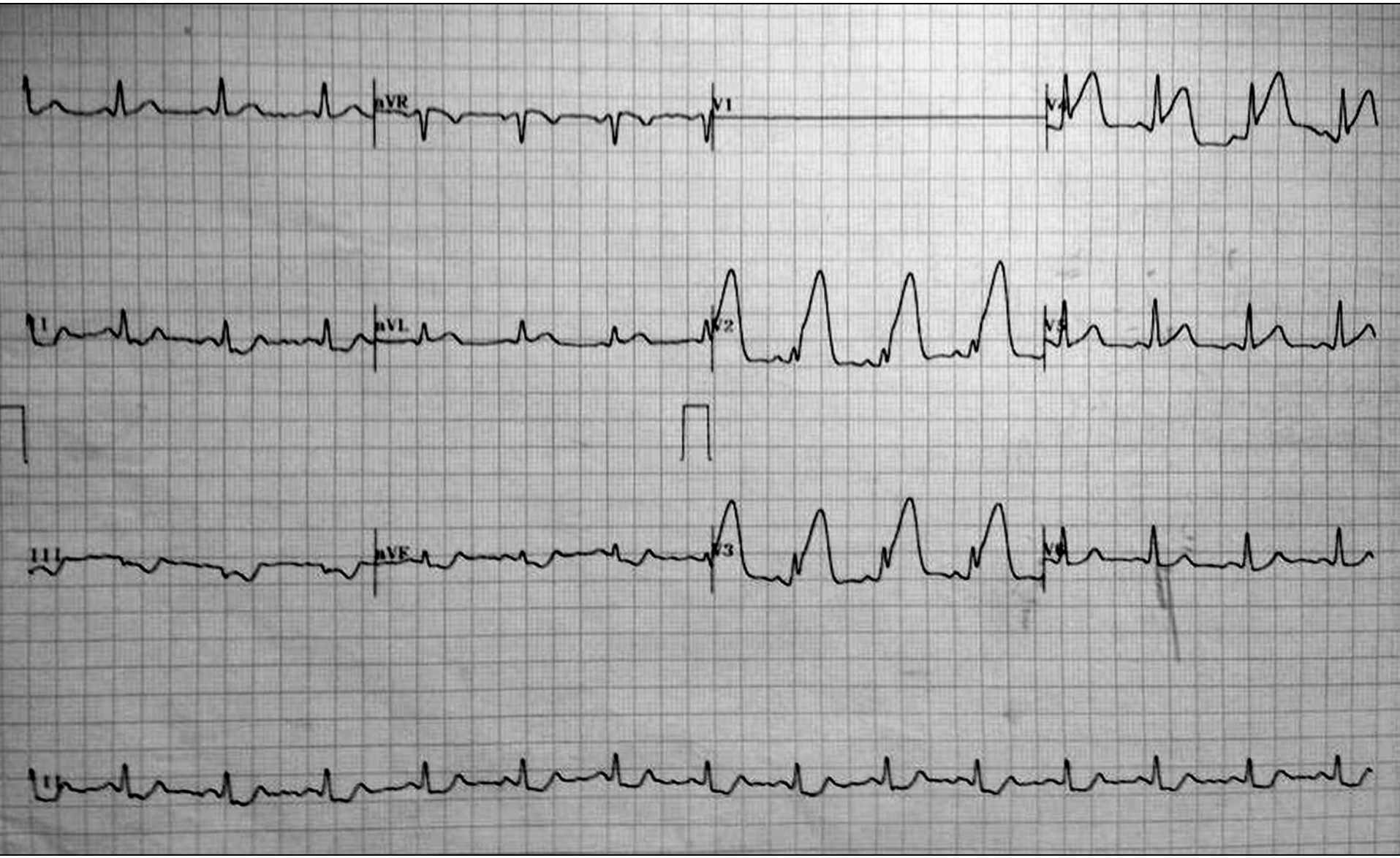
Hombre de media edad usuario de anfetamínicos y canabis sativa con cuadro de sindrome coronario agudo con elevación del segmento ST que presentó parada cardiaca súbita después de la administración del trombolítico.

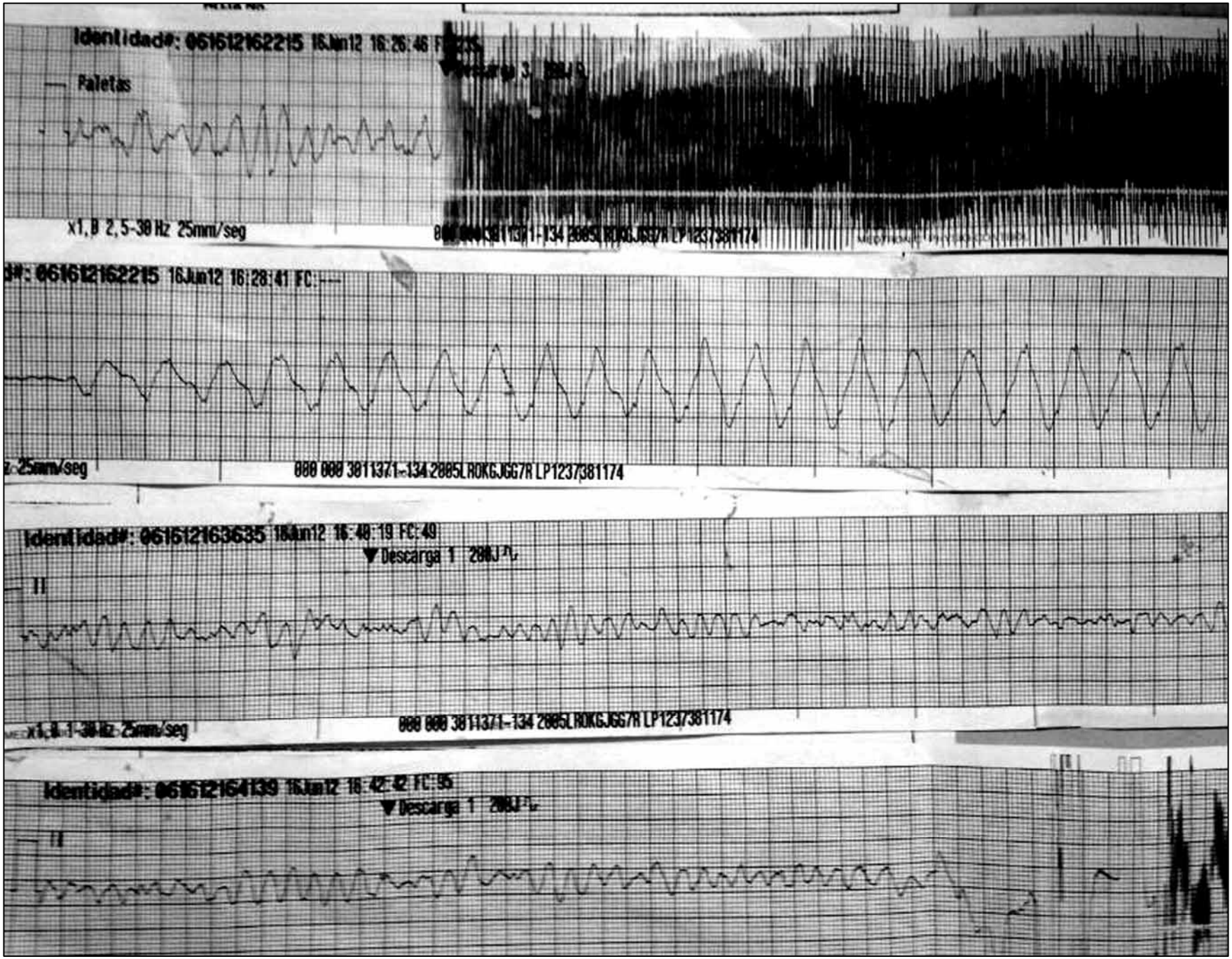
Middle-aged man user of amphetamines and cannabis sativa with picture of segment elevation ST Acute Coronary Syndrome who presented sudden cardiac arrest after thrombolytic administration

Jesus Antonio Campuzano Chacon M.D.
Guadalupe NL. Mex Urgenciologo.

Saludos amigos del foro
En esta ocasión me gustaria compartir esta secuencia de ECGs perteneciente a un hombre de 50 años que ingresa a la sala de urgencias con malestar precordial de >4 horas de evolución, procedente de una clinica familiar donde se ralizó el pimer ECG titulado “admisión“ 12h, Se interpreta como un sindrome coronario agudo con elevación del segmento ST y se le aplica el trombolítico tenecteplasa (desconozco si fue trombolizado previo al ECG 2 o posteriormente.)
Durante el examen físico hace súbito paro cardiopulmonar con deterioro neurológico, respiratório y hemodinámico. Se inician maniobras de reanimación cardio-pulmonar sin suceso.(7 descargas elétricas de 200J cada una). A posteriori, los familiares refirieron que el paciente era dependiente y gran consumidor de canabis satiba (consumo diario) y en los últimos meses estava haciendo uso además cristales de metanfetaminas. Desconocemos eventos previos. Espero sea de interés.
Abrazos Jesus Antonio Campuzano Chacon
Guadalupe NL. Mex Urgenciologo.
Greetings friends of the forum: On this occasion I would like to share this ECGs sequence of belonging to a 50 year old man admitted to the emergency room with chest discomfort for >4 hours of evolution, from a family clinic where preformed the "admission-ECG ". It is interpreted as an acute coronary syndrome with ST segment elevation and applies IV thrombolytic tenecteplase (I do not know if it was before trombolictic aplication or later.).
During the physical examination presented sudden cardiopulmonary arrest with neurological impairment, and hemodynamic unstability. Cardiopulmonary resuscitation maneuvers were initiated without success. (7 electric shock of 200 J each) In hindsight, the relatives said the patient was dependent and major consumer of cannabis sativa or Marijuana (daily) and in recent months also using crystals of methanfetamine. Unknown to previous events.
Hope will be of interest.
Hugs
Jesus Antonio Campuzano Chacon
Guadalupe NL. Mex emergency physician.

Admission-ECG midd-day 12.00h

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Paletas
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25mm/seg
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Descarga 1 200J
II
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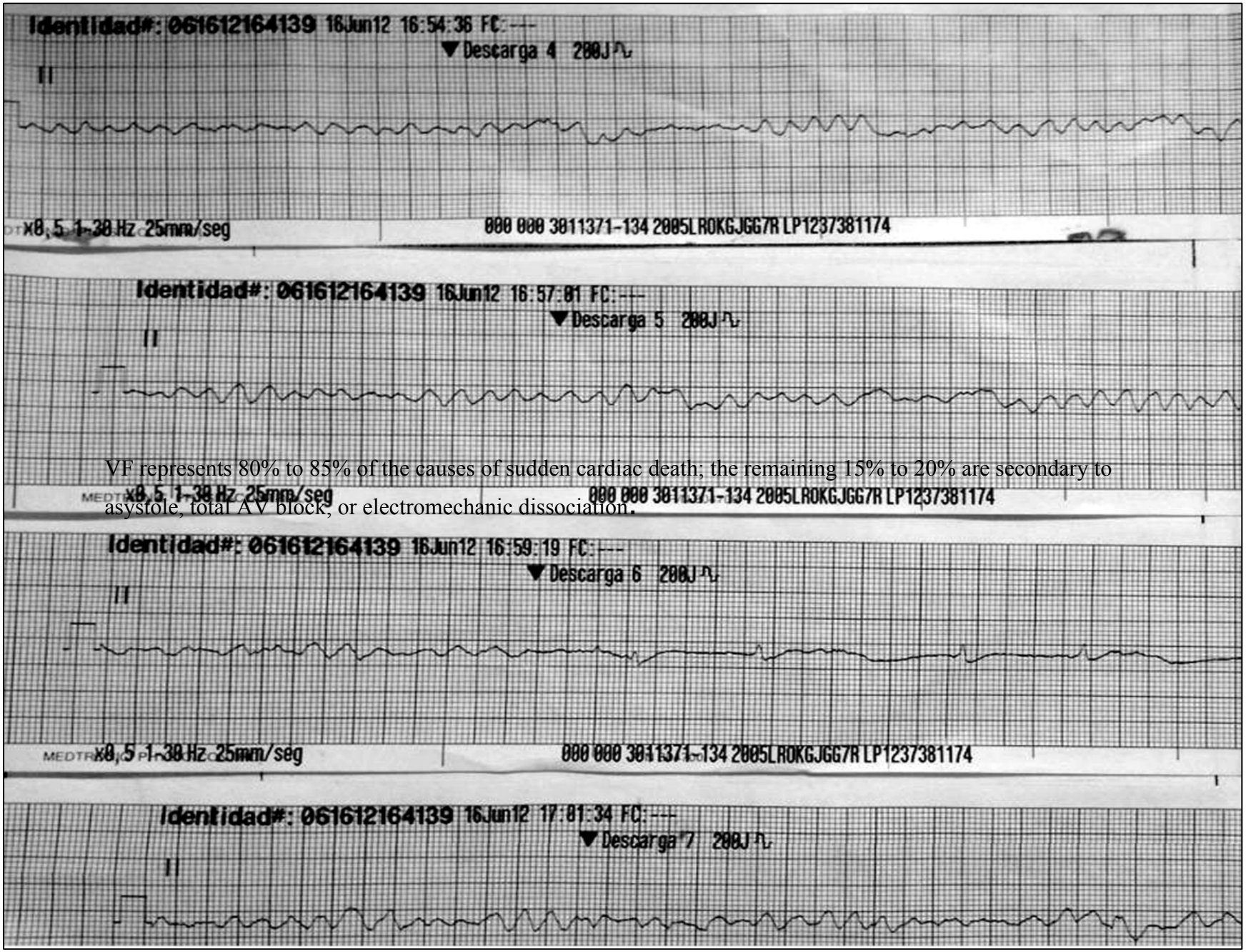
Descarga 1 200J
II



VF represents 80% to 85% of the causes of sudden cardiac death; the remaining 15% to 20% are secondary to asystole, total AV block, or electromechanic dissociation.

Colleagues opinions

Análisis del caso del Dr Jesus Antonio Campuzano

El ECG de admisión muestra un patrón de infarto anteroseptal por obstrucción proximal de la artéria coronária descendente anterior,(por la remodelacion con ST deprimido y onda T invertida en DII, DIII aVF y onda T positiva en aVL). con borde protegido por una artéria segunda marginal (V5y V6 sin elevación del segmento ST) Desde el punto de vista patofisiologico se trata de un miocardio desprotegido (sin circulación colateral y sin precondiciomiento)

La arritmia que aparece posiblemente después del tratamiento trombolítico es inicialmente una taquicardia ventricular polimórfica la cual después del choque eléctrico se transforma en disociación electro-mecánica seguida de fibrilación ventricular agónica. No se si cannabis y la anfetamina (cocaina ?) podrian tener un efecto agravante en el proceso Por ser una evolución muy dramática hace pensar que talvez hizo un hemopericardio iatrogénico por el tratamiento trombolítico y talvez se haya administrado previamente aspirina y heparina ?

Un fraternal abrazo

Samuel Sclarovsky

Analysis of the case of Dr. Jesus Antonio Campuzano

The admission-ECG shows a pattern of anteroseptal myocardial infarction due to obstruction of the proximal left anterior descending coronary artery (for the remodeling with ST depression and inverted T wave in II, III and aVF positive T wave in aVL). with edge protected by the second marginal coronary artery (V5 withouth ST-segment elevation) From the pathophysiological point of view this is an unprotected myocardium (without collateral circulation and without ischemic precondicioning)

The arrhythmia may appear after thrombolytic therapy is initially a polymorphic ventricular tachycardia transformed into electro-mechanical dissociation followed by agonic VF.

I don't know if cannabis and amphetamine (cocaine?) Could have an aggravating effect on the process Being a very dramatic evolution suggests that maybe an iatrogenic hemopericardium consequence of thrombolytic therapy and perhaps previously been administered aspirin and heparin?

A fraternal embrace

Samuel Sclarovsky M.D. Israel

Estimado Dr Jesus: interesante ECG impresiona un AMI hiperagudo de menos de 4 hs de evolución en território de DA, con supradesnivel de ST de V2 a V4 (no se registró V1), por el infradesnivel del segmento ST en DII, DIII y AVF oclusión proximal a la primera diagonal.

Es confuso en que momento recibió la terapia de reperfusión y cuales eran los signos vitales del paciente prévio a indicarse.

Las metanfetaminas pueden ocasionar crisis hipertensivas y espasmo de las arterias coronarias. Obviamente tambien el consumo de cannabis aumenta el riesgo de IAM por rotura de placa y aumento de la trombogenicidad.

Examen fisico al ingreso, signos vitales y que tratamiento se instauro previo a la terapia de reperfusion? vasodilatadores coronarios? Beta-bloqueadores?

Al ingreso a emergencias tampoco está claro, si presentó deterioro neurológico seguido de descompensacion hemodinámica, es esto asi?

Un cordial saludo

Martin Ibarrola

Gracias Martin por tu comentario.

Desgraciadamente a tus preguntas no puedo darle respuestas porque apenas tengo los ECGs rescatados por fotos tomadas con un iPhone por un residente de urgencias, ya que cuando ocurre una muerte tan precoz en nuestro servicio habitualmente todo el protocolo posterior nos impide accesar al expediente original. Apenas cuento con lo comentado ya que como mencioné en el correo previo no se en que momento fue trombolizado, ni las circunstancias previas o posteriores a la muerte. Las tiras de ECG de cada fragmento corresponden a una descarga eléctrica o al menos asi lo dice el papel de registro. A este paciente le fueron administradas al parecer 7 descargas todas de 200 J, primero por TV y posteriormente FV, otra cosa importante tambien es que el primer ECG de ingreso fue registrado a las 12:00 y el paciente ingresa al hospital mas de 4 horas después.

Gracias nuevamente

Jesus Campuzano

El mecanismo de afectación de la irrigación cardíaca, (circulación colateral) se ve afectada no solo por la presencia de trombo/s sino también por los espasmos producidos por la cocaína u otros estupefacientes. En este paciente debido al infarto anterior por afectación, probablemete de la DA, no hay duda que tenía un compromiso secundario al consumo de cocaína. Tenemos actualment un paciente ingresado en la UCI por un infarto cerebral importante, infarto renal derecho y de bazo. Desde el punto cardiológico: recuperado. La cocaína como principal factor de espasmos coronarios (la clínica de ingreso fue dolor torácico y dolor abdominal). La formación de trombos como resultado de la alteración d ela agregación por la cocaína y, aunque no encontramos indicios de punción parenteral, la afectación de la válvula aórtica ha sido espectacular.

Aunque no es un caso del forum, me gustaría enviaros en pdf las imágenes con las vegetaciones. En 72 horas el Staphyilococcus Aureus acabó con los velos aórticos.Se implantó protésis aórtica biológica, volvió a tener fiebre y bajo tratamiento antibiótico, pero el ETE de ayer mostró nuevos abscesos.

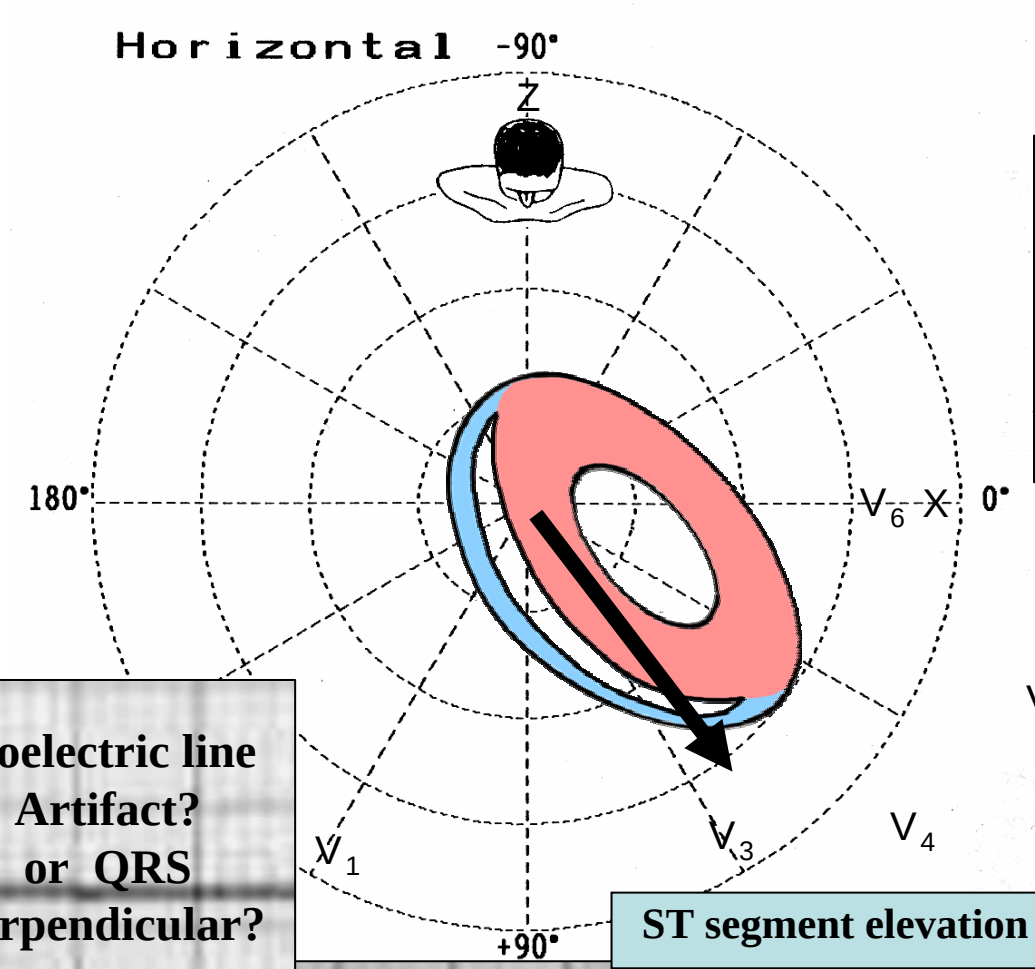
Un caso muy interesante.

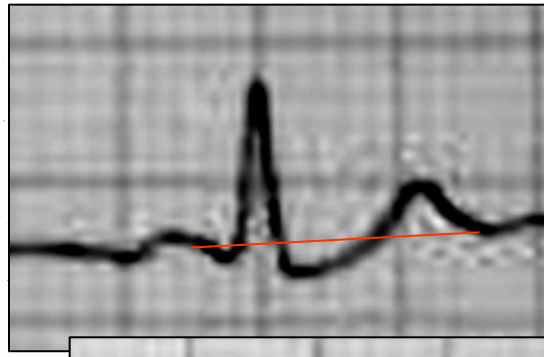
Os envio un artículo publicado sobre un estudio de muerte en jovenes consumidores de cocaína en España. Como sabéis, España es el comsumidor número uno de Europa. Saludos.

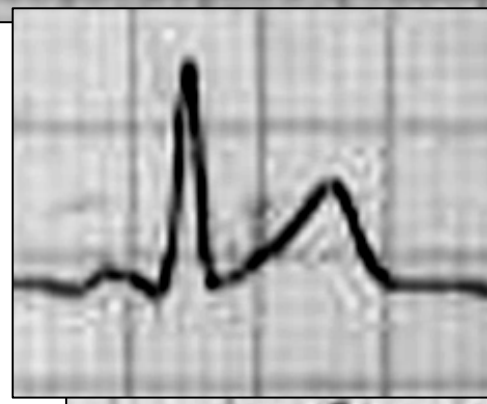
Dr. Londono

Finals comments

By Andrés Ricardo Pérez-Riera M.D. Ph.D.

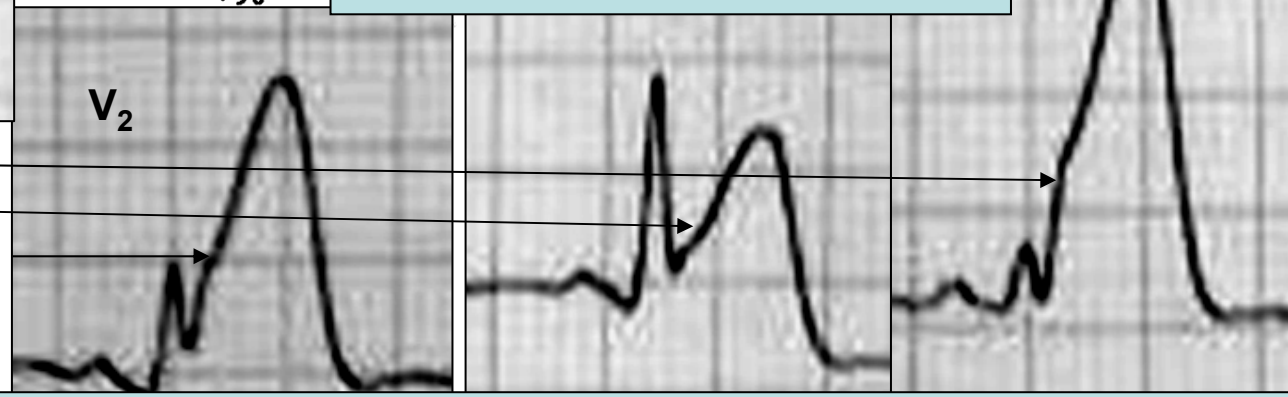






Isoelectric line Artifact? or QRS perpendicular?

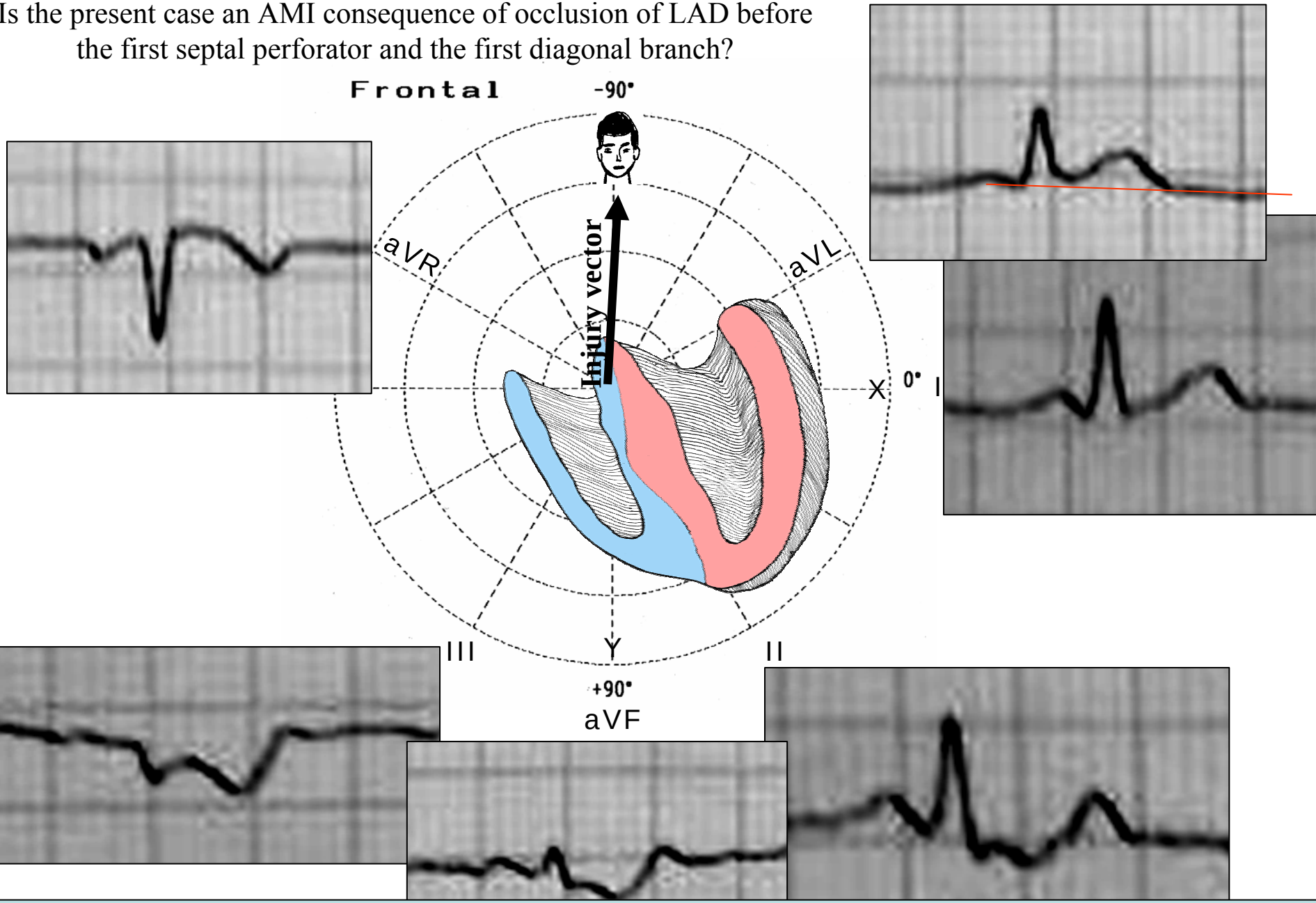
ST segment elevation MI (STEMI)



ST segment elevation in at least 2mm ST elevation in the precordial leads. These elevations must be present in anatomically contiguous leads.

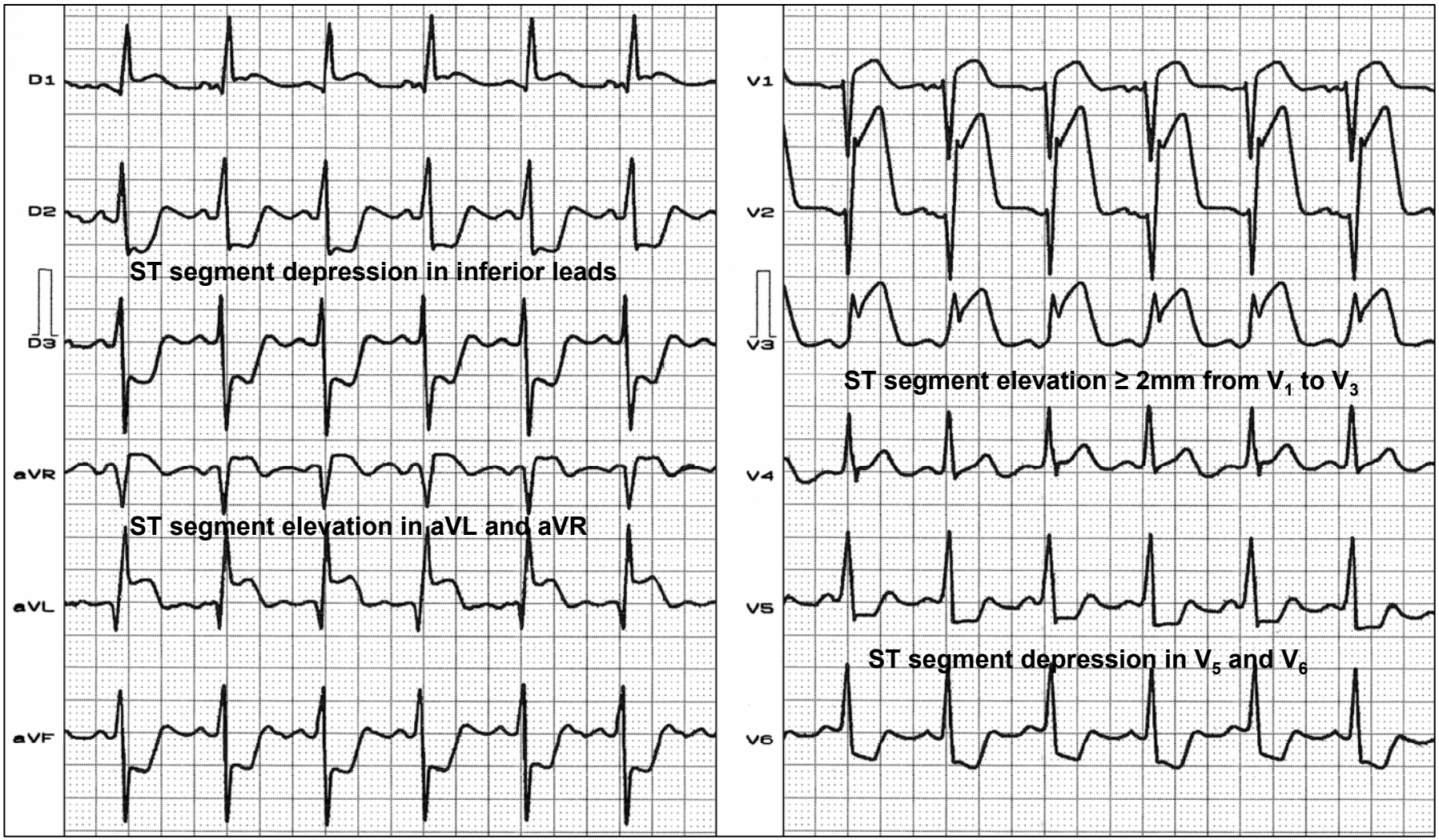
Subepicardial injury current J point and ST segment elevation from V2 to V4 anterior MI

Is the present case an AMI consequence of occlusion of LAD before the first septal perforator and the first diagonal branch?

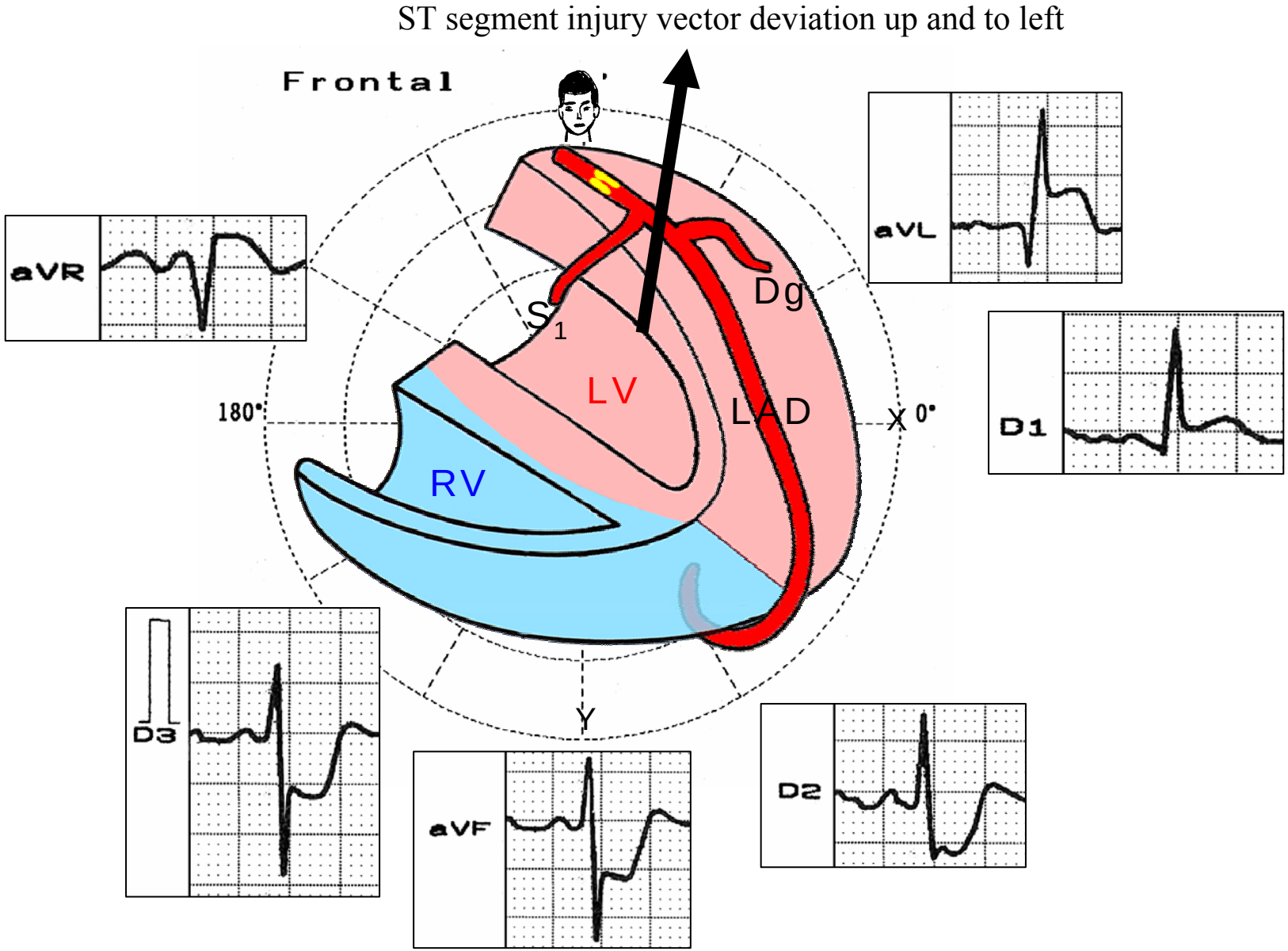


ST segment depression in III, aVF and II because injury vector directed to up

Typical example of AMI consequence of occlusion of LAD before the first septal perforator and the first diagonal branch

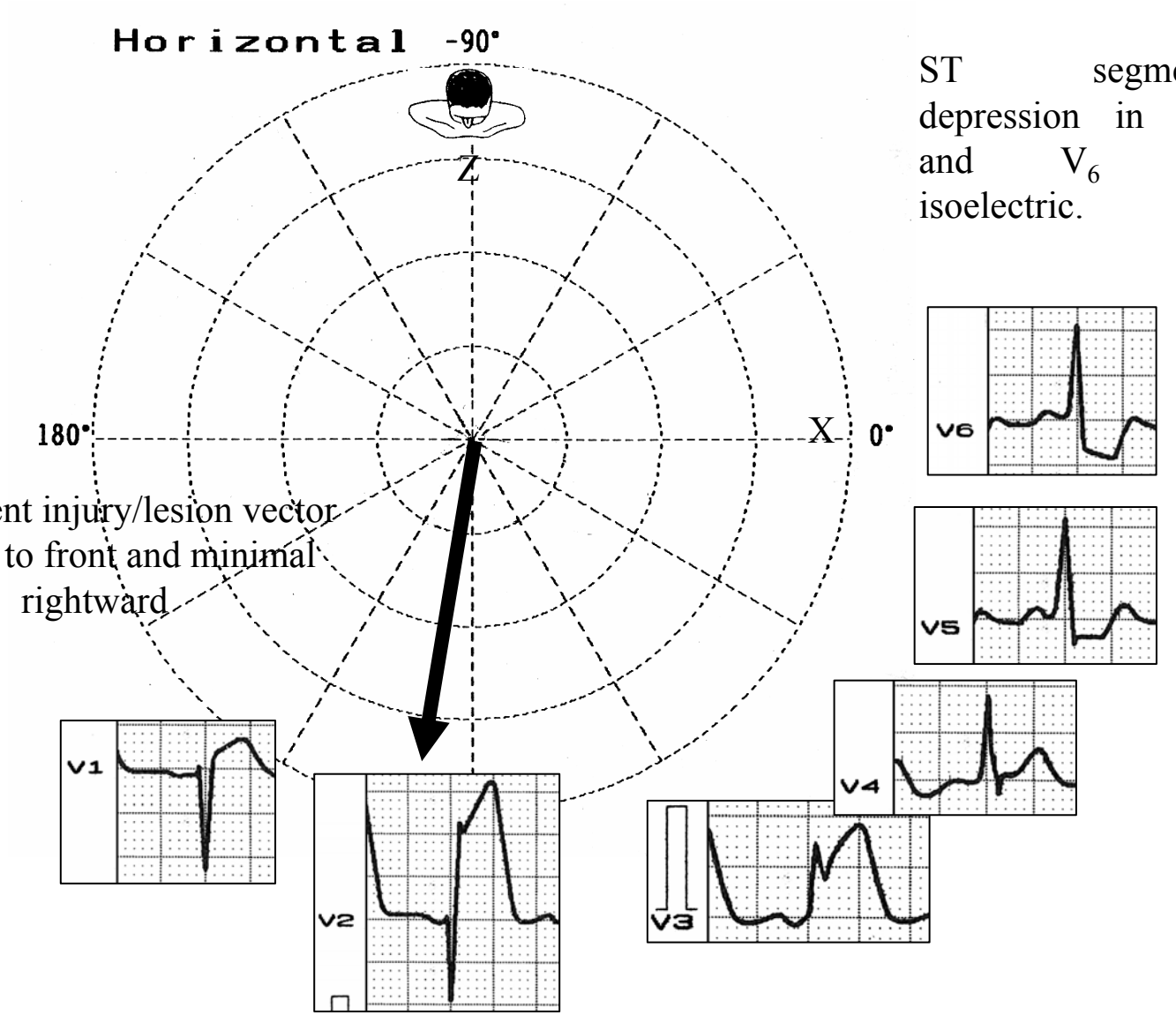


Why we observe this pattern?



ST segment injury lesion vector pointing to up, causing st segment elevation in aVL and aVR and ST segment depression in inferior leads.

ST segment elevation ≥ 2mm from V_1 to V_3 or V_4 (ST segment injury/lesion vector directed to front). ST segment depression in V_5 and V_6 or isoelectric. Eventually CRBBB and/or LAFB and/or LSFB.

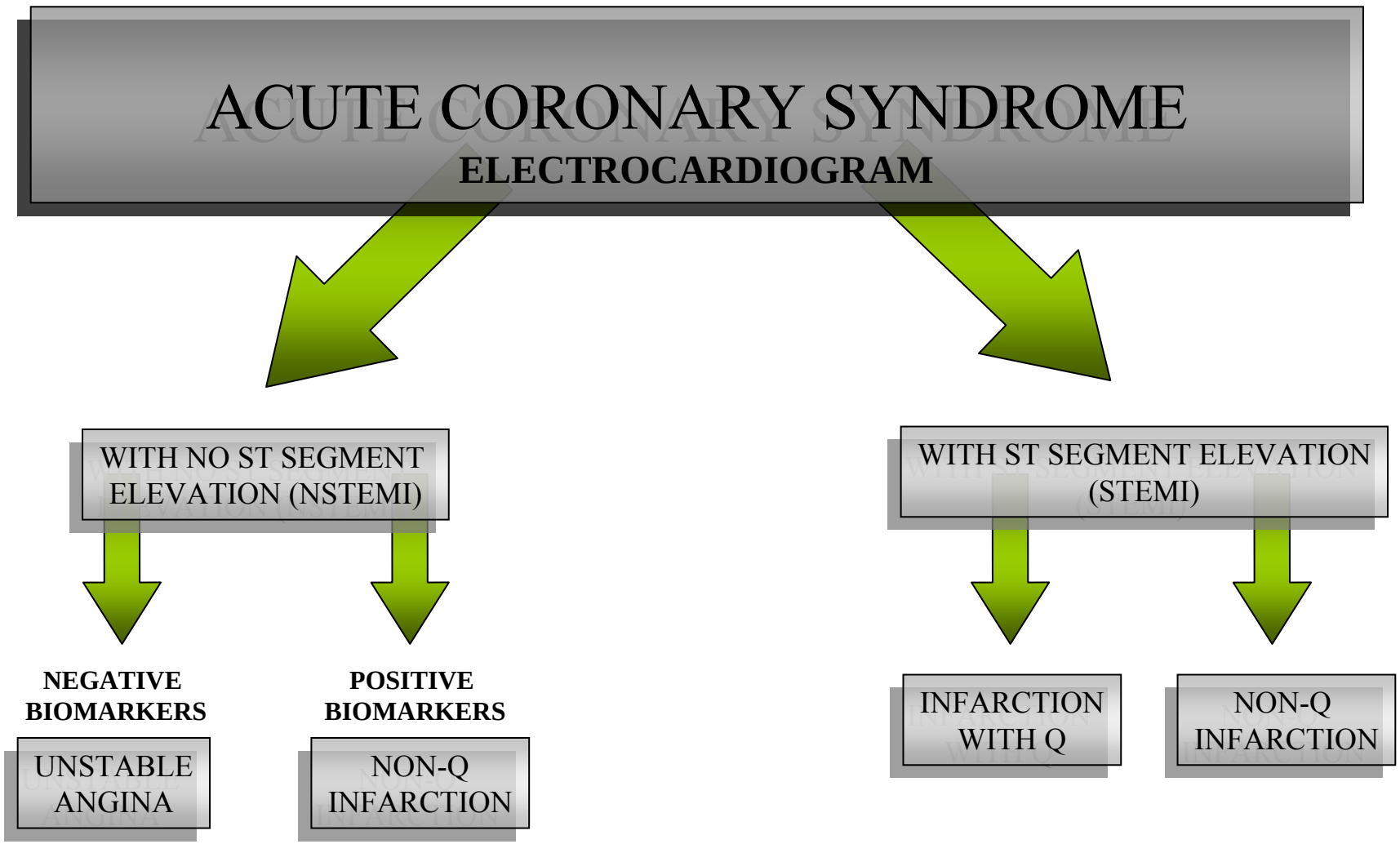


ST segment depression in V_5 and V_6 or isoelectric.

ST segment injury/lesion vector directed to front and minimal rightward

ST segment elevation ≥ 2mm from V_1 to V_3 or V_4

CLINICAL CLASSIFICATION OF ACUTE CORONARY SYNDROMES



Clinical classification of acute coronary syndromes.

THE ECG IN ACUTE CORONARY SYNDROME(ACS)

Patients with ACS include those whose clinical presentations cover the following range of diagnoses:

I) Unstable angina: ***New-onset exertion angina, angina increasing frequency or duration or refractory to nitroglycerin, or angina at rest.***

II) Non–ST-Elevation Myocardial Infarction (NSTEMI)

III) ST-elevation Myocardial Infarction (STEMI).

ST-segment Elevation Myocardial Infarction (STEMI)

New or presumably recent J point and ST segment elevation in 2 or more adjacent leads

$\geq$ 2 mm in V_1, V_2 or V_3 or $\geq$ 1 mm in other leads

Congenital heart disease

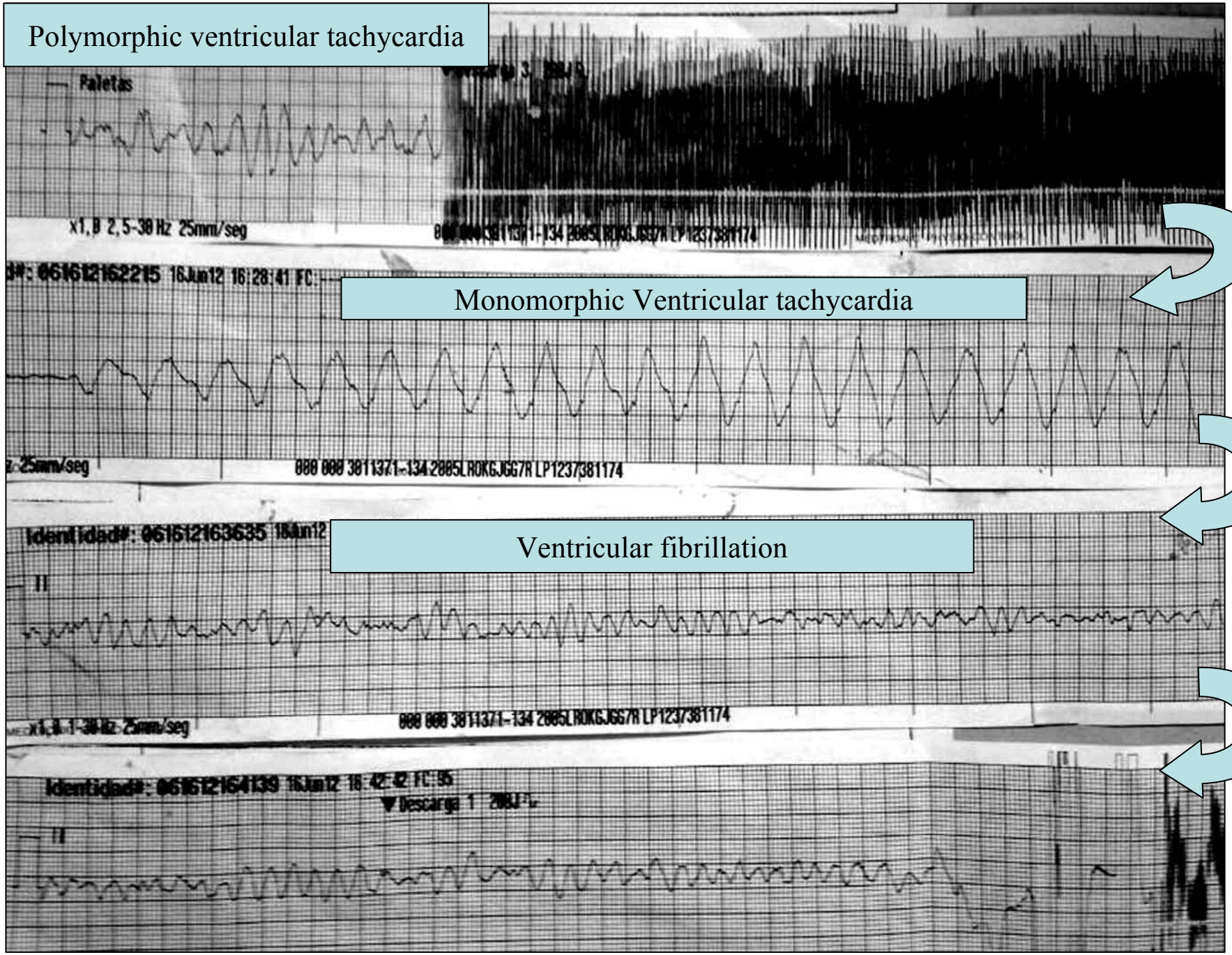
Non-ST segment Elevation Myocardial Infarction (NSTEMI)

ST segment depression

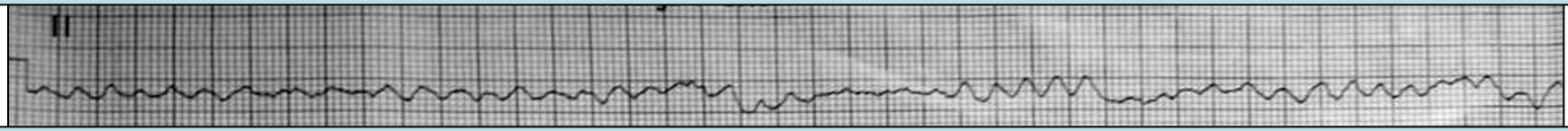
Isolated alterations of the T wave

This ACS spectrum concept is a useful framework for developing therapeutic strategies

1. **Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol. 2000 Sep;36:959-969. Erratum in: J Am Coll Cardiol 2001 Mar 1;37:973.**


Polymorphic ventricular tachycardia
Paletas
x1,0 2,5-30 Hz 25mm/seg
Monomorphic Ventricular tachycardia
Identidad#: 061512163635 16Jun12
Ventricular fibrillation
Descarga 1

Ventricular fibrillation (VF): is a pre-fatal ventricular arrhythmia, consisting of uncoordinated or chaotic contraction of the fibers of the ventricular myocardium, which in all cases lead to symptoms of cardiorespiratory arrest (class IV) by sudden interruption of mechanical ventricular activity, and that demands immediate resuscitation measures.



Ventricular fibrillation (VF): is applied to a ventricular tachyarrhythmia, which has totally chaotic morphology. The distinction between VF and polymorphic VT may be difficult, but the absence of a QRS that can have a specific morphology applied to it is characteristic of VF. This most often occurs in the setting of structural hear disease, most commonly prior myocardial infarction, but may be seen in otherwise healthy people as a consequence of an ion channelopathy; that is, long QT and short QT syndrome, BrS, and CPVT.

$N/_2$

VF represents 80% to 85% of the causes of sudden cardiac death; the remaining 15% to 20% are secondary to asystole, total AV block, or electromechanic dissociation.

It is pseudo fine amplitude fibrillatory waves(≤0.2mV) because ECG standard is $N/_2$.
Fine waves identify patients with worse survival rates and are sometimes confused with asystole

Ventricular Fibrillation prevalence

Ventricular fibrillation (VF): Life-threatening heart arrhythmia with rapid beating in lower chambers. VF is a condition in which there is uncoordinated contraction of the cardiac muscle of the ventricles in the heart, making them quiver rather than contract properly. While there is activity, it is undetectable by palpation (feeling) at major pulse points of the carotid and femoral arteries especially by the lay person. Such an arrhythmia is only confirmed by ECG. VF is a medical emergency that requires prompt Basic Life Support/Advanced Cardiac Life Support interventions because should the arrhythmia continue for more than a few seconds, it will likely degenerate further into asystole ("flatline"). The condition results in cardiogenic shock, cessation of effective blood circulation, and SCD will result in a matter of minutes. If however the patient is revived after a sufficient period (at room temperature, roughly 5 minutes) of cerebral hypoxia, the patient could sustain irreversible brain damage and possibly be left brain dead (death often occurs if normal sinus rhythm is not restored within 90 seconds of the onset of VF, especially if it has degenerated further into asystole). From the 200,000 SDs/year that occur in Brazil, more than 160,000 are subsequent to VF, which in most cases occurs in relatively young patients (average, 45 years old).Nowadays, the unexpected death that occurs within one hour after abrupt change from stable clinical state or the onset of symptoms, is considered to be Sudden cardiac arrest is the leading cause of death in the industrialized world. The majority of these deaths are due to VF secondary to MI, or "heart attack". During VF, cardiac output drops to zero, and, unless remedied promptly, death usually ensues within minutes. Within the context of acute phase of MI, it occurs in three possible manners: 1) As a mechanism of sudden death.; 2) Primary VF (the one that occurs unexpectedly in patient without ventricular dysfunction).; 3) Secondary VF (terminal event of ventricular dysfunction with a high mortality rate: 50%). This would be 9.5% in the first hour; 4.5% in the second hour; 1.5% in the third and the fourth hour. Within the first 4 hours, 15.5% of the patients with acute infarction develop ventricular fibrillation.The primary form presents an incidence of 0.35%.

Patients with Diabetes Mellitus (DM) have significantly higher prevalence of VF independent of CAD or CHF, which in part may explain the higher risk of sudden death in patients with DM.(1)

1. **Movahed MR, Hashemzadeh M, Jamal M. Increased prevalence of ventricular fibrillation in patients with type 2 diabetes mellitus. Heart Vessels. 2007 Jul;22:251-253**

History of Knowledge of Ventricular Fibrillation

Lyman Brewer suggests that the first recorded account of VF dates as far back as 1500 BC, and can be found in the Ebers papyrus of ancient Egypt. The extract recorded 3500 years ago may even date from as far back as 3500 BC. It states: "*When the heart is diseased, its work is imperfectly performed: the vessels proceeding from the heart become inactive, so that you cannot feel them … if the heart trembles, has little power and sinks, the disease is advanced and death is near.”* A book authored by Jo Miles suggests that it may even go back farther. Tests done on frozen remains found in the Himalayas seemed fairly conclusive that the first known case of VF dates back to at least 2500 BC.(1)

Whether this is a description of VF is debatable.[13] The next recorded description occurs 3000 years later and is recorded by Vesalius, who described the appearance of "worm-like" movements of the heart in animals prior to death.The significance and clinical importance of these observations and descriptions possibly of VF were not recognized until John Erichsen in 1842 described VF following the ligation of a coronary artery (Erichsen JE 1842). Subsequent to this in 1850, VF was described by Ludwig and Hoffa when they demonstrated the provocation of VF in an animal by applying a "Faradic" (electrical) current to the heart.

In 1874, Edmé Félix Alfred Vulpian (January 5, 1826 – May 18, 1887) was a French physiologist and neurologist coined the term *mouvement fibrillaire*. Among other noted discoveries and experiments Vulpian discovered adrenaline in the adrenal medulla. He was the first to use the term "fibrillation" to describe a chaotic irregular rhythm of the heart VF(2). Additionally he was the co-discoverer of Vulpian-Bernhardt spinal muscular atrophy and the Vulpian-Heidenhain-Sherrington phenomenon.

1. **Brewer LA (1983). "Sphygmology through the centuries. Historical notes". *Am. J. Surg. 1983;* Jun;145 (6): 695–702.**
2. ***Vulpian EFA. Essai sur l'origine réelle de plusieurs nerfs crâniens*. Doctoral thesis, Paris, 1853.**

Portrait of the French neurologist and physiologist Edmé Félix Alfred Vulpian. He was the first to use the term "fibrillation" ***mouvement fibrillaire***

* 1826 **VULPIAN** † 1887

Membre de l'Académie de Médecine, 1866
Prof. d'Anatomie pathologique, 1867
Prof. de Pathologie expérimentale et comparée, 1872
Doyen de la Faculté de Médecine de Paris, 1878
Membre de l'Institut (Académie des Sciences), 1876

Alfred Vulpian monument,
rue Antoine Dubois, Paris, France

John A. MacWilliam, a physiologist who had trained under Ludwig and who subsequently became Professor of Physiology at the University of Aberdeen, gave an accurate description of the arrhythmia in 1887.
This definition still holds today, and is interesting in the fact that his studies and description predate the use of the ECG. His description is as follows:

"The ventricular muscle is thrown into a state of irregular arrhythmic contraction, whilst there is a great fall in the arterial blood pressure, the ventricles become dilated with blood as the rapid quivering movement of their walls is insufficient to expel their contents; the muscular action partakes of the nature of a rapid incoordinate twitching of the muscular tissue … The cardiac pump is thrown out of gear, and the last of its vital energy is dissipated in the violent and the prolonged turmoil of fruitless activity in the ventricular walls."

MacWilliam spent many years working on VF and was one of the first to show that VF could be terminated by a series of induction shocks through the heart. He also describes the electrical stimulation of the heart in cases of "fatal syncope" in man. *"A single induction shock readily causes a beat in an inhibited heart, and a regular series of induction shocks (for example, sixty or seventy per minute) gives a regular series of heartbeats at the same rate*."(1;2) In 1899, J A McWilliam reported in the British Medical Journal of his experiments in which application of an electrical impulse to the human heart in asystole caused a ventricular contraction and that a heart rhythm of 60-70 beats per minute could be evoked by impulses applied at spacings equal to 60-70/minute

1. *McWilliam JA. Cardiac Failure and Sudden Death. Br Med J 1889;1:6-8.*
2. *McWilliam JA. Electrical stimulation of the heart in man. Br Med J 1889;1:348-50.*

The first ECG recording of VF was by August Hoffman in a paper published in 1912 . At this time, two other researchers, Mines and Garrey, working separately, produced work demonstrating the phenomenon of circus movement and re-entry as possible substrates for the generation of arrhythmias. This work was also accompanied by Lewis, who performed further outstanding work into the concept of "circus movement."

Later milestones include the work by Kerr and Bender in 1922, who produced an ECG showing VT evolving into VF . The re-entry mechanism was also advocated by DeBoer, who showed that VF could be induced in late systole with a single shock to a frog heart. The concept of "R on T ectopics" was further brought out by Katz in 1928. This was called the “vulnerable period” by Wiggers and Wegria in 1940, who brought to attention the concept of the danger of PVBs occurring on a T wave.

Another definition of VF was produced by Wiggers in 1940. He described VF as *"an incoordinate type of contraction which, despite a high metabolic rate of the myocardium, produces no useful beats. As a result, the arterial pressure falls abruptly to very low levels, and death results within six to eight minutes from anemia of the brain and spinal cord"*.

Spontaneous conversion of VF to a more benign rhythm is rare in all but small animals. Defibrillation is the process that converts VF to a more benign rhythm. This is usually by application of an electric shock to the myocardium and is discussed in detail in the relevant article.

TYPES OF VENTRICULAR FIBRILLATIONS

IDIOPATHIC: the one that occurs in absence of any evidence of structural heart disease or primary electrical disorder, ischemia, recurrent infarction, decompensated heart failure and/or other mechanical complications; that is to say, in absence of known heart disease: absence of organic substrate. It presents 30% of recurrence two years later. It is one of the causes of arrhythmic sudden death. The treatment of choice is implantable cardioverter defibrillator.

PRIMARY: it arises in the setting of acute myocardial infarction, which occurs unexpectedly in absence of ventricular dysfunction; however, with evidences of structural heart disease.

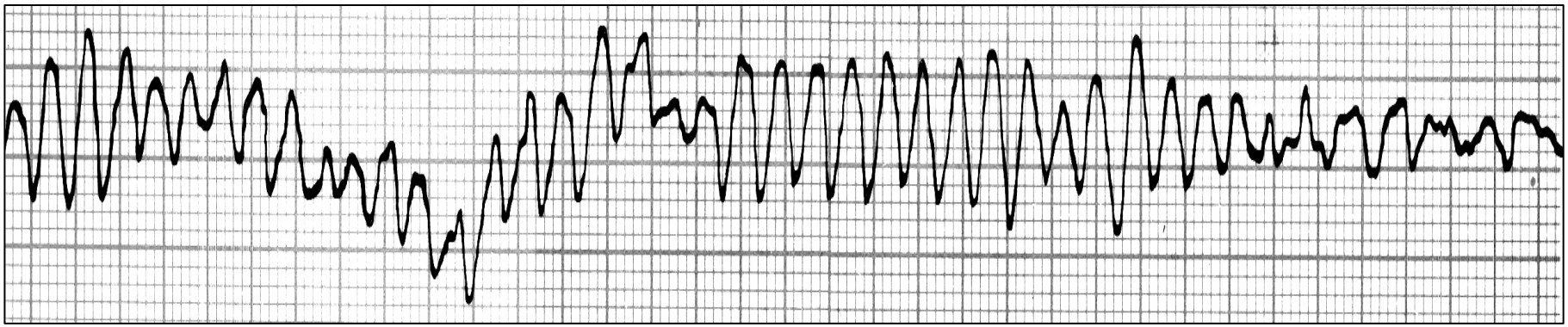
SECONDARY: caused by pump failure of different degrees up to cardiogenic shock.
Within the setting of acute myocardial infarction, it represents a terminal event of ventricular dysfunction, with a high rate of mortality (50%). This group is the one with greatest risk, with 28% after 5 years with conventional antiarrhythmic treatment, and 74% with implantable cardioverter defibrillator.

ELECTRICAL STORM: it is defined as recurrent or multiple episodes of VF or VT: 20 or more per day, or 4 or more per hour. This type of event, with ominous meaning, may be observed in the acute phase of myocardial infarction and in Brugada Syndrome.

Conditions that can lead to Ventricular Fibrillations

1. Coronary heart disease: acute myocardial infarction, ACS, Prinzmetal angina Takotsubo cardiomyopathy
2. Cardiomyopathies;
3. Myocarditis,
4. Mitral valve Prolapse
5. Electrocution accidents or direct injury to the heart.
6. Channelopaties
7. Short-coupled variant of torsade de pointes short-coupled TdP, a normal QTc interval and without demonstrable structural heart disease.
8. Early repolarization
9. Commotio cordis: ventricular fibrillation triggered by chest impact
10. Idiopathic Ventricular Fibrillation
11. WPW syndrome
12. Intoxication and adverse drug reactions Illicit drugs
13. Metabolic diabetic ketoacidosis
14. Electrolyte disturbances
15. Congenital heart disease
16. Cerebral
17. Sepsis
18. Accidental hypothermia
19. Non-traumatic aortic dissection or rupture:aortic is rare, and mortality remains very high, even when circulation can be restored initially. Common features such as previously known aortic aneurysm, old age, male gender and pulseless electrical activity as initial cardiac rhythm should increase suspicion of the condition.
20. Non-cardiac causes were mostly due to pulmonary causes

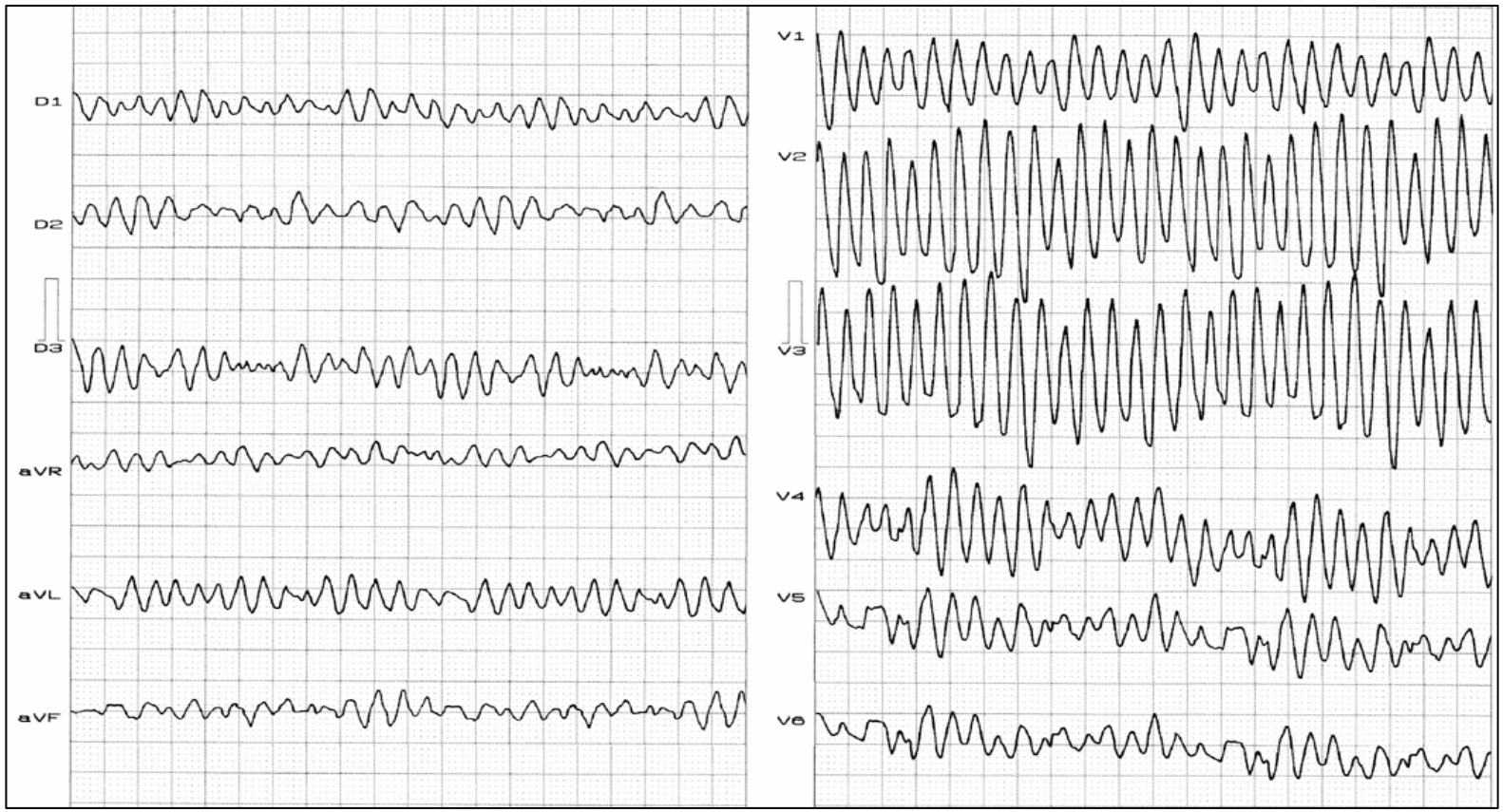
VENTRICULAR FIBRILLATION ELECTROCARDIOGRAPHIC CHARACTERIZATION OF VF



1) Rapid waves (300 to 500 bpm): irregular, bizarre, erratic.
2) Complexes variable in width, frequency and duration.
3) Width may be greater at the onset of the event (coarse VF) to decrease progressively until reaching a reduced voltage in prolonged forms (fine VF: <0.2 mv). This may be difficult to distinguish from asystole.
4) If the waves are wider, the potential to reverse with electrical cardioversion is greater than when they are slow and/or with less voltage.
5) It is impossible to identify any wave in the tracing.

Example of VF in the monitor.

GENUINE IDIOPATHIC VENTRICULAR FIBRILLATION (GIVF)



12-lead ECG that records VF of recent onset. GIVF is a disorder of the sodium channel that affects the cardiac alpha subunit in the SCN5A gene. Akai et al[1], identified a *missense* mutation, heterozygotic serine 1710-leucine of the SCN5A gene, in a 39-year-old man, who was admitted in the hospital with recurrent syncopes and symptoms of spontaneous VF during hospitalization. The ICD implantation was successful. There was no Brugada syndrome present. The grandfather and uncle from the father's side had died suddenly at the age of 60, by unknown causes. Both the parents and the brothers were asymptomatic.

1) Akai J, et al. FEBSLett. 2000; 479: 29-34.

Example of idiopathic VF (IVF) in 12-lead ECG.

CONDITIONING FACTORS OF OMINOUS PROGNOSIS IN VENTRICULAR FIBRILLATION

1) Reduced prior left ventricular ejection fraction;
2) Presence of ventricular dysfunction;
3) Significant alterations in the movement of LV walls: aneurysms, extensive akinesia, dyskinesia;
4) Significant bradycardia or asystole;
5) Secondary to anterior wall infarction;
6) Poor socioeconomic condition;
7) Fine VF;
8) Late therapeutic procedure of resuscitation:

Up to 4 minutes: rate of survival 30%;

Up to 7 minutes: rate of survival 20%;

>10 minutes: rate of survival 6%.

Methamphetamine (MAP)

Turnipseed et al.(1) reviewed the frequency of ACS in patients presenting to emergency department with chest pain after methamphetamine (MAP) use during a 2-year interval. Thirty-three patients (25 males, 8 females; average age 40.4 +/- 8.0 years) with a total of 36 visits met study inclusion criteria:

1) Non-traumatic chest pain,
2) Positive MAP urine toxicology screen,
3) Admission to "rule-out" myocardial infarction,
4) Chest radiograph demonstrating no infiltrates. An ACS was diagnosed in 9 patients (25%).

Three patients (8%) (2 ACS and 1 non-ACS) suffered cardiac complications (VF, VT, supraventricular tachycardia, respectively). Age, gender, cardiac risk factors, prior CAD, initial systolic blood pressure and heart rate did not differ significantly in the ACS and non-ACS groups. The initial and subsequent ECGs were normal in 1/9 (11%) patients with ACS and 16/27 (59%) without ACS ($p < 0.05$). These findings suggest that:

1) ACS is common in patients hospitalized for chest pain after MAP use, and
2) The frequency of other potentially life-threatening cardiac complications is not negligible.
3) A normal ECG lowers the likelihood of ACS, but an abnormal ECG is not helpful in distinguishing patients with or without ACS.

Methamphetamine increases alertness, concentration, energy, and in high doses, can induce euphoria, enhance self-esteem and increase libido. Methamphetamine has high potential for abuse and addiction, activating the psychological reward system by triggering a cascading release of dopamine in the brain. Methamphetamine is FDA approved for the treatment of ADHD and exogenous obesity. As a result of methamphetamine-induced neurotoxicity to dopaminergic neurons, chronic abuse may also lead to post-withdrawal syndrome which persist beyond the withdrawal period for months, and even up to a year.

1. Turnipseed SD, Richards JR, Kirk JD, Diercks DB, Amsterdam EA. Frequency of acute coronary syndrome in patients presenting to the emergency department with chest pain after methamphetamine use. J Emerg Med. 2003 May;24:369-373.

Cannabis

Cannabis, also known as marijuana (from the Mexican Spanish**marihuana**) and by other names, refers to preparations of the *Cannabis* plant intended for use as a psychoactive drug and as medicine.

Chemically, the major psychoactive compound in cannabis is delta-9-tetrahydrocannabinol (Δ9-THC); it is one of 400 compounds in the plant, including other cannabinoids, such as cannabidiol (CBD), cannabinol(CBN), and tetrahydrocannabivarin (THCV), which can produce sensory effects unlike the psychoactive effects of THC. Cannabis abuse is responsible for a wide range of pathologies, including cognitive impairment, a rise in the prevalence of lung, head and neck tumors, atrial and ventricular arrhythmias, and an increase in the risk of ischemic cardiovascular events. A history of cocaine use in African Americans with ICD is a risk factor for high DFT and race itself (being African American) may be a risk for high defibrillation threshold (DFT). Use of high-energy ICDs and other DFT lowering techniques may be considered for patients who have used or continue to use cocaine or in whom DFT testing cannot be performed at the time of implantation.(2)The long-term use of cannabis, particularly at high intake levels, is associated with several adverse psychosocial features, including lower educational achievement and, in some instances, psychiatric illness. There is little evidence, however, that long-term cannabis use causes permanent cognitive impairment, nor is there is any clear cause and effect relationship to explain the psychosocial associations. There are some physical health risks, particularly the possibility of damage to the airways in cannabis smokers. Overall, by comparison with other drugs used mainly for ‘recreational’ purposes, cannabis could be rated to be a relatively safe drug. Contemporary uses of cannabis are as a recreational drug, as religious or spiritual rites, or as medicine; the earliest recorded uses date from the 3rd millennium BC. In 2004, the United Nations estimated that global consumption of cannabis indicated that approximately 4.0 percent of the adult world population(162 million people) used cannabis annually, and that approximately 0.6 percent (22.5 million) of people used cannabis daily.Since the early 20th century cannabis has been subject to legal restrictions with the possession, use, and sale of cannabis preparations containing psychoactive cannabinoids currently illegal in most countries of the world; the United Nations has said that cannabis is the most used illicit drug in the world.

1. **Perrine SA, Nayak R, Bharadwaj AS, et al. Effect of substance abuse on defibrillation threshold in patients with implantable cardioverter-defibrillator. Pacing Clin Electrophysiol. 2011 Feb;34:193-199.**

Cardiovascular Effects of Cannabis

One of the most consistent effects of cannabis intoxication is an increased heart rate(1). For this reason alone it would not be normally recommended for patients with cardiovascular problems. However, THC also acts as a smooth-muscle relaxant, relaxing the walls of the arteries, which can result in lower blood pressure and increased blood flow to the tissues(2;3). The effect taken together is analogous to a car changing down a gear. Cannabis intoxication has been found to reduce the level of exercise which can be tolerated before the onset of angina(4).to a greater extent than a high-nicotine tobacco cigarette(5). Cardiovascular symptoms have been attributed to cannabis use, either alone (stroke)(6), or in combination with alcohol and cocaine(7).

1. **Nahas G, Trouve R (1985) Effects and interactions of natural cannabinoids on the isolated heart. Proc Soc Exp Biol Med 180(2):312-6**
2. **Malit LA, Johnstone RE, Bourke DI, Kulp RA, Klein V, Smith TC (1975) Intravenous delta9-Tetrahydrocannabinol: Effects of ventilatory control and cardiovascular dynamics. Anesthesiology 42(6):666-73**
3. **Johnstone RE, Lief PL, Kulp RA, Smith TC (1975) Combination of delta9-tetrahydrocannabinol with oxymorphone or pentobarbital: Effects on ventilatory control and cardiovascular dynamics. Anesthesiology 42(6):674-84**
4. **Editorial (1978) Cannabis, 1977. Ann Intern Med 89(4):539-49**
5. **Aronow WS, Cassidy J (1975) Effect of smoking marihuana and of a high-nicotine cigarette on angina pectoris. Clin Pharmacol Ther 17(5):549-54**
6. **Lawson TM, Rees A (1996) Stroke and transient ischaemic attacks in association with substance abuse in a young man. Postgrad Med J 72(853):692-3**
7. **D aisley H, Jones-Le Cointe A, Hutchinson G, Simmons V (1998) Fatal cardiac toxicity temporally related to poly-drug abuse. Vet Hum Toxicol 40(1):21-2**

The presence and action of CB1 cannabinoid receptors in arterial tissue was described by Bilginger et al(1), who reported: "the data demonstrate that cannabinoid signalling is involved with the regulation of the microvascular environment" Cannabinoids such as CBD and the synthetic HU-211(2) have been shown to reduce ischaemic cell damage following cardiac arrest or stroke. CBD also counteracts the increase in HR associated with THC[x] - THC and CBN both appear to increase HR, while CBD tends to decrease HR. There is conflicting evidence as to whether changes in cardiovascular function are related to myocardial contractility(3;4). Animal studies are conflicting, the effect in dogs appears opposite to that in humans(5;6). Part of the increase in HR can be counteracted by use of β-blocker drugs(7), but not by opiate antagonists such as Naloxone. From a clinical study of long-term marijuana smokers, Tashkin et al(3) concluded ***"in long-term heavy users of cannabis, marihuana has no significant effect on myocardial contractility independent of its effect on HR."***

1. Bilfinger TV, Salzet M, Fimiani C, et la Pharmacological evidence for anandamide amidase in human cardiac and vascular tissues. Int J Cardiol 1998; 64 Suppl 1:S15-22
2. Belayev L, Busto R, Watson BD, Ginsberg MD Post-ischemic administration of HU-211, a novel non-competitive NMDA antagonist, protects against blood-brain barrier disruption in photochemical cortical infarction in rats: a quantitative study. Brain Res.1995; 702:266-70
3. Tashkin DP, Levisman JA, Abbasi AS, Shapiro BJ, Ellis NM Short-term effects of smoked marihuana on left ventricular function in man. Chest. 1977; 72:20-26
4. Smiley KA, Karler R, Turkanis SA Effects of cannabinoids on the perfused rat heart. Res Commun Chem Pathol Pharmacol 1976; 14(4):659 -75
5. Jandhyala BS, Malloy KP, Buckley JP (1976) Effects of acute administration of delta9-tetrahydrocannabinol on pulmonary hemodynamics of anesthetized dogs. Eur J Pharmacol 38(1):183-7
6. Daskalopoulos N, Schmitt H, Laubie M (1975) Action of delta 9 tetrahydrocannabinol on the central cardiovascular regulation : mechanism and localization. Encephale 1(2):121-32
7. Kanakis C Jr, Pouget JM, Rosen KM The effects of delta-9-tetrahydrocannabinol (cannabis) on cardiac performance with and without beta blockade. Circulation 1976;53:703-707

Blood Pressure

Early studies on rats bred for high blood pressure[xviii] found that THC reduced levels of blood pressure(2;3), and that tolerance developed to this effect(4). Mechoulam(5) predicted in 1978 "Numerous synthetic cannabinoids are currently being investigated as analgetics and as sedative-relaxants." Zaugg & Kyncl(6) reported "hydroxyacetyl and gamma-hydroxybutyryl (cannabinol) derivatives were potent antihypertensive agents (minimum effective dose, 3-5 mg/kg, orally) of the same order of activity as the highly CNS-active N-propargyl derivatives“

Hanus et al(7) reported that the specific CB2 receptor agonist HU-308 "reduces blood pressure... The hypotension... produced by HU-308 (is) blocked (or partially blocked) by the CB(2) antagonist SR-144528, but not by the CB(1) antagonist SR-141716A. These results demonstrate the feasibility of discovering novel nonpsychotropic cannabinoids that may lead to new therapies for hypertension..." Garcia et al(8) reported "Anandamide produced a dose-dependent decrease in mean arterial pressure due to a drop in systemic vascular resistance (SVR) that was accompanied by a compensatory rise in cardiac output. Anandamide also elicited an increase in both portal venous flow and pressure, along with a decline in mesenteric vascular resistance (MVR). Pretreatment with 3 mg/kg SR-141716A, a CB(1) antagonist, prevented the decline of SVR and MVR from the lower dose of anandamide.“

1. **Birmingham MK. [1973] Reduction by 9-tetrahydrocannabinol in the blood pressure of hypertensive rats bearing regenerated adrenal glands. Br J Pharmacol 1 48(1):169-71**
2. **Williams RB, Ng LK, Lamprecht F, Roth K, Kopin IJ [1973] 9 -Tetrahydrocannabinol: a hypotensive effect in rats. Psychopharmacologia 28(3):269-74**
3. **Varma DR, Goldbaum D. [1975] Effect of delta9-tetrahydrocannabinol on experimental hypertension in rats. J Pharm Pharmacol 27(10):790-1**
4. **Nahas GG, Schwartz IW, Adamec J, Manger WM. [1973] Tolerance of delta-9-tetrahydrocannabinol in the spontaneously hypertensive rat Proc Soc Exp Biol Med 142(1):58-60**
5. **Mechoulam R, Carlini EA. [1978] Toward drugs derived from cannabis Naturwissenschaften 65(4):174-9**
6. **Zaugg HE, Kyncl J. [1983] New antihypertensive cannabinoids. J Med Chem 26(2):214-7**
7. **Hanus L, Breuer A, Tchilibon S, Shiloah S, Goldenberg D, Horowitz M, Pertwee RG, Ross RA, Mechoulam R, Fride E. [1999] HU-308: a specific agonist for CB(2), a peripheral cannabinoid receptor. Proc Natl Acad Sci U S A 96(25):14228-33**
8. **Garcia N Jr, Jarai Z, Mirshahi F, Kunos G, Sanyal AJ. [2001] Systemic and portal hemodynamic effects of anandamide. Am J Physiol Gastrointest Liver Physiol 280(1):G14-20**

Gardiner et al(1), rats studying the effects of the cannabinoid receptor agonist WIN 55212-2 in normal (HSD) and hypertensive (TG), concluded "Collectively, the results indicate that the predominant cardiovascular effects of WIN 55212-2 in conscious HSD and TG rats (i.e., pressor and vasoconstrictor actions) can be attributed largely to indirect, pentolinium-sensitive mechanisms, which appear to differ little in the normotensive and hypertensive state, at least in con scious animals. Under the conditions of our experiments, signs of cannabinoid-induced vasodilatation were modest." Studying anandamide in anaesthetised and conscious rats, Gardiner et al(2) reported *"At all doses of anandamide, there was a significant, short-lived increase in mean arterial blood pressure associated with vasoconstriction in renal, mesenteric and hindquarters vascular beds. The higher doses (2.5 and 3 mg kg(-1)), caused an initial, marked bradycardia accompanied, in some animals, by a fall in arterial blood pressure which preceded the hypertension. In addition, after the higher doses of anandamide, the hindquarters vasoconstriction was followed by vasodilatation... None of the cardiovascular actions of anandamide were influenced by the CB(1)-receptor antagonist, AM 251*"

Jarai & Kunos(2) noted "cannabinoids were found to be potent CB1-receptor dependent vasodilators in the coronary and cerebrovascular beds" concluding "the endogenous can nabinoid system plays an important role in cardiovascular regulation, and pharmacological manipulation of this system may offer novel therapeutic approaches in a variety of pathological conditions."

1. **Gardiner SM, March JE, Kemp PA, Bennett T Complex regional haemodynamic effects of anandamide in conscious rats. Br J Pharmacol. 2002; 135:1889-1896**
2. **Jarai Z, Kunos G. Cardiovascular effects of cannabinoids. Orv Hetil. 2002; 143:1563-568.**

Wagner et al(1)report "Activation of peripheral cannabinoid CB(1) receptors elicits hypotension" and noted "We conclude that cannabinoids elicit profound coronary and cerebral vasodilation in vivo by direct activation of vascular cannabinoid CB(1) receptors, rather than via autoregulation, a decrease in sympathetic tone or, in the case of anandamide, the action of a non-cannabinoid metabolite." However, in a review article for the Bulletin on Narcotics, Husan & Khan(2) warned "The use of cannabis causes prominent and predictable effects on the heart, including increased work-load, increased plasma volume and postural hypotension, which could impose threats to the cannabis users with hypertension, cerebrovascular disease or coronary arteriosclerosis."

Lake et al(3) no ted "in anesthetized rats anandamide elicits bradycardia and a triphasic blood pressure response: transient hypotension secondary to a vagally mediated bradycardia, followed by a brief pressor and prolonged depressor response, the latter two effects being similar to those of delta 9-tetrahydrocannabinol (THC)“

Krowicki et al(4) found that, in anaesthetised rats "Intravenously administered delta9-THC evoked ... bradycardia, and hypotension“.The picture is slowly becoming clearer, indicating that endo-cannabinoids modify aspects of blood flow at a subtle local level. In a 2001 review, Schiffrin(5) noted "The endothelium produces a variety of substances that play important roles in regulation of the circulation and vascular wall homeostasis. The control of blood vessel wall homeostasis is achieved via production of vasorelaxants and vasoconstrictors. Among the vasorelaxants are ... metabolites of arachidonic acid like epoxyeicosatrienoic acids, and endocannabinoid s)"

1. Wagner JA, Jarai Z, Batkai S, Kunos G. Hemodynamic effects of cannabinoids: coronary and cerebral vasodilation mediated by cannabinoid CB(1) receptors. Eur J Pharmacol. 2001; 423:203-210
2. Husain S, Khan I. An update on cannabis research. Bull Narc 1985 Oct-Dec;37:3-13
3. Lake KD, M artin BR, Kunos G, Varga K. Cardiovascular effects of anandamide in anesthetized and conscious normotensive and hypertensive rats. Hypertension.1997; 29:1204-1210.
4. Krowicki ZK, Moerschbaecher JM, Winsauer PJ, Digavalli SV, Hornby PJ. Delta9-tetrahydrocannabinol inhibits gastric motility in the rat through cannabinoid CB1 receptors. Eur J Pharmacol. 1999; 371:187-196
5. Schiffrin EL. A critical review of the role of endothelial factors in the pathogenesis of hypertension. J Cardiovasc Pharmacol.2001; 38 Suppl 2:S3-6

Summary - Cardiovascular effects of Cannabis

1. Cannabis increases heart rate in nave users although tolerance develops to this effect.
2. Cannabinoids can also reduce blood pressure via arteriollar dilatation in a variety of tissues, although the effect on blood flow varies at a local level, with some organs or brain regions experiencing vasoconstriction, others vasodilation.
3. In the withdrawal phase following cessation of chronic use, cerebral blood flow may be significantly reduced.
4. Cannabis use has been implicated as a causative factor in a small number of patients suffering strokes or transient ischaemic attacks, and may represent a risk factor to susceptible individuals.
5. However cannabinoids, in particular CB1-receptor agonists, have been shown to protect against nerve cell death following stroke, and dexanabinol at an advanced stage of the licensing process as a drug to be administered to victims of stroke or closed-head injuries to minimise the long-term brain damage caused by such events, and to improve survival and recovery prospects.

IDENTIFICATION OF PATIENTS WITH POTENTIAL FOR ARRHYTHMIC SUDDEN DEATH

1. Significant decrease of LVEF;
2. High density of premature ventricular contractions in Holter;
3. Presence of complex ventricular arrhythmias: polymorphic, early, coupled and runs of VT;
4. Presence of congenital or acquired long QT interval in ECG;
5. Highly changing T waves that go from negative to isoelectric and wide biphasic, inverted, alternating and bifid with notches with a great velocity: “enigmatic ECG”.
6. Presence of delayed potentials in high resolution ECG;
7. Decreased variability of R-R intervals: heart rate variability (HRV);
8. Great dispersion of QTc interval;
9. Presence of microvolt T wave alternans;
10. Symptomatic WPW with rapid anomalous pathway: anterograde refractory period <270 ms and effective ventricular refractory period <220 ms;
11. Patients who recovered from cardiac arrest with baseline ECG with “Brugada sign” or idiopathic J wave in right precordial leads.
12. Early repolarization type 3 of Antzelevitch and Yan: This variant display an ER pattern globally in the inferior, lateral, and right precordial leads(1),

1. **Antzelevitch C, Yan GX. J-wave syndromes. from cell to bedside. J Electrocardiol. 2011 Nov-Dec;44:656-61.**