYNCOPE

Classific-ation	Test for diagnosis	Time from standing to symptoms	Pathophysiology	Most frequent symptoms	Most frequent associated conditions
Initial OH	Beat-to-beat SBP on lying-to-standing test (active standing).	0-30 s	Mismatch betwen CO and SVR.	Lighteadedness/dizziness, visual disturbances a few seconds after standing up, (syncope rare).	Young asthenic subjects, old age, drug induced (α-blockers), CSS.
Classical OH (classical autonomic failure)	Lying-to-standing test (active standing) or tilt table.	30 -3 min	Impaired increase in SVR in autonomic failure resulting in pooling of blood/or severe volume depletion over-riding reflex adjustments.	Dizziness, pre-syncope, fatigue, weakness, palpitations, visual and hearing disturbances (syncope rare).	Old age, drug induced (any vasoactive drugs and diuretics).
Delayed (progressive) OH	Lying-to-standing test (active standing) or tilt table.	3-30 min	Progressive fall in venous return: low CO, diminished vasoconstriction capacity (failing adaptation reflex), no reflex bradycardia.	Prolonged prodrome (dizziness, fatigue, weakness, palpitations, visual and hearing disturbances, hyperhydrosis, low back pain,	Old age, autonomic failure, drug induced (any vasoactive drugs and diuretics), co-morbidities.

DIAGNOSTIC TEST
OTHER METHODIC

- Holter ECG
- ILR and ELR
- Electrophysiological study
- Echocardiography
- Exercise testing
- Psychiatric evaluation
- Neurological evaluation

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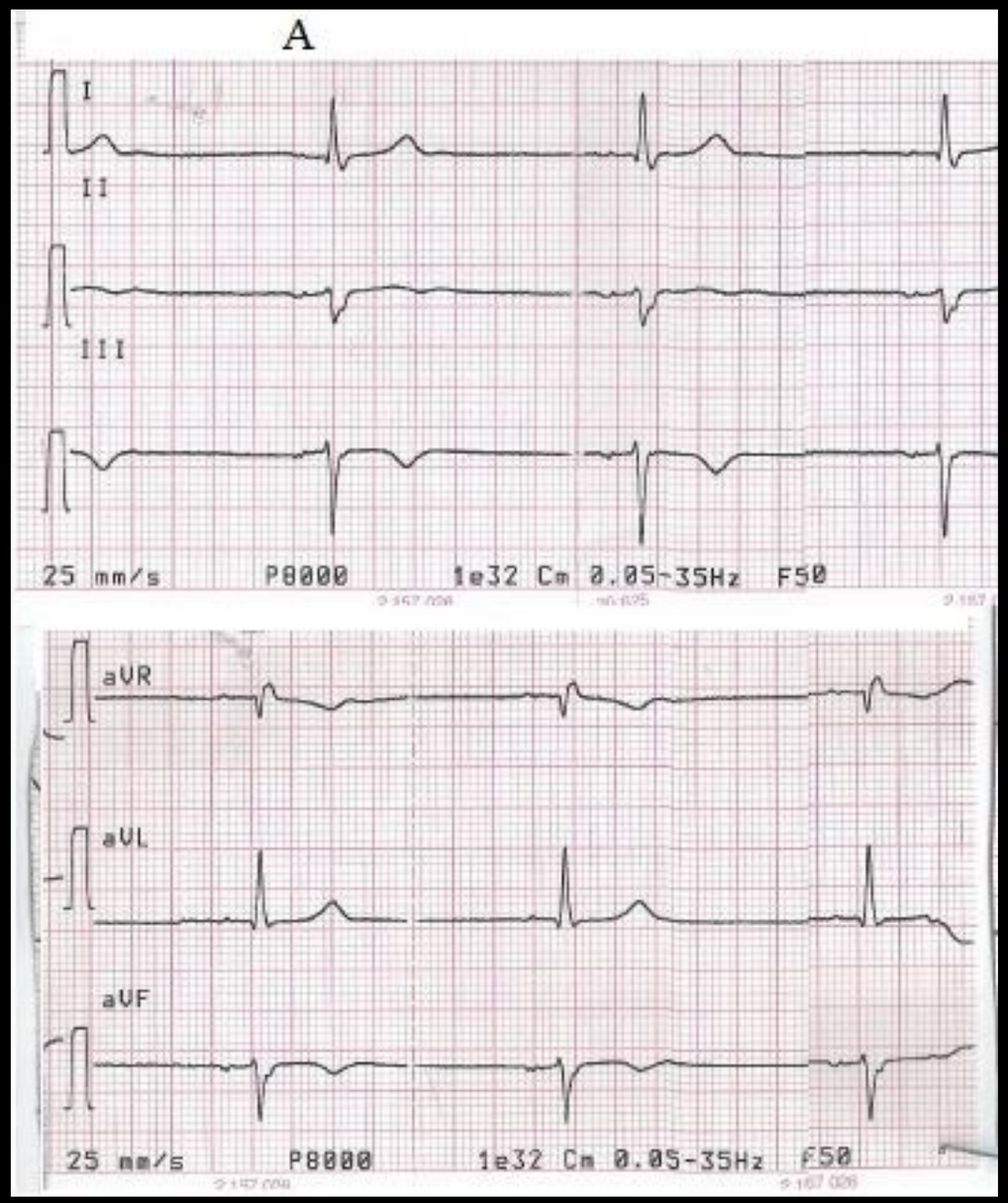
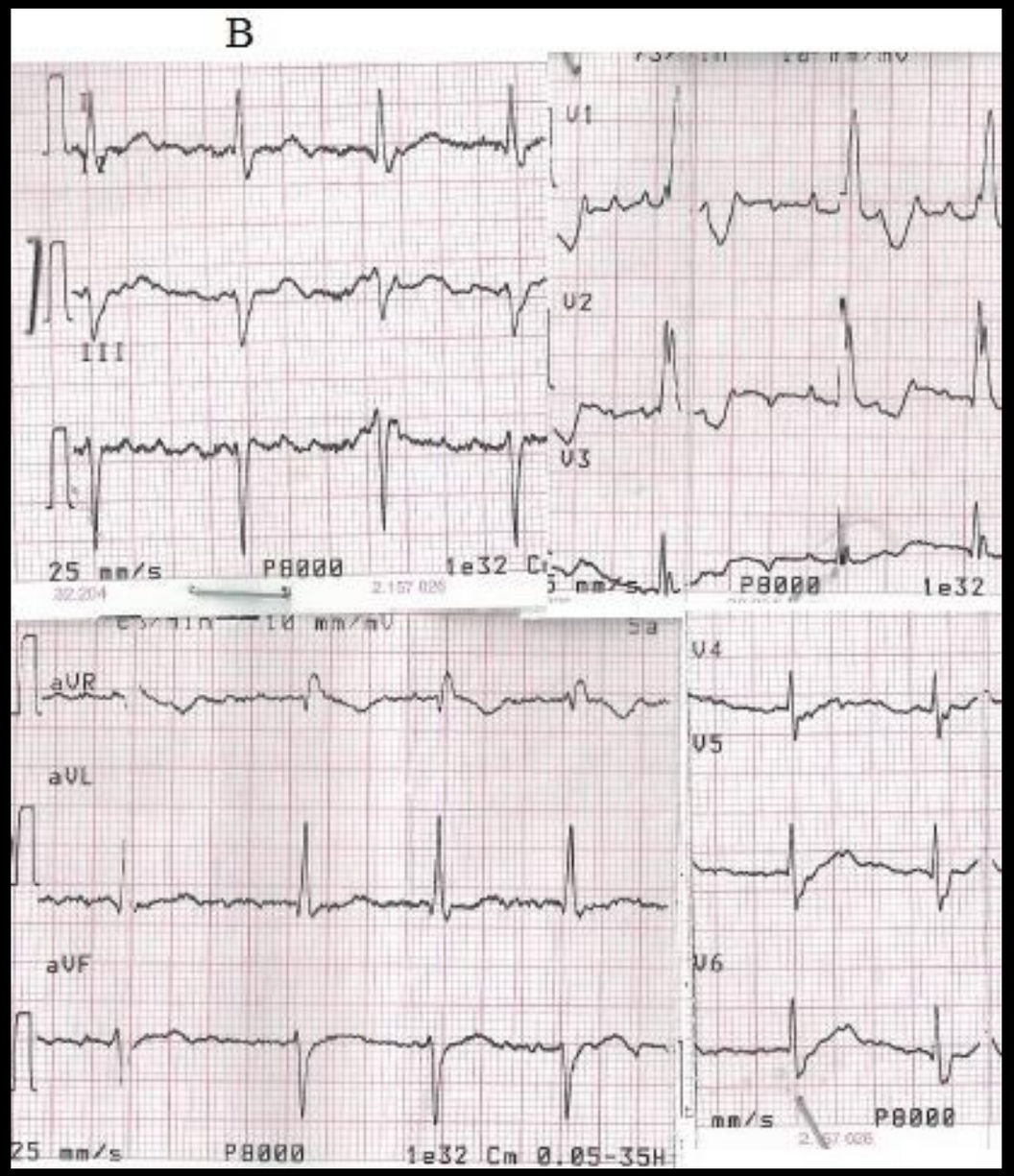
Cardiac Syncope





Sick sinus syndrome

Cardiac Syncope

Table 2. Arrhythmias in Patients with Sick Sinus Syndrome

Bradyarrhythmias
Ectopic atrial bradycardia
Greater than three-second pause following carotid massage
Long pause following cardioversion of atrial tachyarrhythmias
Sinoatrial exit block
Mobitz type I block (Wenckebach block)
Mobitz type II block
Sinus arrest (with or without junctional escape)
Sinus bradycardia
Tachyarrhythmias
Atrial fibrillation
Atrial flutter
Atrial tachycardia
Paroxysmal supraventricular tachycardia
Alternating bradyarrhythmias and tachyarrhythmias
Tachycardia-bradycardia syndrome

Adapted with permission from Wahls SA. Sick sinus syndrome. Am Fam Physician. *1985;31(3):120, with additional information from reference 3.*

Sick sinus syndrome

Cardiac Syncope

Table 1. Causes of Sick Sinus Syndrome

Intrinsic causes

Degenerative fibrosis

Infiltrative disease processes

- Amyloidosis
- Connective tissue diseases
- Hemochromatosis
- Sarcoidosis

Ion channel dysfunction

Remodeling of the sinoatrial node

Extrinsic factors that mimic or exacerbate sick sinus syndrome

Autonomic dysfunction

- Carotid sinus hypersensitivity
- Neurocardiogenic syncope
- Vasovagal syncope

Increased vagal tone (occurs in athletes and during sleep)

Extrinsic factors that mimic or exacerbate sick sinus syndrome *(continued)*

Metabolic disturbances

- Hyperkalemia
- Hypocalcemia
- Hypokalemia
- Hypothermia
- Hypothyroidism
- Hypoxia

Obstructive sleep apnea

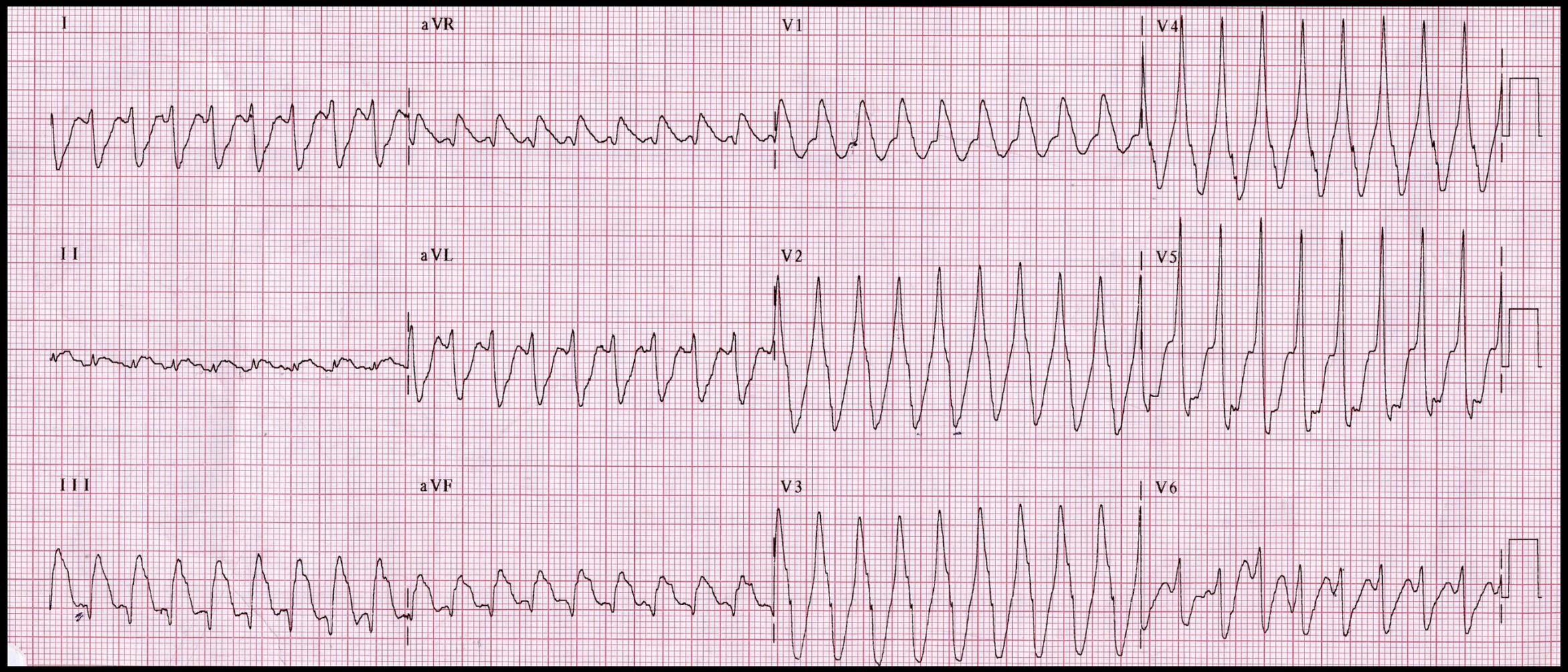
Pharmacologic agents

- Antiarrhythmic medications (class I and III)
- Beta blockers
- Calcium channel blockers (nondihydropyridine)
- Digoxin
- Lithium
- Sympatholytic medications

Toxins

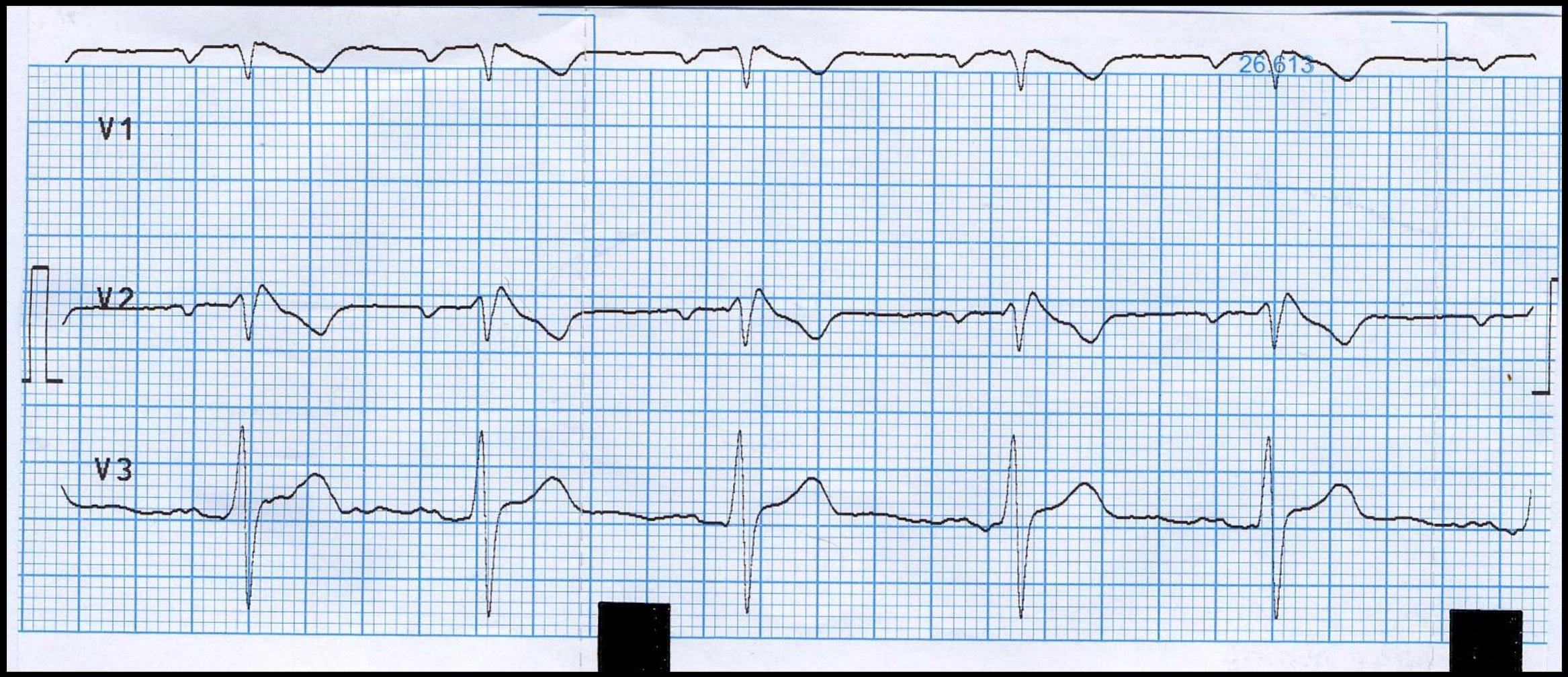
Sick sinus syndrome

Cardiac Syncope



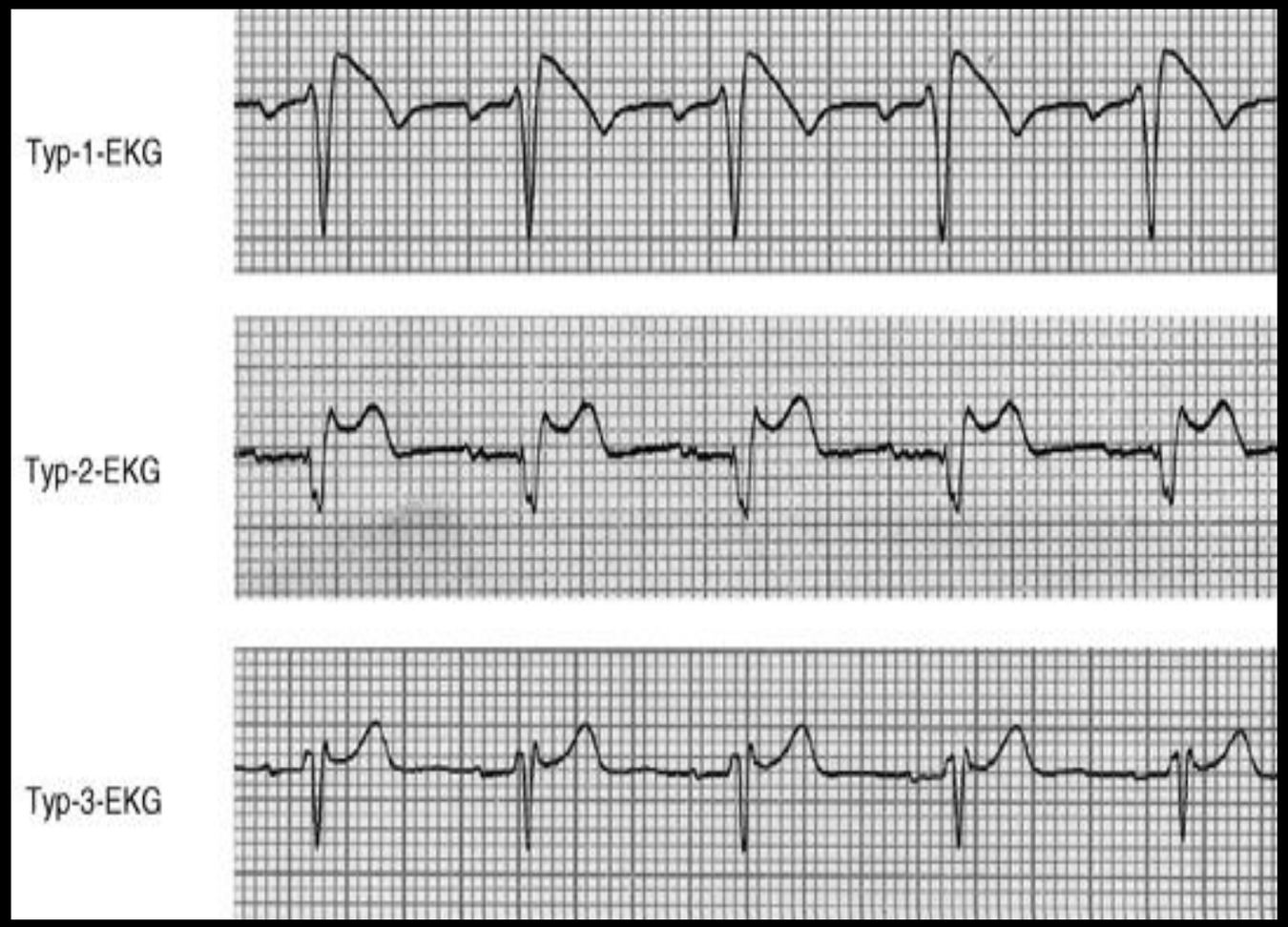
Sustained Ventricular tachycardia

Cardiac Syncope



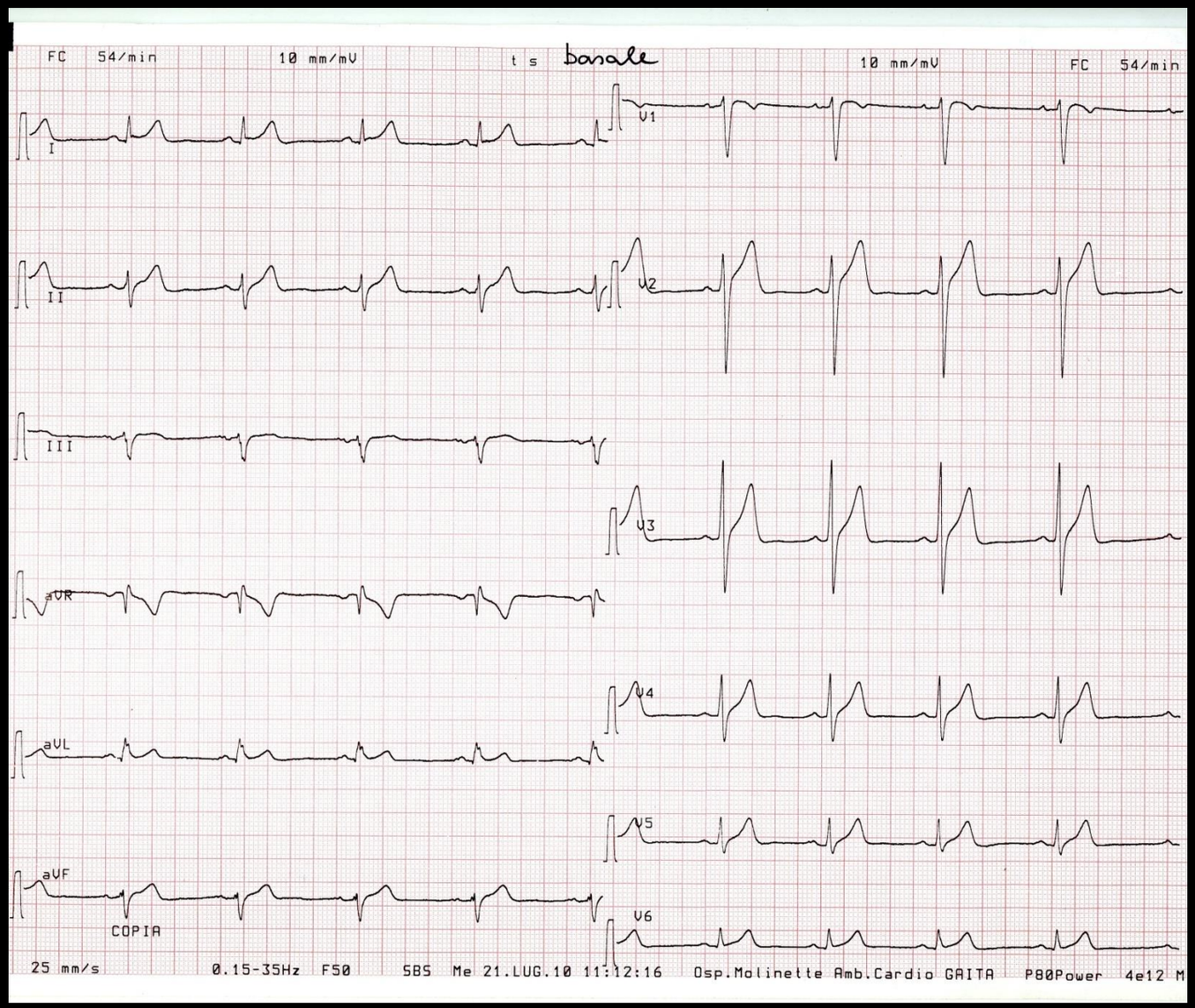
Brugada’s syndrome
type I

Cardiac Syncope



Brugada’s syndrome

Cardiac Syncope



Brugada’s syndrome
type II

B

ID#:

anni

Sesso: Sconosciuta

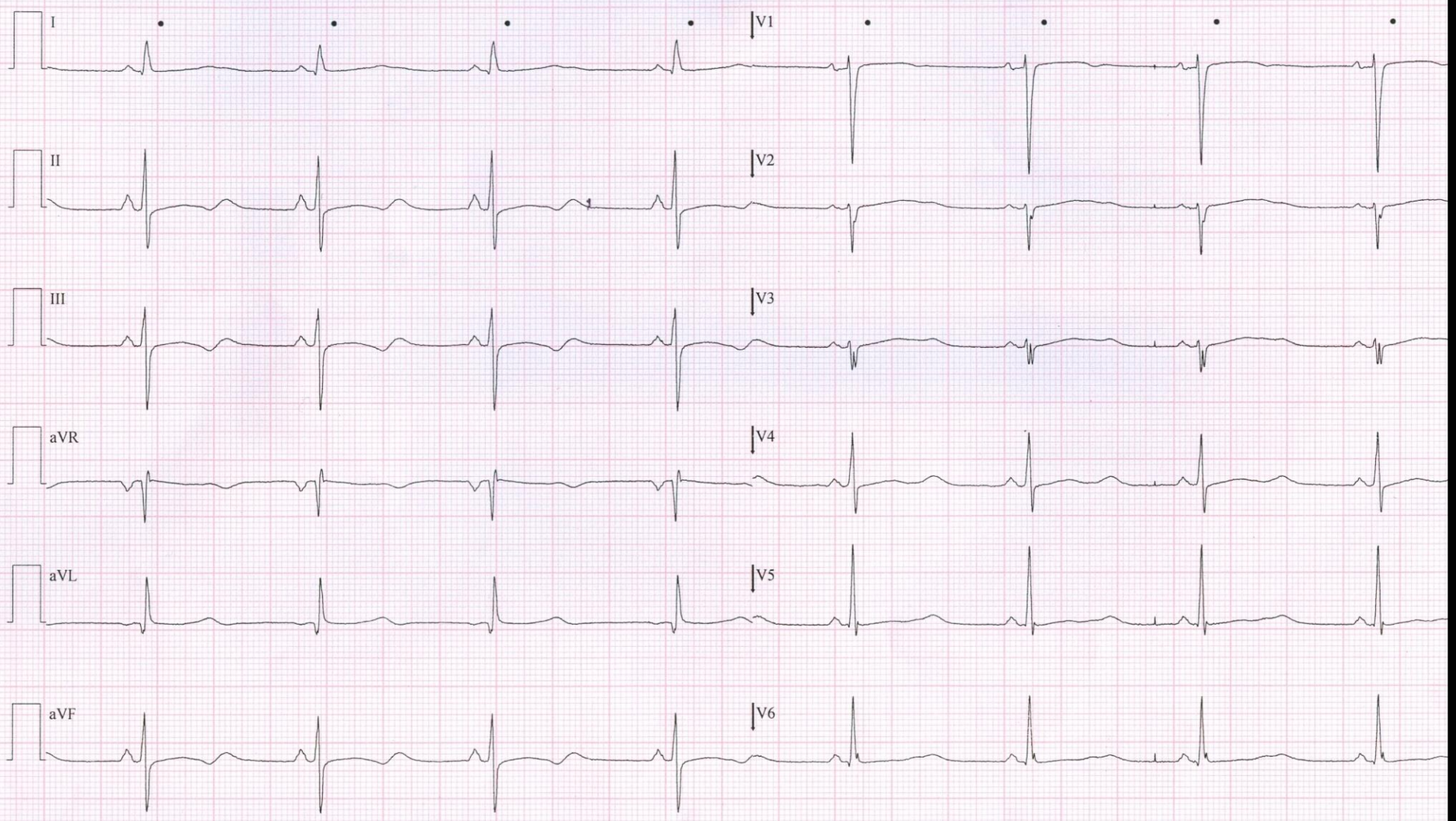
15/10/2009 00:17:24

Freq. Ventricolare	48
Interv. PR	141
Durata QRS	88
QT/QTc	453/418
QTc Bazett	405
QTc Fridericia	420
Asse P-R-T	70 -14 56
RR Medio	1246

BRADICARDIA SINUSALE
POSSIBILE INGRANDIMENTO ATRIALE DESTRO
ANOMALIE DELL'ONDA T ASPECIFICHE
ECG ANORMALE

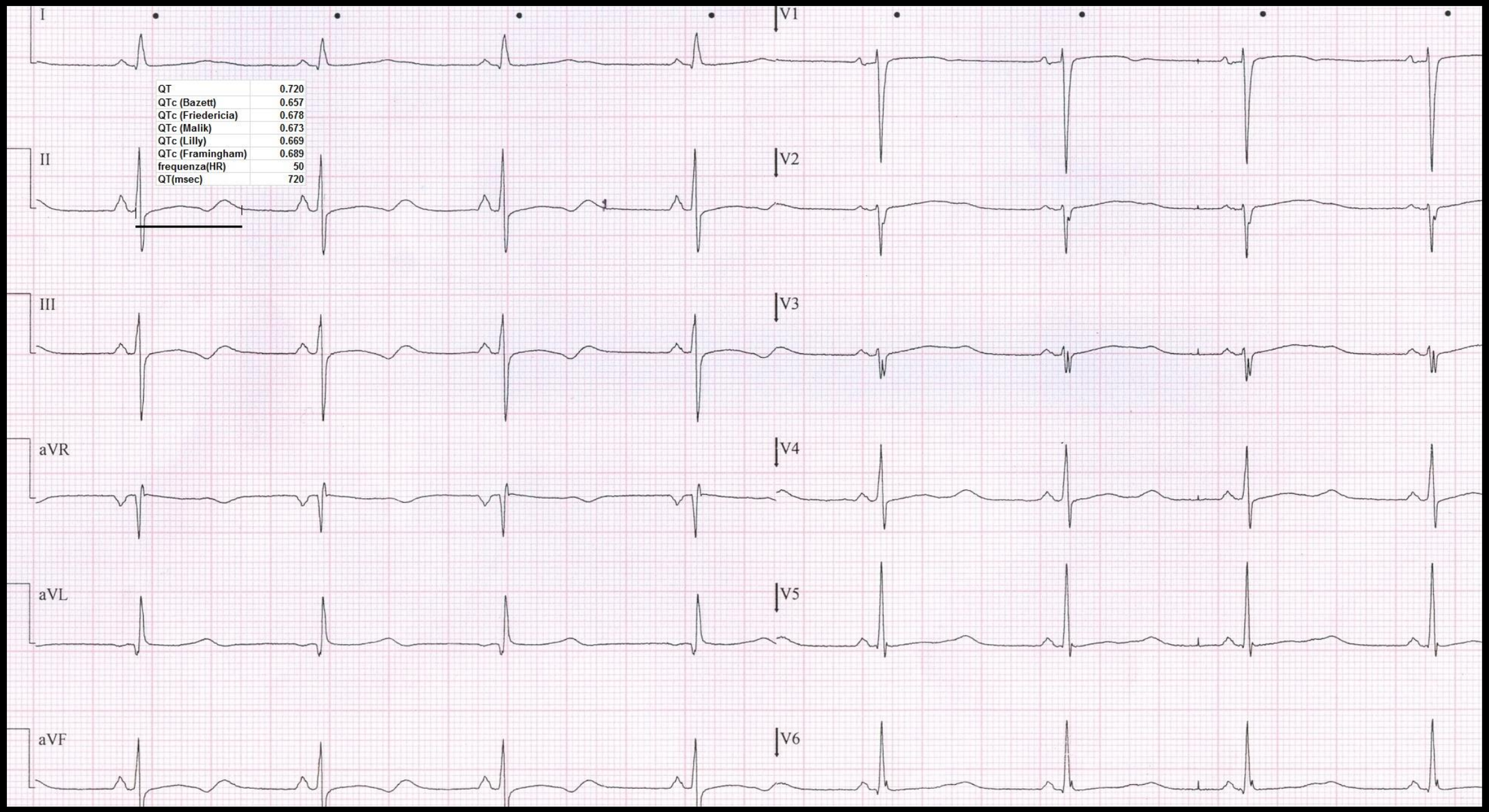
Nota: Probabile posizionamento elettrodi periferici sul torace

NON CONFERMAT



ECG: 10 mm/mV, 25 mm/s, Sito#0, Telemetria 7, [0.05 - 150

Cardiac Syncope



LQTS

B CONSOLO

ID#:

anni

Sesso: Sconosciuta

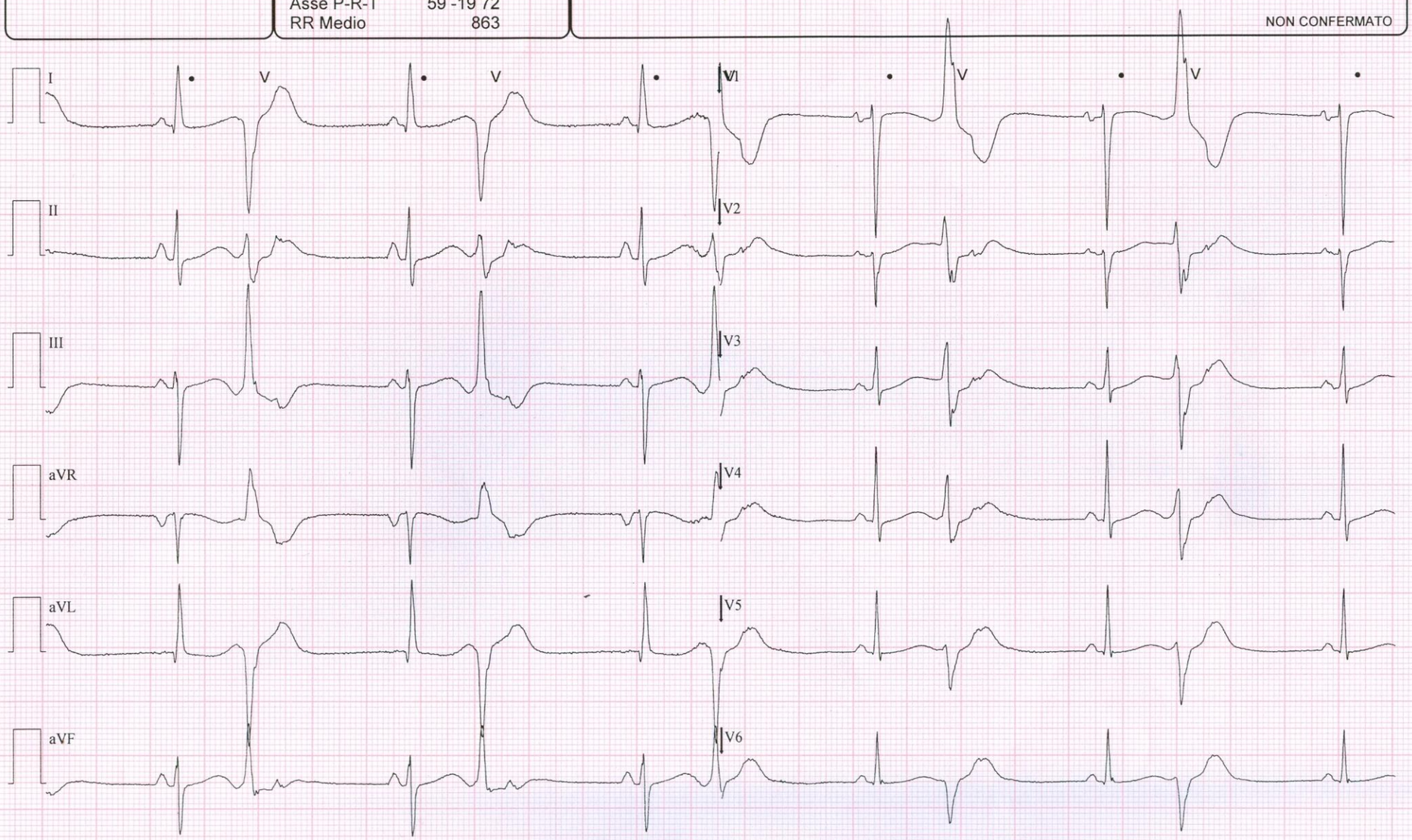
14/10/2009 22:19:24

Freq. Ventricolare	69
Interv. PR	141
Durata QRS	90
QT/QTc	381/400
QTc Bazett	410
QTc Fridericia	400
Asse P-R-T	59 -19 72
RR Medio	863

RITMO SINUSALE CON FREQUENTI EXTRASISTOLI VENTRICOLARI CAUSANTI RITMO BIGEMINO
POSSIBILE INGRANDIMENTO ATRIALE DESTRO
IVS CON ALTERAZIONI DELLA RIPOLARIZZAZIONE
ECG ANORMALE

Nota: Probabile posizionamento elettrodi periferici sul torace

NON CONFERMATO



U.O. Cardiologia - Belcolle Viterbo

ECG: 10 mm/mV, 25 mm/s, Sito#0, Telemetria 7, [0.05 - 150]

B CONSOLO

ID#:

anni

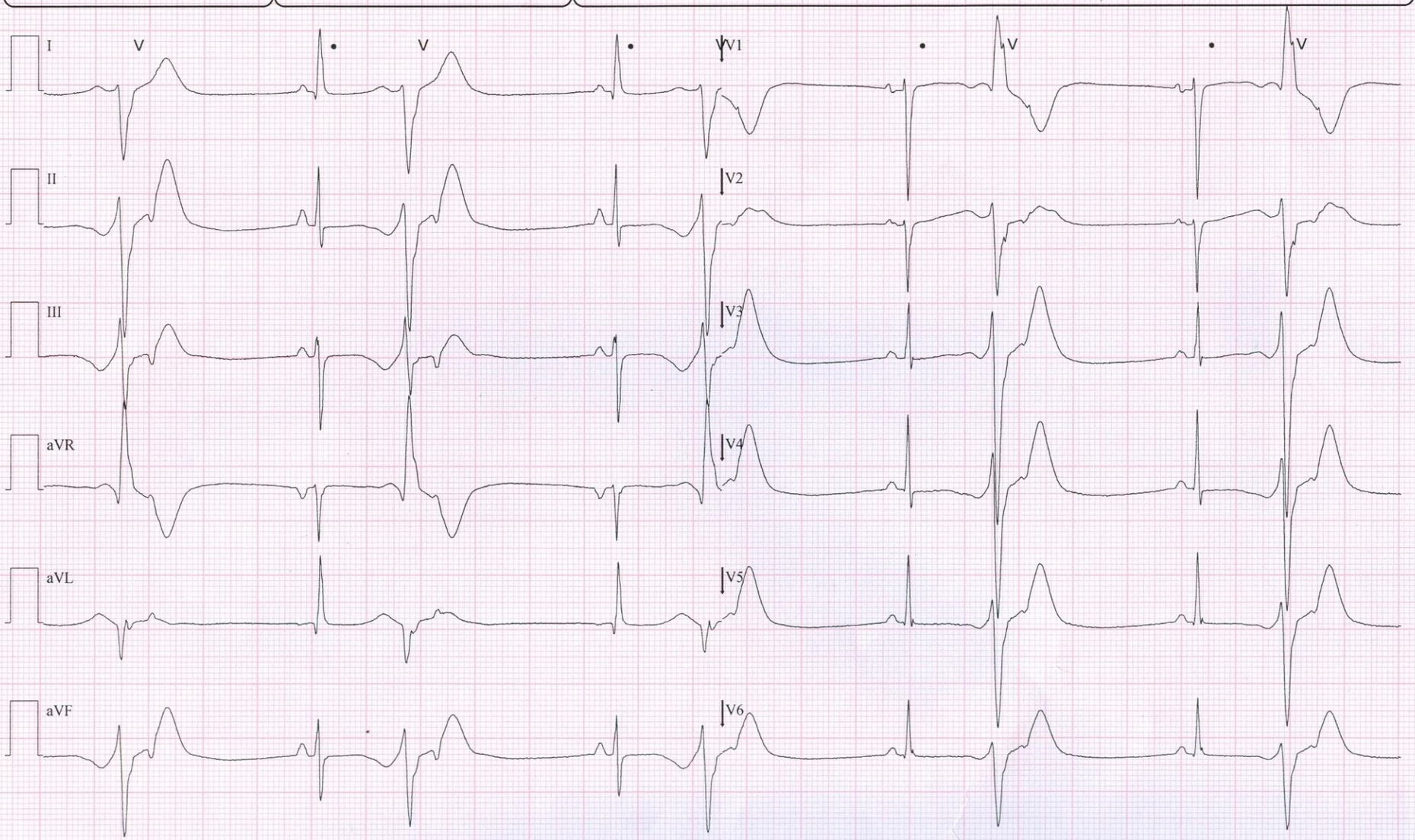
Sesso: Sconosciuta

15/10/2009 07:07:40

Freq. Ventricolare	56
Interv. PR	140
Durata QRS	88
QT/QTc	486/476
QTc Bazett	469
QTc Fridericia	475
Asse P-R-T	66 -8 -57
RR Medio	1070

BRADICARDIA SINUSALE CON FREQUENTI EXTRASISTOLI VENTRICOLARI
CAUSANTI RITMO BIGEMINO
POSSIBILE INGRANDIMENTO ATRIALE DESTRO
CRITERI DI VOLTAGGIO PROBABILI PER IVS, O VARIANTE NORMALE
ANOMALIE DI ST E DELL'ONDA T ASPECIFICHE
INTERVALLO QT ALLUNGATO
ECG ANORMALE

NON CONFERMATO



U.O. Cardiologia - Belcolle Viterbo

ECG: 10 mm/mV, 25 mm/s, Sito#0, Telemetria 7, [0.05 - 150]

B

ID#:

anni

Sesso: Sconosciuta

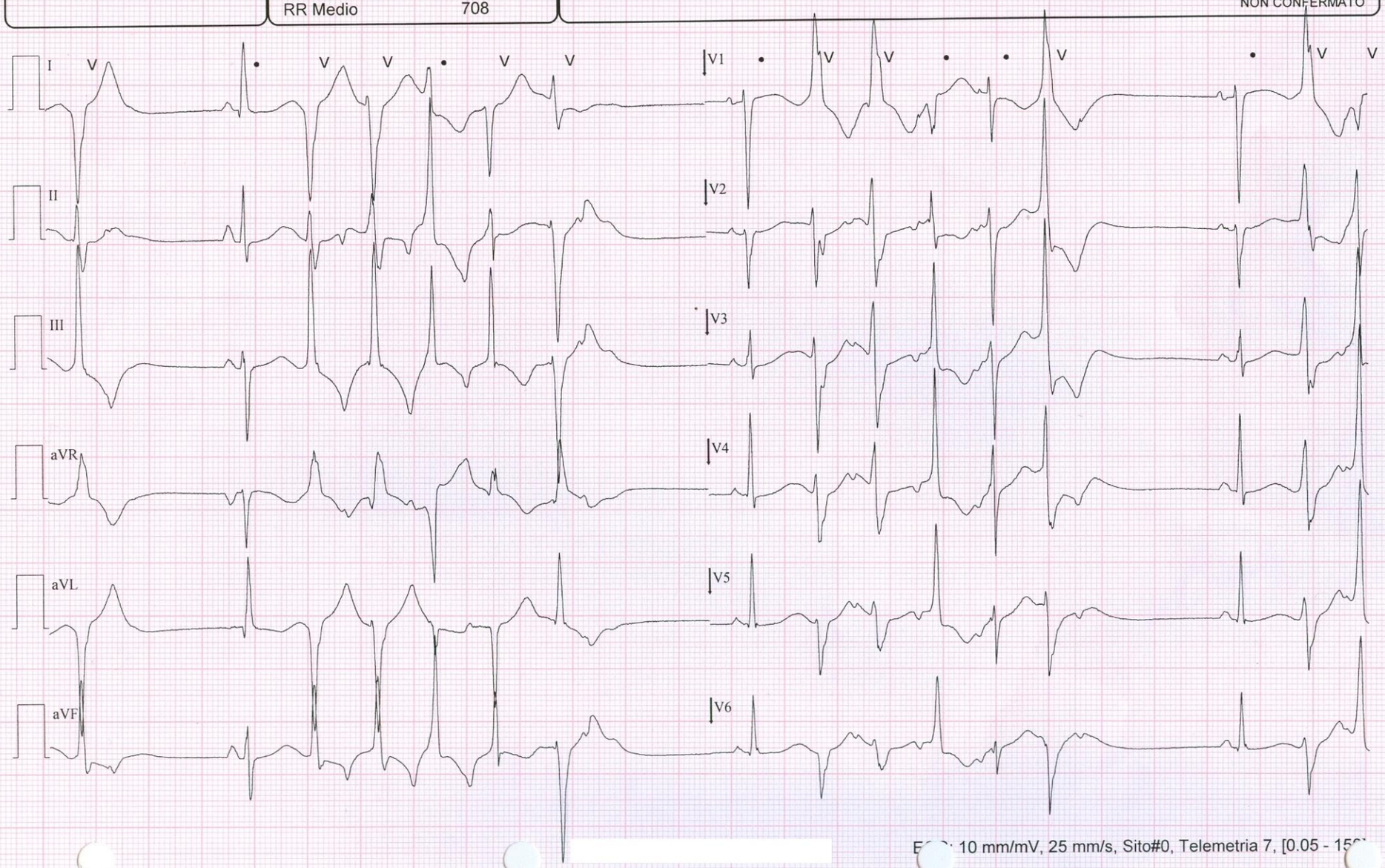
14/10/2009 22:07:05

Freq. Ventricolare	84
Interv. PR	124
Durata QRS	87
QT/QTc	550/591
QTc Bazett	653
QTc Fridericia	617
Asse P-R-T	58 -6 60
RR Medio	708

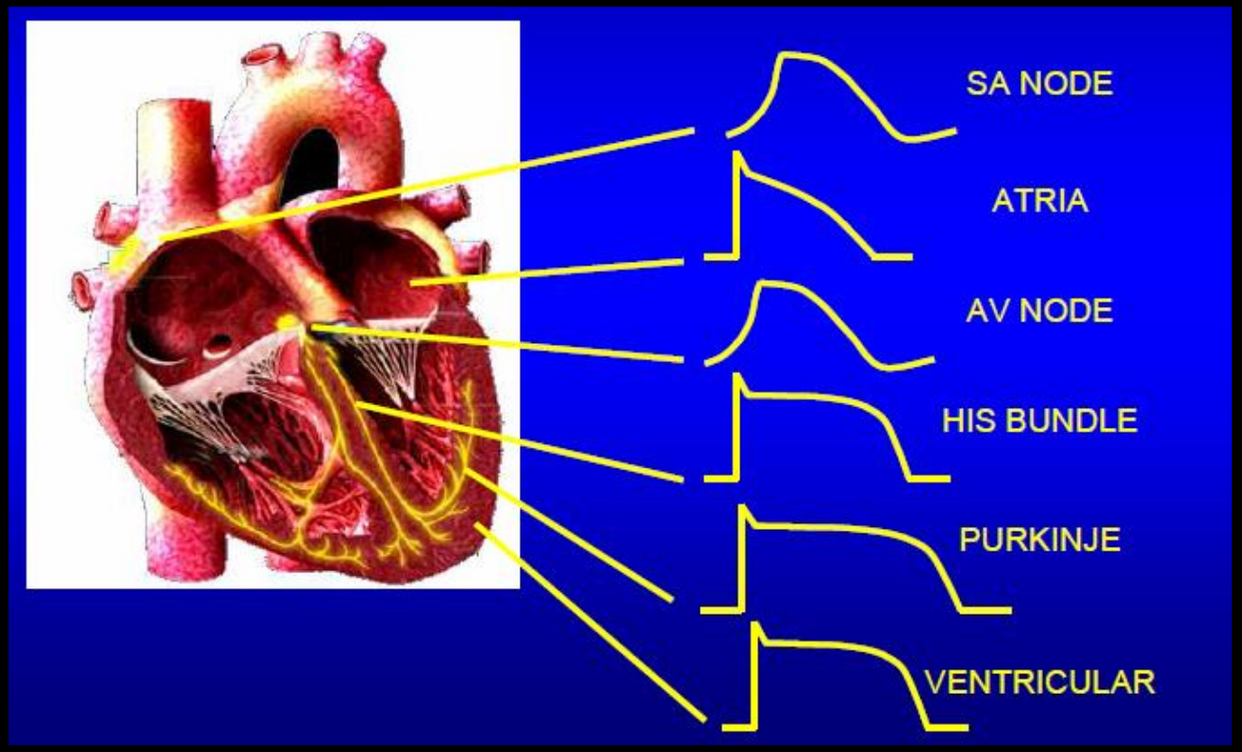
RITMO SINUSALE CON FREQUENTI EXTRASISTOLI VENTRICOLARI
POSSIBILE INGRANDIMENTO ATRIALE DESTRO
IVS CON ALTERAZIONI DELLA RIPOLARIZZAZIONE
ECG ANORMALE

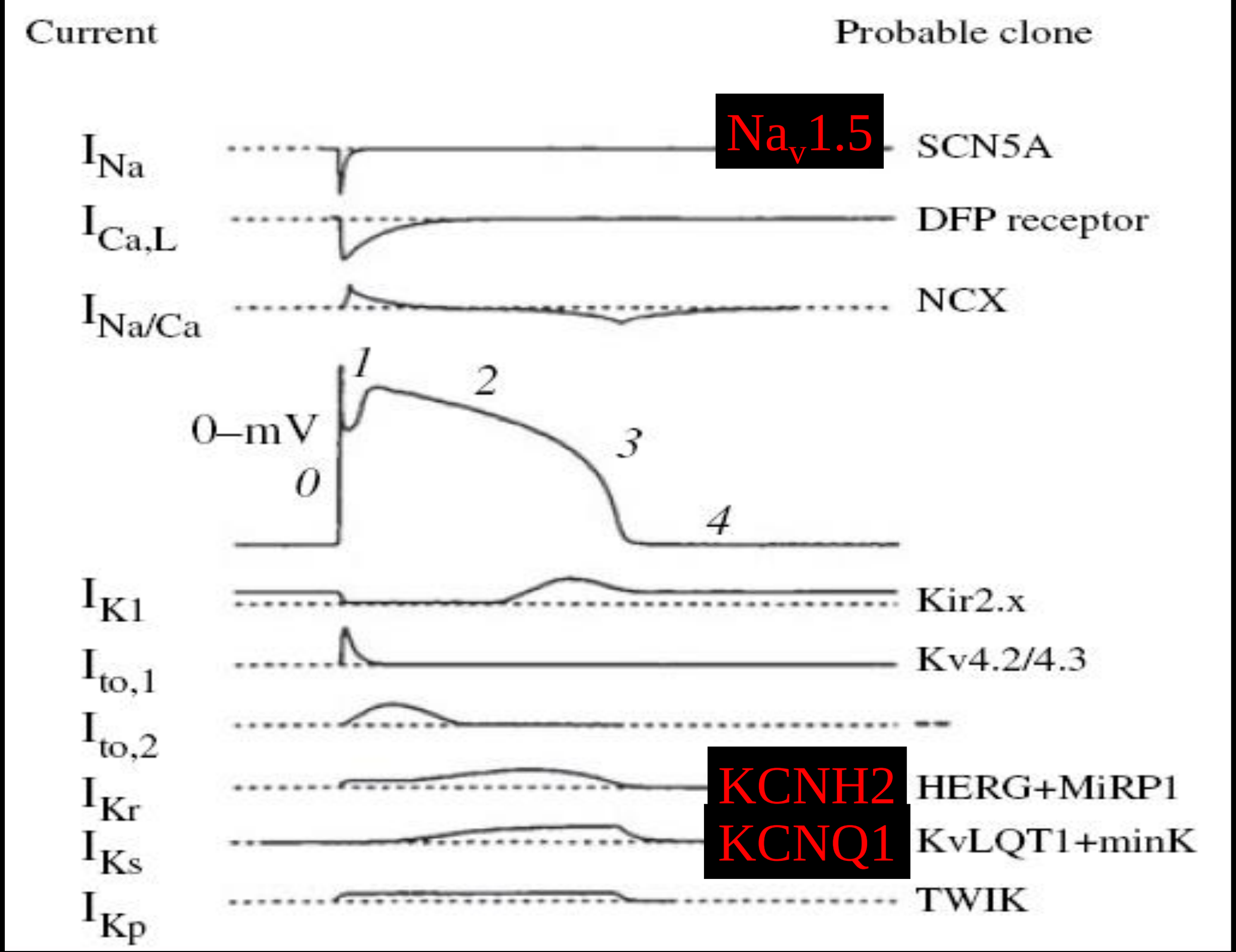
Nota: Probabile posizionamento elettrodi periferici sul torace

NON CONFERMATO



E[illegible]: 10 mm/mV, 25 mm/s, Sito#0, Telemetria 7, [0.05 - 15[illegible]


SA NODE
ATRIA
AV NODE
HIS BUNDLE
PURKINJE
VENTRICULAR

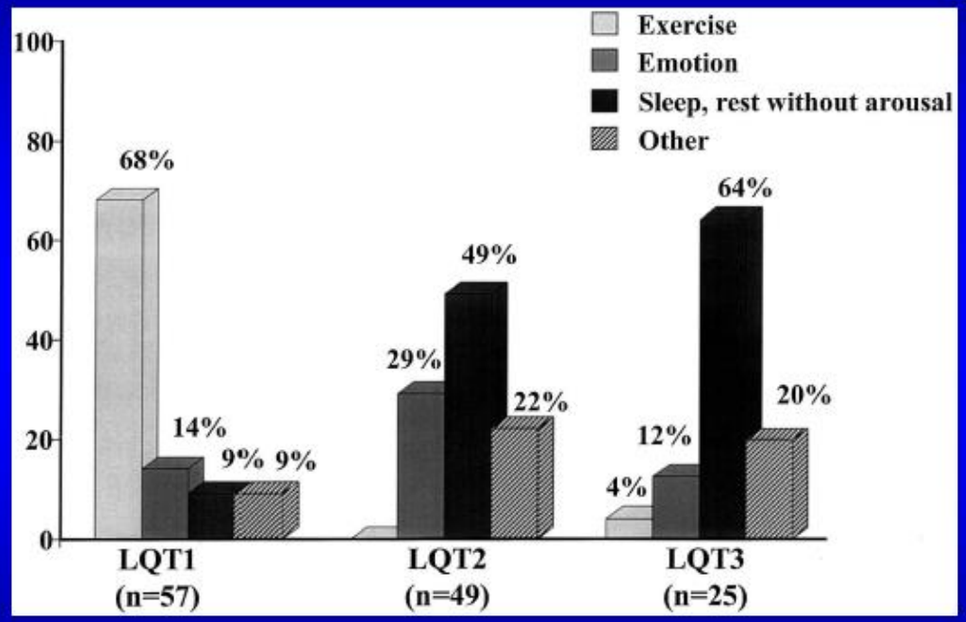


Rosen MR, *Int J Med* 2006; 259: 7-23

Ventricular	Rhythm	Inheritance	Locus	Ion channel	Gene
Long QT syndrome (RW)	TdP	AD			
LQT1			11p15	I_{Ks}	*KCNQ1, KvLQT1*
LQT2			7q35	I_{Kr}	*KCNH2, HERG*
LQT3			3p21	I_{Na}	*Na_v1.5, SCN5A*
LQT4			4q25		*ANKB, ANK2*
LQT5			21q22	I_{Ks}	*KCNE1, minK*
LQT6			21q22	I_{Kr}	*KCNE2, MiRP1*
LQT7	(Andersen–Tawil syndrome)		17q23	I_{K1}	*KCNJ2, Kir 2.1*
LQT8	(Timothy syndrome)		6q8A	$I_{Ca\text{-}L}$	*Ca_v1.2, CACNA1C*
Long QT syndrome (JLN)	TdP	AR	11p15	I_{Ks}	*KCNQ1, KvLQT1*
			21q22	I_{Ks}	*KCNE1, minK*
Brugada syndrome	VT/VF	AD	3p21	I_{Na}	*Na_v1.5, SCN5A*
			3p22-25		
Short QT syndrome					
SQT1	VT/VF	AD	7q35	I_{Kr}	*KCNH2, HERG*
SQT2		AD	11p15	I_{Ks}	*KCNQ1, KvLQT1*
SQT3		AD	17q23.1-24.2	I_{K1}	*KCNJ2, Kir2.1*
Catecholaminergic VT					
CPVT1	VT	AD	1q42-43		*RyR2*
CPVT2	VT	AR	1p13-21		*CASQ2*

Antzelevitch C, *Int J Med* 2006; 259: 48-58

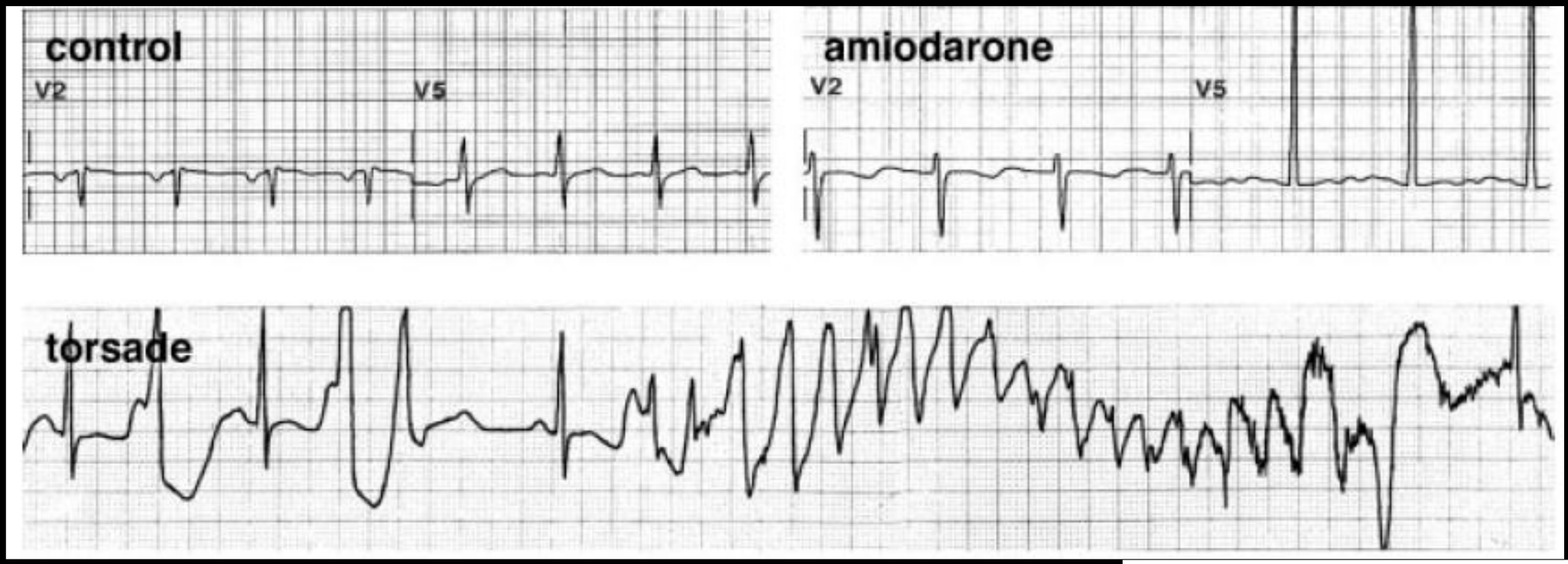
Lethal cardiac events according to 3 classified triggers in 3 genotypes

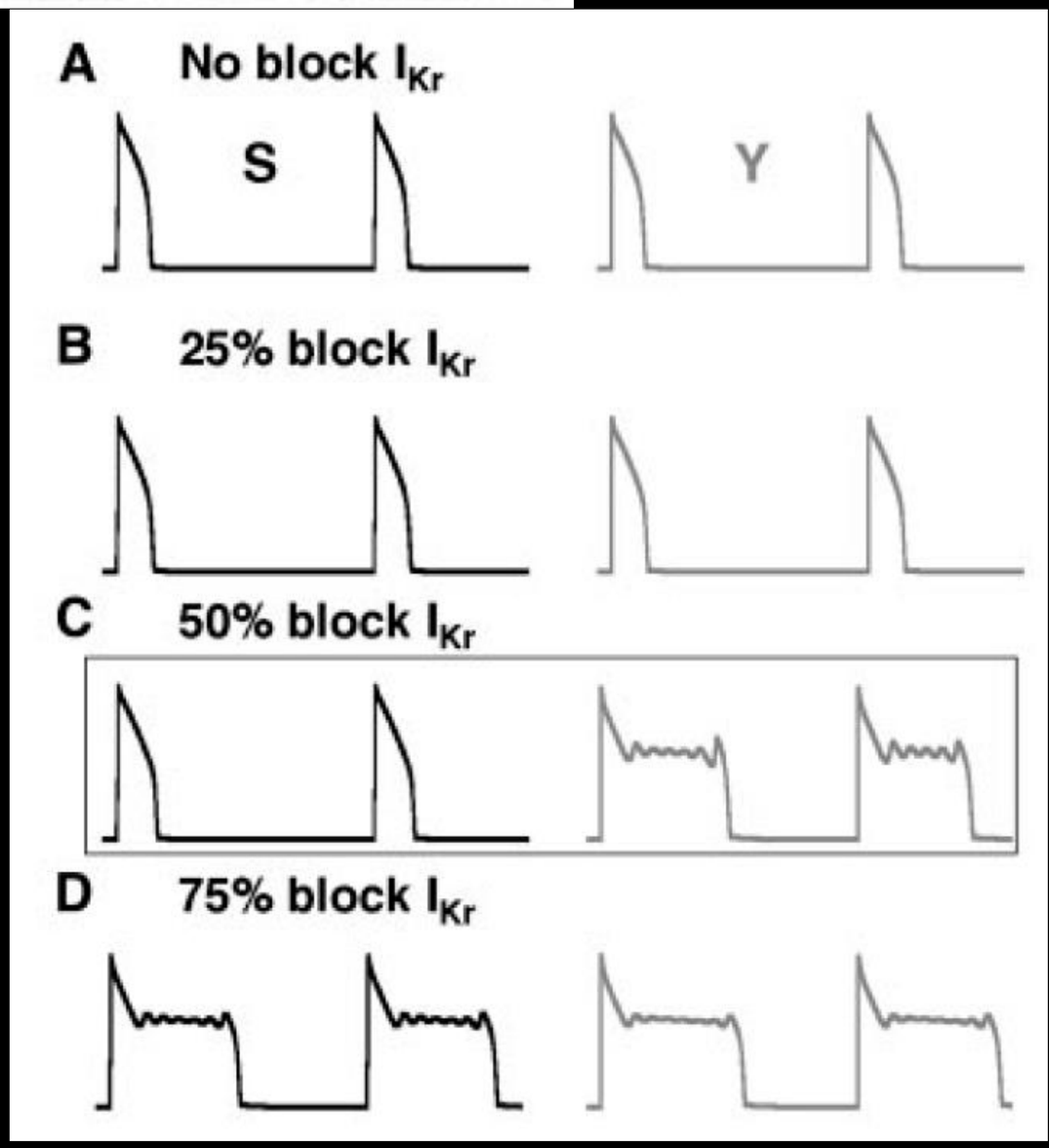


Schwartz, P. J. et al. Circulation 2001;103:89-95

Repolarization reserve

DNA polymorphisms of ionic channels





Splawski I,*Science* 2002; 297: 1333-1335

SCN.5A
(S1102Y, H558R)

KCNE1
(D85N)

Female gender
Hypokalaemia Hypomagnesaemia
Drugs
Bradycardia
Hypertrophy
CHF

QTc: 0.400 sec → **QTc: 0.500-0.600 sec** → **Torsades de Pointes**

SCD

Rosen MR, *Int J Med* 2006; 259: 7-23

D85N KCNE1 2% black white

S1102Y SCN5A 6-7% black

H558R SCN5A 29% black

23% Hispanic

20% white

9% Asiatic

Table 1 Overview of mutations and functional polymorphisms in cLQTS genes that have been reported in acquired LQTS patients. *n.s.* Not specified

Gene	Base pair change	Amino acid change	Drugs	Age (years)	Sex	Additional risk factors	Symptoms	Reference
KCNE1	253G→A	D85N	Sotalol	80	Female	–	TdP	This study
	253G→A	D85N	Quinidine	71	Male	Hypokalaemia	TdP	This study
KCNE2	22A→G	T8A	Amiodarone	12	Male	–	TdP	This study
	22A→G	T8A	Quinidine	n.s.	n.s.	–	TdP	13
	22A→G	T8A	Sulfametoxazole	45	Male	–	QTc>600 ms	14
	25C→G	Q9E	Clarithromycin	76	Female	Hypokalaemia, diabetic, history of stroke	TdP, VF	13
	161T→C	M54T	Procainamide	n.s.	n.s.	–	TdP	14
	170T→C	I57T	Oxatomide	n.s.	n.s.	–	TdP	14
	347C→T	A116V	Quinidine, mexiletine	55	Female	History of cardiac arrest	Syncope with TdP	14
KCNH2	1039C→T	P347S	Cisapride, clarithromycin	77	Female	–	TdP	21, this study
	1048C→T	R328C	n.s.	45	Male	–	TdP	15
	2350C→T	R784W	Amiodarone	n.s.	n.s.	–	TdP	16
KCNQ1	944A→G	Y315C	Cisapride	77	Female	Hypokalaemia	Cardiac arrest	22
	1663C→T	R555C	Terfenadine	38	Female	cLQTS family	Sudden death	29
	1747C→T	R583C	Dofetilide	n.s.	n.s.	–	TdP	16
SCN5A	1844G→A	G615E	Quinidine	n.s.	n.s.	–	TdP	16
	1852C→T	L618F	Quinidine	n.s.	n.s.	–	TdP	16
	3748T→C	F1250L	Sotalol	n.s.	n.s.	–	TdP	16
	5474T→C	L1825P	Cisapride	70	Female	–	Tdp	30

Paulussen AD, *J Mol Med* 2004; 82: 182-188

https://crediblemeds.org/new-drug-list/

CredibleMeds :: QTDrugs Li...

Pagina ▾ Sicurezza ▾ Strumenti ▾

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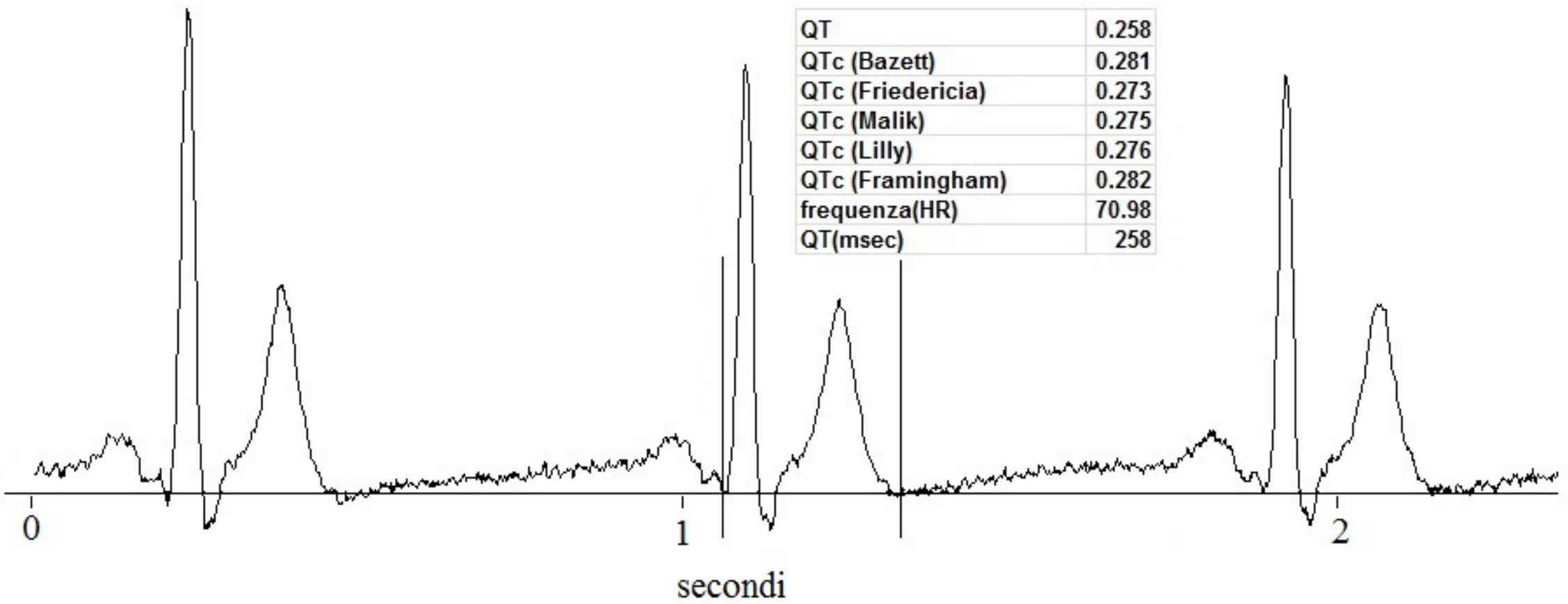
Risk Categories for Drugs that Prolong QT & induce Torsades de Pointes (TdP)

Based on ongoing systematic analysis of all available evidence, CredibleMeds® places drugs into broad categories based on whether each can cause QT prolongation or TdP. Because these actions are highly dependent on the circumstances of each drug's use AND each patient's clinical characteristics, we do not attempt to rank-order the drugs within each category. Therefore, we do not recommend that these lists be used to rank-order the drugs for their relative toxicity.

https://crediblemeds.org/new-drug-list/

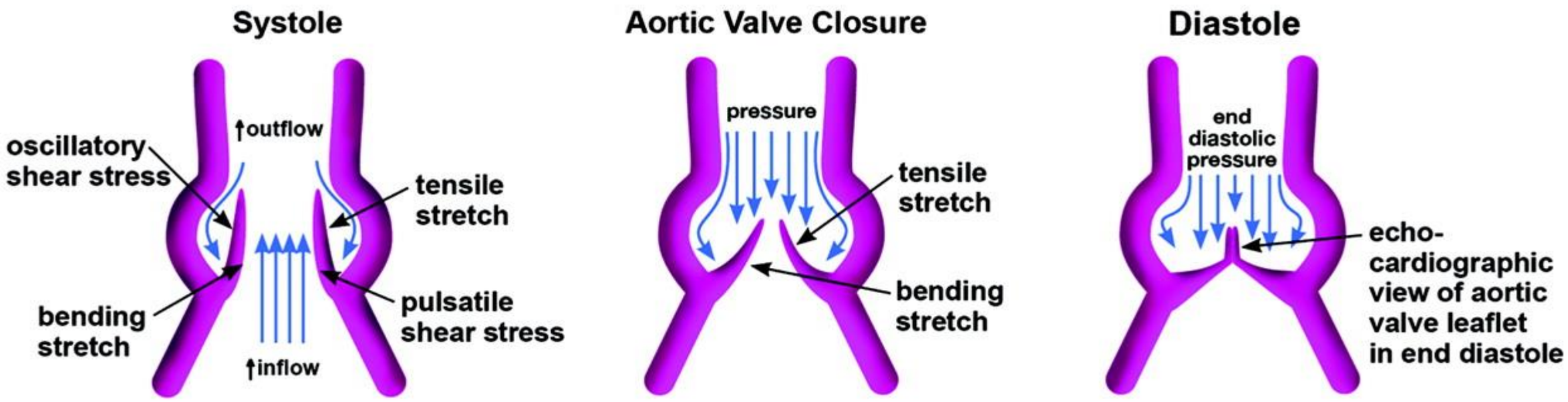
Cardiac Syncope



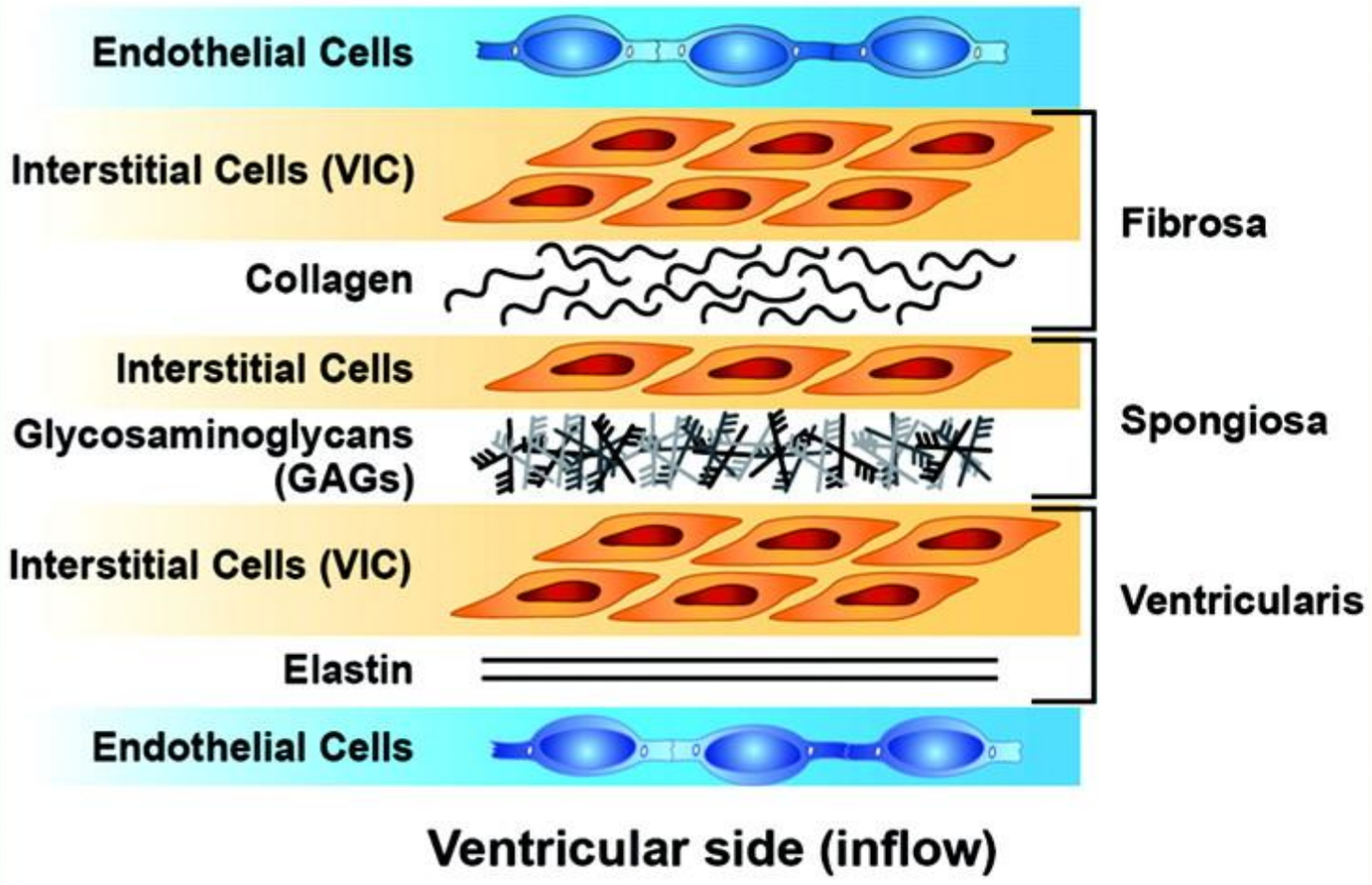
SQTS

Neurally-mediated syncope	Orthostatic hypotension syncope	Arrhitmics syncope	Cardiopulmonary syncope	Neurological syncope
• Vasovagal • Carotid sinus hypersensitivity • Situational	• Pure autonomic failure (PAF, MSA, m. Parkinson, Lewy body dementia • Secondary autonomic failure(diabetes, kidney failure,…) • Drugs	• Bradycardia syndrome (sick sinus syndrome) • Tachicardia syndrome	• Aortic stenosis • AMI • Acute Cor Pulmonale • Pulmonary hypertension	• Vascular thievery • TIA • Ictal bradycardia

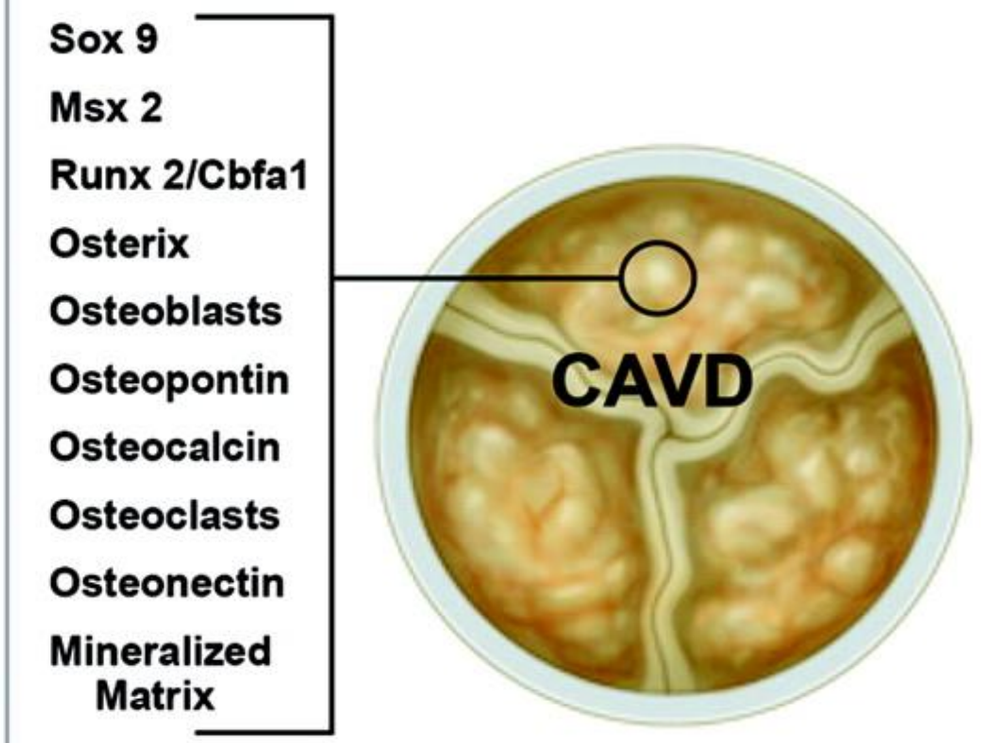
A Hemodynamic Flow Across the Aortic Valve



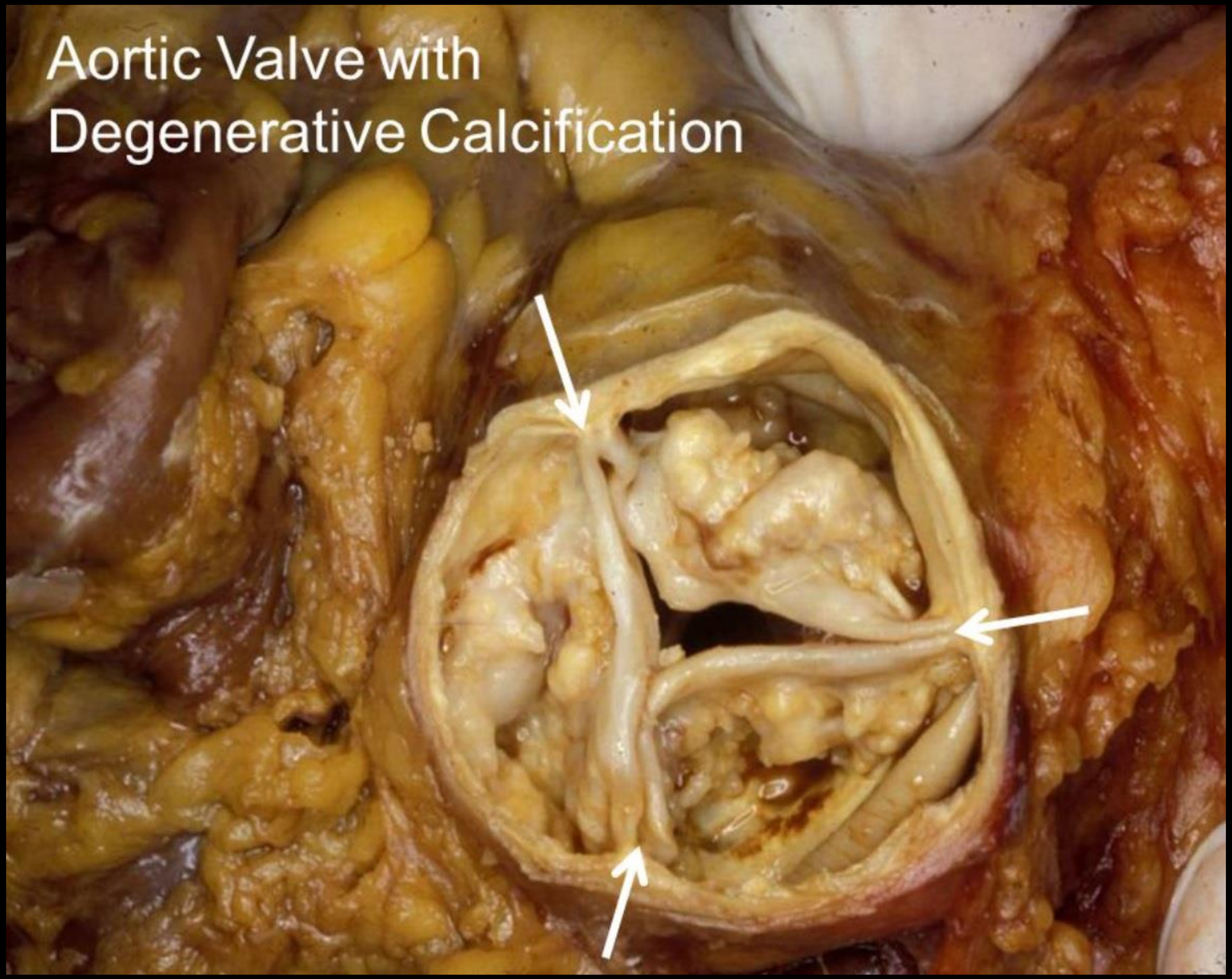
B Cellular Architecture of the Aortic Valve

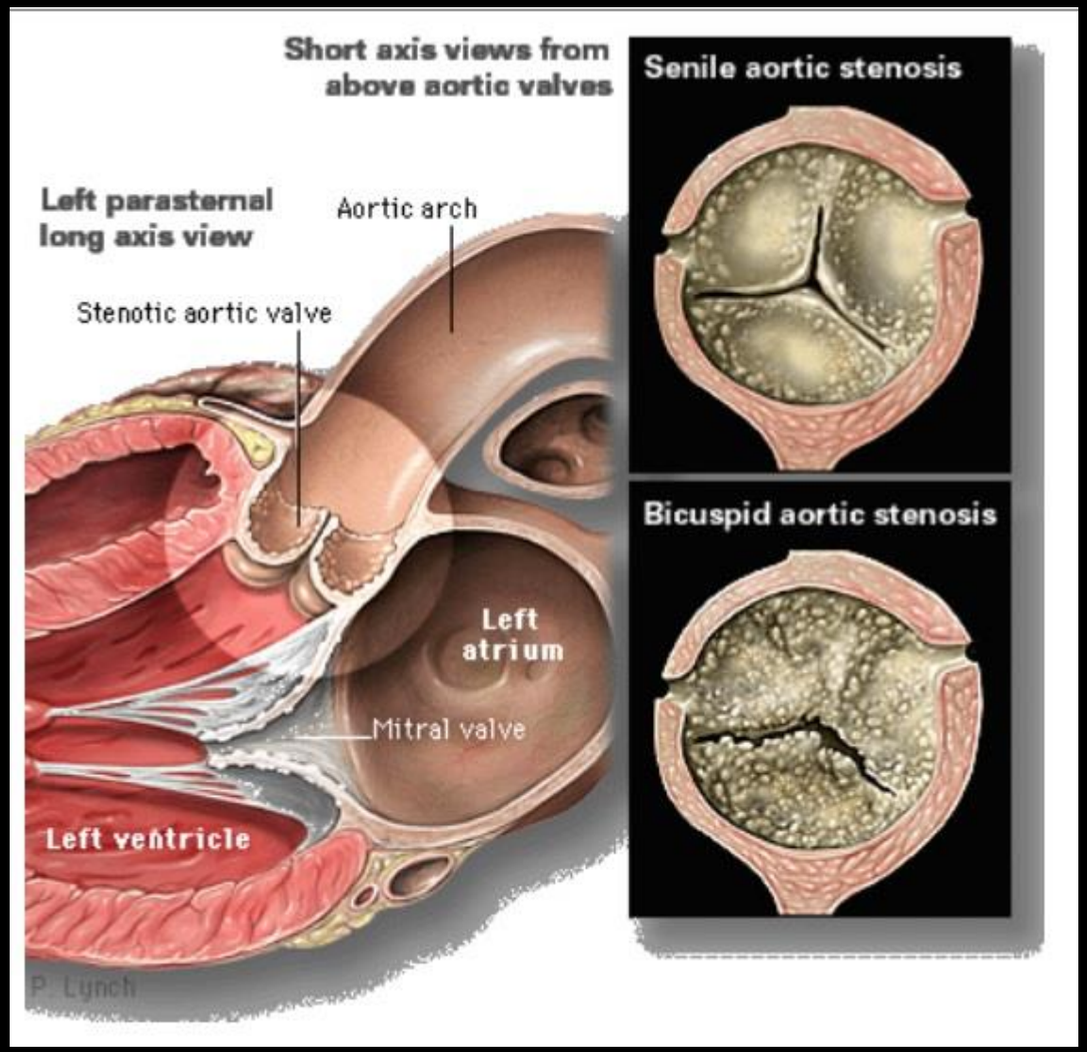


C Calcified Nodules Via Osteogenic Gene Regulation in VIC Cell



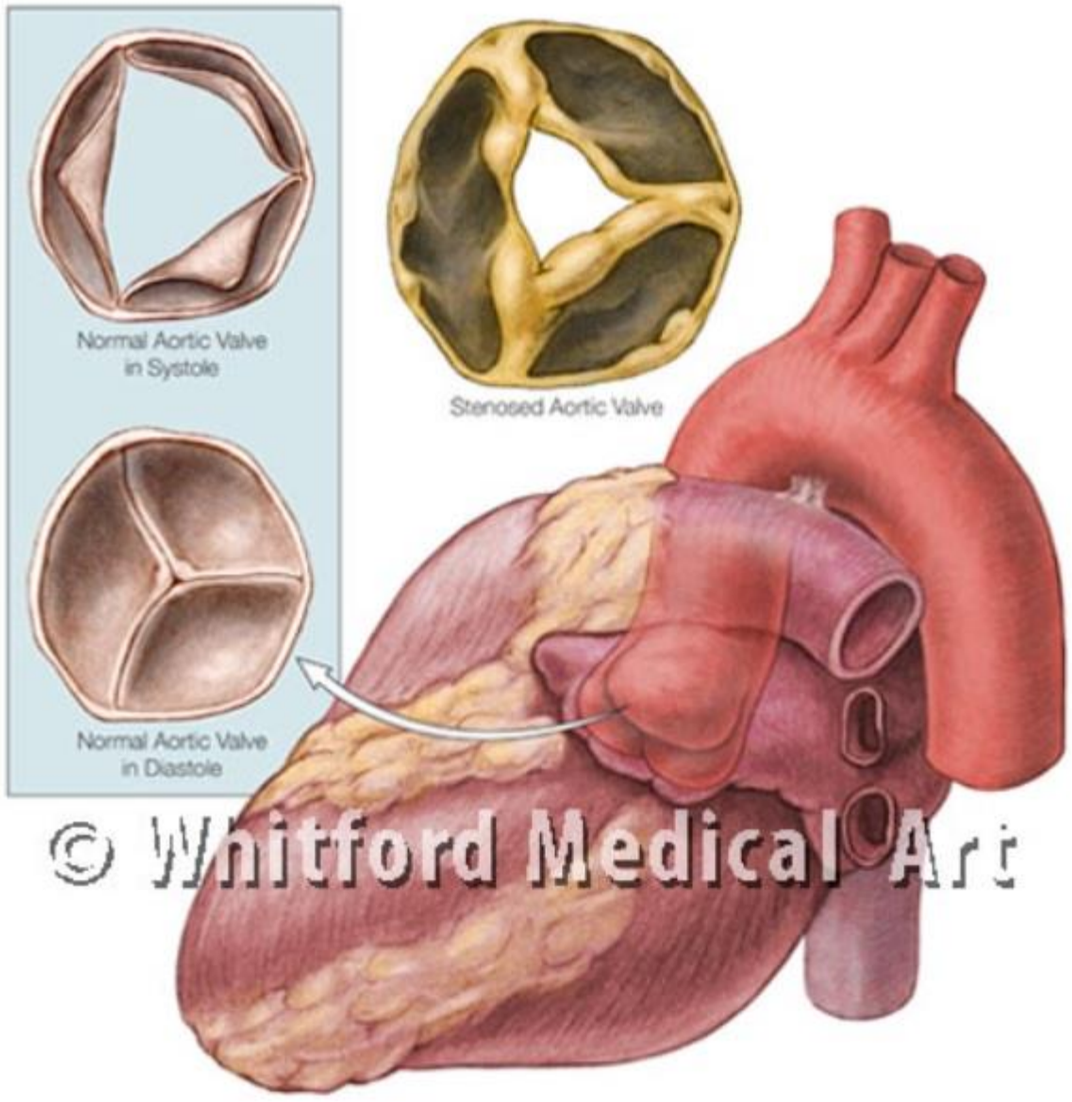
Aortic Valve with Degenerative Calcification




Short axis views from above aortic valves
Left parasternal long axis view
Aortic arch
Stenotic aortic valve
Left atrium
Mitral valve
Left ventricle
P. Lynch
Senile aortic stenosis
Bicuspid aortic stenosis

Rheumatic Aortic Valve Stenosis

Aortic valve stenosis is one possible result of the postinflammatory scarring caused by rheumatic heart disease. Rheumatic aortic stenosis is characterized by commissural fusion and a thickening and distortion of the valve cusps. Because the aortic valve cannot fully open or close, the left ventricle must compensate with more forceful contractions resulting in myocardial hypertrophy. Ensuing symptoms include angina pectoris, congestive heart failure or syncope. The only treatment is surgical replacement of the damaged valve.



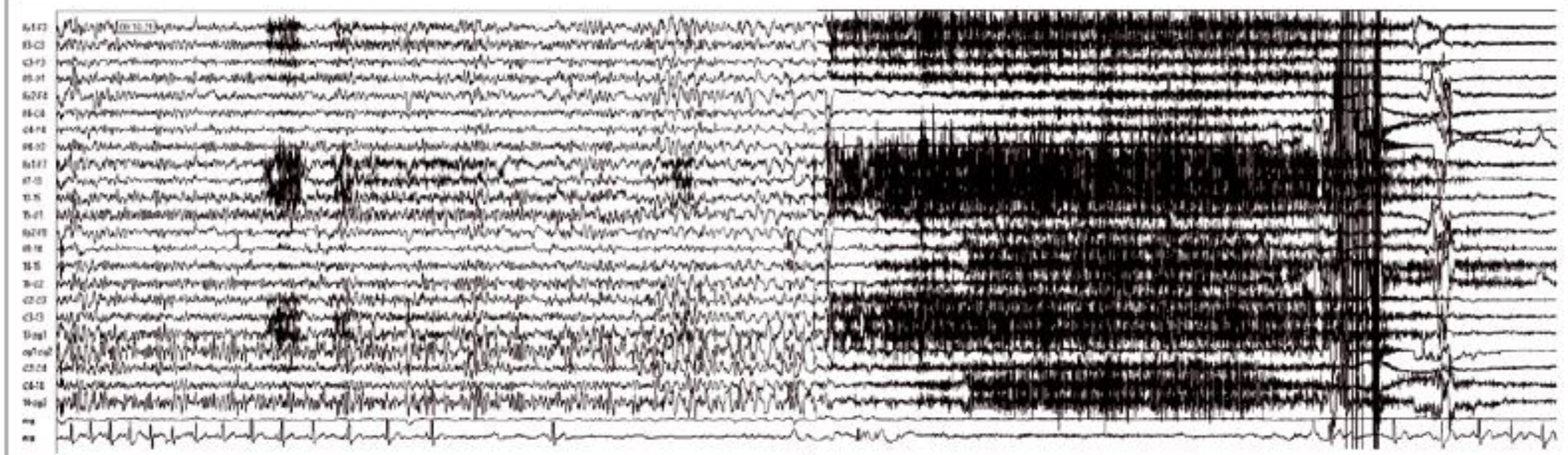
Heart Team:
geriatrician’s role

-Heart team: group of specialists who visit the patient,
evaluating their eligibility for the TAVR procedure

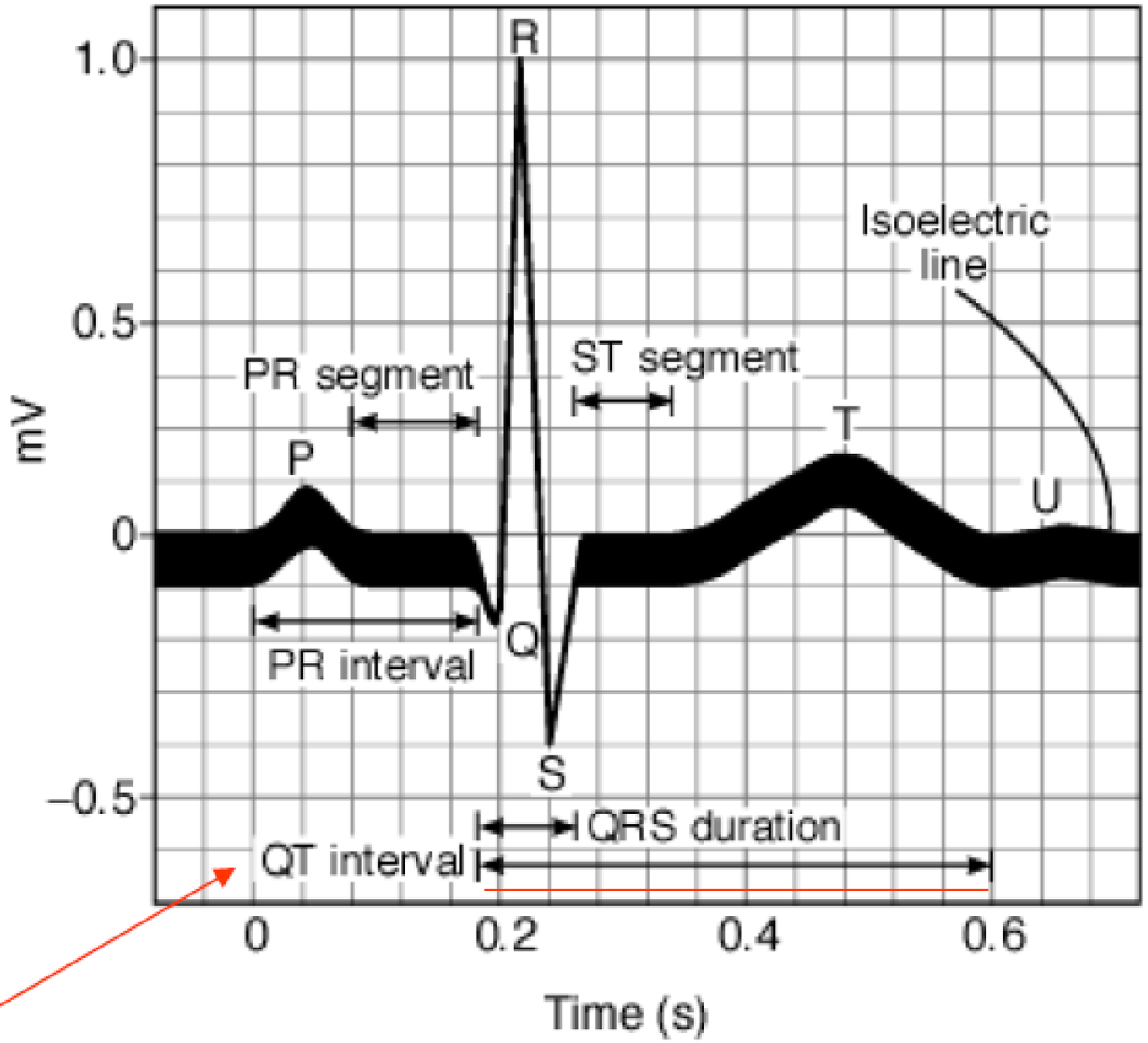
-It is composed by: cardiologist, heart surgeon, anesthetist, vascular surgeon,
geriatrician

.-The geriatrician performs a specific multidimensional assessment
(MMSE, CIRS, ADL, IADL, MNA, Rockwood, SF36 for QoL,
Chair test and Afilalo criteria).

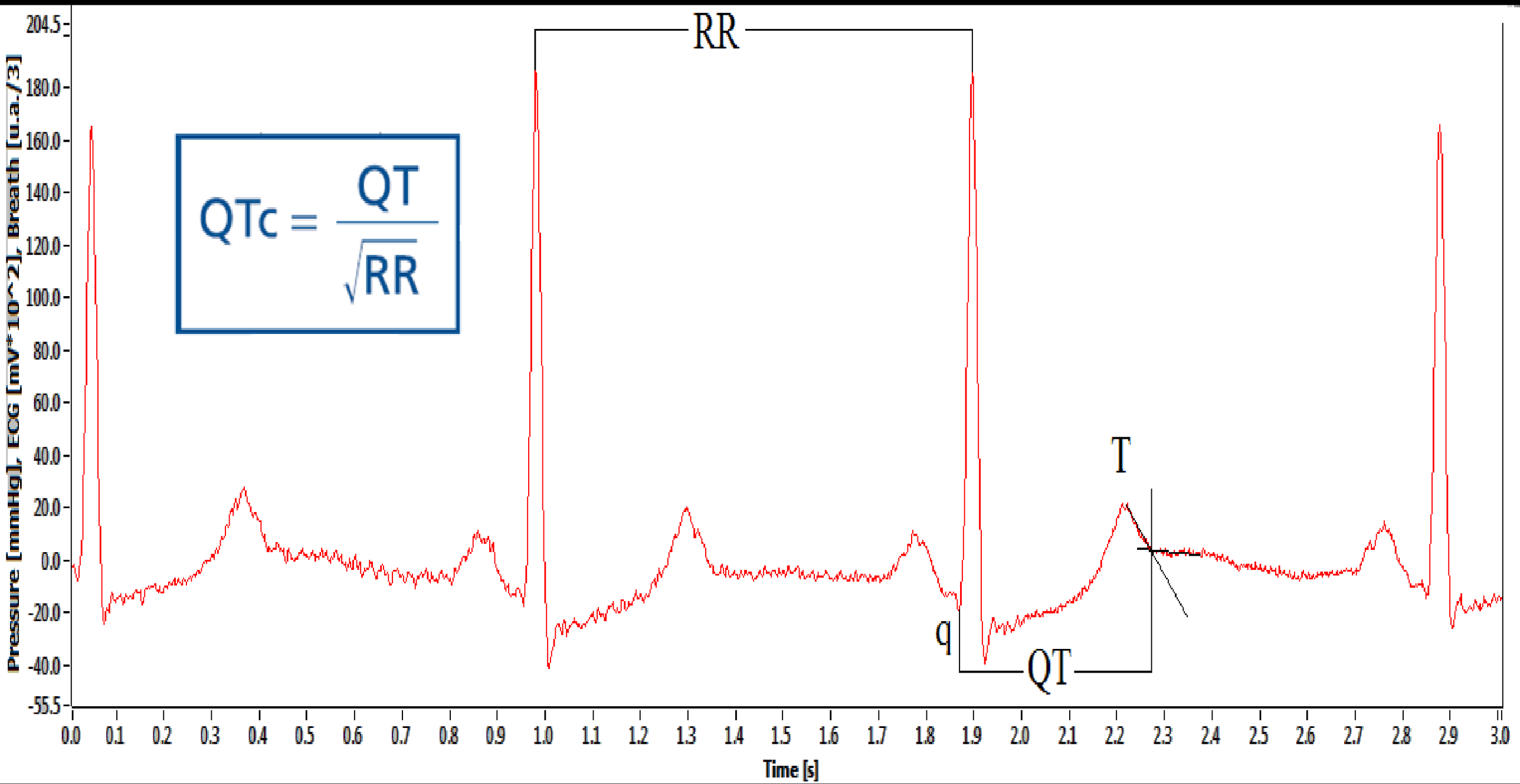
- If the patient, independently from the performance obtained in the tests,
has a life expectancy lower than one year, or an MMSE of less than 24,
is not eligible for the procedure.


Paura, cardiopalmo
Perdita di coscienza

L'ECG


1.0
0.5
0
−0.5
mV
R
P
Q
S
T
U
PR segment
ST segment
Isoelectric line
PR interval
QRS duration
QT interval
0
0.2
0.4
0.6
Time (s)

$$QTc = \frac{QT}{\sqrt{RR}}$$



25 QTc Zang una derivazione (Bazett-Friedericia-Malic-Lilly-Framingham- Normogramma) - Co

FILE | HOME | INSERISCI | LAYOUT DI PAGINA | FORMULE | DATI | REVISIONE | VISUALIZZA

Incolla | Appunti | Arial | 10 | Carattere | Testo a capo | Unisci e allinea al centro | Allineamento | Generale | Numeri | Formattazione condizionale

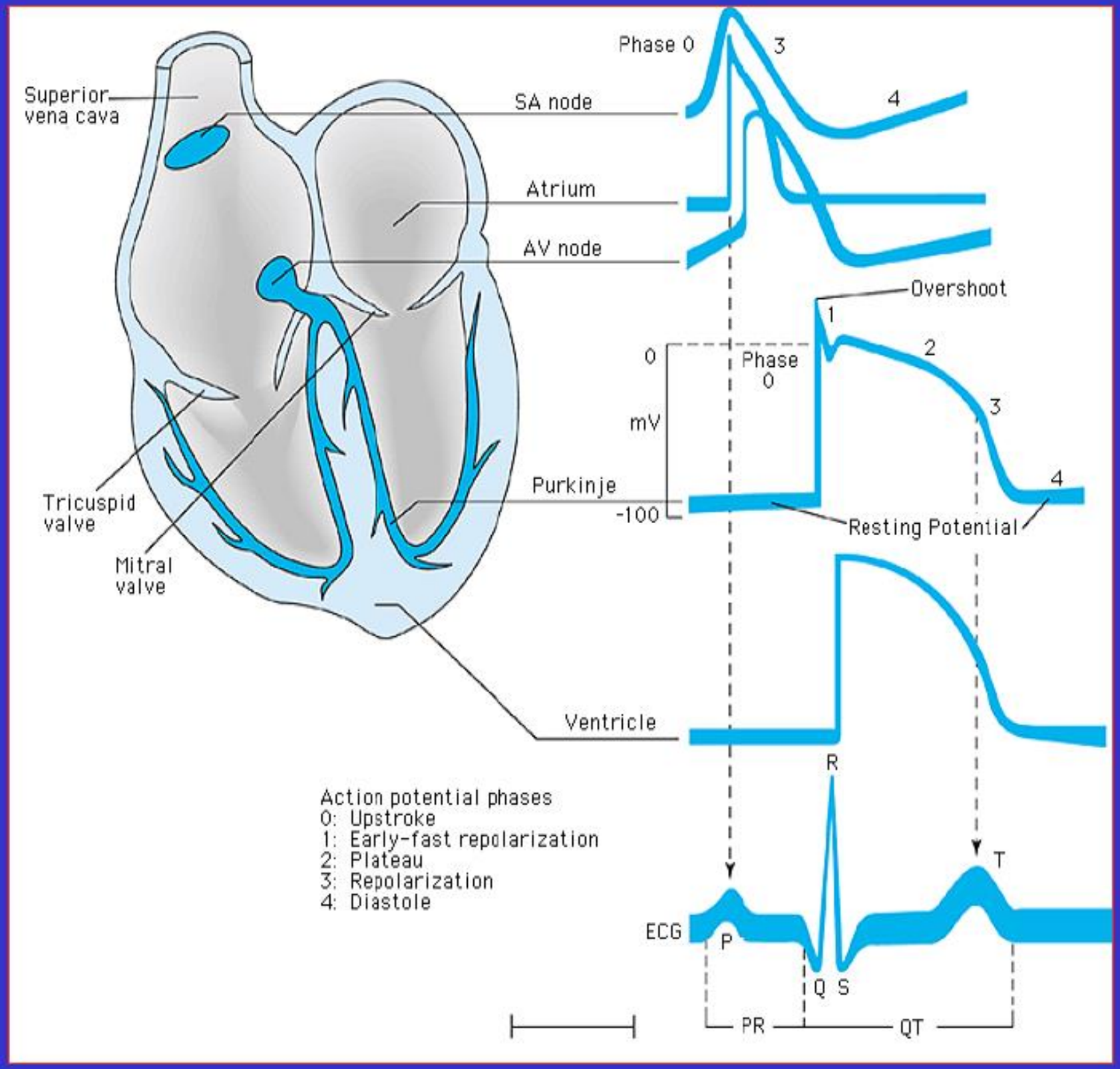
F7 | =POTENZA(F5;0.3333)

	A	B	C	D	E	F	G	H
1		mm QT	mm RR		QT(sec)	RR(sec)	QTms	RRms
2	II a			25	0.35	0.8	350	800
3	II b			25	0.35	0.8	350	800
4	II c			25	0.35	0.8	350	800
5				QT	0.35	0.8	RR	
6				QTc (Bazett)	0.3913	0.894427		
7				QTc (Friedericia)	0.377	0.928325		
8				QTc (Malik)	0.3801	0.920753		
9				QTc (Lilly)	0.3827	0.91461		
10				QTc (Framingham)	0.3808	0.0308		
11				frequenza(HR)	75			
12				QT(msec)	350			
13								
14								
15								
16								
17								

	Maschi adulti	Femmine adulte
Normale	< 430	< 450
Borderline	430-450	450-470
Patologico	> 450	> 470

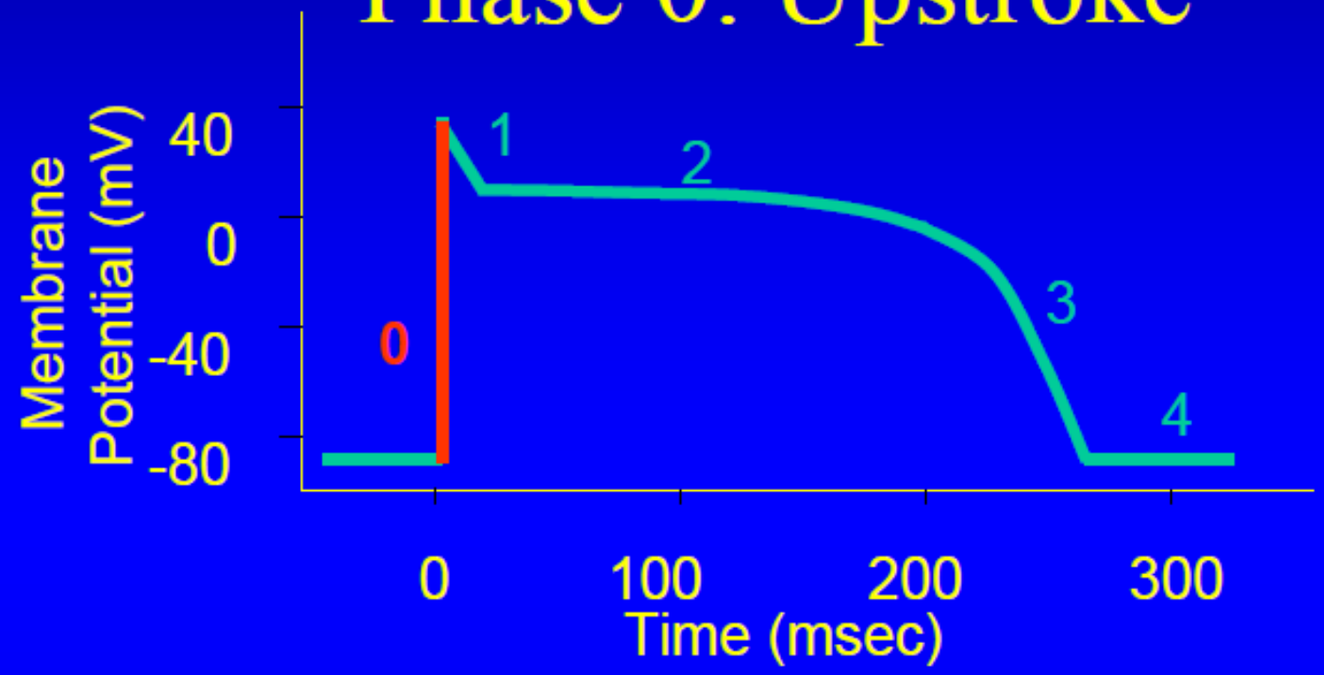
Adattata da: Yap YG, Camm AJ. *Heart* 2004;89:1363.

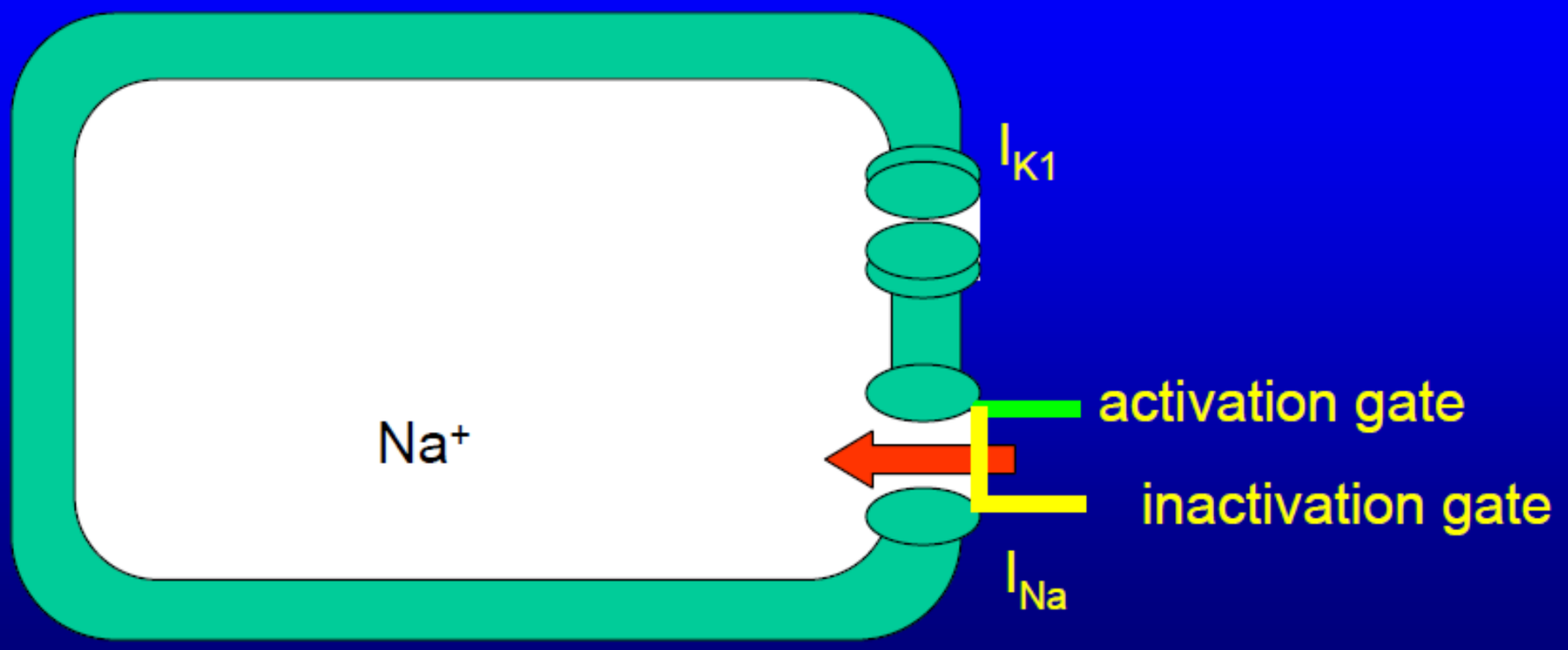
Dal potenziale d'azione all'ECG



Fast Response Action Potential

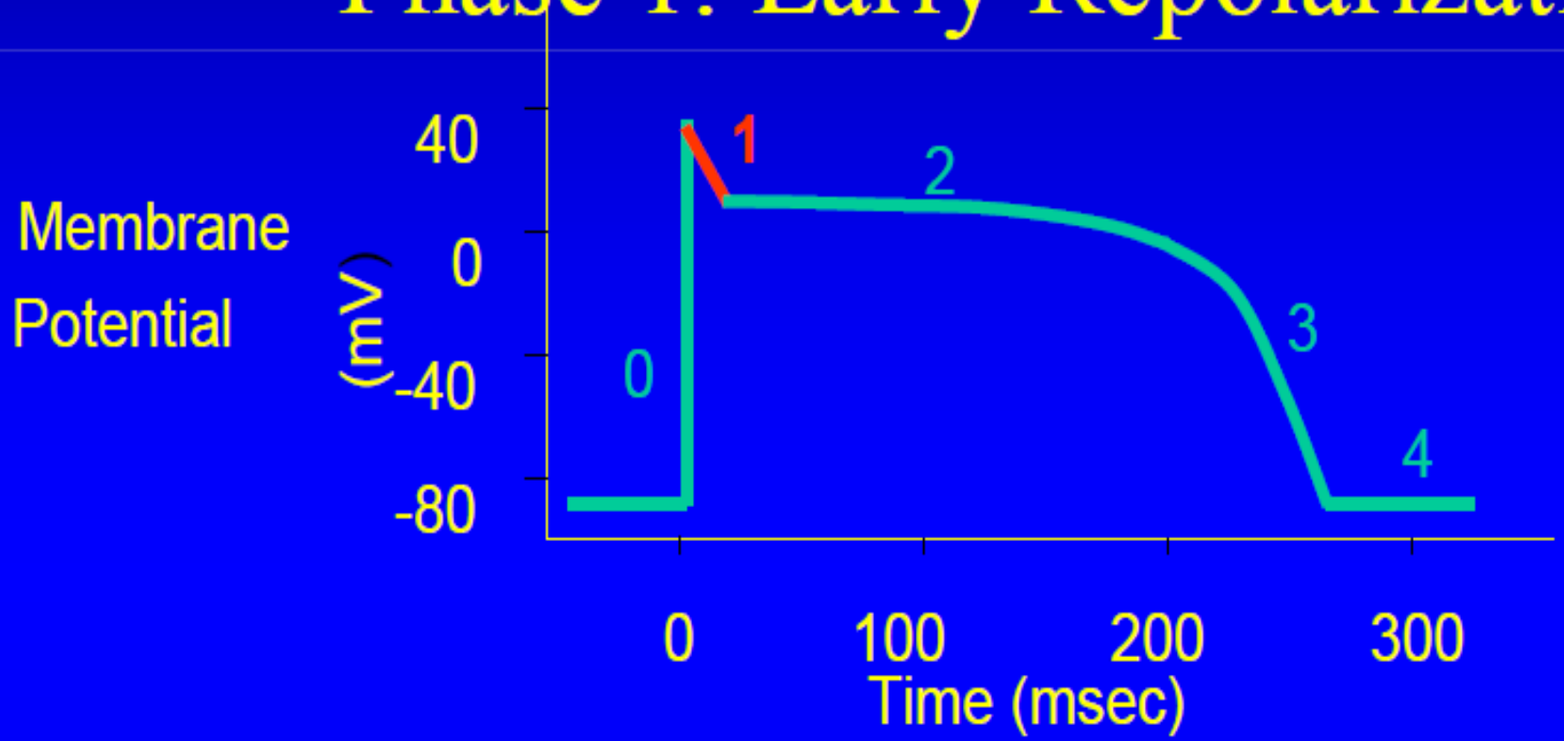
Phase 0: Upstroke

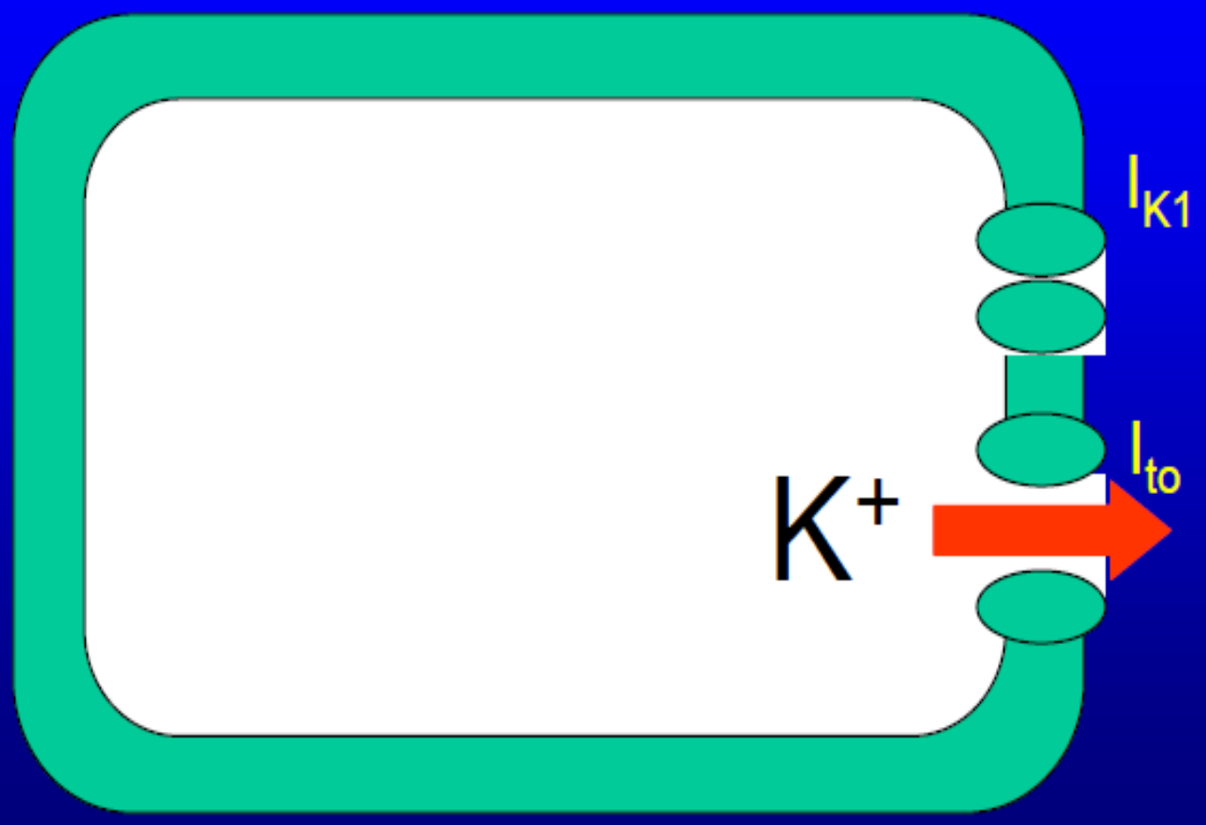




Fast Response Action Potential

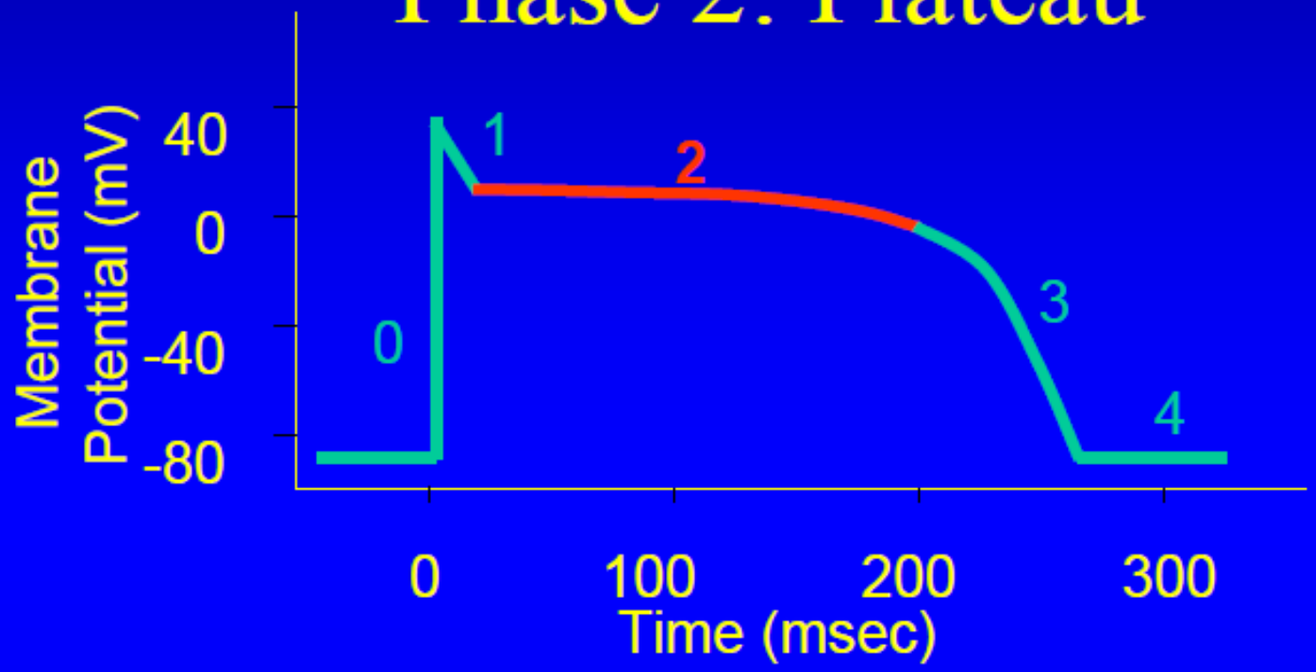
Phase 1: Early Repolarization

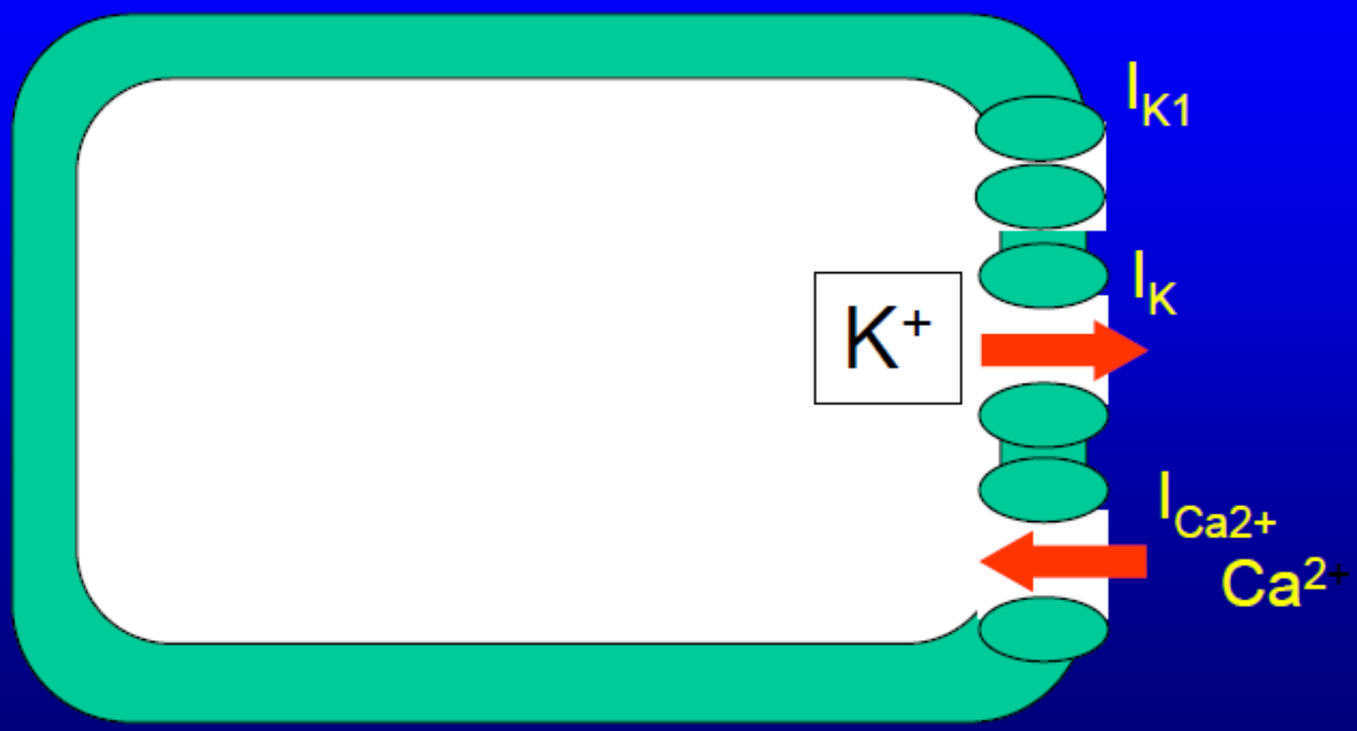




Fast Response Action Potential

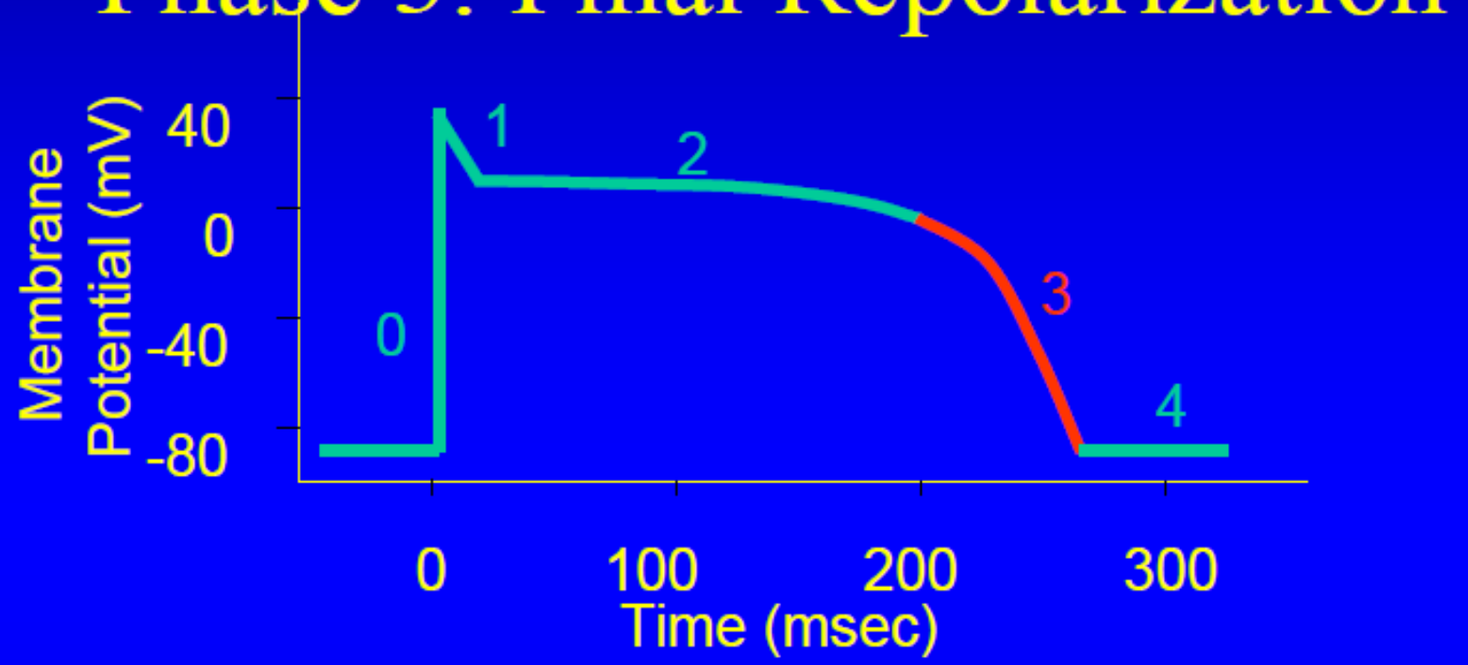
Phase 2: Plateau

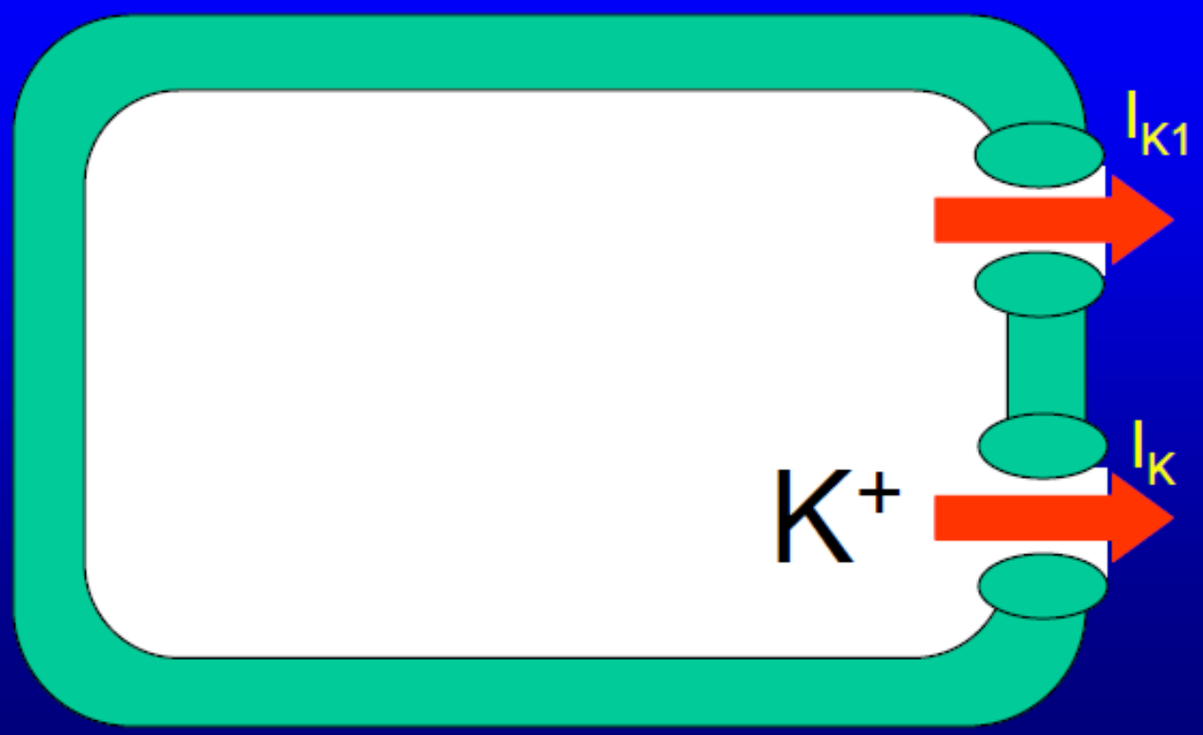




Fast Response Action Potential

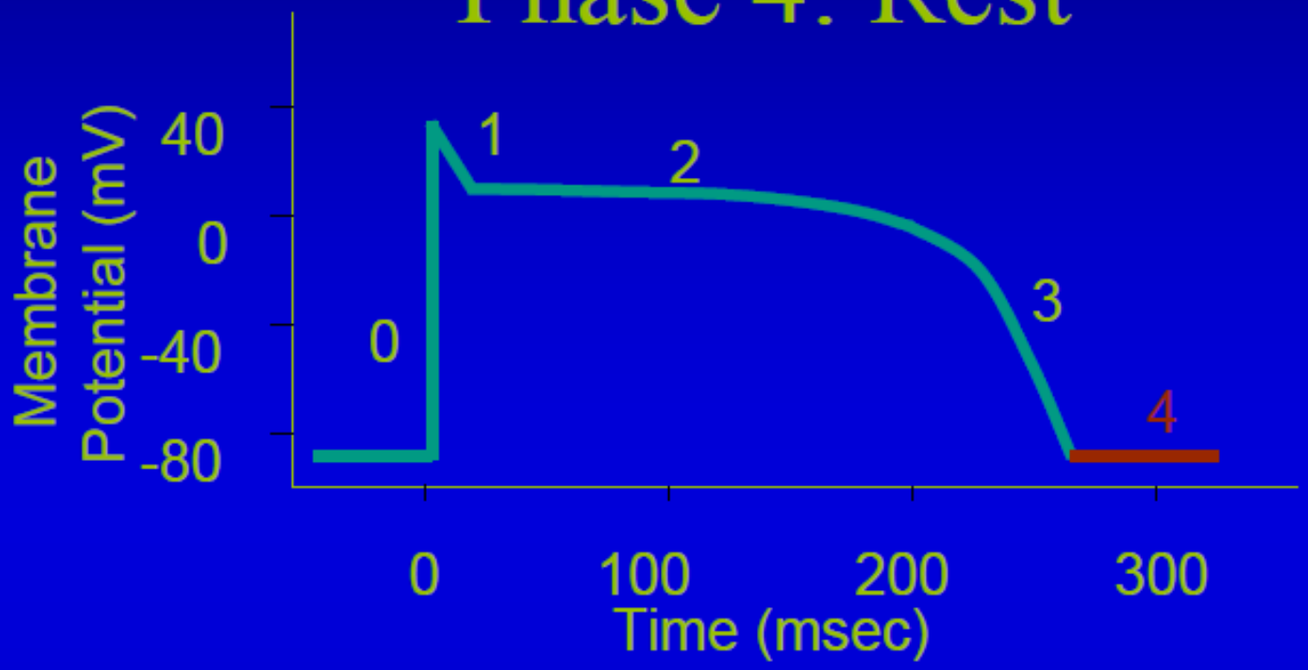
Phase 3: Final Repolarization

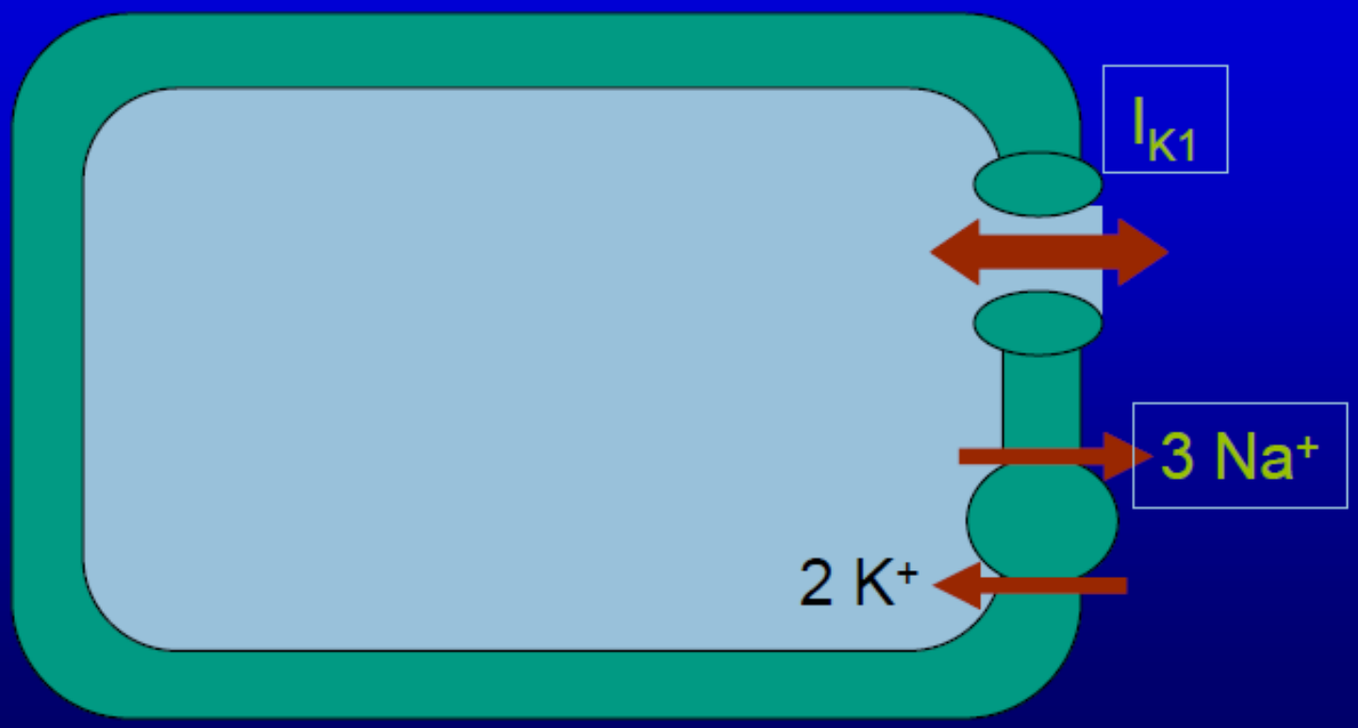


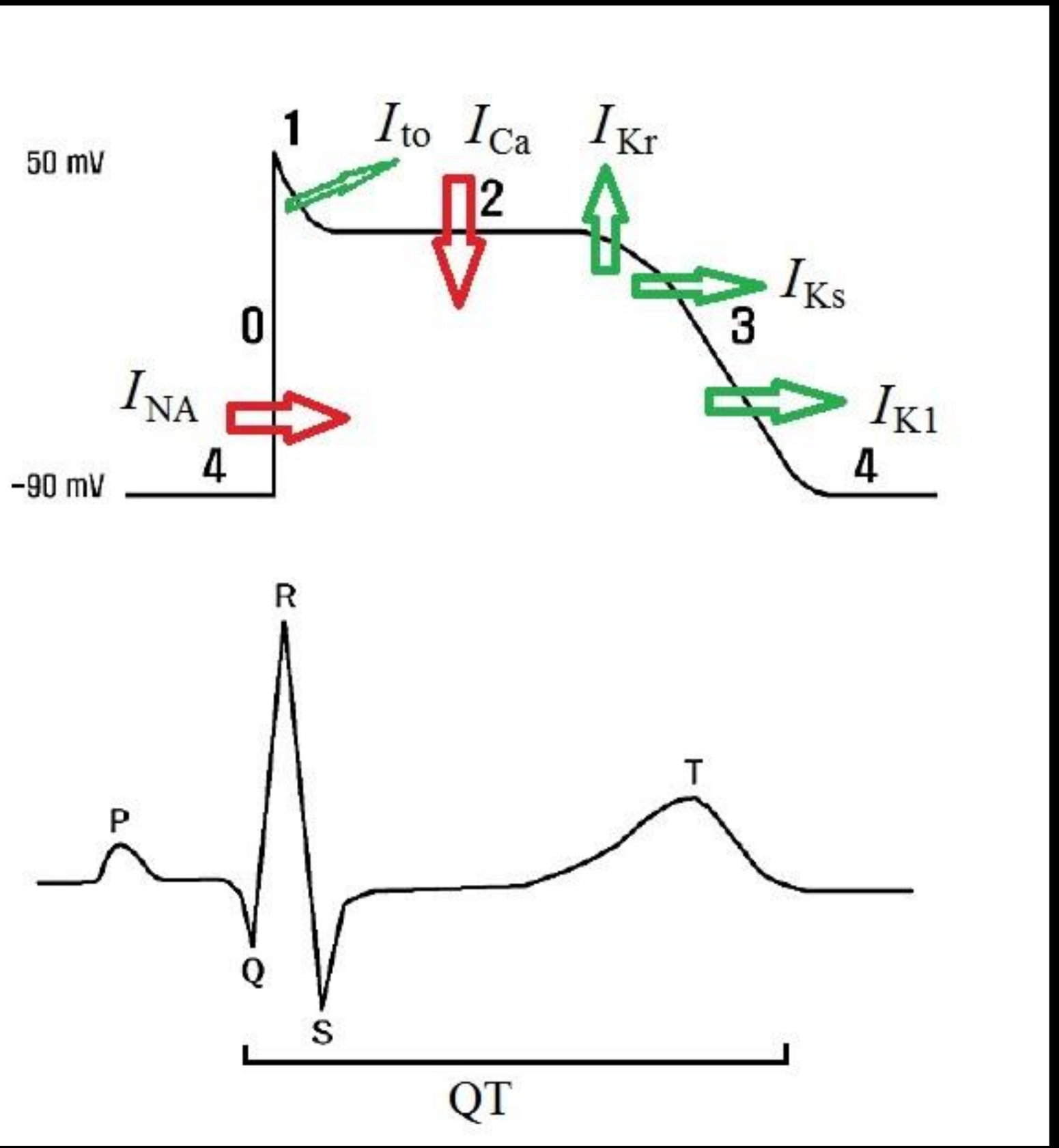


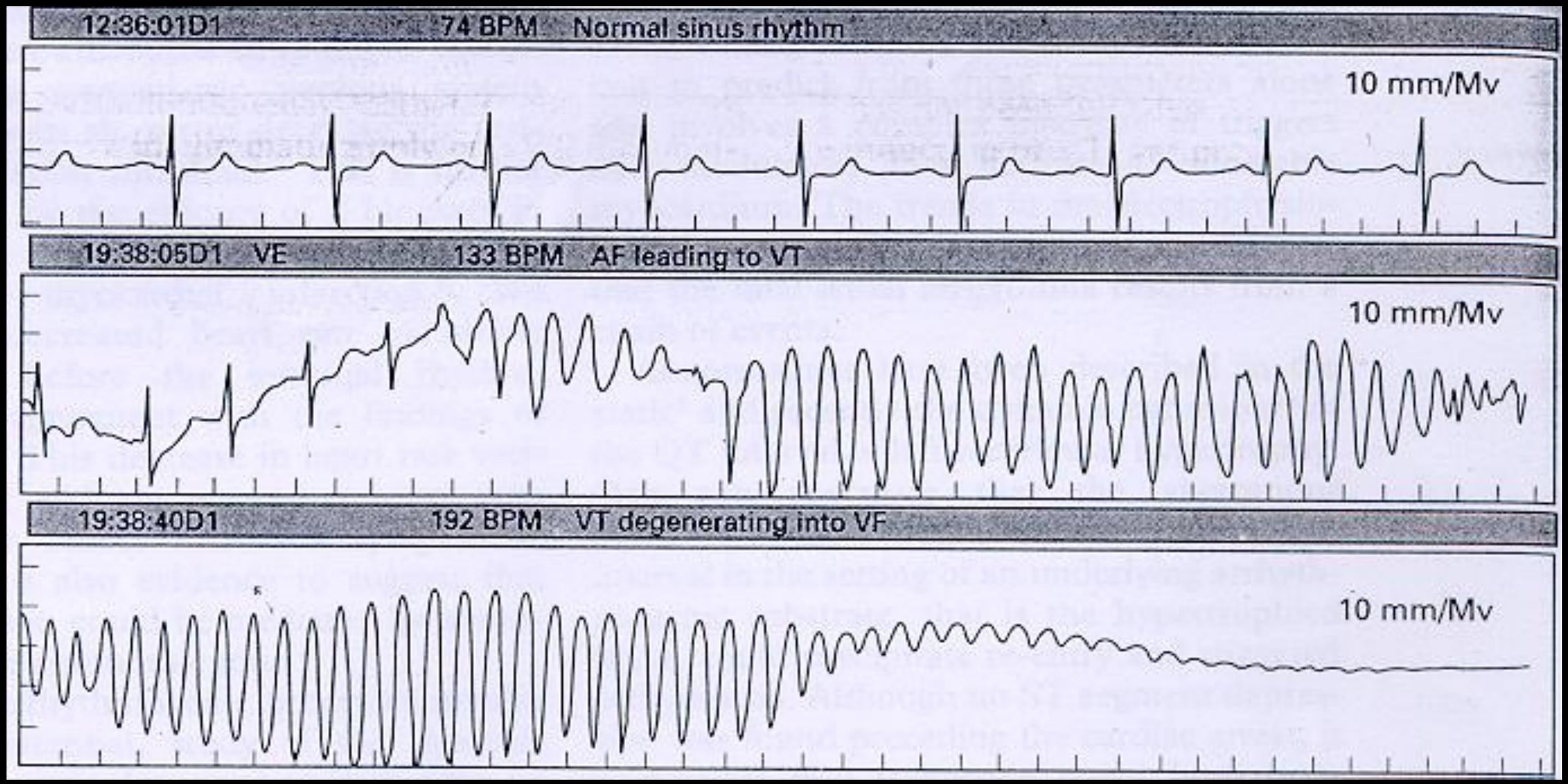
Fast Response Action Potential

Phase 4: Rest

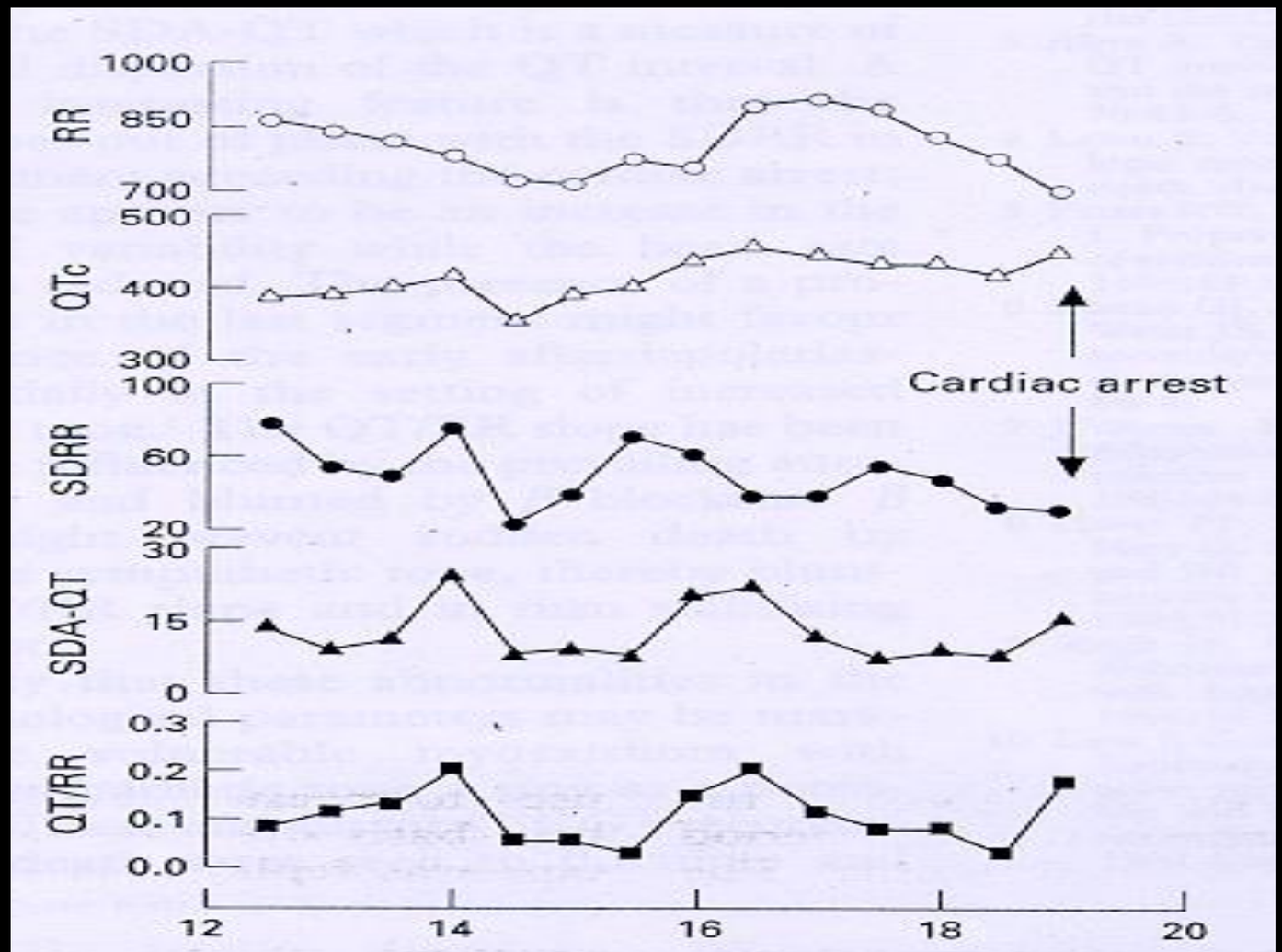





50 mV
-90 mV
1
2
3
4
0
4
I_{to}
I_{Ca}
I_{Kr}
I_{Ks}
I_{K1}
I_{NA}
R
P
Q
S
T
QT



Singh JP, *Heart* 1997

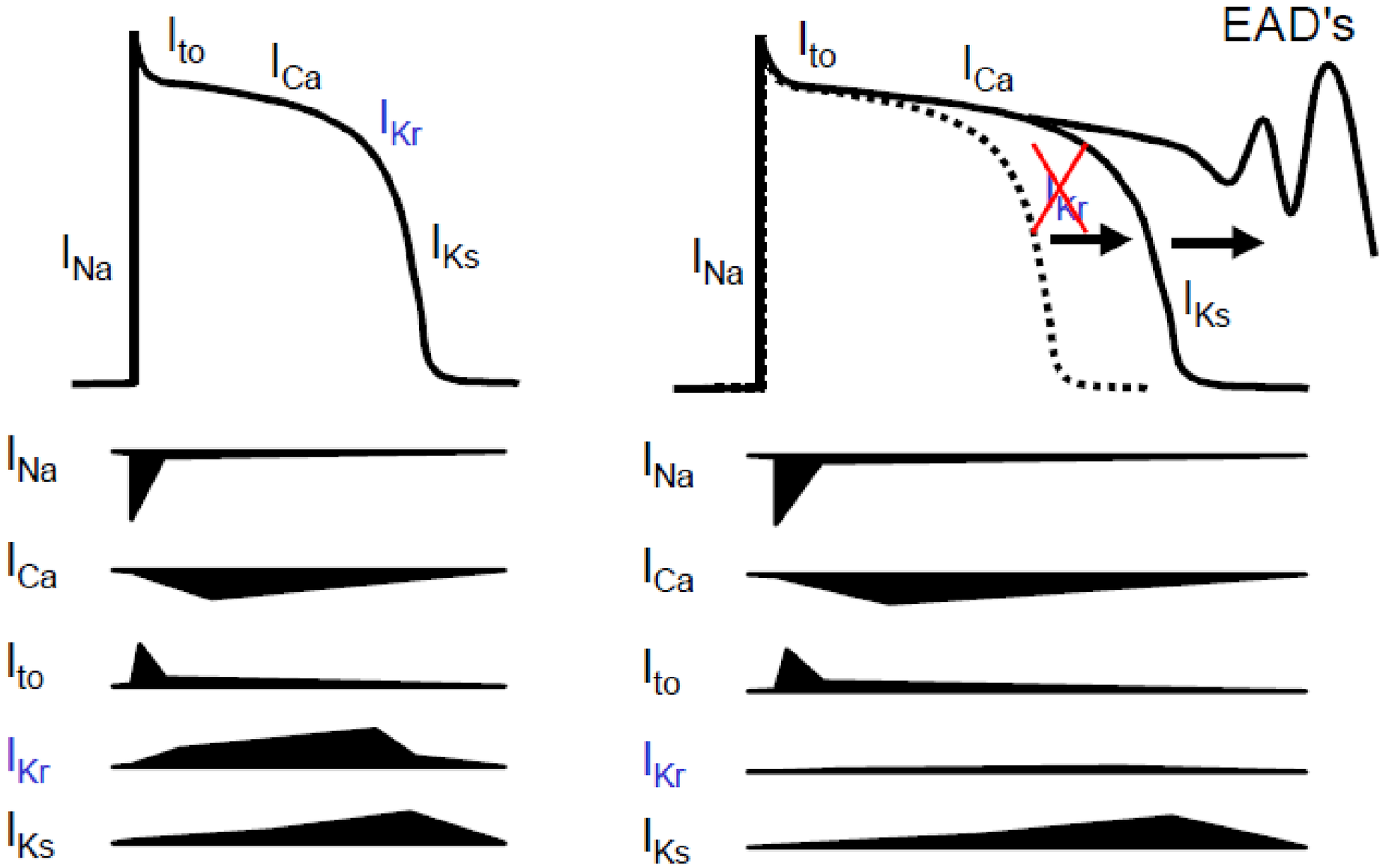


QT/RR slope and SDRR in the hour preceding the terminal rhythm

Time (min)	*QT/RR slope*	*SDRR (ms)*
−60	0·032	43·2
−50	0·043	37·3
−40	0·068	56·8
−30	0·026	40·5
−20	0·018	25·3
−10	0·293	33·1

SDRR, standard deviation of consecutive RR intervals over 5 min intervals.

Singh JP, *Heart* 1997


I to
I Ca
I Kr
I Ks
I Na
EAD's
I to
I Ca
I Kr
I Ks
I Na
I Na
I Ca
I to
I Kr
I Ks
I Na
I Ca
I to
I Kr
I Ks

	Chromosome	Gene	Protein	Ion current affected	Trigger	Special features/ occurrence
LQTS type						
1	11p15.5	*KCNQ1*	KvLQT1 (Kv7.1)	I_{Ks}	Exercise (swimming), emotion	42–54%
2	7q35–36	*KCNH2*	HERG, (Kv11.1)	I_{Kr}	Rest, emotion, exercise (acoustic, post partum)	35–45%
3	3p24–21	*SCN5A*	Nav1.5	I_{Na}	Rest, sleep, emotion	1·7–8%; High lethality
4	4q24–27	*ANK2*	Ankyrin-B	$I_{Na\text{-}K}$, $I_{Na\text{-}Ca}$, I_{Na}	Exercise	<1%
5	21q22	*KCNE1*	MinK	I_{Ks}	Exercise, emotion	<1%
6	21q22	*KCNE2*	MiRP1	I_{Kr}	Rest, exercise	<1%
7	17q23	*KCNJ2*	Kir2.1	I_{K1}	Rest, exercise	Periodic paralysis, dysmorphic feature
8	12p13.3	*CACNA1C*	Cav1.2	I_{Ca}	Exercise, emotion	Rare, syndactyly
9	3p25.3	*CAV3*	Caveolin-3	I_{Na}	Non-exertional, sleep	Rare
10	11q23.3	*SCN4B*	NaVβ4	I_{Na}	Exercise, post partum	<0·1%
Short QT syndrome type						
1	7q35–36	*KCNH2*	HERG (Kv11.1)	I_{Kr}	Exercise, rest (acoustic)	..
2	11p15.5	*KCNQ1*	KvLQT1 (Kv7.1)	I_{Ks}	..	..
3	17q23	*KCNJ2*	Kir2.1	I_{K1}	Sleep	..
4	12p13.3	*CACNA1C*	Cav1.2	I_{Ca}	..	..
5	10p12.33	*CACNB2b*	CaVβ2b	I_{Ca}	..	..
Jervell and Lange-Nielsen syndrome type						
1	11p15.5	*KCNQ1*	KvLQT1 (Kv7.1)	I_{Ks}	Exercise (swimming), emotion	1–7%; deafness
2	21q22	*KCNE1*	MinK	I_{Ks}	Exercise (swimming), emotion	<1%; deafness

I_{Ks}=rectifier K^+ current, slow component. I_{Kr}=rectifier K^+ current, rapid component. I_{Na}=inward Na^+ current. $I_{Na\text{-}K}$=Na^+-K^+ ATPase current. $I_{Na\text{-}Ca}$=Na^+-Ca^{2+} exchanger current. I_{K1}=inward rectifier K^+ channel. I_{Ca}=Ca^{2+} current.

Table 2. Genes Involved in the Long-QT Syndrome

Variant	Gene	Protein	Effect of Mutations
LQT1	*KCNQ1*	KvLQT1	Reduced I_{Ks}
LQT2	*KCNH2*	HERG	Reduced I_{Kr}
LQT3	*SCN5A*	Nav1.5	Increased I_{Na}
LQT4	*ANK2*	Ankyrin B	Reduced membrane expression of Na^+ and Ca^{2+} channels
LQT5	*KCNE1*	MinK	Reduced I_{Ks}
LQT6	*KCNE2*	MiRP	Reduced I_{Kr}
LQT7, Andersen syndrome	*KCNJ2*	Kir2.1	Reduced outward I_{K1}
LQT8, Timothy syndrome	*CACNA1c*	Cav1.2	Increased I_{Ca}
LQT9	*CAV3*	Cardiac caveolin gene	Increased I_{Na} resulting from altered gating kinetic
LQT10	*SCN4B*	Sodium channel β_4 subunit	Reduced subunit expression causing increased I_{Na}
LQT11	*AKAP9*	Yotiao	Impaired I_{Ks} activation by catecholamines
LQT12	*SNTA1*	Syntrophin	Reduced NaV1.5 nitrosylation and increased current
LQT13	*KCNJ5*	Kir3.4/GIRK4	Reduced I_{KAch}, acetylcholine-dependent potassium current

Table 1 Risk factors for drug-induced torsades de pointes

Female gender
Hypokalaemia
Hypomagnesaemia
Bradycardia
Shortly after conversion of atrial fibrillation
Congestive heart failure
Left ventricular hypertrophy
High drug concentrations (exception: quinidine)
Unrecognized congenital long QT syndrome
Predisposing DNA polymorphisms

Rosen MR, *Int J Med* 2006; 259: 7-23

Repolarization reserve

DNA polymorphisms of ionic channels

Polimorfismo Genetico dei Canali Ionici

QTc< 0.40 SEC

Rosen MR, *Int J Med* 2006; 259: 7-23

Polimorfismo dei Canali Ionici

SCN.5A
(S1102Y, H558R)

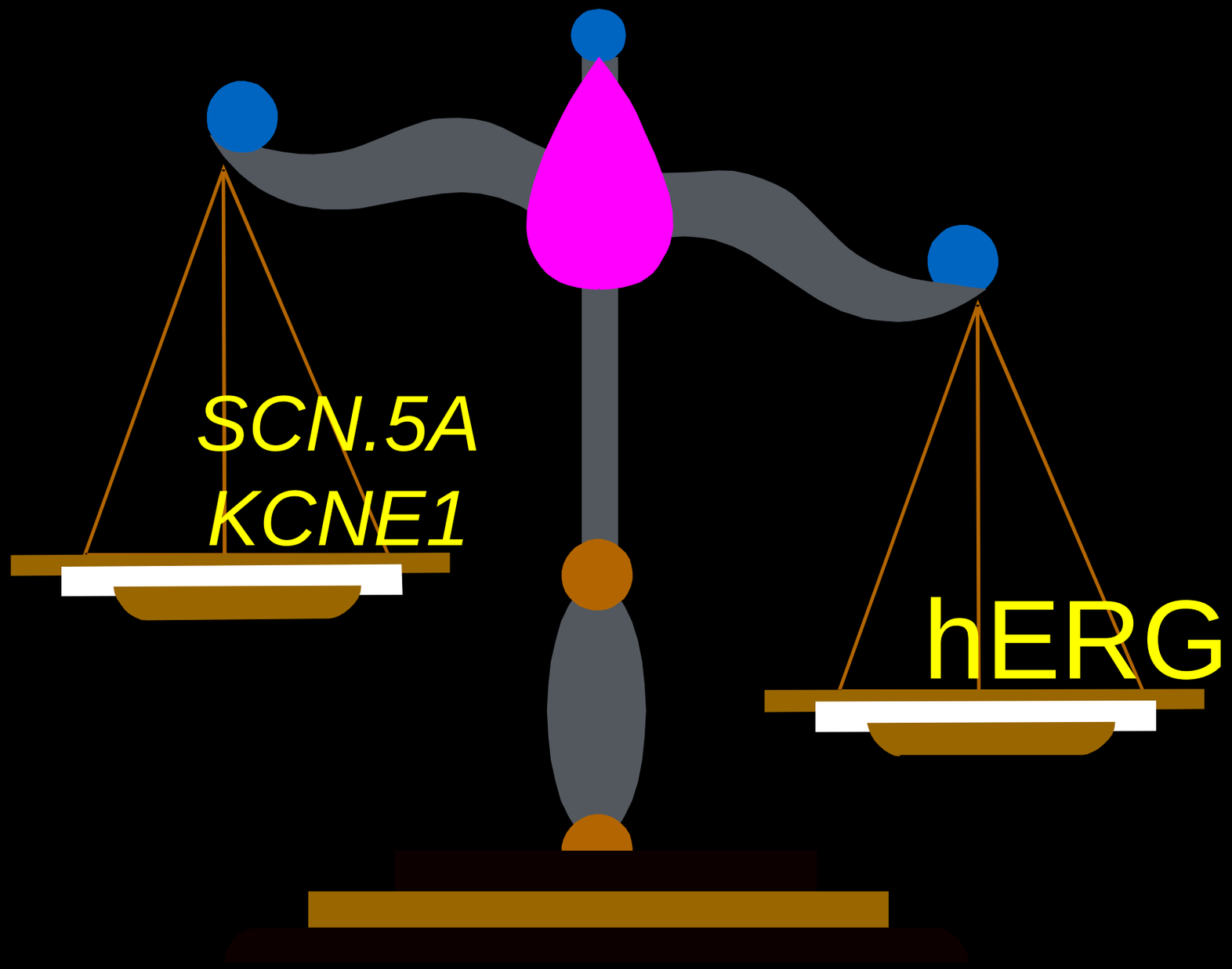
KCNE1
(D85N)

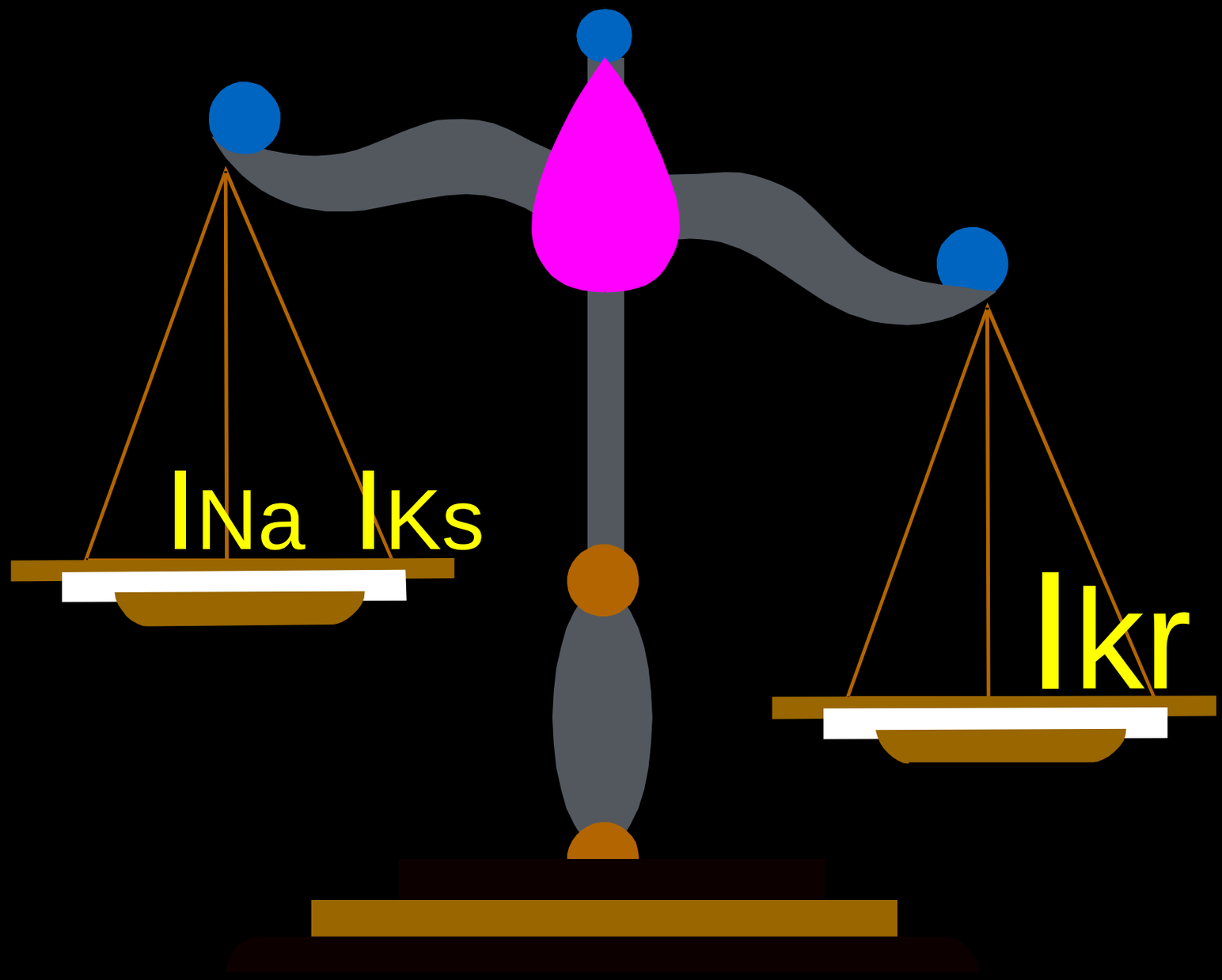
Ipokalemia
Farmaci
Ischemia
Ipertrofia
CHF

QTc: 0.400 sec → **QTc: 0.500-0.600 sec** → **T.di Punta**

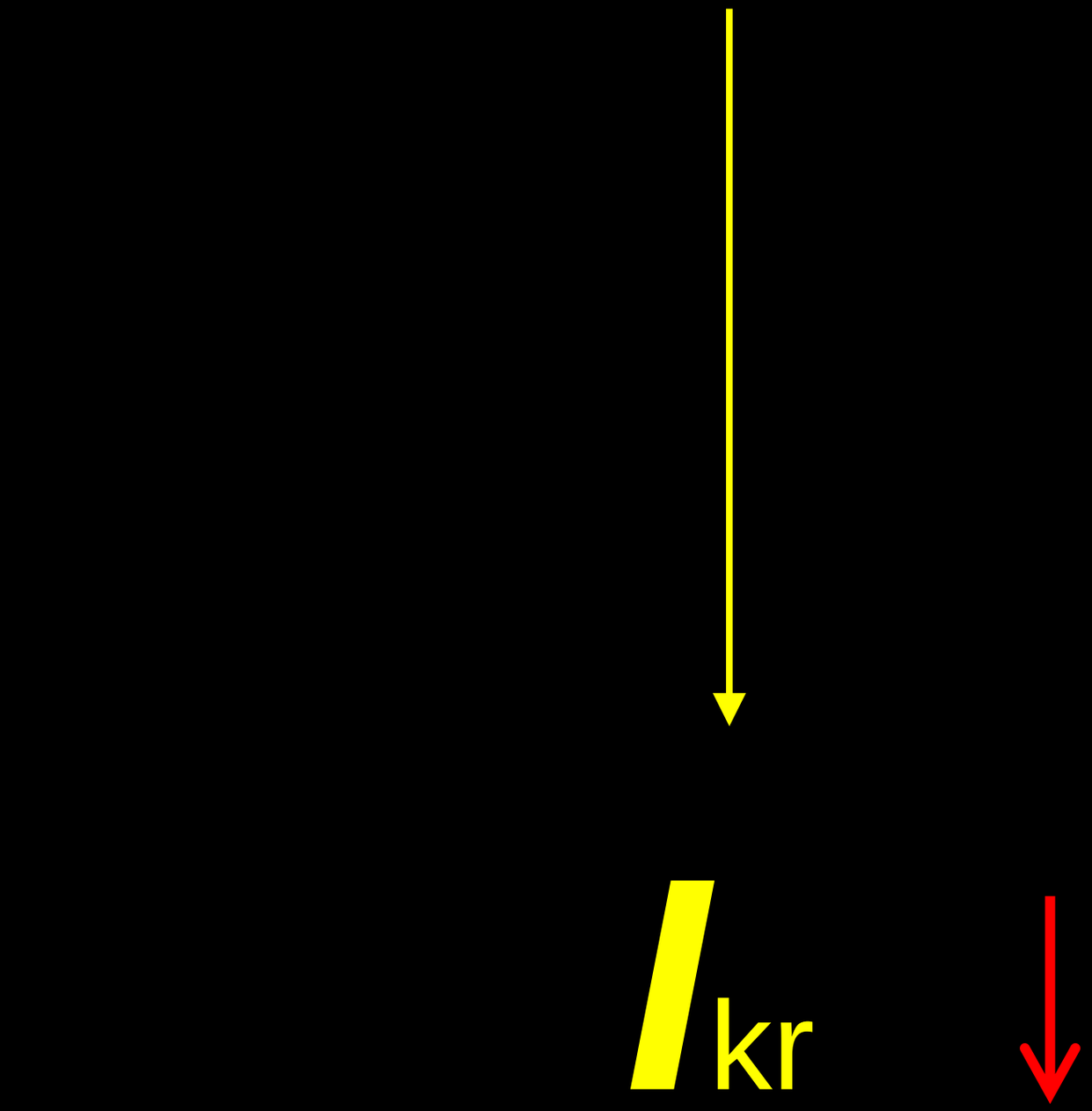
M.I.

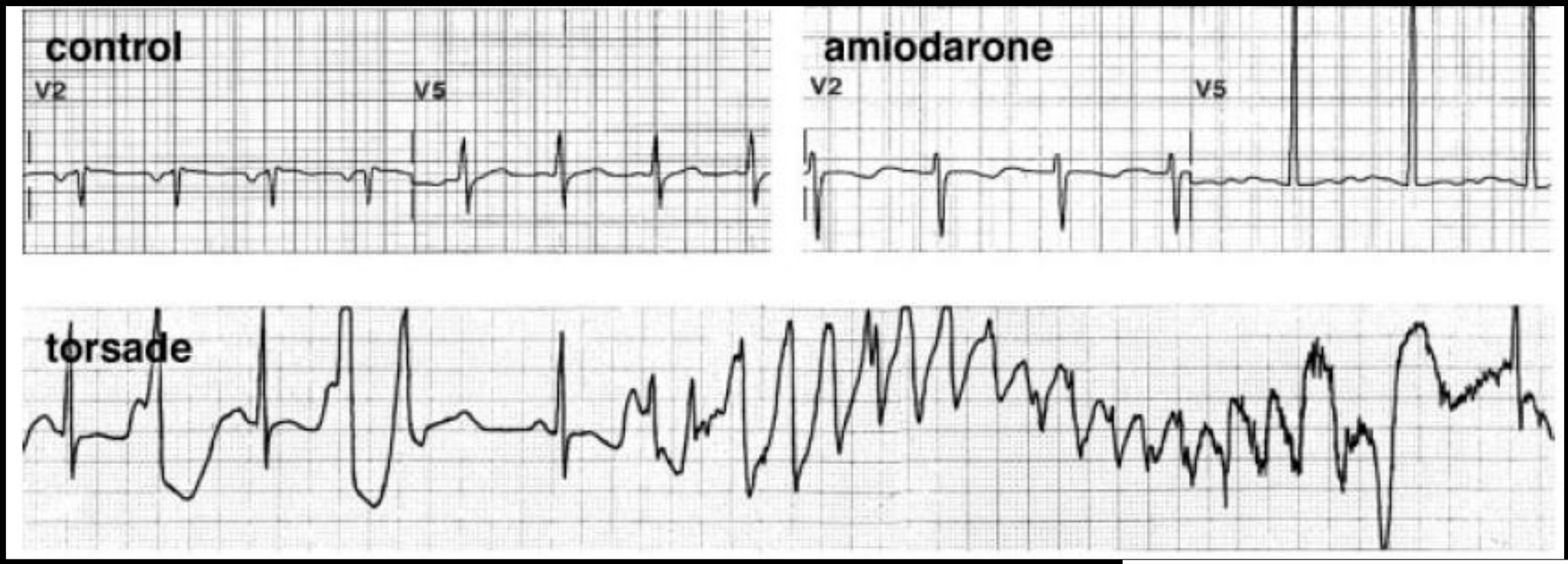
Rosen MR, *Int J Med* 2006; 259: 7-23

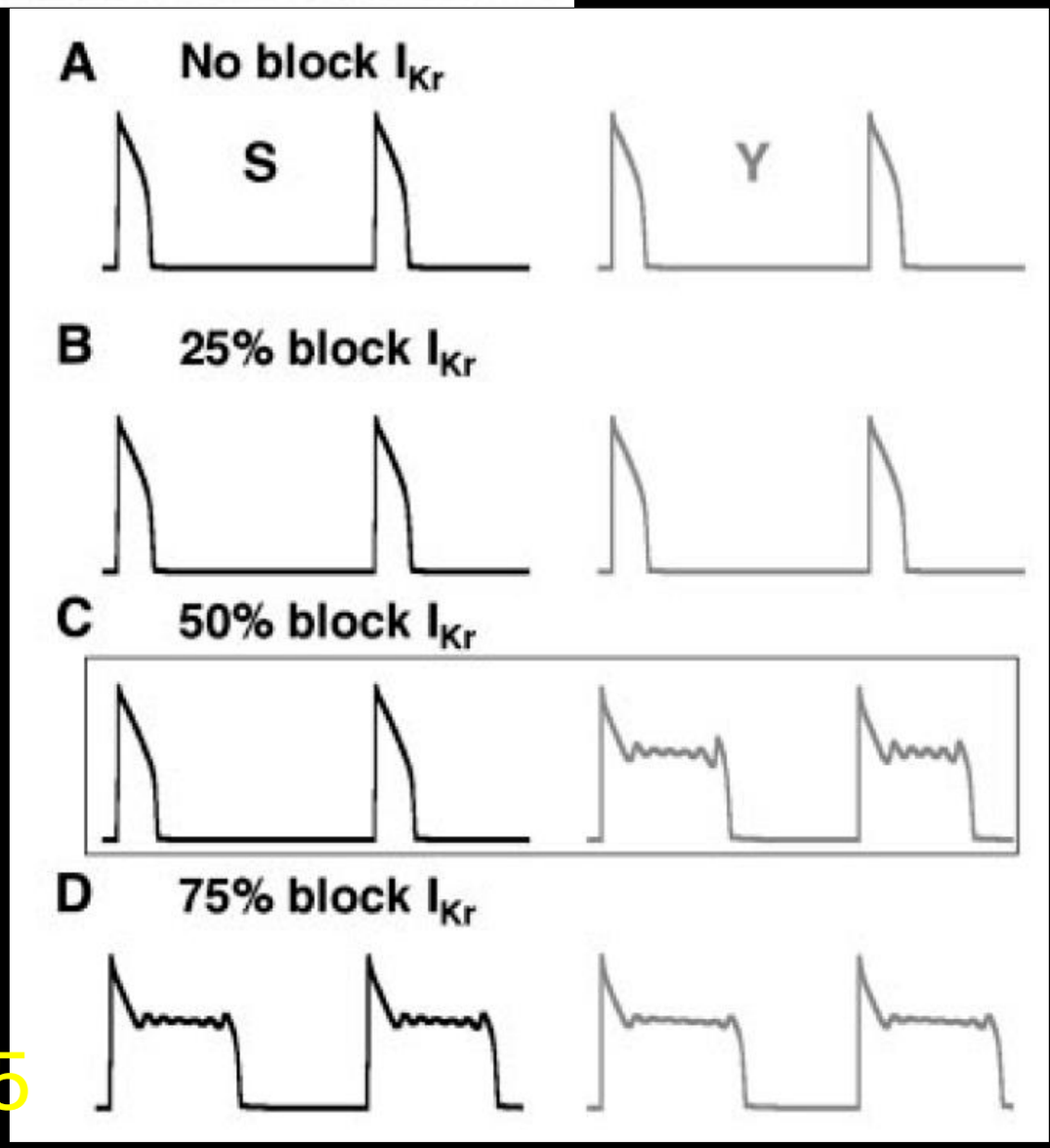

SCN.5A
KCNE1
hERG


INa IKs
IKr

Ipokalemia







plawski I,*Science* 2002; 297: 1333-1335

Genotype	Arrhythmia cases (n = 23) (%)	Controls (n = 100) (%)	Odds ratio (95% CI)*	P †
Y,Y	2 (8.7)	0 (0.00)		
S,Y	11 (47.8)	13 (13.0)		
S,S	10 (43.5)	87 (87.0)		
S,Y + Y,Y	13 (56.5)	13 (13.0)	8.7 (3.2–23.9)	0.000028

*Odds ratio for the likelihood of arrhythmia in Y carriers (S,Y + Y,Y) versus noncarriers (S,S). †P value for the comparison of carriers (S,Y + Y,Y) and noncarriers (S,S) in cases and controls (Fisher's exact test).

Splawski I,*Science* 2002; 297: 1333-1335

Table 1 Overview of mutations and functional polymorphisms in cLQTS genes that have been reported in acquired LQTS patients. *n.s.* Not specified

Gene	Base pair change	Amino acid change	Drugs	Age (years)	Sex	Additional risk factors	Symptoms	Reference
KCNE1	253G→A	D85N	Sotalol	80	Female	–	TdP	This study
	253G→A	D85N	Quinidine	71	Male	Hypokalaemia	TdP	This study
KCNE2	22A→G	T8A	Amiodarone	12	Male	–	TdP	This study
	22A→G	T8A	Quinidine	n.s.	n.s.	–	TdP	13
	22A→G	T8A	Sulfametoxazole	45	Male	–	QTc>600 ms	14
	25C→G	Q9E	Clarithromycin	76	Female	Hypokalaemia, diabetic, history of stroke	TdP, VF	13
	161T→C	M54T	Procainamide	n.s.	n.s.	–	TdP	14
	170T→C	I57T	Oxatomide	n.s.	n.s.	–	TdP	14
	347C→T	A116V	Quinidine, mexiletine	55	Female	History of cardiac arrest	Syncope with TdP	14
KCNH2	1039C→T	P347S	Cisapride, clarithromycin	77	Female	–	TdP	21, this study
	1048C→T	R328C	n.s.	45	Male	–	TdP	15
	2350C→T	R784W	Amiodarone	n.s.	n.s.	–	TdP	16
KCNQ1	944A→G	Y315C	Cisapride	77	Female	Hypokalaemia	Cardiac arrest	22
	1663C→T	R555C	Terfenadine	38	Female	cLQTS family	Sudden death	29
	1747C→T	R583C	Dofetilide	n.s.	n.s.	–	TdP	16
SCN5A	1844G→A	G615E	Quinidine	n.s.	n.s.	–	TdP	16
	1852C→T	L618F	Quinidine	n.s.	n.s.	–	TdP	16
	3748T→C	F1250L	Sotalol	n.s.	n.s.	–	TdP	16
	5474T→C	L1825P	Cisapride	70	Female	–	Tdp	30

Paulussen AD, *J Mol Med* 2004; 82: 182-188

Farmaci che allungano il QT

Antiaritmici
IA: chinidina, procainamide, disopiramide
III: amiodarone, dofetilide, ibutilide, sotalolo
IV: bepridil, mibefranil, terodilina

Antzelevitch C, *Int J Med* 2006; 259: 70-80

Farmaci che allungano il QT

Antistaminici
Terfenadina
Astemizole
Difenilidramina

Antzelevitch C, *Int J Med* 2006; 259: 70-80

Farmaci che allungano il QT

Antimicrobici
Eritromicina, Azitromicina, Claritromicina
Trimethoprim-sulfametolaxazolo
Ciprofloxacina, Grepafloxacina, Sparfloxacina
Chetoconazolo
Pentamidina
Clorochina. Alofantrina

Antzelevitch C, *Int J Med* 2006; 259: 70-80

Farmaci che allungano il QT

Psicotropi
Aloperidolo, Droperidolo
Clorpromazina
Tioridazina
Pimozide
Risperidone, Amisulpride, Quetiapina
Sertindole
Antidepressivi triciclici e tetraciclici
Inibitori del reuptake della serotonina

Antzelevitch C, *Int J Med* 2006; 259: 70-80

Farmaci che allungano il QT

Antischemici/Vasodilatatori
Bepridil
Lidoflazine
Ketanserina
Prenilamina

Antzelevitch C, *Int J Med* 2006; 259: 70-80

Farmaci che allungano il QT

Ipolipemizzanti
Probucol
Agenti Gastrointestinali
Cisapride
Agenti Antimpotenza
Sildenafil

Antzelevitch C, *Int J Med* 2006; 259: 70-80

1. Farmaci associati a rischio di TdP	2. Farmaci potenzialmente associati a rischio di TdP	3. Farmaci da evitare in pazienti affetti o sospetti di LQTS cong.
Farmaci che sono generalmente accettati dalle autorità regolatorie come a rischio di causare TdP	*Farmaci che, in qualche segnalazione sono associati a TdP, ma per i quali mancano ancora sostanziali evidenze*	*Farmaci da evitare in pazienti con LQTS congenita diagnosticata o sospetta (anche gruppo 1, 2 e 4)*
Aloperidolo	Amantadina	Albuterolo
Amiodarone	Azitromicina	Chinidina
Arsenico triossido	Cloralio idrato	Cocaina
Chinidina	Dolasetron	Dobutamina
Clorpromazina	Felbamato	Dopamina
Claritromicina	Flecainide	Droperidolo
Disopiramide	Foscarnet	Efedrina
Domperidone	Grasinetron	Epinefrina
Droperidolo	Indapamide	Fenilefrina
Eritromicina	Isradimina	Fenilpropanolamina
Ibutilide	Levofloxacina	Midodrina
Metadone	Litio	Pseudoefedrina
Pentamidina	Moexipril-idroclorotiazide	Ritodrina
Pimozide	Moxifloxacina	Sibutramina
Procainamide	Nicardipina	Terbutalina
Sotalolo	Ocreotide	
Tioridazina	Ondasentron	
	Quetiapina	
	Risperidone	
	Salmeterolo	
	Tacrolimus	
	Tamoxifene	
	Telitromicina	
	Tizanidina	
	Venflaxina	
	Voriconazolo	

https://crediblemeds.org/new-drug-list/

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Risk Categories for Drugs that Prolong QT & induce Torsades de Pointes (TdP)

Based on ongoing systematic analysis of all available evidence, CredibleMeds® places drugs into broad categories based on whether each can cause QT prolongation or TdP. Because these actions are highly dependent on the circumstances of each drug's use AND each patient's clinical characteristics, we do not attempt to rank-order the drugs within each category. Therefore, we do not recommend that these lists be used to rank-order the drugs for their relative toxicity.

https://crediblemeds.org/new-drug-list/