I) Coronary Artery Disease Overview (CAD)

And…….

II) Time for a new paradigm shift in myocardial infarction.

Introduction

Coronary artery disease (CAD) is one of the major cardiovascular diseases affecting the global human population. CAD is a major cause of death in both the developed and developing countries. CAD is the leading cause of death in both men and women in the United States. Although incidence of MI has demonstrated a significant decline over the past few years, Americans still experience approximately 610,000 deaths annually (estimated 1 in 4 deaths) and is the leading cause of mortality in the United States. It is the third leading cause of mortality worldwide and is associated with 17.8 million deaths annually Early recognition and appropriate management of myocardial infarction are imperative to improving patient outcomes.

Risk factors for CAD can be categorized into nonmodifiable and modifiable.

A) Nonmodifiable risk factors include:

- **Age** of more than 45 years in men and more than 55 years in women. CAD prevalence increases after 35 years of age in both men and women. The lifetime risk of developing CAD in men and women after 40 years of age is 49% and 32%, respectively;[1]
- **Family history of early heart disease** is associated with a higher risk of CAD, especially if a close relative developed heart disease at an early age. Patients with a family history of premature cardiac disease younger than 50 years of age have an increased CAD mortality risk.[2] A father or brother diagnosed with CAD before 55 years of age, and a mother or sister diagnosed before 65 years of age are considered risk factors;[3]
- **Ethnicity:** African American race. (**Boudi FB. Risk factors for coronary artery disease. In: Subhi Y, editor. MedScape. Available at: https://emedicine.medscape.com/article/164163-overview. Accessed May 3, 2018.)** Hispanics, Latinos, and Southeast Asians, are ethnic groups with an increased risk of CAD morbidity and mortality.[4-6]

- **Genetic factors:** Genome-wide association studies have suggested the association of chromosome 9p21.3 in the premature onset of CAD. Genome-wide association studies have identified a CAD risk locus in a non-coding region at 9p21.3, the nearest genes being CDKN2A and CDKN2B.

B) Modifiable risk factors include:

- **Lifestyle, environmental factors, and for the development of these entities.**
- **Diabetes mellitus or insulin resistance:** The USPSTF recommends screening for abnormal glucose in patients aged 40 to 70 years old who are overweight or obese. Early screening for diabetes can also be a consideration for patients in higher-risk groups. This risk pool includes patients with a family history of diabetes, history of gestational diabetes or polycystic ovarian syndrome, or members of specified racial/ethnic groups (African Americans, American Indians, Alaskan Natives, Asian Americans, Hispanics or Latinos, Native Hawaiians or Pacific Islanders).[7] The American Diabetes Association states that three years is a reasonable screening interval. A 2019 meta-analysis of 12 cardiovascular outcomes trials indicated that a 0.5% reduction in A1C conferred a 20% hazard risk reduction (95% CI 4-33%) for major cardiovascular events. This analysis included patients on peptidase-4 inhibitors, GLP-1 agonists, and SGLT-2 inhibitors.[8]
- **High blood pressure:** About 1 out of every three patients has hypertension. Hypertension and smoking were responsible for the largest number of deaths in a 2009 review comparing twelve modifiable risk factors.[9] Yet, only 54% of these patients achieve adequate blood pressure control.[10] Hypertension has long been a major risk factor for heart disease through both oxidative and mechanical stress; it places on the arterial wall.[11, 12] A 1996 article reported that in the Framingham cohort, a systolic of 20mmHg and diastolic of 10 mmHg increase was observed from age 30 years to 65 years.[13]
- **Smoking:** The USPSTF recommends screening for tobacco use in all adults with each clinical encounter and to provide behavioral and pharmacologic smoking cessation interventions.[14] The USPSTF also

recommends educating children and adolescents about the risks of smoking to prevent the initiation of tobacco use.[15] The American Heart Association recommends a combined behavioral and pharmacologic approach to maximize quit rates.[16] The risk of CAD drops to a level of lifetime nonsmokers within four years of quitting, according to the FDA, and within ten years, according to the CDC.[17, 18] Behavioral interventions include motivational interviewing (Ask, Advise, Assess, Assist, Arrange for follow-up). Pharmacologic interventions such as nicotine replacement therapy, varenicline (Chantix), and bupropion (Wellbutrin) reduce cravings and withdrawal symptoms. A 2014 Cochrane review revealed that nicotine replacement therapies, such as nicotine gum and the nicotine patch increased the chances of smoking cessation by 49% (55 trials, RR 1.49, 95% CI 1.40-1.60) and 64% (43 trials, RR 1.64, 95% CI 1.52-1.78), respectively. The nicotine oral tablets/lozenges (6 trials, RR 1.95, 95% CI 1.61-2.36), inhaler (4 trials, RR 1.90, 95% CI 1.36-2.67), and nasal sprays (4 trials, RR 2.02, 95% CI 1.49-2.73) approximately doubled the chances of success. The combination of bupropion and nicotine replacement therapy increased the likelihood of success by 24% compared to bupropion alone (4 trials, RR 1.24, 95% CI 1.06-1.45).[19] Varenicline doubled the chances of smoking cessation.[20] There have been rare reports of neuropsychiatric adverse effects with varenicline. The FDA removed this black box warning in 2016 after noting that the risk was lower than expected. A 2014 Cochrane review showed that bupropion increases the chances of smoking cessation by 62% (44 trials, N=13,728, RR 1.62, 95% CI 1.48-2.78).[21, 22] A 2016 Cochrane review indicated that the combined use of behavioral support and pharmacotherapy had a higher chance of success.[23]

- **Hyperlipidemia** (a high level of low-density lipoprotein (LDL) cholesterol, cholesterol and or a low level of high-density lipoprotein (HDL), High triglycerides: The USPSTF recommends evaluation for statin use for the primary prevention of cardiovascular disease between 40 to 75 years of age.[24] The USPSTF gives a grade I (current evidence insufficient) recommendation for routine screening for lipid disorders in children and adolescents.[25] In 2011, the National Heart, Lung, and Blood Institute

(NHLBI) recommended universal screening between 9 to 11 years of age and again at 17 to 21 years of age. The American Academy of Pediatrics subsequently endorsed this. Despite the publication of these guidelines, pediatric lipid screening practice patterns have not followed suit.[26] An early 1994 review showed that a 10% reduction in serum cholesterol leads to a 50%, 40%, 30%, and 20% drop in CAD risk at age 20, 50, 60, and 70, respectively.[27] The Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) study demonstrated that statins reduce the risk of major cardiovascular events.[28] Treatment with a moderate-intensity statin resulted in a CAD absolute risk reduction of 2.7% (NNT 37). Treatment with a high-intensity statin resulted in a 4.1% absolute risk reduction (NNT 24).[29]

- **High-sensitivity C-reactive protein (hs-CRP),**
- **Overweight or obesity,**
- **Sleep apnea,**
- **Sedentary lifestyle,**
- **Unhealthy diet:** The DASH, Mediterranean, and vegetarian diets have the most evidence for cardiovascular disease prevention.[30] The DASH diet can reduce systolic blood pressure up to 11.5 mmHg in adults with hypertension.[31, 32] A 2013 meta-analysis and systematic review revealed a 21% coronary artery disease risk reduction (RR 0.79, 95% CI 0.71-0.88) with the DASH diet. A 2017 meta-analysis and systematic review revealed an 8% risk reduction (15 studies, RR 0.92, 95% CI 0.90-0.95) of coronary artery disease for every 200 grams per day of fruits and vegetables. This effect was observable at up to 800 grams per day.[33] A 2016 meta-analysis and systematic review revealed a 29% risk reduction (29 studies, RR 0.71, 95% CI 0.63-0.80) of CAD for every 28 grams per day of nut consumption.[34] A 2017 narrative review revealed a decreased risk of about 20 to 25% with the Mediterranean diet on cardiovascular disease. It was also showed positive effects on endothelin function, arterial stiffness, and cardiac function.[35] The American Heart Association recommends the replacement of saturated fat with polyunsaturated and monounsaturated fats.[21] A 5% exchange in saturated fat consumption with polyunsaturated fat is associated with a 10% lower CAD risk (RR 0.90, 95% CI 0.83-0.97).[31,

[36] A 2018 review, however, challenged the strength of the traditional link between saturated fat and higher CAD risk, compared to other nutrients.[37] In a separate review, the lack of a significant association between saturated fat and cardiovascular disease was due to studies replacing saturated fat with highly refined carbohydrates. If saturated fats were replaced by polyunsaturated fat, then coronary heart disease is indeed reduced.[38] While it is challenging to carry out research relating to diet practices and coronary artery disease, much research has taken place in the past.[37] The AHA/ACC guidelines recommend a diet consisting mostly of vegetables, fruits, legumes, nuts, whole grains, and fish. Dietary intake of processed meats, refined carbohydrates, and sweetened beverages should be reduced, while avoiding trans fats altogether. Saturated fats should be replaced with polyunsaturated and monounsaturated fats.[21] The USPSTF recommends offering or referring adults who are obese/overweight and have one additional cardiovascular risk factor intensive behavioral counseling to promote a healthful diet and physical activity. The USPSTF also recommends individualizing the decision to offer or refer patients without obesity or other cardiovascular risk factors for behavioral counseling.

- **Alcohol abuse.**
- **Autoimmune diseases: Lupus, rheumatoid arthritis,**
- **High levels of homocysteine,**
- **Low serum testosterone levels,**
- **Psychosocial stress,**
- **Preeclampsia.**
- **Cocaine use** Chest pain after cocaine or other stimulant use: ECG changes are common among cocaine users. Chances of developing MI are highest within 1–3 h of cocaine abuse. (**Mittleman MA, Mintzer D, Maclure M, Tofler GH, Sherwood JB, Muller JE. Triggering of myocardial infarction by cocaine. *Circulation.* 1999;99:2737–41**.). The cocaine users with chest pain suggestive of ACS be managed similarly to nonusers

Main studies

The Framingham Heart Study enrolled its first participant in 1948 and is currently studying its third generation of participants. This was the first study that elucidated risk factors associated with cardiovascular disease. Since then, cohort studies have continued to study the impact of different risk factors on cardiovascular disease.[39]

The FINRISK study is an ongoing Finnish population-based observational study that began in 1972.

The ULSAM, PIVUS, POEM, EpiHealth, and SCAPIS studies were cohort studies completed at Uppsala University in Sweden.

The PREDICT Cardiovascular Disease Cohort study was another study completed in New Zealand.

The eradication and management of CAD has been established through extensive studies and trials. Antiplatelet agents, nitrates, β-blockers, calcium antagonists, and ranolazine are some of the few therapeutic agents used for the relief of symptomatic angina associated with CAD.

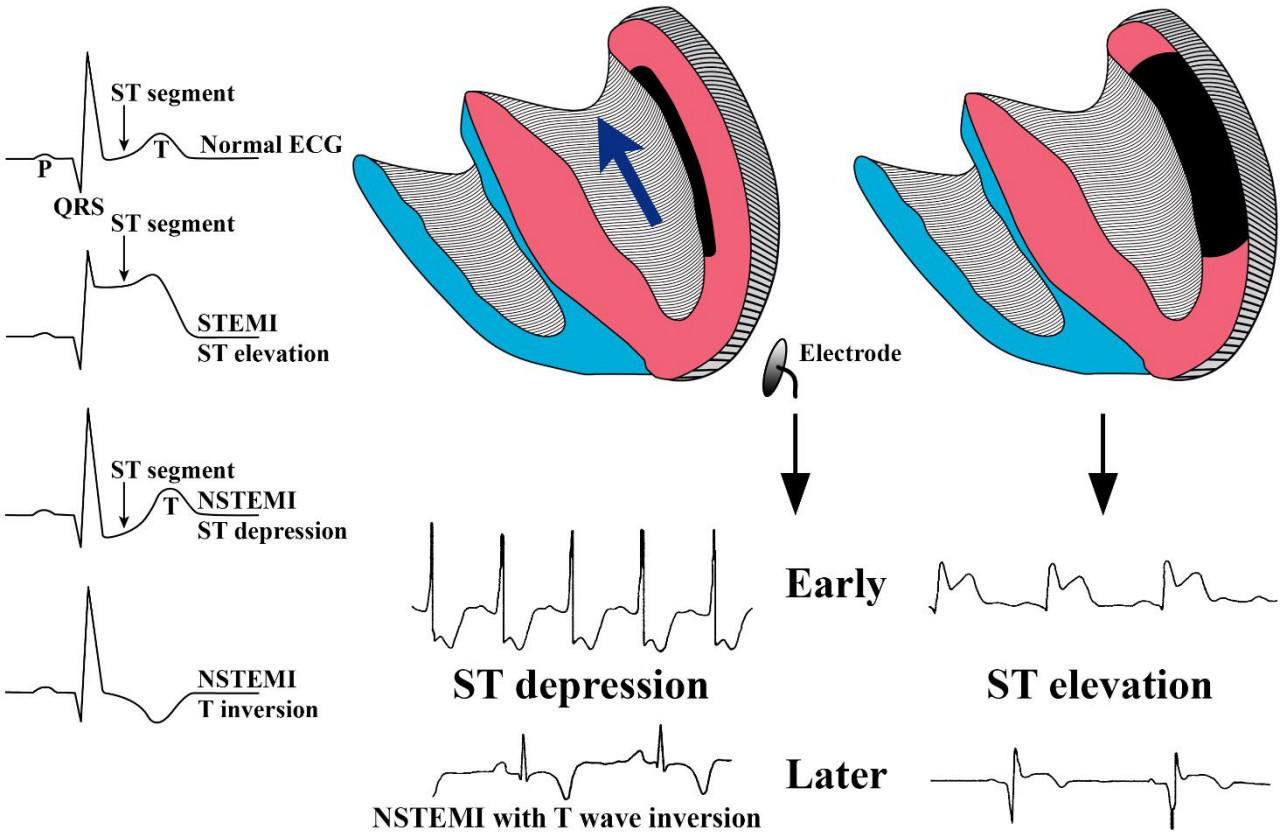
Coronary artery diseases: Clinical-electrocardiographic types

- Stable angina
1. Unstable angina **Yeghiazarians Y, Braunstein JB, Askari A, Stone PH (January 2000). "Unstable angina pectoris". N. Engl. J. Med. 342 (2): 101–14. doi:10.1056/NEJM200001133420207. PMID 10631280**
- Non-ST elevation myocardial infarction (NSTEMI)
- ST elevation myocardial infarction (STEMI)
- Other cardiac diseases; e.g., coronary emboli, coronary dissection

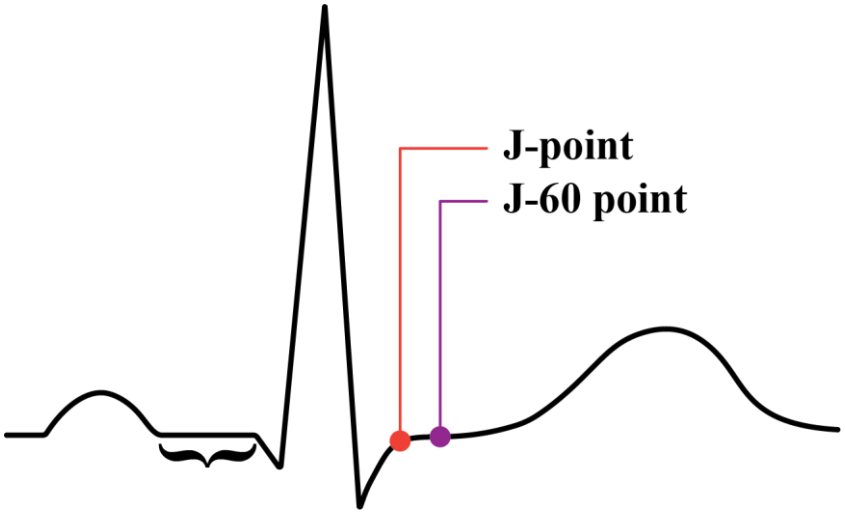
Unstable angina or sometimes referred to as acute coronary syndrome (ACS) causes unexpected chest pain, and usually occurs while resting. The most common cause is reduced blood flow to the heart muscle because the coronary arteries are narrowed by fatty buildups (atherosclerosis) which can rupture causing injury to the coronary blood vessel resulting in blood clotting which blocks the flow of blood to the heart muscle. Unstable angina should be treated as an emergency. In presence of new, worsening or persistent chest discomfort, it is necessary to go to the ER. You could be having a heart attack which puts you at increased risk for severe cardiac arrhythmias or cardiac arrest, which could lead to sudden death.

NSTEMI, as well as unstable angina, typically cause ST-segment depressions and inverted T waves. Current guidelines indicate that diagnosis of ischemia is made when ST-segment depression is new and there is horizontal or down sloping in at least 2 anatomically contiguous leads ≥0.5 mm.[40] Criteria for ischemic T-wave inversions require inversion that is ≥1 mm in at least 2 anatomically contiguous leads with presence of R waves.10 In a small minority of patients presenting with NSTEMI, initial ECG may be normal; thus, it is important to evaluate additional factors such as history, physical examination, cardiac biomarkers, and serial ECGs before excluding a diagnosis of NSTEMI.[41]

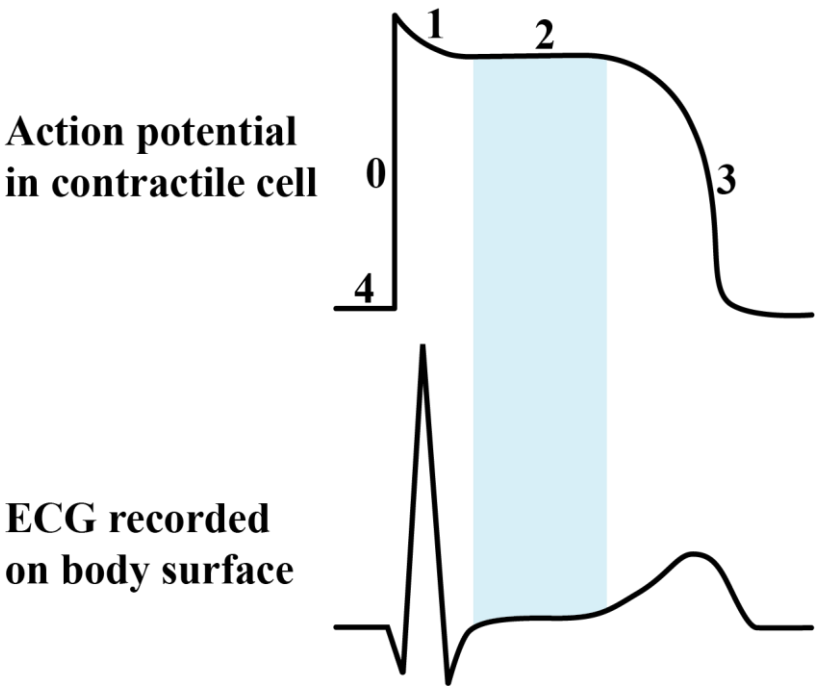
A) Sub – endocardial ischemia **B) Transmural ischemia**



Dimension points

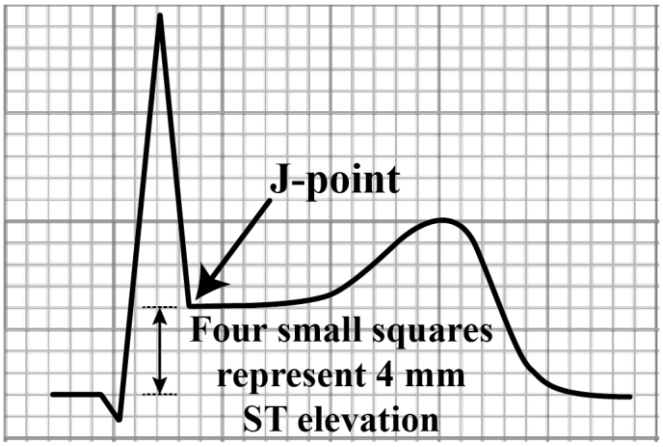


The PR segment is the baseline for measuring deviation of the ST segment

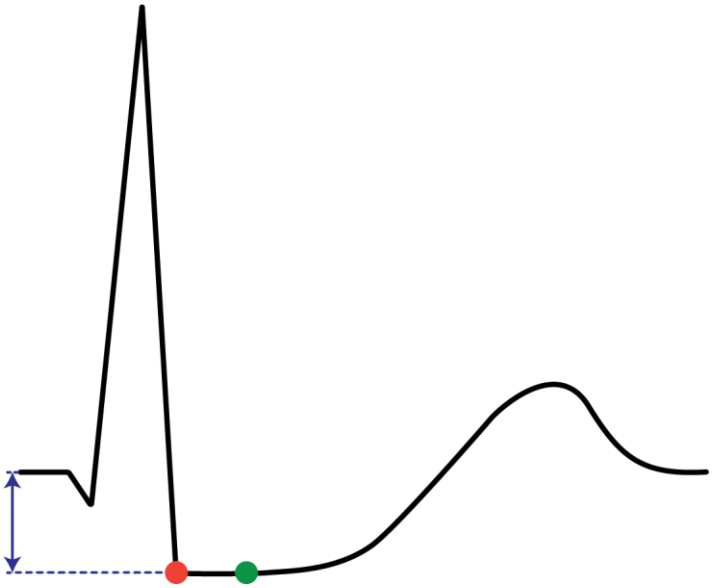


The plateau phase or phase 2 corresponds to the ST segment on the surface ECG. The membrane potential is relatively unchanged during this phase and most ventricular cells are in this phase simultaneously (more or less). Therefore, there are no electrical potential differences in the myocardium during phase 2 which results in a flat and isoelectric ST segment.

Acute ischemia is virtually always confined to a specific area, where the cell´s membrane potentials change (due to is ischemia). Thus, electrical potential difference in the myocardium and this displaces the ST-segment up or down.

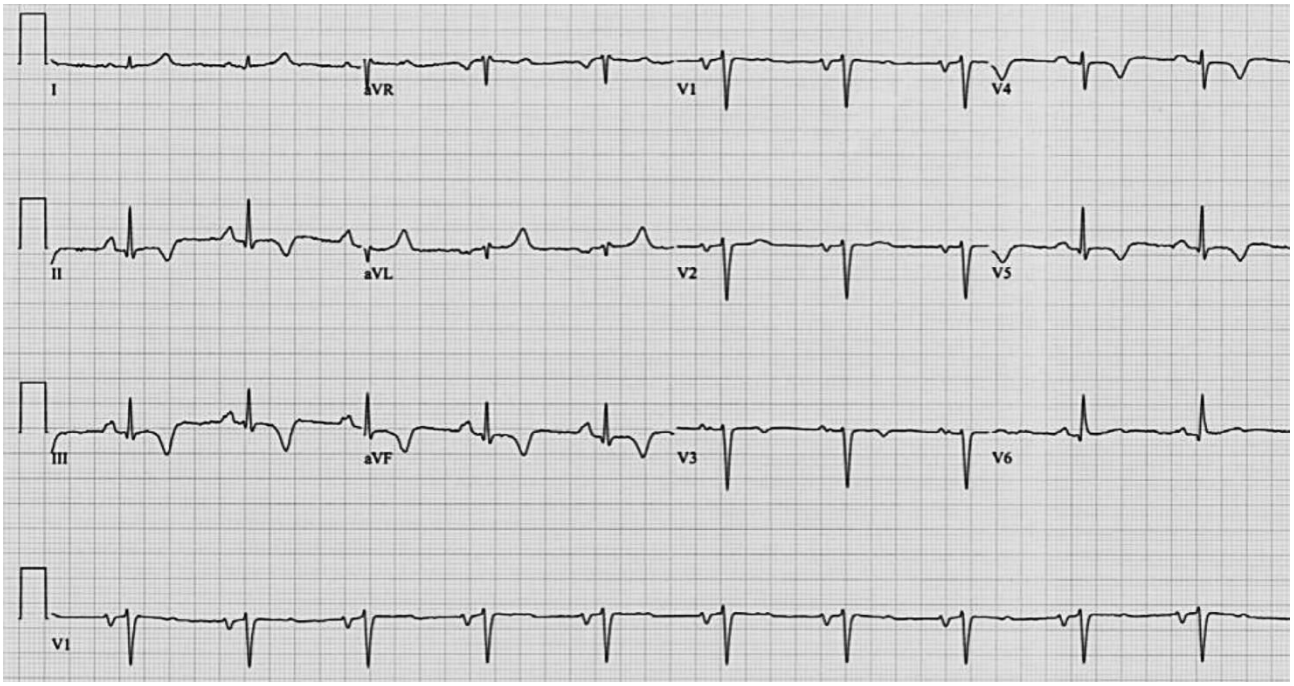


The magnitude of ST segment elevation is measured in the J point.



The magnitude of ST segment depression is measured in the J point in most instances. Occasionally it is advised that the J-60 point be used instead (particularly during exercise stress testing). If the ST segment is horizontal then there is no difference in the magnitude of the ST depression in J and I-60.

Example



NSTEMI with T-wave inversion

In a small minority of patients presenting with NSTEMI, initial ECG may be normal; thus, it is important to evaluate additional factors such as history, physical examination, cardiac biomarkers, and serial ECGs before excluding a diagnosis of NSTEMI (**Ellis KM. Myocardial infarction. In: EKG plain and simple. 4th edition. Boston: Pearson Education; 2016. p. 311–43**) . (**Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012;60(16):1581–98**.)

A) **Subendocardial ischemia:**

In subendocardial ischemia only the sub endocardium is affected. **Diffuse subendocardial ischemia** is more often due to supply/demand mismatch in the absence of ACS than it is due to ACS. Common etiologies of supply/demand mismatch are hypoxia, tachydysrhythmias, hypotension (from whatever cause), anemia, coronary artery stenosis without ACS, or (intraventricular) hypertension. --Oxygen supply is determined by:

1) Oxygen (O_2) carrying capacity,
2) O_2 saturation, and
3) Coronary flow.

Thus, in the absence of athero-thrombotic mechanism (ACS), myocardial ischemia can be brought on by:

1) Hypotension (diastolic hypotension, as all coronary flow happens during diastole because intramyocardial pressure during systole stops blood flow). Hypotension may of course be a result of a brady- or tachydysrhythmia.
2) Hypoxia, including poisons of oxidative phosphorylation such as HS, Carbon Onoxide (CO), CN.
3) Anemia, or poisons of hemoglobin such as methemoglobin or CO.
4) Fixed coronary stenosis that limits flow. --Oxygen demand is determined by: Afterload (high resistance to LV outflow), which is increased by elevated blood pressure or by aortic stenosis. Heart rate: sinus tachycardia --Decreased supply (hypotension) and increased demand from 1) high afterload (LV pressures are very high because of the aortic stenosis outflow resistance) and high heart rate. --This demonstrates that there may be some value to heart auscultation, to listen for an aortic murmur. In fact, bedside ultrasound might even find severe aortic stenosis. If you can use Doppler, then you can diagnose it.

Myocardial Ischemia Background

Non-ST-elevation acute coronary syndrome (NSTEACS) encompasses two main entities:

Non-ST-elevation myocardial infarction (NSTEMI).

Unstable angina (UA).

The differentiation between these two conditions is usually retrospective, based on the presence/absence of raised cardiac enzymes at 8-12 hours after the onset of chest pain.

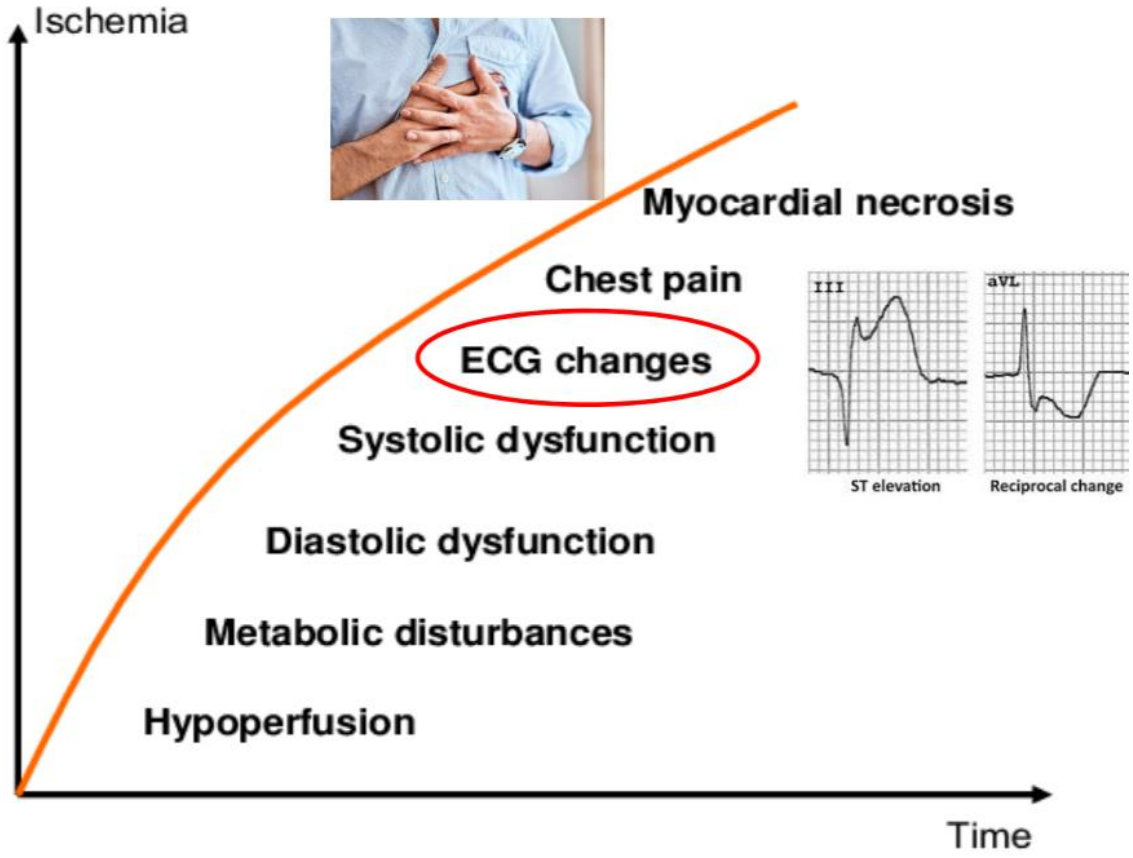
Both produce the same spectrum of ECG changes and symptoms and are managed identically in the Emergency Department.

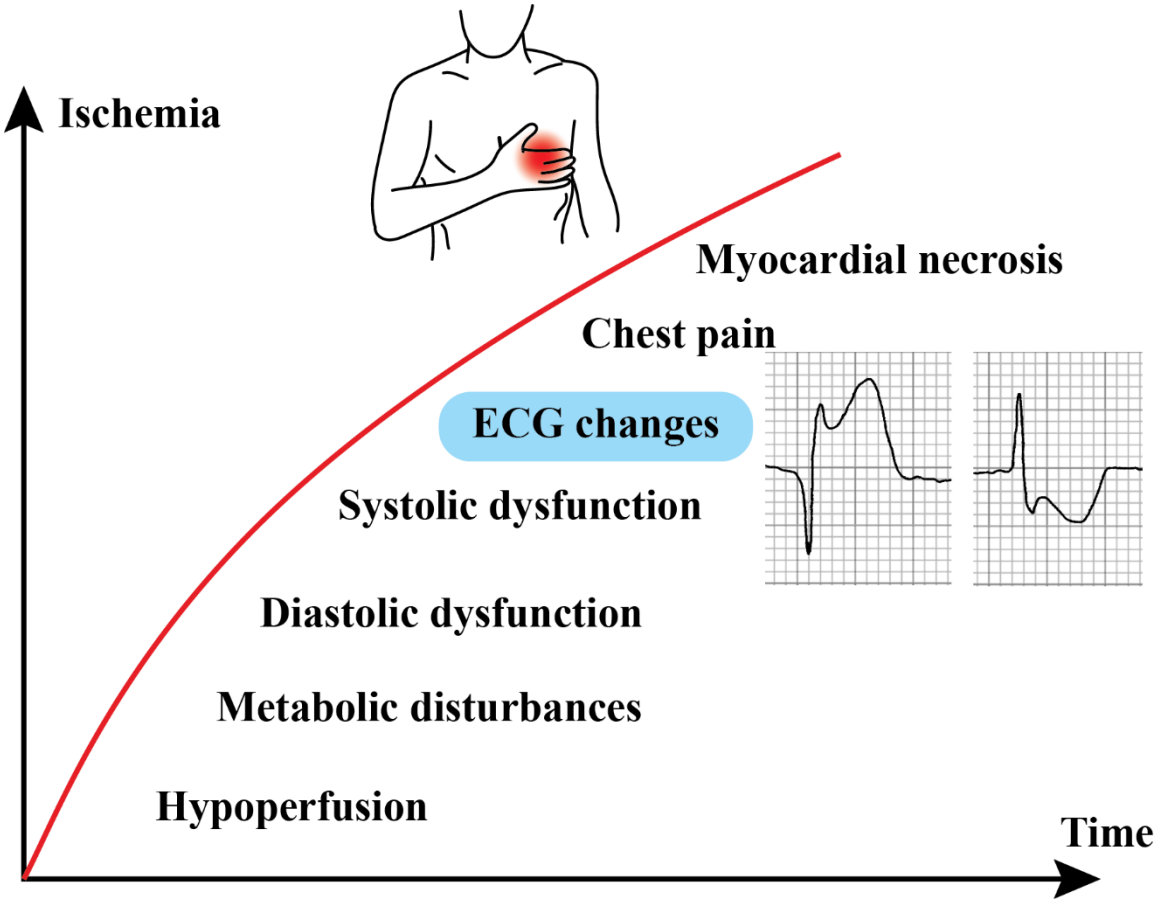
B) **Transmural ischemia**

Its implies that the entire wall thickness – from endocardium to epicardium – is affected in the area supplied by the occluded artery. Transmural heterogeneities of the properties of sodium and ATP-sensitive potassium channels may contribute to the genesis of ST–T changes during mild or moderate transmural ischemia, while ST elevation may be induced without the contribution of heterogeneity under severe transmural ischemia.

George J. Tayor , MD , 150 Practice ECGs: Interpretation and Review , ISBN – 13: 978-1-4051-0483-8

Ischemic cascade





Diagnose of MI; ECG role

Detection of rise and / or fall of cardiac troponin -T values with at least one of the following:

1. Symptoms of acute myocardial ischemia
2. New ischemic ECG change
3. Development of pathological Q waves
4. If the initial ECG is not diagnostic for STEMI and there is a high index of clinical suspicion of ACS, ECGs should be done serially and repeated if pain recurs (***Fesmire FM, Percy RF, Bardoner JB, Wharton DR, Calhoun FB* Usefulness of automated serial 12-lead ECG monitoring during the initial emergency department evaluation of patients with chest pain. *Ann Emerg Med. 1998 Jan; 31(1):3-11***.)
5. ECGs should be interpreted by qualified emergency physicians in the ED. ECGs should not routinely be taken to a cardiologist for interpretation nor should a cardiologist be asked to consult on every patient who presents to the ED with chest pain. Exceptions for emergent cardiology consultation

include ECGs with borderline findings suggestive of a possible acute STEMI

6. Imaging evidence of new loss of viable myocardium or new regional wall abnormality in pattern consistent with an ischemic etiology
7. Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy

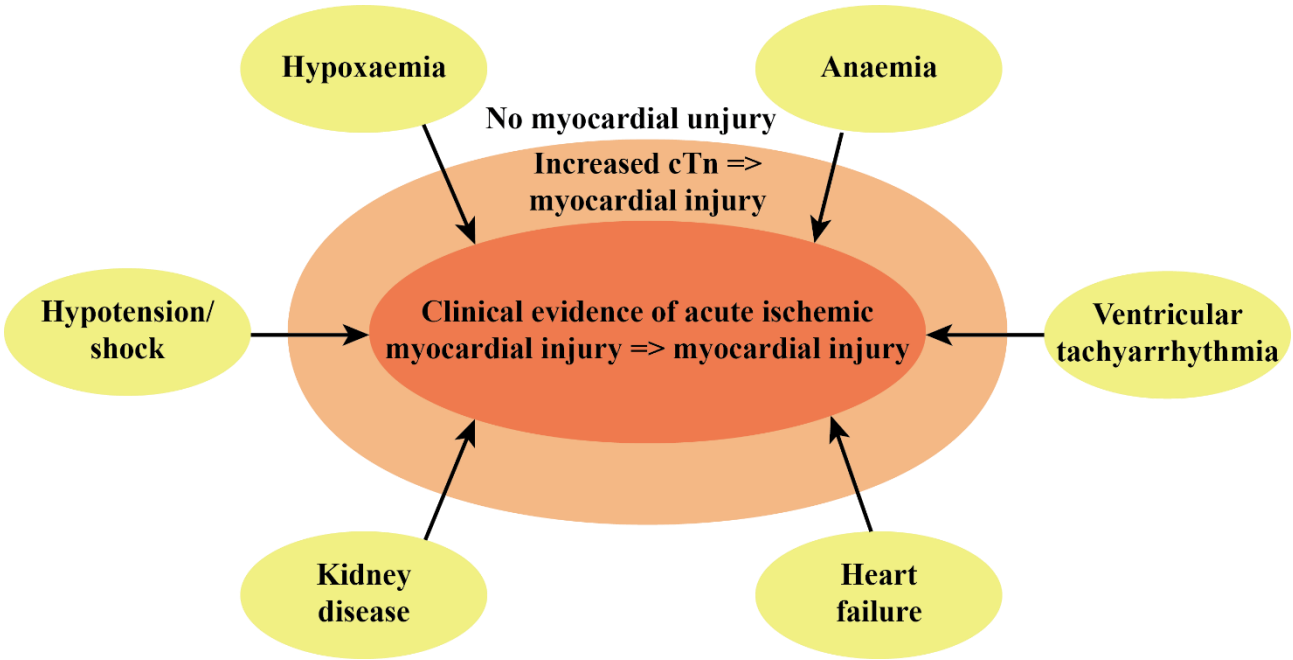
Fourth universal definition of myocardial infarction, EHJ (2018) 00,1-33

A 12-lead ECG should be completed immediately on arrival to the ED. The patient should be placed on a monitor, intravenous (IV) access established, and blood for cardiac troponin levels should be sent to the laboratory for quantitative measurement in all patients with chest pain suggestive of ACS within 10 min of presenting to the ED

However; Troponin T raising in many conditions:

Other systemic disease(s):

- Sepsis, infectious disease
- Stroke, SAH
- Pulmonary embolism
- Chemotherapeutic agents
- Critical ill patients
- Strenuous exercise



STEMI – “trans-mural ischemia”

♣ Life – threatening condition

♣ Plaque rupture

♣ Acute obstruction of infarct artery (s)

♣ Immediate management is essential

♣ Mortality is higher if a greater number of ECG leads show ST elevation

Management Early Diagnosis Early treatment Time = myocardium

ECG evaluation

12-lead ECG recording as soon as possible and interpretation is indicated at the point of first medical contact (FMC), with a maximum target delay of 10 minutes (**Diercks DB, Peacock WF, Hiestand BC, Chen AY, Pollack CVJr, Kirk JD, Smith SCJr, Gibler WB, Ohman EM, Blomkalns AL, Newby LK, Hochman JS, Peterson ED, Roe MT. Frequency and consequences of recording an electrocardiogram >10 minutes after arrival in an emergency room in non-ST-segment elevation acute coronary syndromes (from the CRUSADE Initiative). Am J Cardiol 2006;97(4):437–442.)(Rokos IC, French WJ, Koenig WJ, Stratton SJ, Nighswonger B, Strunk B, Jewell J, Mahmud E, Dunford JV, Hokanson J, Smith SW, Baran KW, Swor R, Berman A, Wilson BH, Aluko AO, Gross BW,**

Rostykus PS, Salvucci A, Dev V, McNally B, Manoukian SV, King SB3rd. Integration of pre-hospital electrocardiograms and ST-elevation myocardial infarction receiving center (SRC) networks: impact on door-to-balloon times across 10 independent regions. JACC Cardiovasc Interv 2009;2(4):339–346.) If the ECG is equivocal, repeat ECGs and compared with previous recording Monitor ECG with defibrillator capacity. ECG monitoring with defibrillator capacity is indicated as soon as possible in all patients with suspected STSE,

(**O'Doherty M, Tayler DI, Quinn E, Vincent R, Chamberlain DA. Five hundred patients with myocardial infarction monitored within one hour of symptoms. BMJ (Clin Res Ed) 1983;286(6375**):**1405–1408**.)(**Mehta RH, Starr AZ, Lopes RD, Hochman JS, Widimsky P, Pieper KS, Armstrong PW, Granger CB. Incidence of and outcomes associated with ventricular tachycardia or fibrillation in patients undergoing primary percutaneous coronary intervention. JAMA 2009;301(17):1779–1789**.)

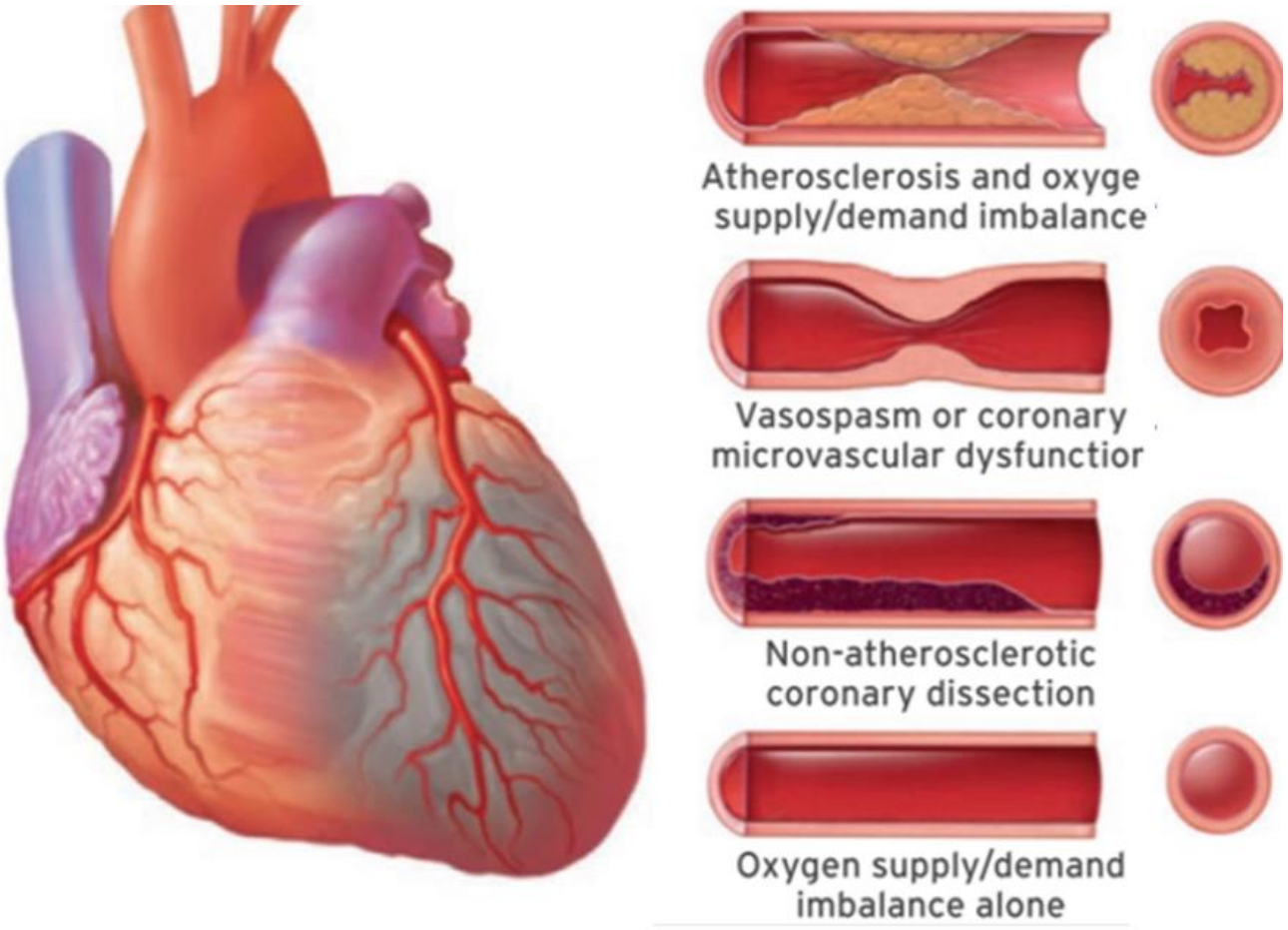
Clinical Classification of Myocardial Infarction

Myocardial infarction type 1 MI caused by atherothrombotic CAD and usually precipitated by atherosclerotic plaque disruption (rupture or erosion) is designated as a type 1 MI. The relative burden of atherosclerosis and thrombosis in the culprit lesion varies greatly, and the dynamic thrombotic component may lead to distal coronary embolization resulting in myocyte necrosis. Plaque rupture may not only be complicated by intraluminal thrombosis but also by hemorrhage into the plaque through the disrupted surface Criteria for type 1 MI: Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and with at least one of the following: Symptoms of acute myocardial ischemia; New ischemic ECG changes; Development of pathological Q waves; Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology; Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.

I. Myocardial infarction Type 2 MI: **The pathophysiological mechanism leading to ischemic myocardial injury in the context of a mismatch between oxygen supply and demand has been classified as type 2 MI 10, 12. By definition, acute atherothrombotic plaque disruption is not a feature of type 2 MI. In patients with stable known or presumed CAD, an acute stressor such as an acute gastrointestinal bleed with a precipitous drop in hemoglobin, or a sustained tachyarrhythmia with clinical manifestations of myocardial ischemia, may result in myocardial injury and a type 2 MI. These effects are due to insufficient blood flow to the ischemic myocardium to meet the increased myocardial oxygen demand of the stressor. Ischemic thresholds may vary substantially in individual patients depending on the magnitude of the stressor, the presence of non-cardiac comorbidities, and the extent of underlying CAD and cardiac structural abnormalities. Studies have shown variable occurrences of type 2 MI depending on criteria used for diagnosis. Some reports rely on specific predetermined oxygen mismatch criteria, whereas others apply more liberal criteria. Most studies show a higher frequency of type 2 MI in women. The short- and long-term mortality rates for patients with type 2 MI are generally higher than for type 1 MI patients in most but not all studies due to an increased prevalence of comorbid conditions. Coronary atherosclerosis is a common finding in type 2 MI patients selected for coronary angiography. In general, these patients have a worse prognosis than those without CAD 54, 55, 56, 57. Prospective evaluations of the importance of CAD with type 2 MI using consistent definitions and approaches are needed. It has been shown that the frequency of ST-SE in type 2 MI varies from 3% to 24% (53). In some cases, coronary embolism caused by thrombi, calcium or vegetation from the atria or ventricles, or acute aortic dissection may result in a type 2 MI. Spontaneous coronary artery dissection with or without intramural hematoma is another non-atherosclerotic condition that may occur, especially in young women. It is defined as spontaneous dissection of the coronary artery wall with accumulation of blood within the false**

lumen, which can compress the true lumen to varying degrees (Figure 4) (58).

II. Criteria for type 2 AMI: **Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL, and evidence of an imbalance between myocardial oxygen supply and demand unrelated to coronary thrombosis, requiring at least one of the following: Symptoms of acute myocardial ischemia; New ischemic ECG changes; Development of pathological Q waves; Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology.**

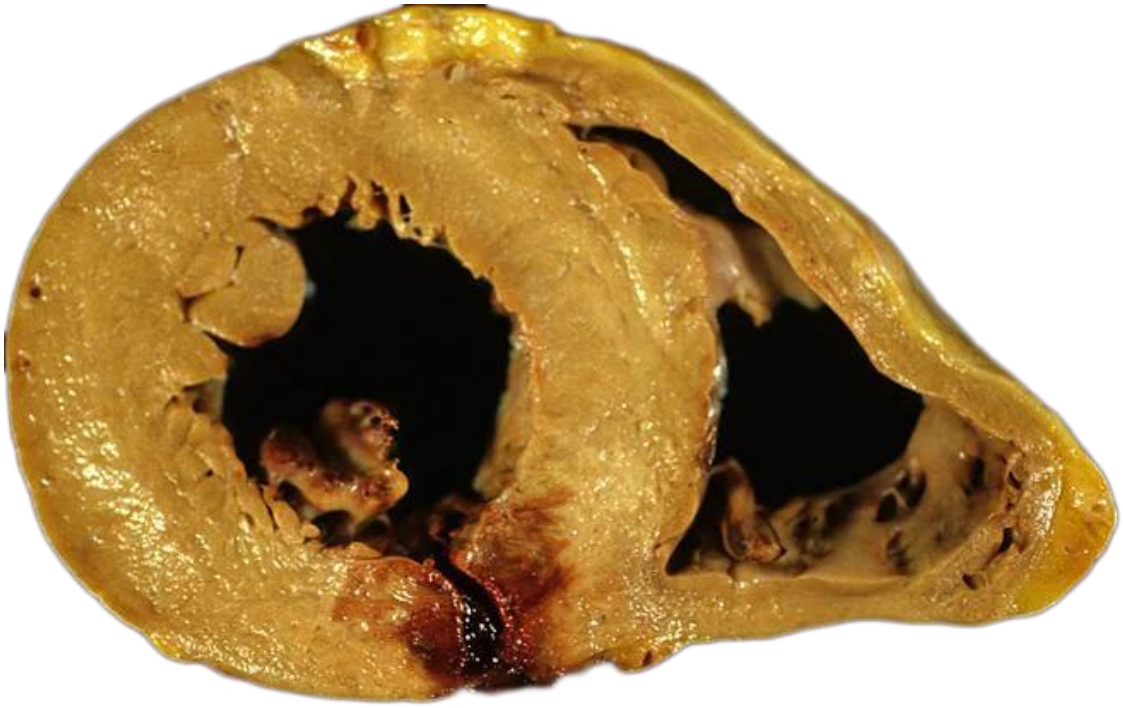


III. Type 3 AMI: **The detection of cardiac biomarkers in the blood is fundamental for establishing the diagnosis of MI 10, 12. However, patients can manifest a typical presentation of myocardial ischaemia/infarction, including presumed new ischaemic ECG changes or ventricular fibrillation, and die before it is possible to obtain blood for cardiac biomarker determination; or the patient may succumb soon after the onset of symptoms before an elevation of biomarker values has occurred. Such patients are designated as having a type 3 MI, when suspicion for an acute myocardial ischaemic event is high, even when cardiac biomarker evidence of MI is lacking 10, 12. This category allows the separation of fatal MI events from the much larger group of sudden death episodes that may be cardiac (non-ischaemic) or non-cardiac in origin. When a type 3 MI is diagnosed and a subsequent autopsy reveals recent evidence of an MI, with a fresh or recent thrombus in the infarct-related artery, the type 3 MI should be reclassified to a type 1 MI. Original investigations addressing the incidence of type 3 MI are sparse, but a study showed an annual incidence below 10/100,000 person-years and a frequency of 3% to 4% among all types of MI. MI resulting in death when biomarker values are unavailable**

Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurring before blood samples could be obtained, before cardiac biomarker could rise, or in cases cardiac biomarkers were not collected

Criteria for Type 3 MI Patients who suffer cardiac death, with symptoms suggestive of myocardial ischemia accompanied by presumed new ischemic ECG changes or ventricular fibrillation, but die before blood samples for biomarkers can be obtained, or before increases in cardiac biomarkers can be identified, or MI is detected by autopsy examination.

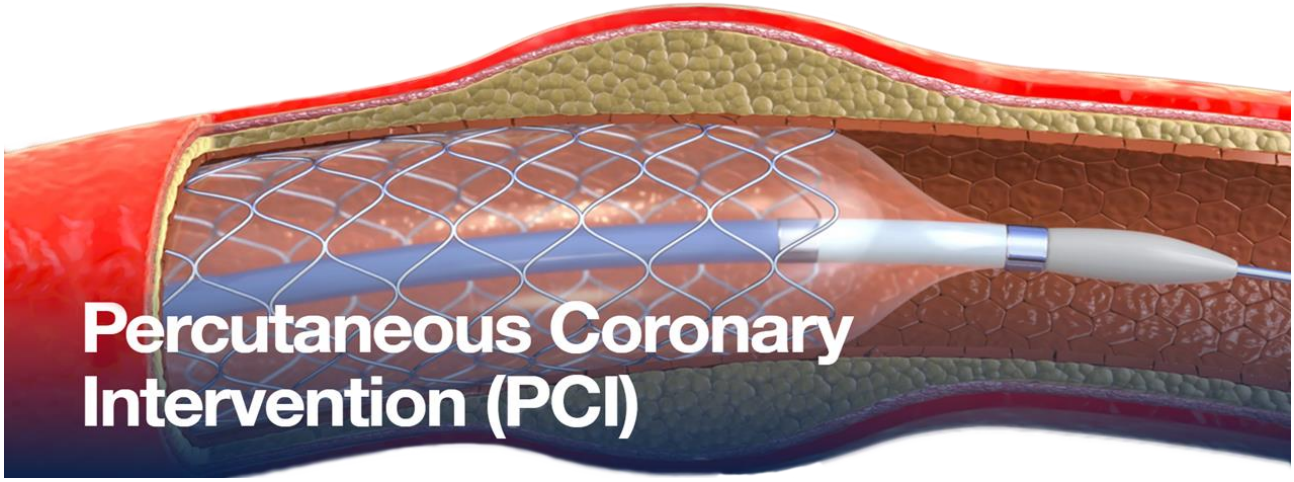
Example



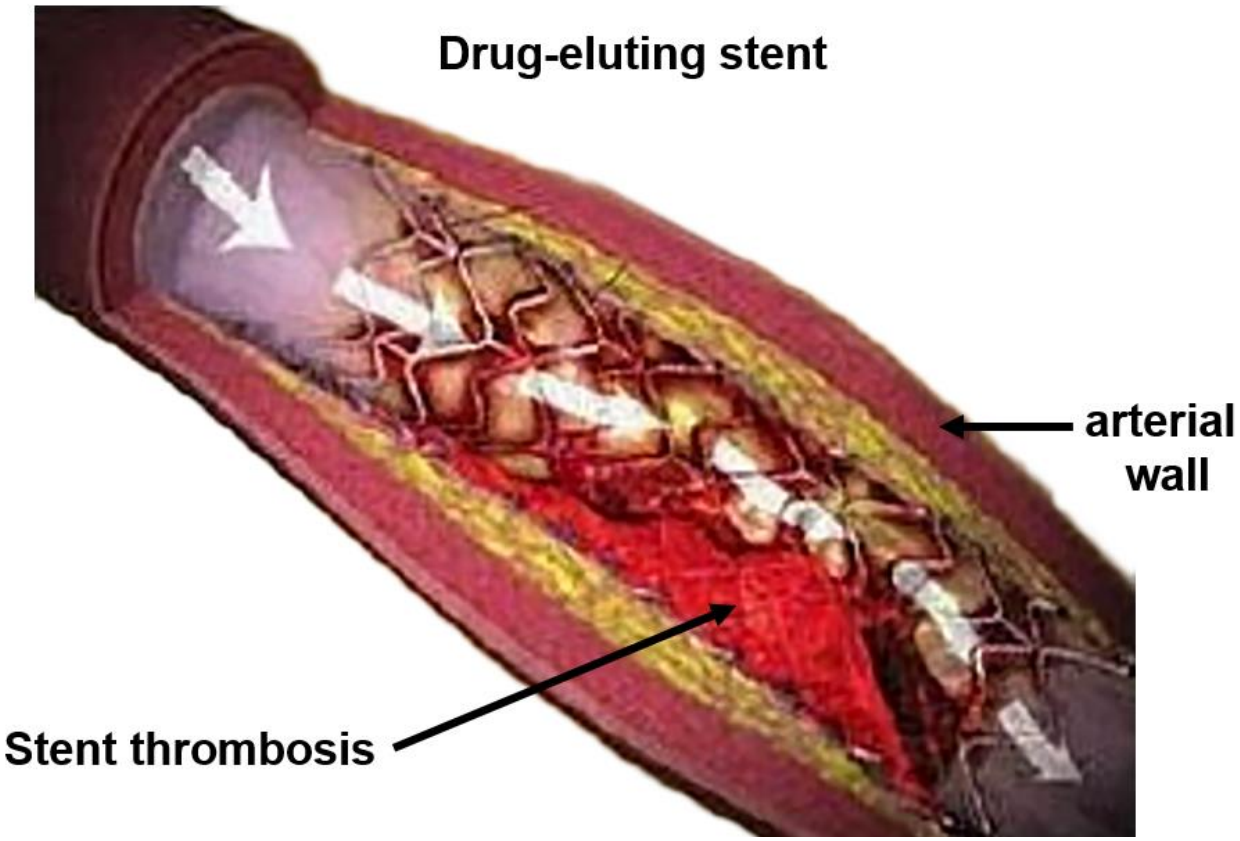
Early cardiac death before biomarkers collection for transmural hem0pericardium AMI: type 3 AMI

Criteria for type 4a AMI related to Percutaneous Coronary Intervention (PCI) (there are complex specific criteria)

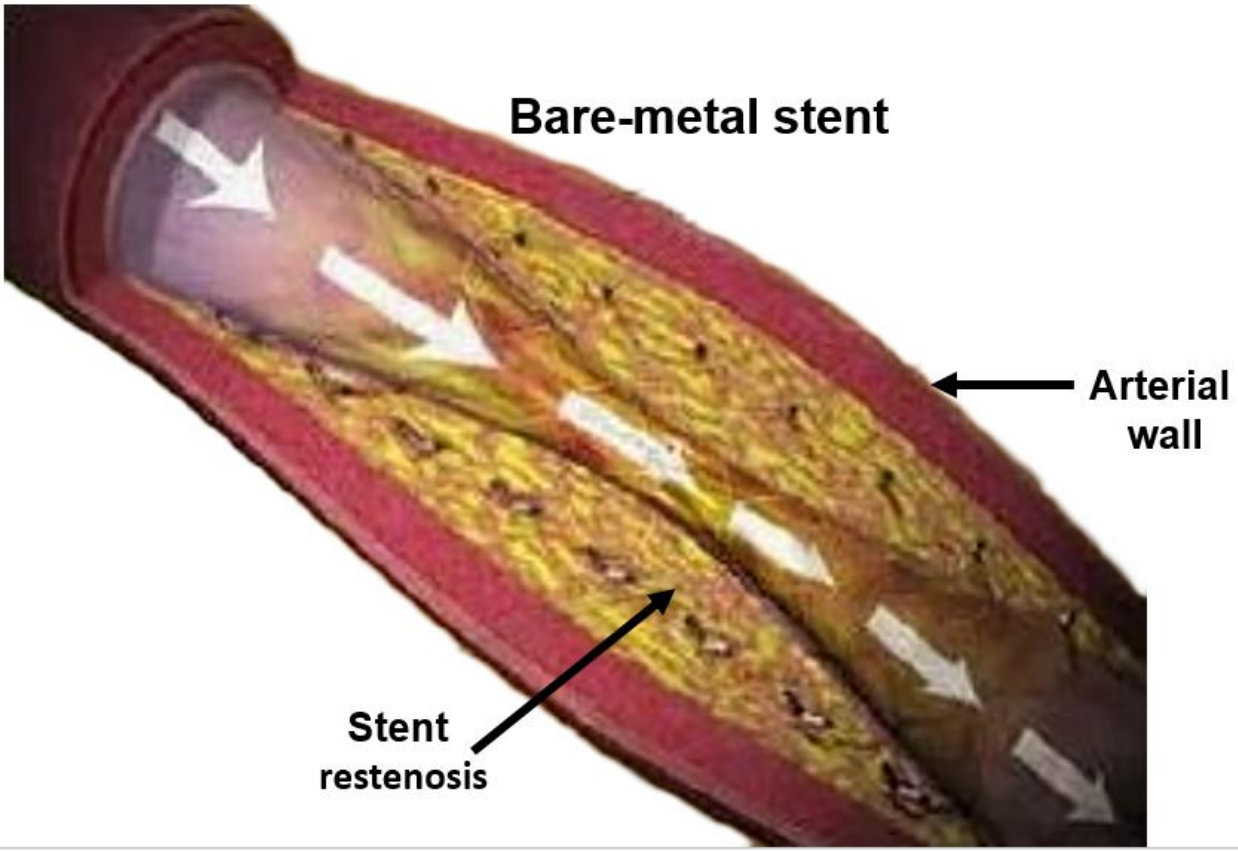
Figure



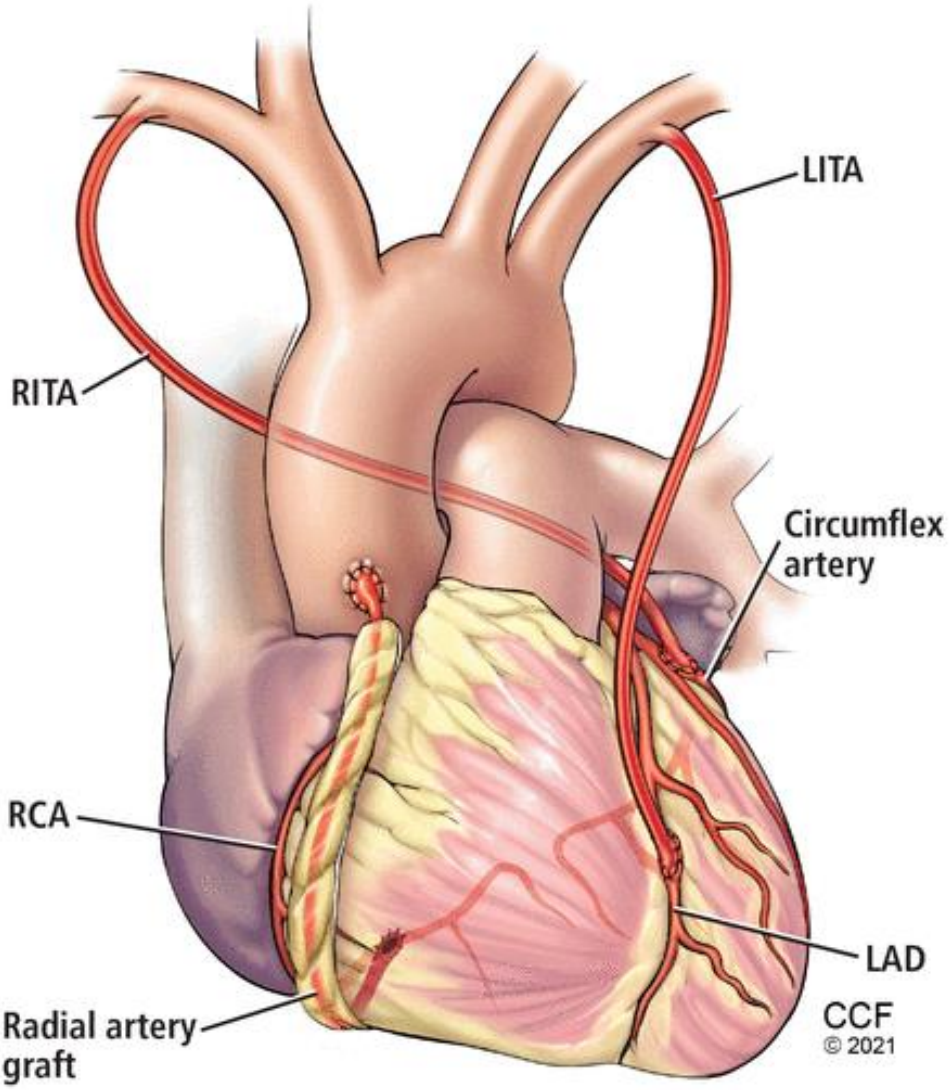
Criteria for type 4B MI. AMI related to stent thrombosis (there are complex specific criteria)



Criteria for type 4C AMI. **Stent restenosis associated with percutaneous coronary intervention.**



Criteria for I type 5AMI; CABG-related AMI (there are complex specific criteria)



Multivessel coronary artery bypass graft surgery. The left internal thoracic artery (LITA: left internal thoracic artery) is used to bypass the left anterior descending artery (LAD: left anterior descending), the right internal thoracic artery (RITA: right internal thoracic artery) to bypass the circumflex artery and the radial artery to bypass the right coronary artery (RCA).

Any AMI resulting from obstruction of these bypasses gives rise to type 5 AMI.

20017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

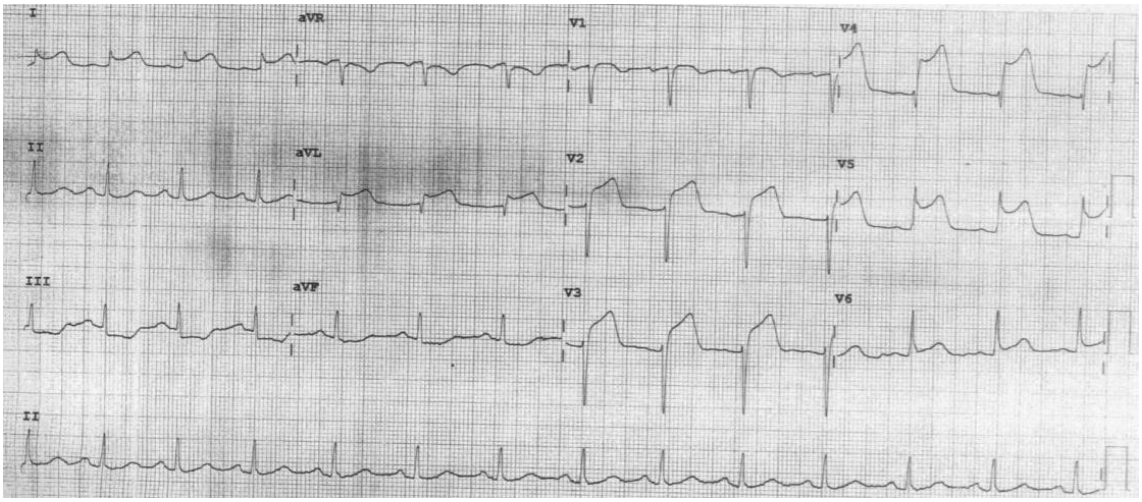
ECG manifestations suggestive of acute MI (in the absence of LVH and BBB)

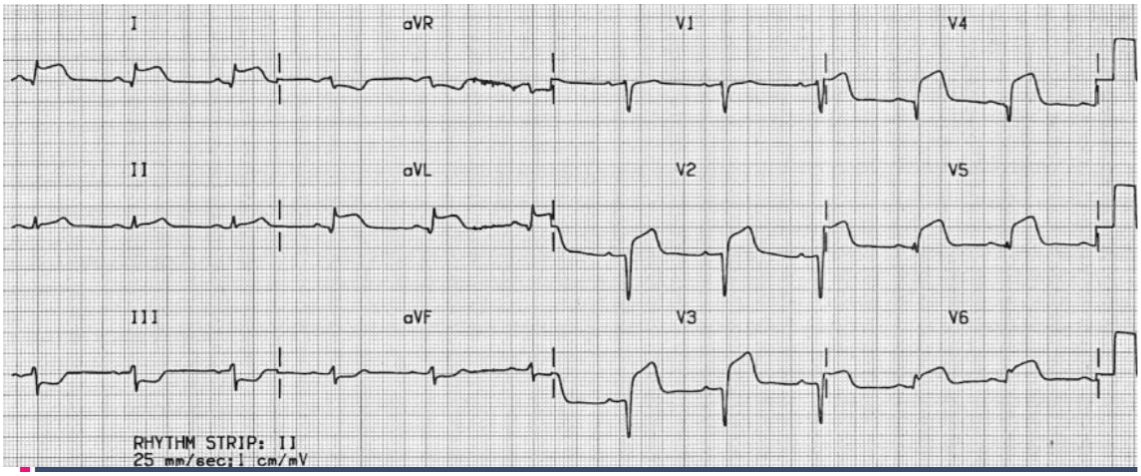
ST-elevation
New ST-elevation at the J-point in two contiguous leads with the cut-point: ≥ 1mm in all leads other than leads V2-V3 where the following cut-point apply: ≥2mm in men≥40 years; ≥2.5 mm in men<40years, or ≥1.5mm in women regardless if age, [a]

KristianThygesen(Denmark)**Fourth Universal definition if myocardial infarction, EHJ (2018)00, 1-33 J Am Coll Cardiol. 2018 Oct 30;72(18):2231-2264. doi: 10.1016/j.jacc.2018.08.1038.**

Examples

Anterior wall STEMI





Tombstone ECG; STEMI anterolateral acute MI Tombstoning ST elevation myocardial infarction can be described as a **STEMI** characterized by tombstoning ST-segment elevation. This myocardial infarction is associated with extensive myocardial damage, reduced left ventricle function, serious hospital complications and poor prognosis.

This ominous ECG pattern first descripted in 1993 by Wimalaratna (**Wimalaratna, H. S. K. (1993). Tombstoning of ST segment in acute myocardial infarction (letter). *The Lancet*, 342, 96 10.1016/0140-6736(93)91622-S**). The term "tombstoning" is used by experienced junior doctors to describe a certain shape of the ST segment in the ECG) of patients with AMI and is noted on admission in some cases. This provocative term is often used to communicate to colleagues a grave prognosis of the patient in question.

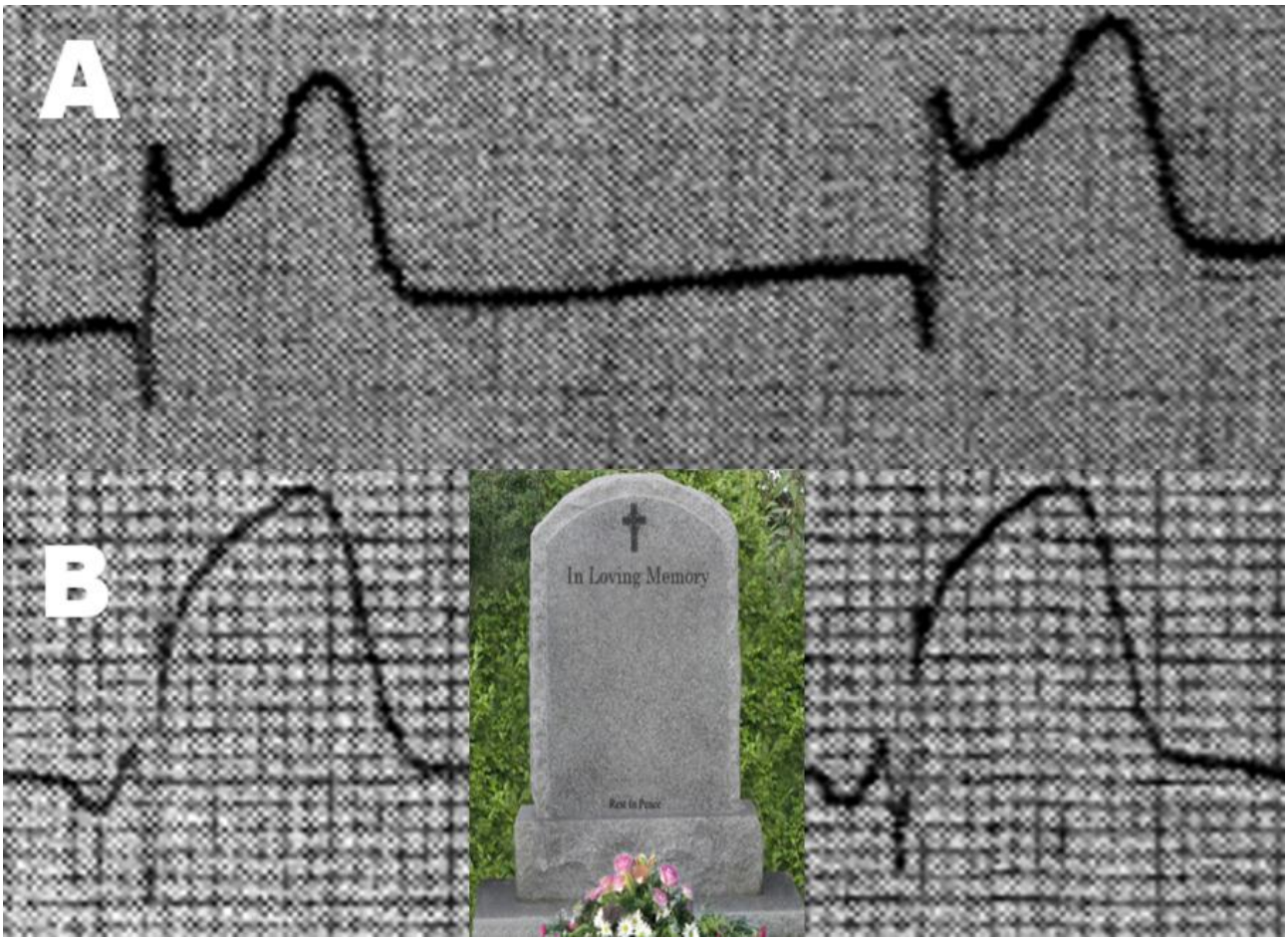


Figure: A= usual ST segment elevation, B= tombstone ECG shape or grave sign: ST-segment elevation: the QRS complex, the ST-segment, and the T

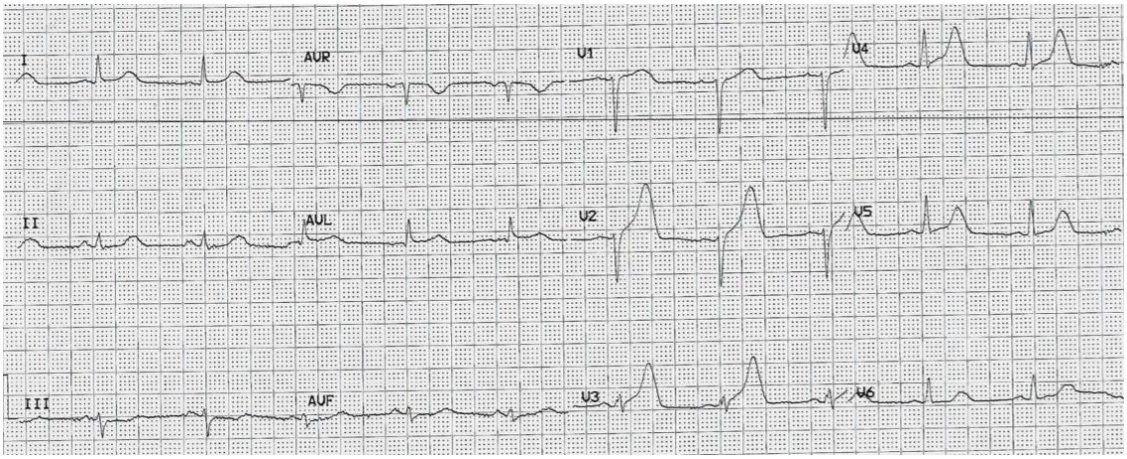
wave merge to form a large upright monophasic deflection called a "tombstone"

Characteristic

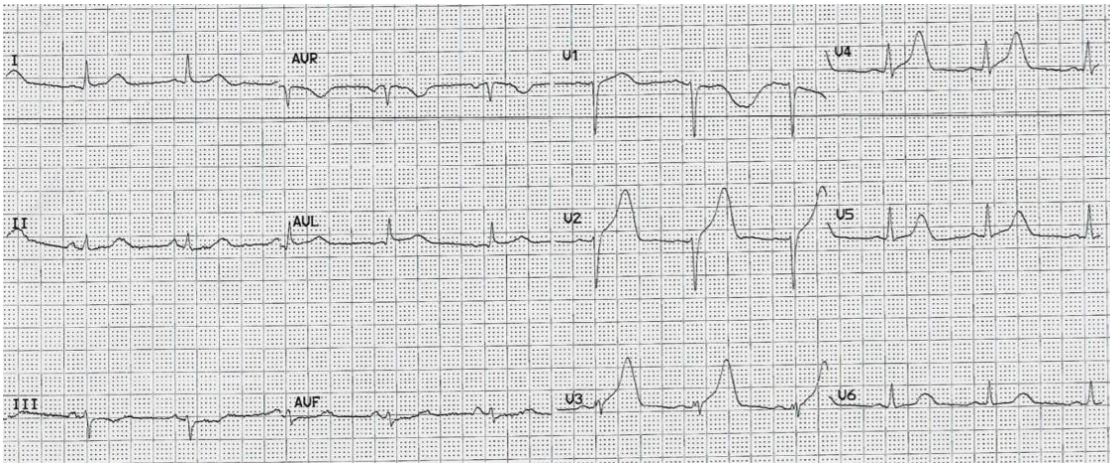
- ***Frequency:*** 25%–30% of STEMI patients (**Guo, X. H., Yap, Y. G., Chen, L. J., Huang, J., & Camm, A. J. (2000). Correlation of coronary angiography with tombstoning electrocardiographic pattern in patients after acute myocardial infarction. Clinical Cardiology, 23, 347–352**.)
- ***Subjacent cause:*** due to the presence of multivessel disease **Balci, B. (2009). Tombstoning ST-Elevation myocardialinfarction. Current Cardiology Reviews, 5, 273–278. https://doi.org/10.2174/157340309789317869**
- ***Cardiac wall affected:*** predominantly in the LV anterior wall > 80% of cases. (**Guo, X. H., Yap, Y. G., Chen, L. J., Huang, J., & Camm, A. J. (2000). Correlation of coronary angiography with tombstoning electrocardiographicpattern in patients after acute myocardial infarction. Clinical Cardiology, 23, 347–352**.)
- ***Underlying Mechanisms:*** multivessel disease + poor collateral circulation + lower LVEF
- ***In-hospital mortality rate***: higher 10 to 13%
- ***6-Month all-cause mortality:*** higher
- ***CK-MB and cardiac troponin:*** higher peak level
- ***Short-term follow-up***, more frequent hospitalization due to HF
- ***Midterm all-cause mortality.*** Higher Although primary PCI is quite successful in a general population patient, a T-pattern among patients with an STEMI is strongly associated with increased hospitalization for heart failure and midterm all-cause mortality.(**ErkanAyhan, et al , 1Patients with Tombstoning Pattern on the AdmissionElectrocardiogram Who Have Undergone Primary Percutaneous CoronaryIntervention for Anterior Wall ST-Elevation Myocardial Infarction: In-Hospitaland Midterm Clinical Outcomes.Ann Noninvasive Electrocardiol. 2012 Oct; 17(4):315–322. doi: 10.1111/j.1542-474X.2012. 00524.x**)

- ***Long-term follow-up***, independent predictor of long-term MACE. (**VeyselOzan Tanık, et al Long-term clinical outcomes andprognoses of ST-segment elevationmyocardial infarction patients who present with tombstoning ST-segment elevation Ann Noninvasive Electrocardiol. 2020 Mar;25(2): e12725. Published online 2019 Nov10. doi: 10.1111/anec.12725**)
- ***Risk stratification:*** Useful for this proposal (**Birnbaum, Y., & Sclarovsky, S. (2001). The grades of ischemia on the presenting electrocardiogram of patientswith ST elevation acute myocardial infarction. Journal of Electrocardiology, 34, 17–26. https://doi.org/10.1054/jelc.2001.28819**)

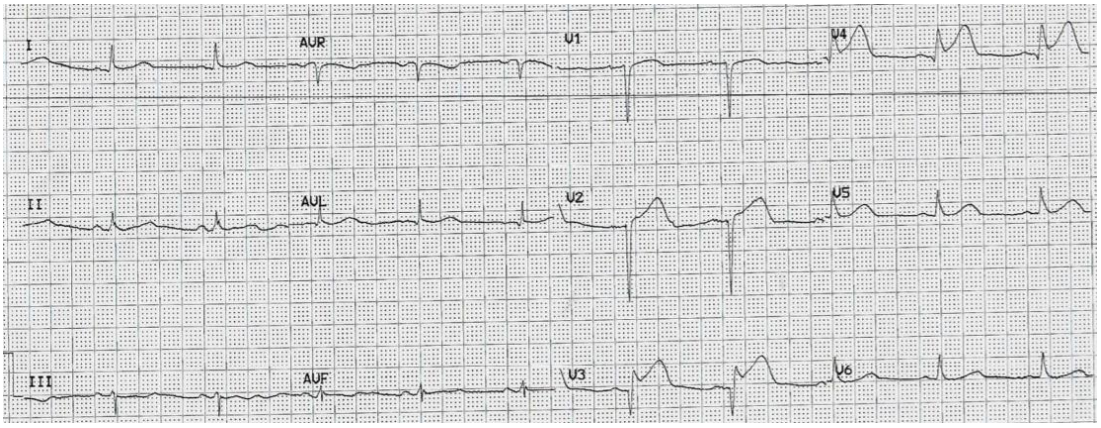
Patient 60-year-old female, with chest pain, admission first ECG print



Patient 60-year-old female, with chest pain, second ECG print

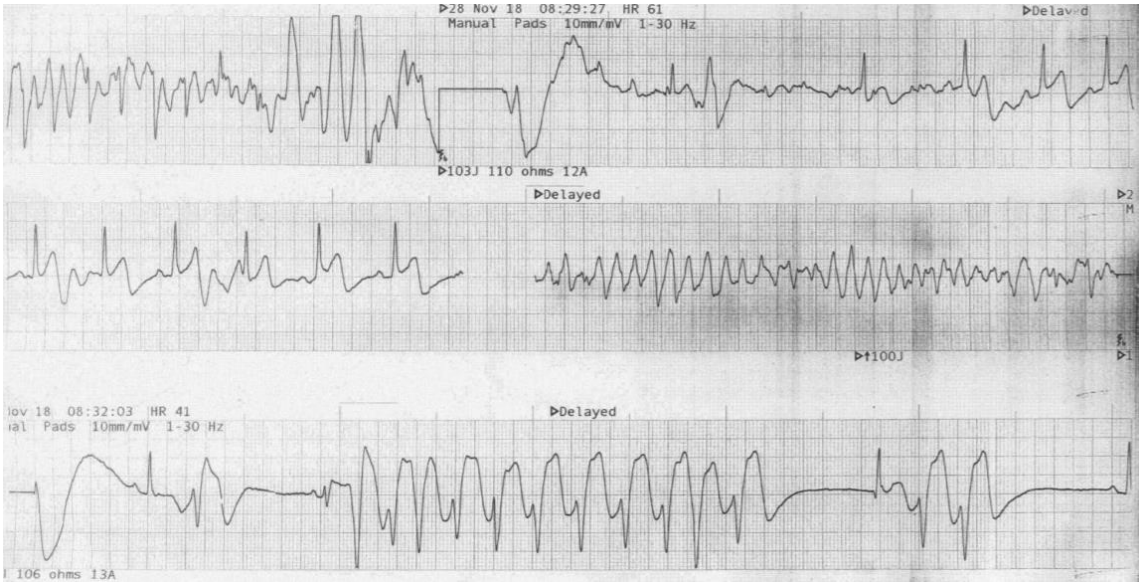


Patient 60-year-old female, with chest pain, third ECG print

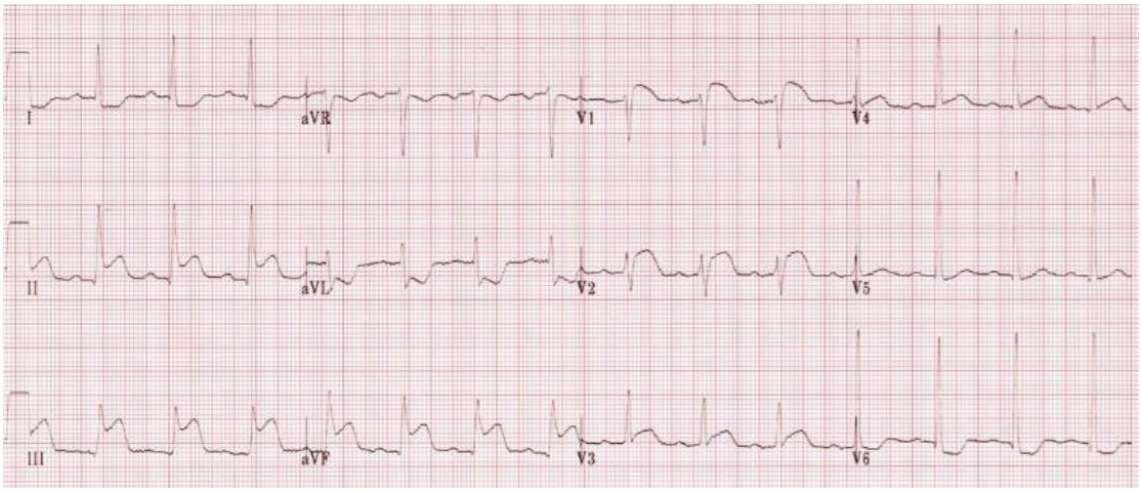


Diagnose; anterior wall STEMI

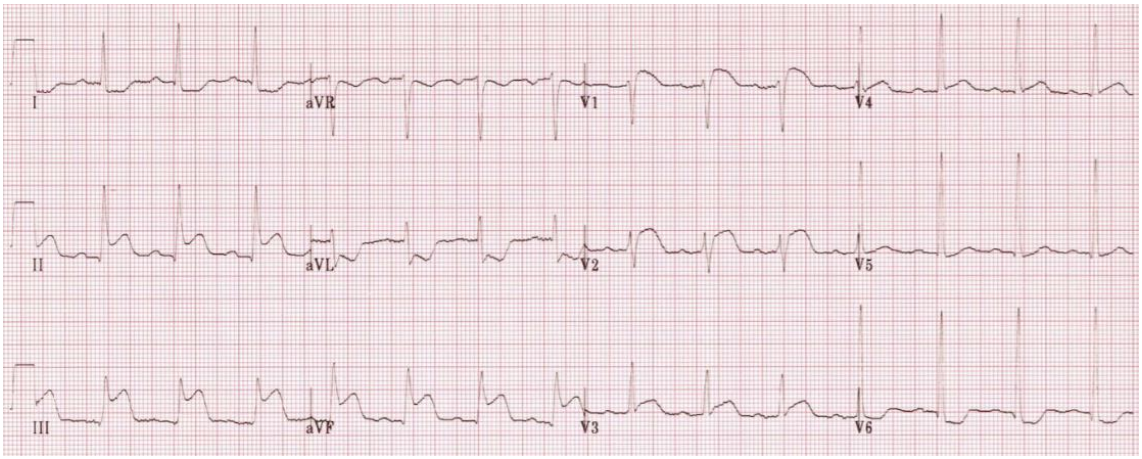
Ventricular fibrillation – complication of STEMI



Inferior wall STEMI

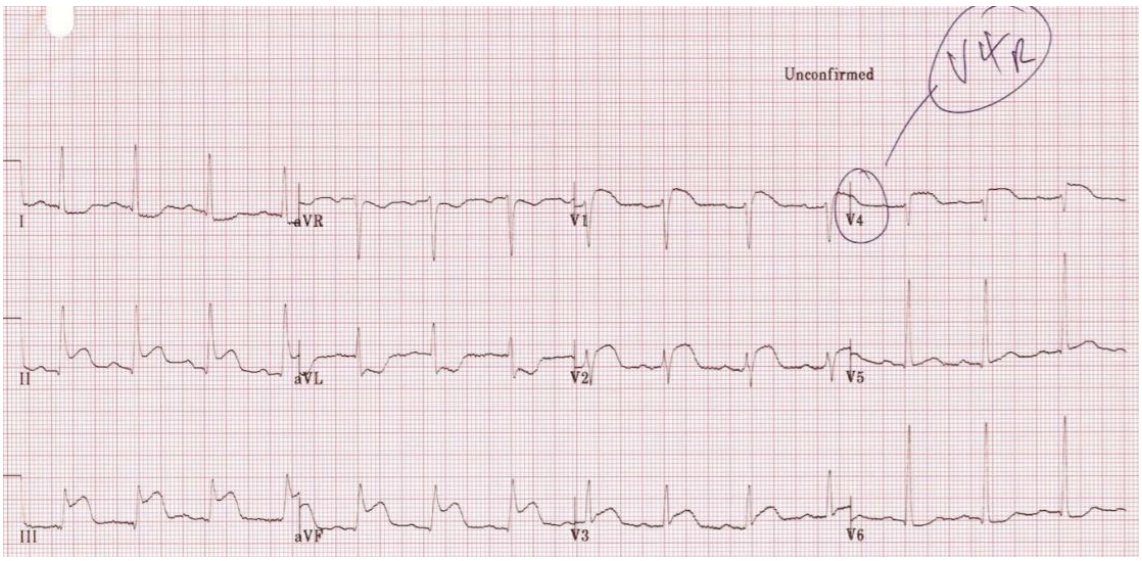


ST elevation in II, III and aVF Right ventricular infarction (concomitant with inferior wall MI)



ST elevation in II, III and aVF and V1

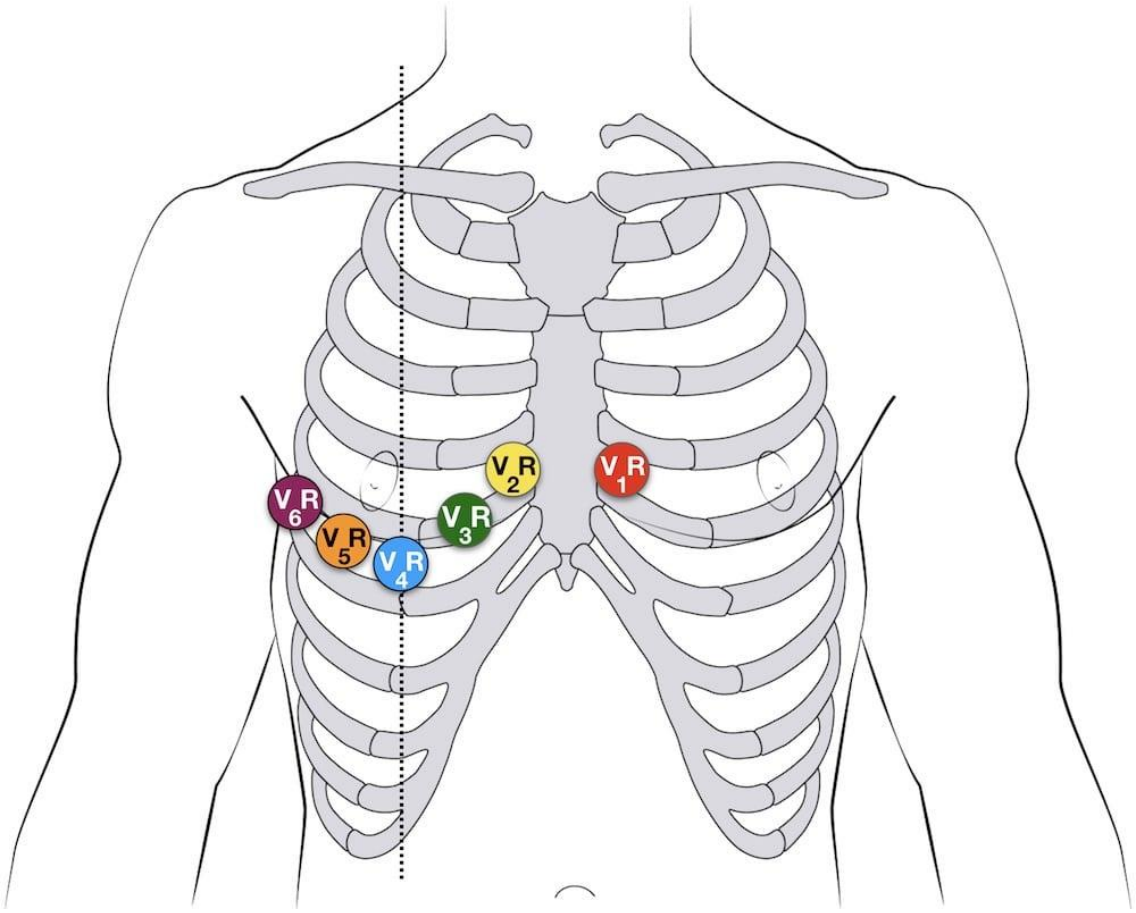
V_{3R}, V_{4R} lead

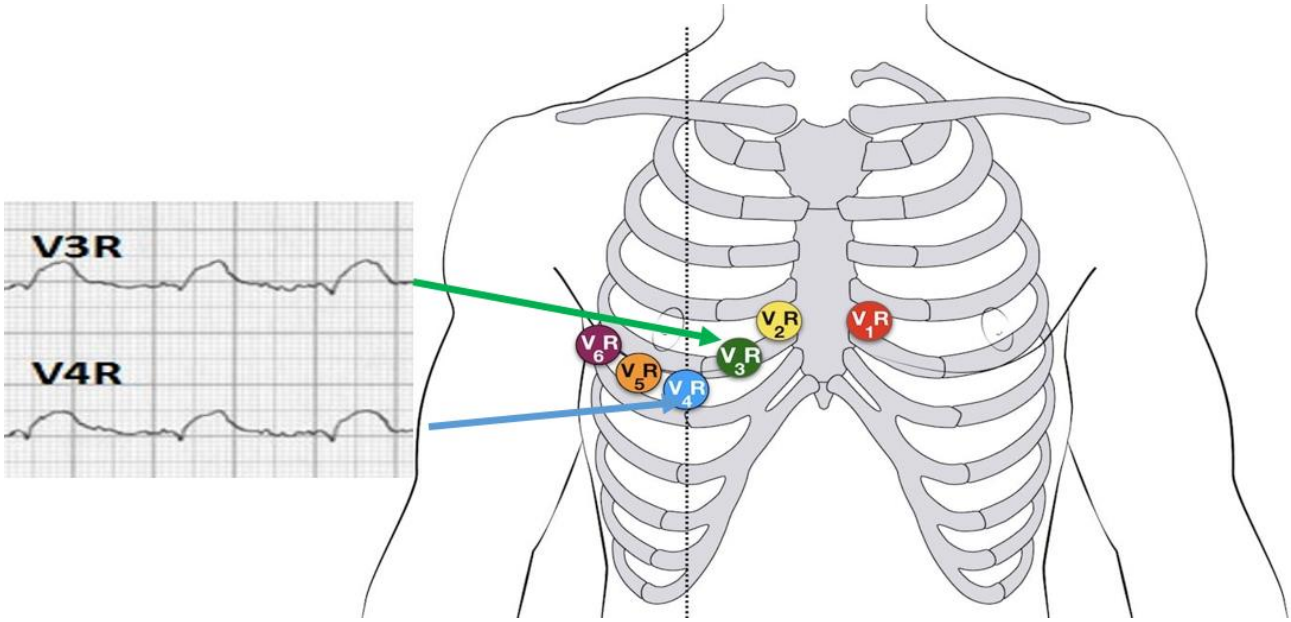


2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

Francis Morris, ABC of clinical electrophysiology, BMJ book, ISBN 0 7279 1536 3

The use of accessory additional right precordial leads V_{3R}, V_{4R} lead





Right sided 12 lead ECG lead placement

The most useful lead is V4R, which is obtained by placing the V4 electrode in the 5th right intercostal space in the mid-clavicular line.

ST elevation in V4R has a sensitivity of 88%, specificity of 78% and diagnostic accuracy of 83% in the diagnosis of RV MI. [see Inferior STEMI]. Additionally, Right-sided precordial leads may be used to better study pathology of the right ventricle or for dextrocardia (and are denoted with an R (e.g., V5R). **The use of accessory additional right precordial leads V_{3R}, V_{4R} lead in patients with inferior MI should be considered to identify concomitant RV infarction. IIa (Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HDWriting Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial InfarctionThygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis**

S, ESC Committee for Practice Guidelines. Third universal definition of myocardial infarction. Eur Heart J 2012;33(20):2551–2567.)(Lopez-Sendon J, Coma-Canella I, Alcasena S, Seoane J, Gamallo C. Electrocardiographic findings in acute right ventricular infarction: sensitivity and specificity of electrocardiographic alterations in right precordial leads V4R, V3R, V1, V2, and V3. J Am Coll Cardiol 1985;6(6):1273–1279.)

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

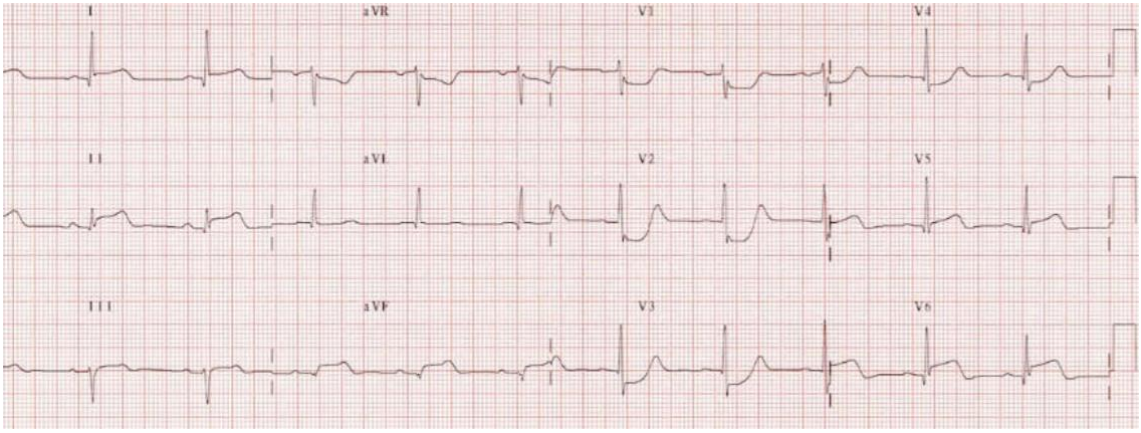
Right ventricular infarction

♣ The diagnosis of right ventricular infarction is important as it may be associated with hypotension

♣ Treatment with nitrates or diuretics may compound the hypotension, though the patient may respond to fluid challenge

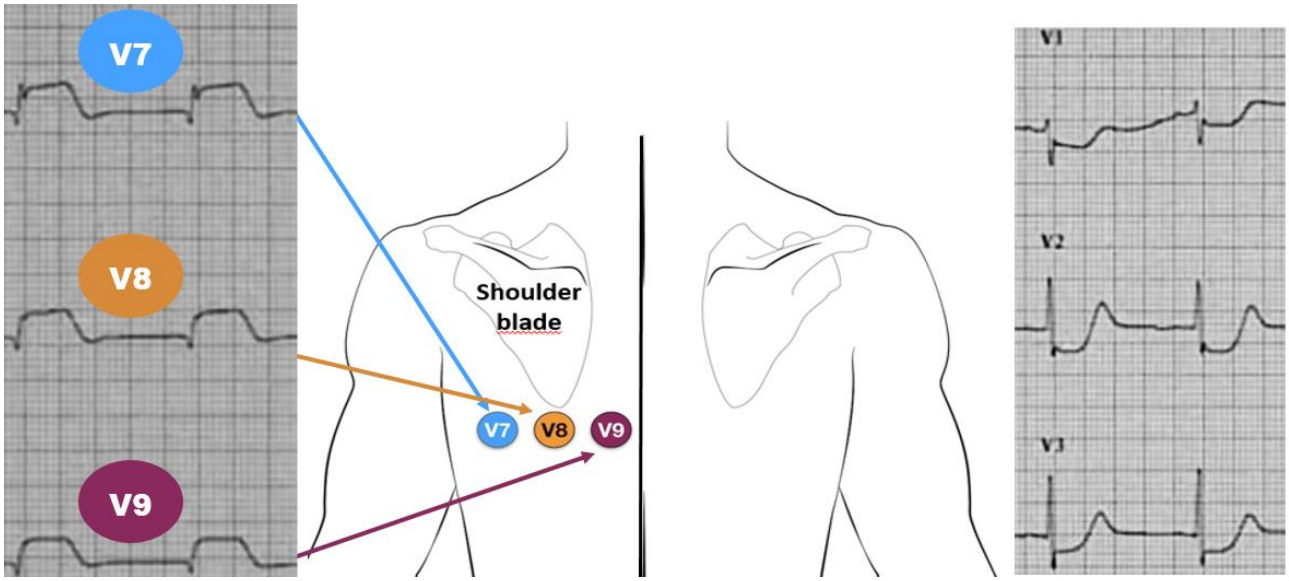
Francis Morris, ABC of clinical electrophysiology, BMJ book, ISBN 0 7279 1536 3

Lateral wall STEMI (concomitant with inferior wall MI) Erroneously called posterior wall STEMI



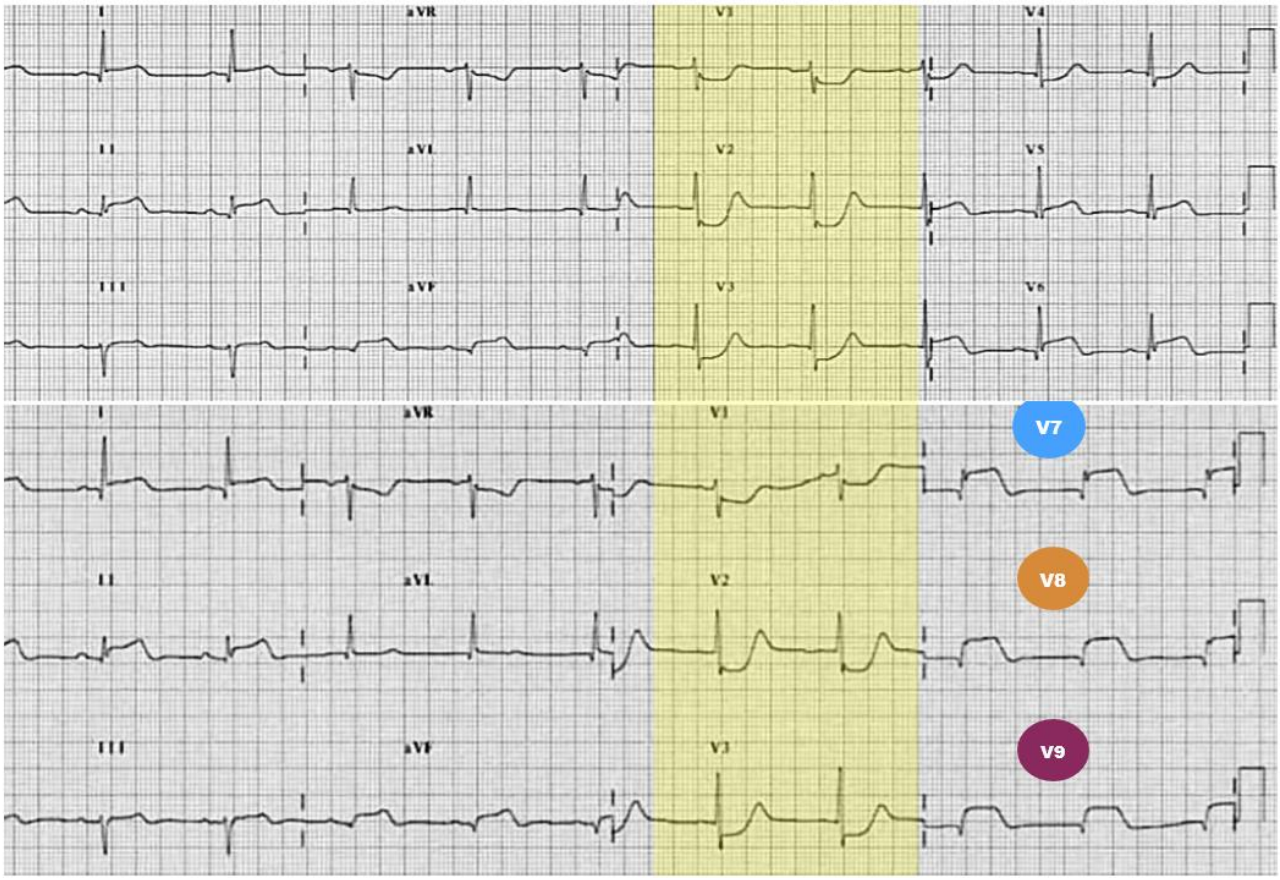
2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

Accessory posterior leads



Leads V7-9 are placed on the posterior chest wall in the following positions:

- V7= Left posterior axillary line, in the same horizontal plane as V6.
- V8 = Tip of the left scapula, in the same horizontal plane as V6.
- V9 = Left paraspinal region, in the same horizontal plane as V6.



The use of additional posterior chest wall leads (V7-V9) in patients with high suspicion or lateral-basal MD (LCx occlusion) should be considered. (**Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HDWriting Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial InfarctionThygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S, ESC Committee for Practice Guidelines. Third universal definition of myocardial infarction. Eur Heart J 2012;33(20):2551–2567.**)(**Rokos IC, Farkouh ME, Reiffel J, Dressler O,**

Mehran R, Stone GW. Correlation between index electrocardiographic patterns and pre-intervention angiographic findings: insights from the HORIZONS-AMI trial. Catheter Cardiovasc Interv 2012;79(7):1092–1098)(Stribling WK, Kontos MC, Abbate A, Cooke R, Vetrovec GW, Dai D, Honeycutt E, Wang TY, Lotun K. Left circumflex occlusion in acute myocardial infarction (from the National Cardiovascular Data Registry). Am J Cardiol 2011;108(7):959–963.) (**Dixon WC4th, Wang TY, Dai D, Shunk KA, Peterson ED, Roe MT. Anatomic distribution of the culprit lesion in patients with non-ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: findings from the National Cardiovascular Data Registry. J Am Coll Cardiol 2008;52(16):1347–1348.**)(**Wang TY, Zhang M, Fu Y, Armstrong PW, Newby LK, Gibson CM, Moliterno DJ, Van de Werf F, White HD, Harrington RA, Roe MT. Incidence, distribution, and prognostic impact of occluded culprit arteries among patients with non-ST-elevation acute coronary syndromes undergoing diagnostic angiography. Am Heart J 2009;157(4):716–723)**

Left circumflex artery occlusion may present with normal ECG. The availability and interpretation of cardiac troponins as described in this statement becomes very important in such lesions (**Huey BL, Beller GA, Kaiser DL, Gibson RS A comprehensive analysis of myocardial infarction due to left circumflex artery occlusion: comparison with infarction due to right coronary artery and left anterior descending artery occlusion.J Am Coll Cardiol. 1988 Nov; 12(5):1156-66**.)

Isolated Lateral wall MI wall MI characterized by isolated ST depression≥0.5 mm inleads V1-V2 and ST elevation (≥0.5 mm) in posterior chest wall leads V7-V9. Should be managed as a **STEMI 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation**

Case report number 3

Acute Myocardial Infarction Due To Acute Total Occlusion Of The Circumflex Coronary Artery Treated as non-ST Segment Elevation Acute Coronary Syndrome (NSTE-ACS)

A seventy-six-year-old man presented to the Emergency Department with oppressive retrosternal chest pain radiating down both arms. Risk factors for coronary artery disease (CAD) included systemic hypertension, diabetes mellitus, and dyslipidemia.

Physical examination: Hemodynamically stable. BP = 130/90 mmHg; HR = 88 bpm and regular; clear lungs; S4 heart sound; absence of murmur.

The 12-lead ECG was obtained without recording of posterior accessory leads (Figure 35). Even with slight ST segment elevation in the inferior leads, a therapy based on non-ST segment elevation acute coronary syndrome (NSTE-ACS) was provided. After 48 h coronary angiography was performed revealing complete occlusion of the circumflex (LCx) artery (arrow, Figure 36). It was decided not to perform percutaneous coronary intervention due to the prolonged time of evolution. The echocardiogram showed akinesis in the inferolateral LV wall.

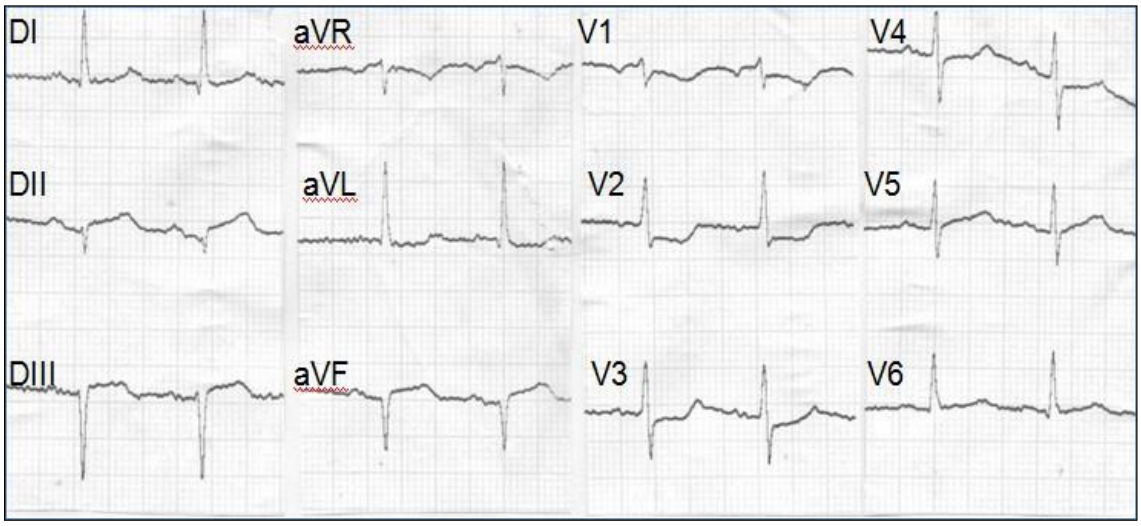


Figure 35. ECG diagnosis: Sinus rhythm, HR 83 bpm. P wave: SAP +60° and posterior; duration 120 ms (prolonged: incomplete interatrial block, LAE, or both?), bimodal P wave in lead II and V3-5; normal PR interval; left axis deviation (SQRS -40°); qR in I and aVL, rS or QS in inferior leads with SIII>SII (LAFB); rs pattern in V1 and Rs in V2 with Q waves in inferior leads and ST depression from V1 to V3; this corresponds to inferolateral infarction according to the new terminology for Q-wave infarctions based on correlation with cardiac nuclear magnetic resonance (lateral wall: segments 6, 3, 11, 12 and 15 and inferior segments 15, 10 and 4 “bullseye” [bullseye heart magnetic resonance image]). ST segment depression is present in V1-V3, and ST segment elevation is present in the inferior leads suggestive of an infero-lateral ST segment elevation AMI (STEMI).

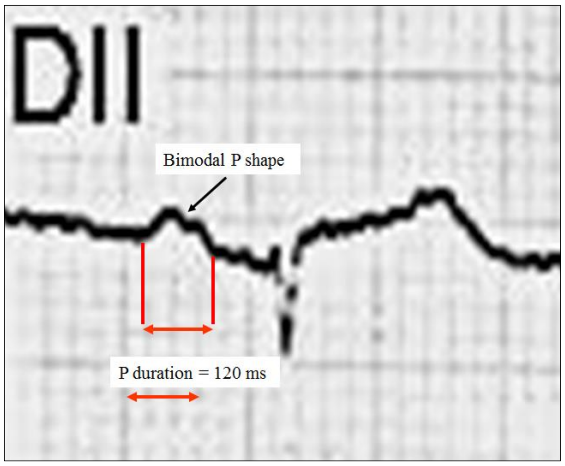


Figure 36. The P wave duration (120 ms) is prolonged suggesting incomplete first degree interatrial block and/or left atrial enlargement (LAE). LAE and interatrial block are frequently related. First degree interatrial block is common and is related to an increased incidence of atrial fibrillation with an increase in overall and cardiovascular mortality [42].

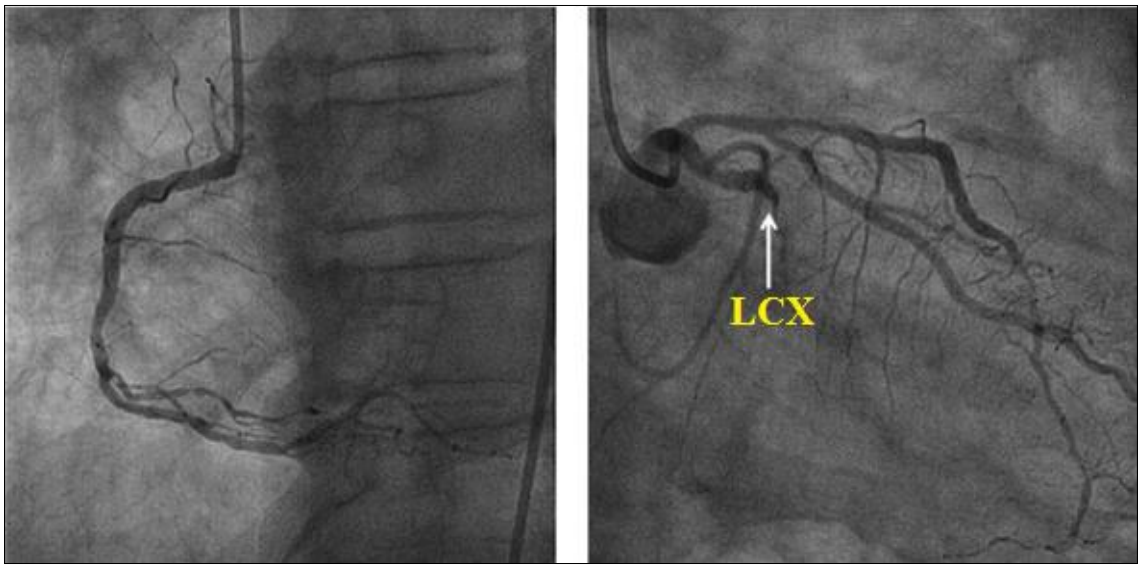


Figure 37. Coronary angiography indicates obstructive lesions in the distal RCA, total occlusion of the LCx artery, and 70% proximal LDA occlusion with distal portion sharpening.

ST segment elevation is the *sine qua non* condition for the diagnosis of transmural AMI resulting from total acute coronary occlusion; however, when the culprit artery is the LCx, ST segment elevation is only observed in approximately 50% of cases [43] [44] [45].

The LCx artery originates from the left main coronary artery and follows a trajectory below the left atrium in the AV groove; it gives off marginal branches that perfuse the LV lateral wall and the left posterior ventricular branch perfusing the infero-basal LV wall (formerly called the dorsal or true posterior wall).

The terms “posterior” or dorsal, used in the International Society for Holter and Noninvasive Electrocardiography (ISHNE) guidelines, should be discontinued [46]. Studies of cardiac NMR-ECG correlation showed that the so-called posterior wall actually corresponds to the basal portion of the inferior wall or segment 4 in the bullseye view.

Q waves never appear in an infarction in segment 4 (basal-inferior) because activation in this region occurs later during the middle and final portions of the QRS (between the 30 and 100 ms); i.e., in the second half of the QRS. Pathologic Q or QS waves occur during the first 40 ms of the QRS.

The infarction of the basal region of the LV causes a late anterior shift of the QRS loop in the horizontal plane because the QRS loop area is located at

least 50% anteriorly (in the front of the orthogonal X). In 40% of the cases this anterior shift of the middle-to-final portion of the QRS loop may cause a triphasic QRS complex (rSr', rSR' or rsR') in V3R or V1 resembling IRBBB (pseudo-IRBBB).

The septal depolarization vectors, vectors 1 (initial septal vector 10-20 ms) and 2 (vector of the low portion of the septum from 20-40 ms), are not affected; only the anterior shift of vector 3 of the LV and RV free walls and vector 4 of the basal wall are significant.

According to the National Cardiovascular Data Registry (NCDR) data, approximately one-third of patients with AMI due to acute LCx occlusion present as NSTE-ACS [45].

Current guidelines for patients presenting with ST segment depression in V1-V4 associated with high R waves and positive T waves consider this to be an infero-lateral STEMI equivalent according to the universal definition of AMI [47, 48 49-51].

When ST segment depression extends into other leads (V4-V6), the differential diagnosis should include subendocardial ischemia, making the identification of the culprit vessel more difficult. Since conventional 12-lead ECG is incapable of detecting ST segment elevation in the infero-lateral wall (basal-inferior portion) this differential diagnosis becomes more difficult [52 53].

Some physicians believe that when the magnitude of the ST segment depression in the V4-V6 leads is much greater than in leads V1-V3, the presence of diffuse subendocardial ischemia and not transmural inferior-lateral ischemia is more likely. One way of resolving this differential diagnosis is the use of accessory posterior leads V7-V9 [54]. These leads enable the identification of up to 20% of the patients with infero-lateral AMI that could benefit with early reperfusion therapy. In spite of the class IIa recommendation by the European Society of Cardiology, use of these additional leads frequently is not made [47, 48].

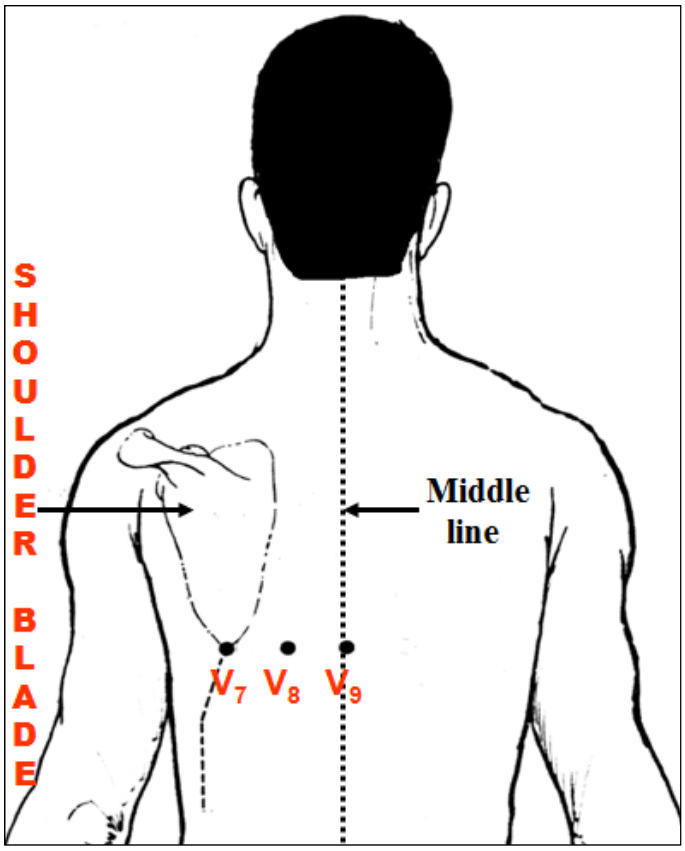


Figure 38. The figure shows the location of the posterior accessory leads V7, V8 and V9.

New electrocardiographic terminology for Q wave infarctions based on the correlation to cardiac NMR in reference to the obstruction in the territory of the left circumflex artery [55] [56] [57]

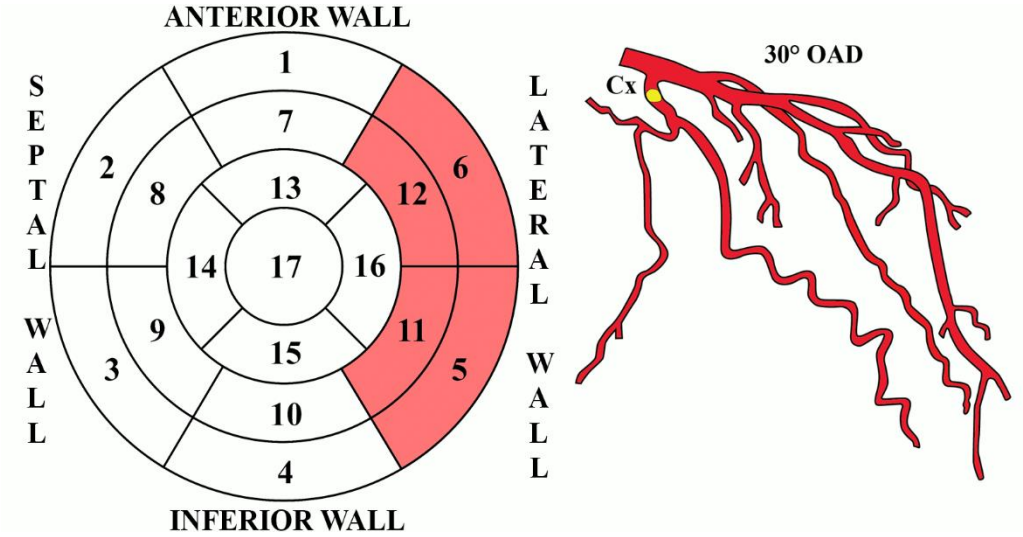


Figure 39. Lateral myocardial infarction: RS in V1-V2 and/or Q in I, aVL, V5-V6, R voltage with minor amplitude. New electrocardiographic terminology for

Q wave infarctions based on the correlation to cardiac NMR in reference to the obstruction in the territory of the left circumflex artery.

- Type: B-1
- Most likely site of occlusion: LCx artery or its marginal oblique branch
- ECG pattern: SR in V1-V2 and/or Q in I, VL, V5-V6. Voltage of R wave in V6 of lower amplitude.
- Segments affected by infarction in cardiac Nuclear Magnetic Resonance (NMR): 6, 5, 12, 11 and 10.
- Sensitivity: 67%
- Specificity: 99%.

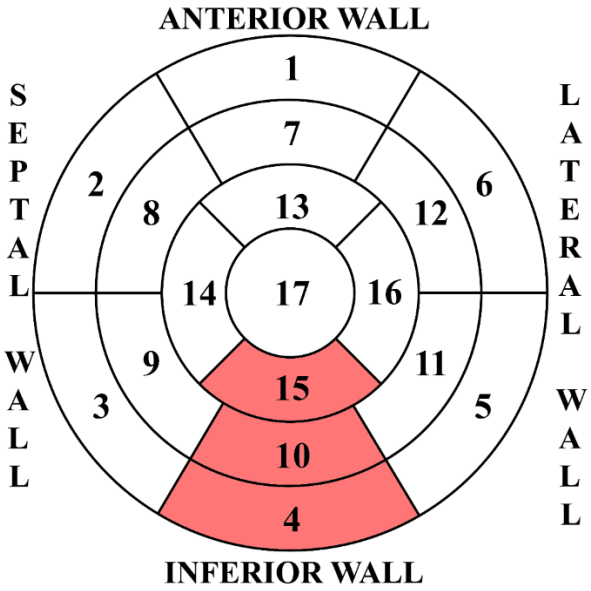


Figure 40. Inferior myocardial infarction (B-2). New electrocardiographic terminology for Q wave infarctions based on the correlation to cardiac NMR in reference to the obstruction in the territory of the left circumflex artery.

- Type: B-2
- Most likely site of occlusion: middle third of RCA.
- ECG pattern: Q and Qr in II, III and aVF.
- Segments affected by infarction in cardiac NMR: 4 and 10.

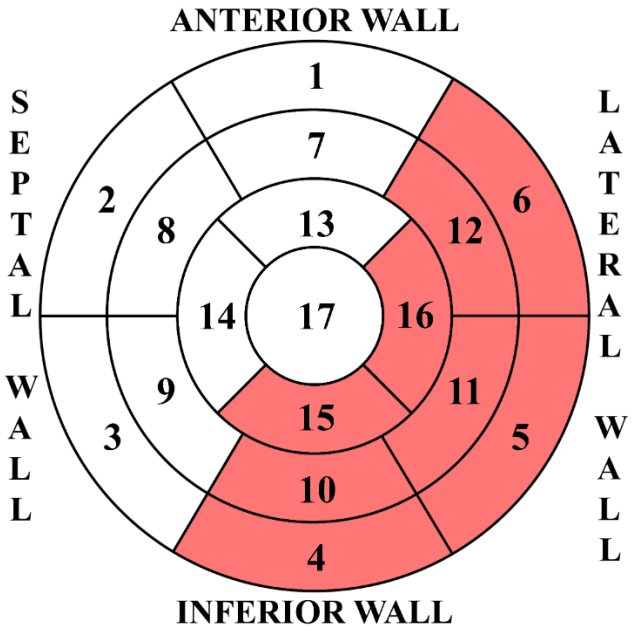


Figure 41. Inferolateral myocardial infarction (B-3). New electrocardiographic terminology for Q wave infarctions based on the correlation to cardiac NMR in reference to the obstruction in the territory of the left circumflex artery.

- Type: B-3
- Most likely site of occlusion: proximal RCA.
- ECG pattern: QS in II, III and aVF and Q in I, aVL, V5-V6.
- Segments affected by infarction in cardiac NMR: 15, 10 and 4/5, 6, 12, 11 and 16.

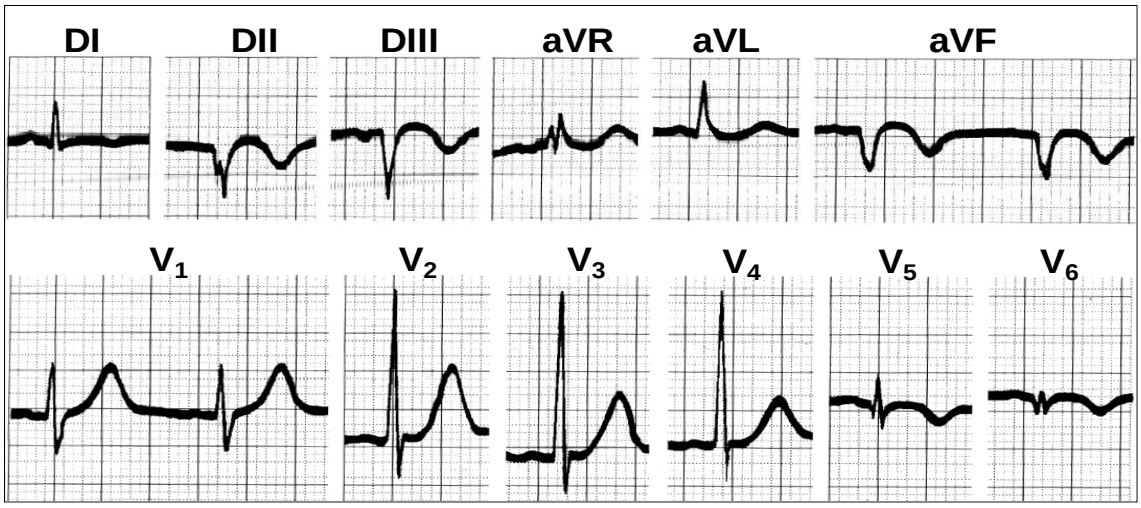


Figure 42. ECG diagnosis: Inferolateral electrically inactive area corresponding to B3 infarction (Figure 5C) using the new ECG/cardiac NMR correlation classification: QS in II, III and aVF with prominent R in V1-V2 and low voltage r/R in V5 and V6. Inferior infarction is extensive, affecting the entire inferior wall, which explains the absence of final r or R wave in II, III and aVF. Involvement of the low lateral or apical wall represented by small r waves in leads V5 and V6 indicates that the necrosis also extends into this wall. Prominent R waves in V1-V2 are no longer thought to be caused by true posterior or dorsal infarction but to lateral left ventricular wall infarction. The coronary angiogram in this case revealed total obstruction of the posterior descending branch of a dominant left circumflex artery.

Figure 43 illustrates an example of a patient with symptoms of acute chest pain, in which the posterior accessory leads were essential for the diagnosis of ST segment elevation AMI. Coronary angiography revealed total acute occlusion of the LCx artery.

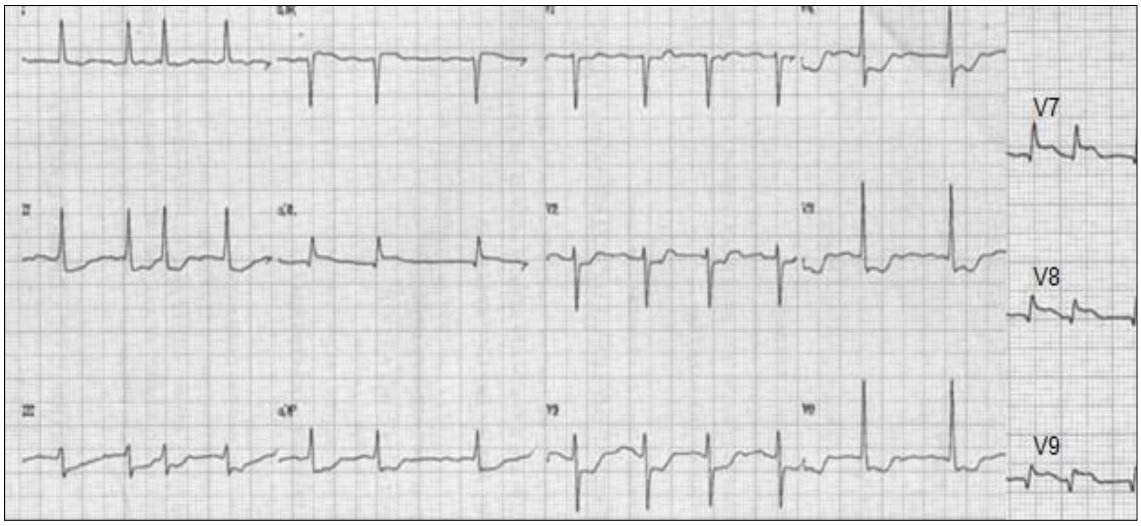


Figure 43. ECG diagnosis: Atrial fibrillation, LVH, and ST segment depression in the inferior leads and leads V2-V6. Only the posterior accessory leads V7-9 revealed pathologic Q waves and ST segment elevation (STE-ACS). A recent study was done evaluating the percent of patients presenting with equivocal ECG criteria of ST segment elevation AMI that were mistakenly managed as non-ST segment elevation AMI. The results showed 55% of patients that exhibited ST segment depression from V1 to V6 and inferior ST segment elevation had angiographic evidence of LCx occlusion [58-60].

Figure 44 shows an example of a patient admitted with prolonged precordial pain and ST segment depression from V1 to V4 without ST segment elevation; coronary angiography the next day revealed total occlusion of marginal branch of the LCx artery.

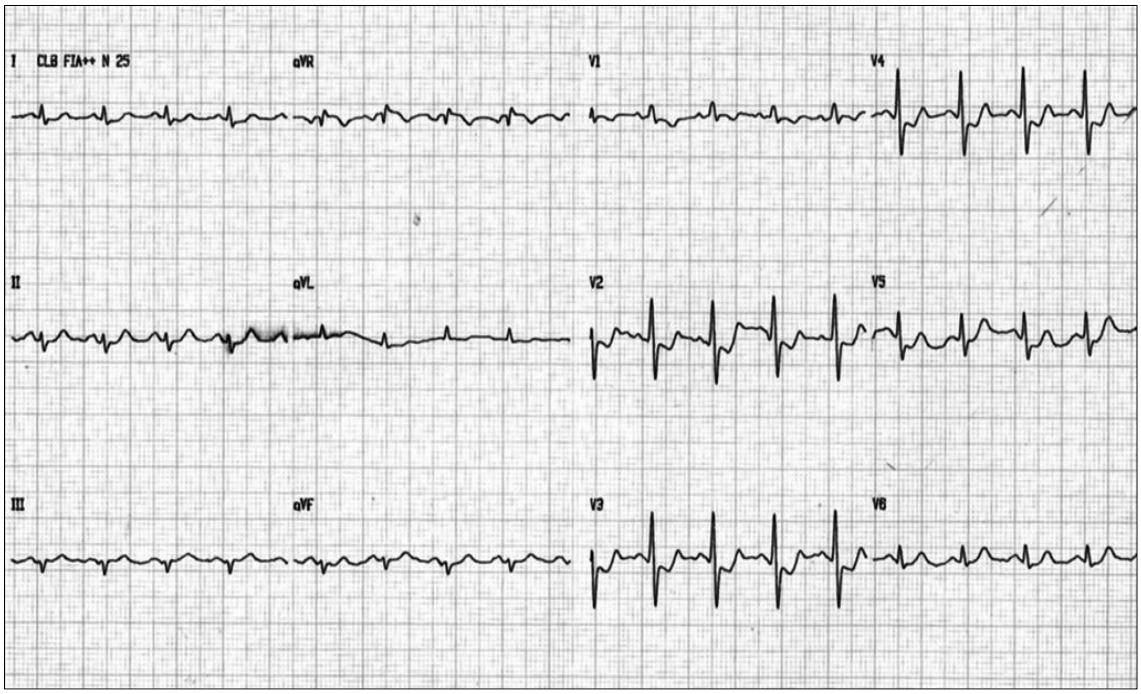


Figure 44.

Consequences of not making an early diagnosis

There are no large, randomized studies in literature to analyze the consequences of not recognizing by ECG an acute occlusion of the LCx artery. However, it is known that acute LCx occlusion with inferior or infero-lateral necrosis can result in rupture of the postero-medial papillary muscle with severe hemodynamic consequences due to mitral valve regurgitation, worsening congestive heart failure, acute pulmonary edema, and cardiogenic shock. Often vasoactive drugs and mitral valve replacement are needed in addition to revascularization in the acute stage [61].

An early diagnosis and emergency surgery are mandatory before these complications develop [62]. Transesophageal echocardiogram has a high sensitivity for this diagnosis. Thus, in the setting of cardiogenic shock associated with acute inferior or infero-lateral infarction, severe mitral valve regurgitation should be suspected and confirmed with this technique even when a regurgitation murmur is not audible. The sensitivity of transthoracic echo and left ventriculography is lower than that of transesophageal echo [63] [64].

Figure 45 below shows an example of a woman mistakenly treated as NSTE-ACS that, on the second day of admission, evolved into acute pulmonary edema. Echocardiogram revealed infero-lateral LV akinesis, EF of 38%, and

severe mitral valve insufficiency. Coronary angiography revealed total LCx marginal branch occlusion; 50% lesion in the middle third of the LDA; 70% in the middle third of the RCA and 90% in the posterior ventricular branch.

Ventriculography confirmed severe mitral valve insufficiency. The patient was referred to emergency surgery with mitral valve replacement.

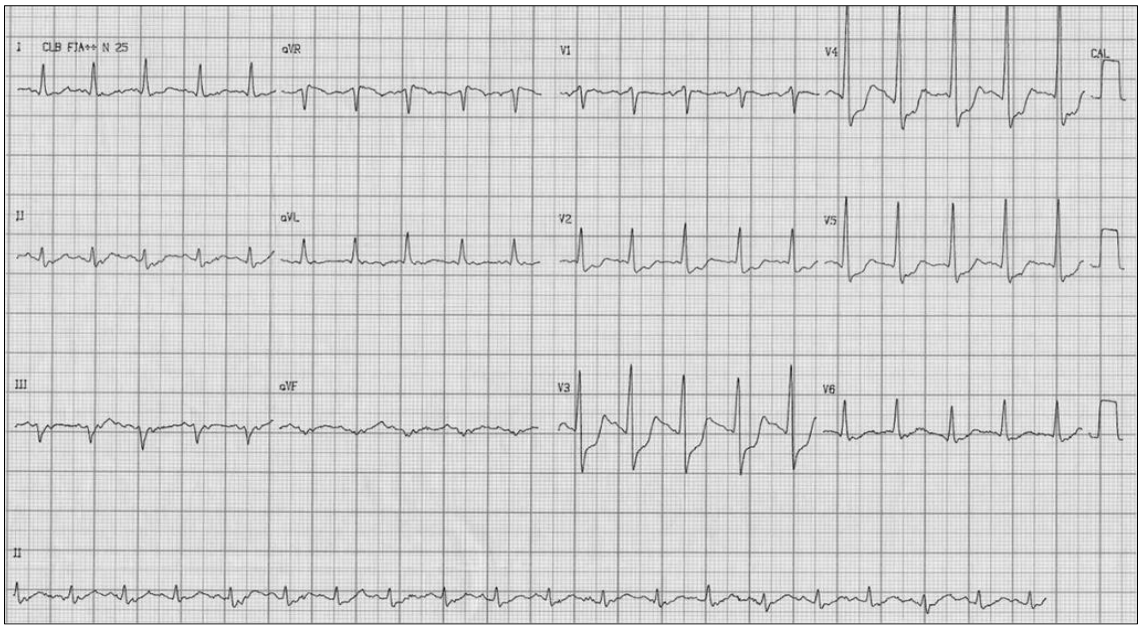


Figure 45. ECG diagnosis: Sinus tachycardia 148 bpm, prominent R in V2 (Rs) and ST segment depression from V2 through V5. On the occasion of total occlusion of the LCx artery, typical inferior or infero-lateral wall ST segment elevation changes of a STEMI appear, enabling appropriate early management.

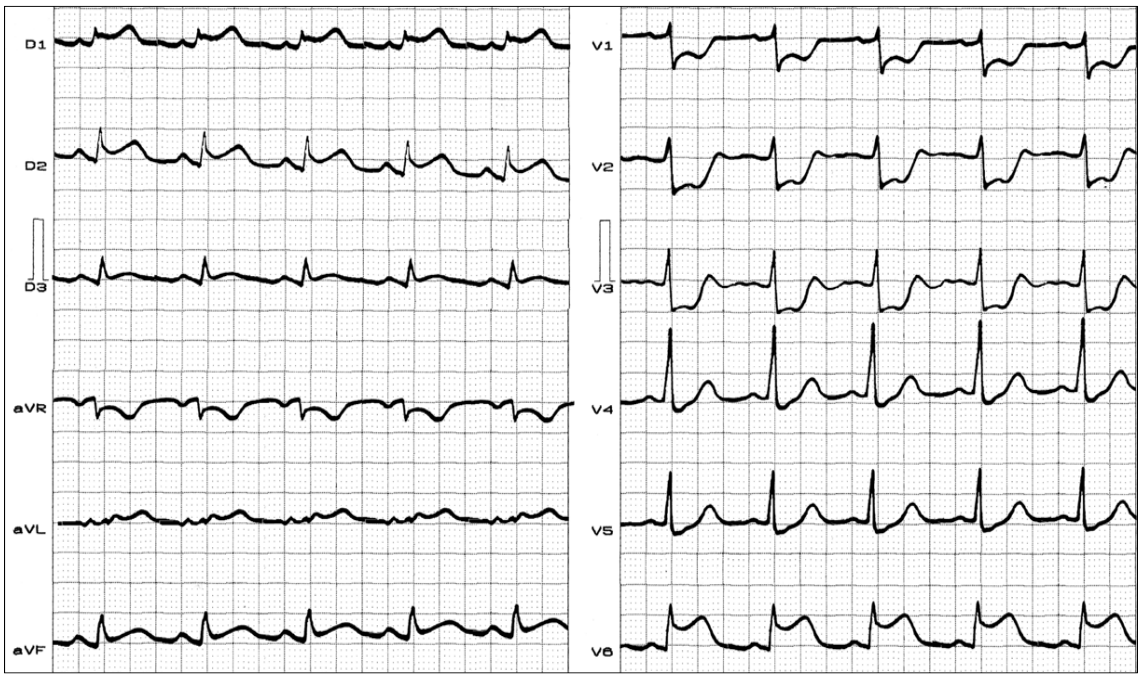


Figure 46. ECG diagnosis: Significant ST segment elevation is observed in the infero-lateral wall leads and significant ST segment depression from V1 to V3. Infarction in the hyperacute phase with ST segment elevation in the infero-lateral region (STEMI-ACS) required an immediate intervention.

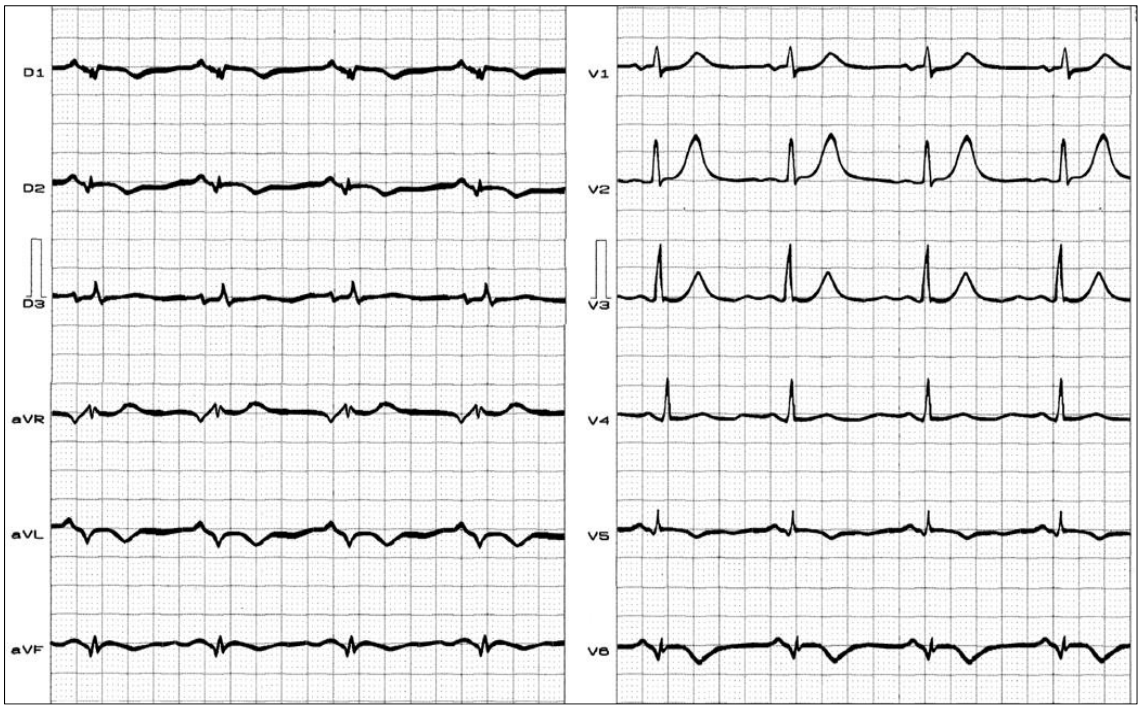


Figure 47. This ECG is from the same patient, made 20 days after the event. Q waves appeared in the inferior wall, prominent R waves from V1 to V3 with positive and symmetrical T waves, low voltage of R in V5-V6 and QS in I and aVL. These changes represent inferolateral myocardial infarction in the late phase.

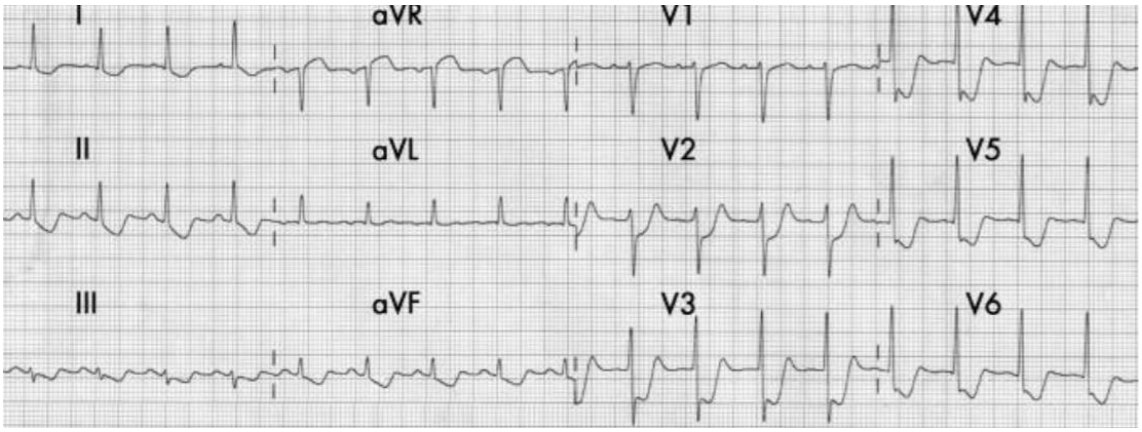
Conclusions:

In ACS patients presenting with new ST segment depression in leads V1-V3 who are suspected of acute occlusion in the LCx artery, it is important to add the posterior accessory leads V7-V9.

If the ST segment elevation is confirmed in these leads, these patients should undergo emergency myocardial reperfusion therapy according to STEMI guidelines.

This approach will often prevent an unfavorable outcome resulting from the lack of identification of circumflex artery occlusion.

ECG in left main coronary artery (LMCA) critical obstruction disease or or multivessel disease



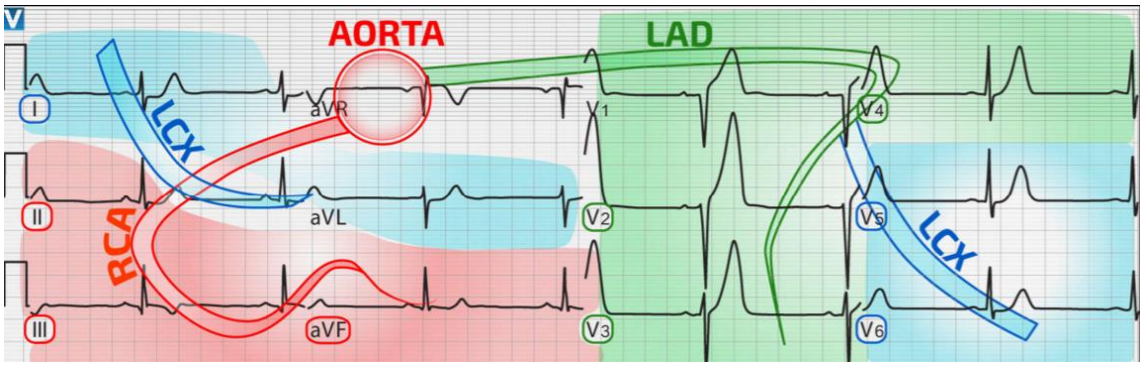
ECG diagnosis ST/T elevation in aVR suspected in LM disease

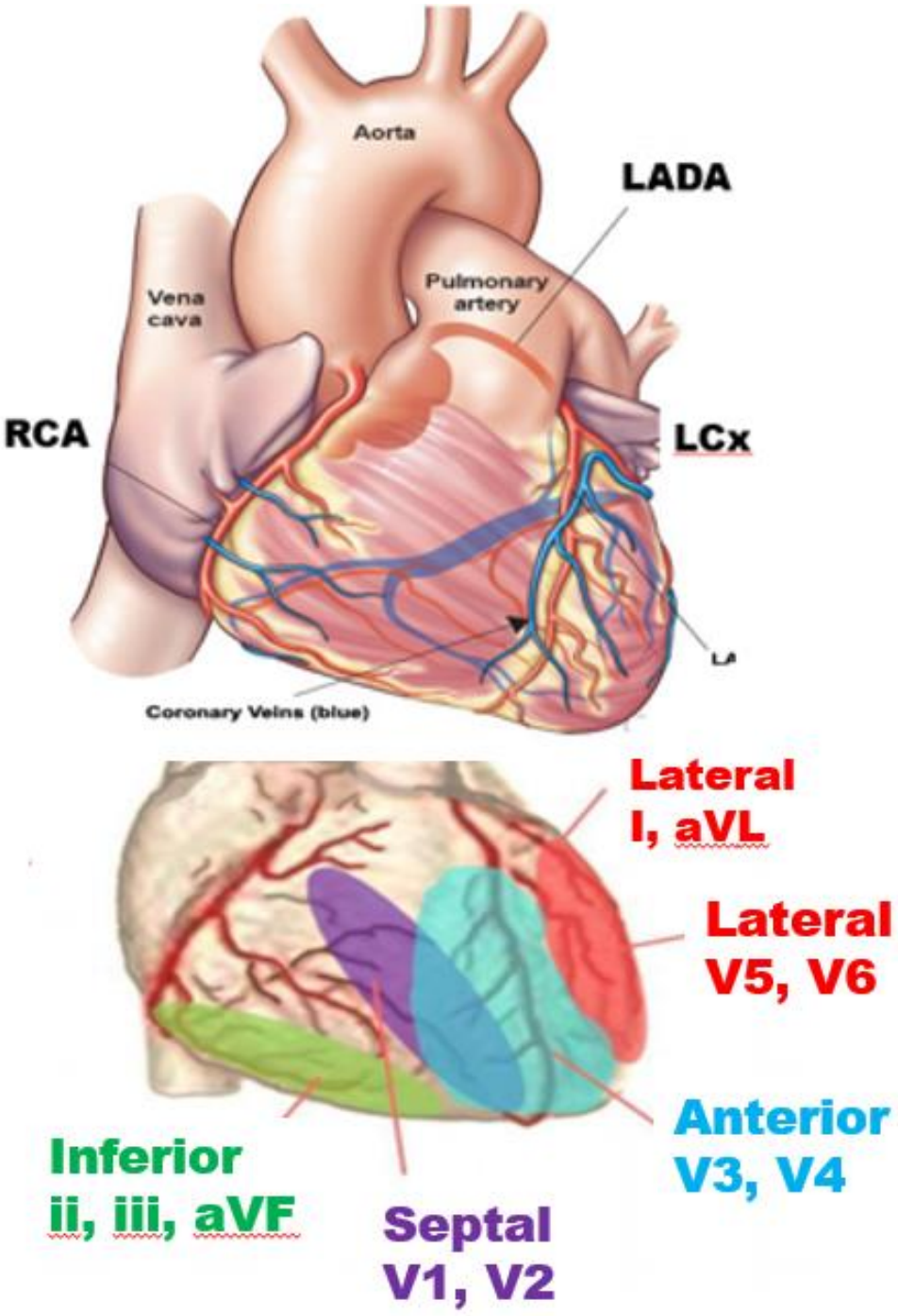
Ischemia due to LMCA occlusion or multivessel disease

ST depression≥1mm in ≥8 surface leads, coupled with ST-segment elevation in aVR and /or V1, suggests LMCA, or left Main equivalent- coronary obstacle, or severe three vessel ischemia

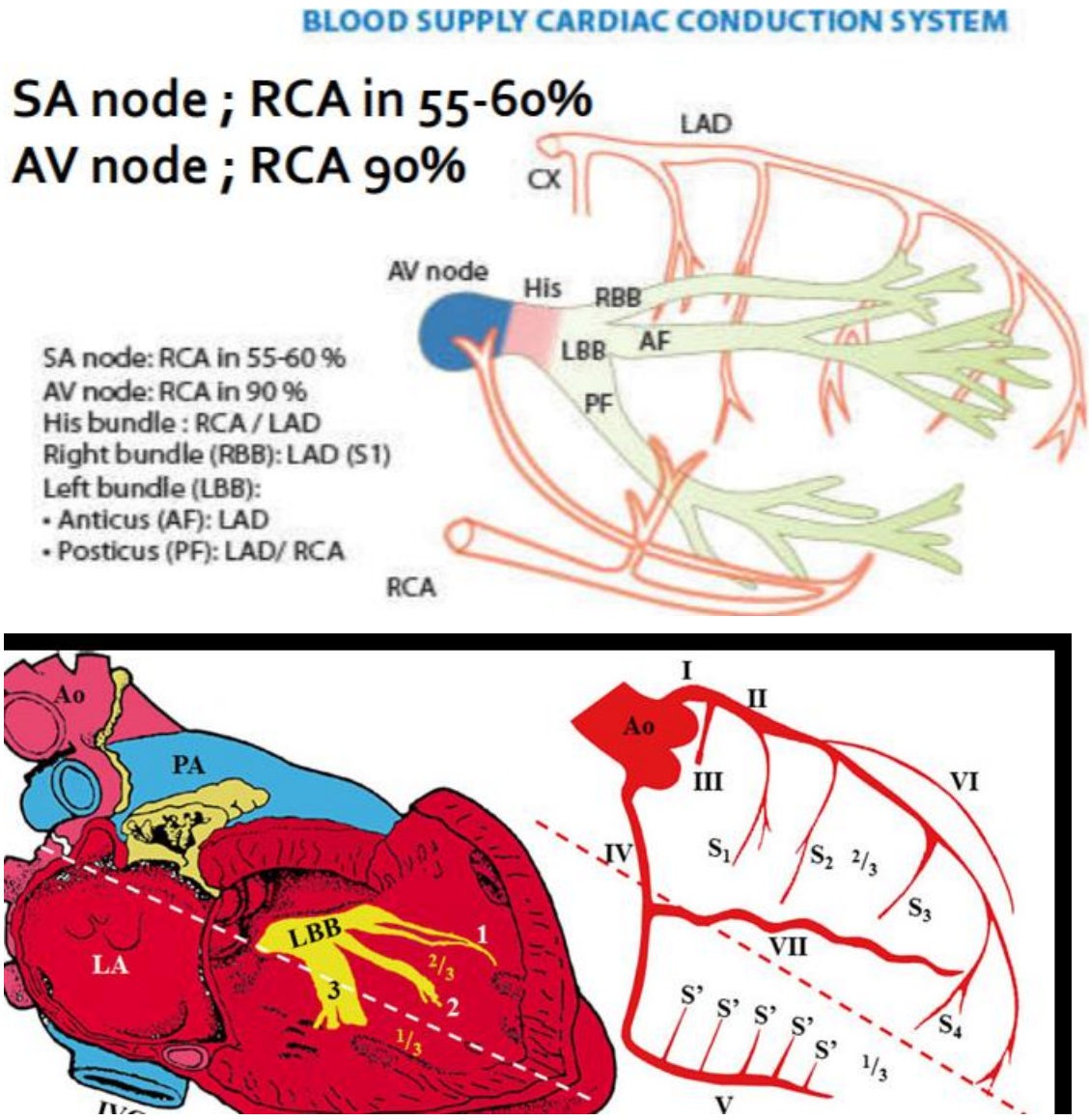
ST-segment elevation in lead aVR with specific repolarization patterns, as a STEMI equivalent ***2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation Fourth universal definition of myocardial infarction, EHJ (2018) 00,1-33***

Coronary blood supply and conduction system as ECG lead





Blood Supply Cardiac of Conduction System



Schematic diagram of blood supply to the cardiac conduction system

Left Main Coronary Artery (LMCA)

Left Anterior Descending Artery (LAD)

Left Circumfl ex Coronary Artery (LCX)

Right Coronary Artery (RCA)

Posterior Descending Artery (PDA). In this case is supplied by the RCA, then coronary circulation

can be classifi ed as “right-dominant”

First Diagonal (Dg)

Acute Marginal (A. Mg)

S1: First Septal Perforator branch

S2: Second Septal Perforator

S3: Third Septal Perforator

S4: Fourth Septal Perforator
2 3 of IVC
S': Posterior Septal Perforating branches: 1 / 3 of IVC
(1) Left Anterior Fascicle (LAF)
(2) Left Septal Fascicle (LSF)
(3) Left Posterior Fascicle (LPF)
Schematic diagram of blood supply to cardiac conduction system. The first septal branch of the left
anterior descending (LAD) coronary artery supplies a critical portion of the interventricular conduction system. The LSF receives its blood supply exclusively from the septal perforating
branches of the LAD. The septal branches of the LAD supply two-thirds of the anterior portion of
the IVS, while the inferior portion of the septum is supplied by septal branches of the PDA, which
usually arises from the RCA and infrequently from the LCX.
Critical lesions of the LAD before the fi rst perforating septal branch (S1) constitute the main cause
of left septal fascicular block (LSFB). It is a major determinant of R wave amplitude during acute
myocardial ischemia. The LSFB may be exercise-induced, transient or intermittent, and may be
the cause of giant anterior precordial R waves (Nakaya et al. 1978 ; Tranchesi et al. 1979 ; Deanfi eld et al. 1983 ; Hassapoyannes and Nelson 1991 ; Moffa et al. 1996). The appearance of LSFB in critical LAD lesions speaks in favor of the proximal lesion, and therefore of a worse prognosis.
Intermittent LSFB, secondary to critical lesions of LAD, was observed during exercise testing
(Uchida et al. 2006), intermittently in acute coronary syndrome (ACS) scenarios including the so called Wellens' syndrome (Riera et al. 2008a , b , c). Wellens' syndrome is also known as: LAD
coronary T-wave syndrome or acute coronary T-wave syndrome.

NSTEMI "subendocardial ischemia"

♣ Clinical spectrum of acute coronary syndrome

♣ sub-total occlusion of coronary vessel

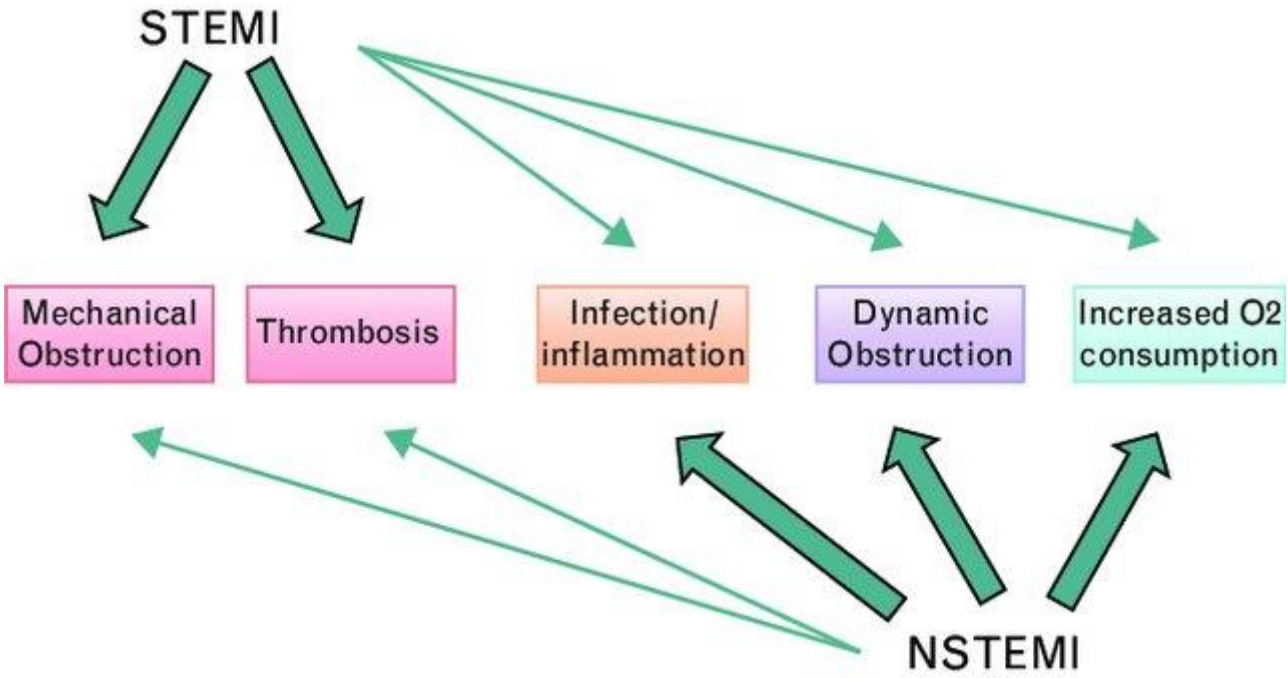
♣ Current guideline emphasizes risk stratification of UA/NSTEMI patients with respect to selecting a conservative versus an early invasive approach.

Ragavendra R. Baliga, MD, MaGraw-Hill Specialty Board Review, ISBN 978-0-07-161410-8

ECG manifestations suggestive of acute NSTEMI (in the absence of LVH and BBB)

Acute coronary syndrome (ACS) can be divided into subgroups of ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina. ACS carries significant morbidity and mortality and the prompt diagnosis, and appropriate treatment is essential. ST-depression and T-wave changes: New horizontal or down sloping ST-depression ≥ 0.5mm in two contiguous leads and/or T inversion>1mm in two contiguous leads with prominent R wae or R/S ratio >1, NSTEMI is diagnosed in patients determined to have symptoms consistent with ACS and troponin elevation but without ECG changes consistent with STEMI. Unstable angina and NSTEMI differ primarily in the presence or absence of detectable troponin leak.

(**Gilutz H, Shindel S, Shoham-Vardi I. Adherence to NSTEMI Guidelines in the Emergency Department: Regression to Reality. Crit Pathw Cardiol. 2019 Mar;18(1):40-46.**)



The pathophysiological mechanisms underlying ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI). While STEMI is due to acute plaque rupture and thrombus formation, NSTEMI is due to dynamic imbalance between myocardial oxygen demand and delivery.

Clinical Criteria for MI The clinical definition of MI denotes the presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia.

Criteria for Myocardial Injury Detection of an elevated cTn value above the 99th percentile URL is defined as myocardial injury. The injury is considered acute if there is a rise and/or fall of cTn values. Kristian **Thygesen et al. ESC/ACC/AHA/WHF EXPERT CONSENSUS DOCUMENT Fourth Universal Definition of Myocardial Infarction (2018)**

Explanation The 99th percentile upper reference limit value of troponin I is given by the manufacturer based upon the results of troponin values obtained from a healthy reference population in that area. The 99th percentile upper reference limit value means that almost every normal person will have a value of troponin below the upper reference range obtained by that sample. So if the value of troponin is above the 99th percentile, that is not normal.

99th percentile values may vary from one ethnicity to the other, even when they come from the same manufacturer.

It is however important to note that level above 99th percentile upper reference limit is not by itself diagnostic of MI. It requires presence of clinical signs and symptoms and ECG changes in addition to troponin levels to diagnose it as MI. Mild elevation of troponin enzymes above reference limits may be found in chronic kidney disease, tachycardia, myocarditis, hypertensive heart disease, cardiomyopathies, atrial fibrillation, and many other disorders.

The problem also arises when one is trying to differentiate between high and low risk chest pain patients.

Vivek Chauhan, et al. have reviewed the low-risk chest pain and how the use of troponin I helps is this. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5357871/ (**Vivek Chauhan, et al. The 2017 International Joint Working Group recommendations of the Indian College of Cardiology, the Academic College of Emergency Experts, and INDUSEM on the management of low-risk chest pain in emergency departments across India. J Emerg Trauma Shock. 2017 Apr-Jun; 10(2): 74–81.doi: 10.4103/JETS.JETS_148_16**)

Morphology of ST-depression and T wave changes

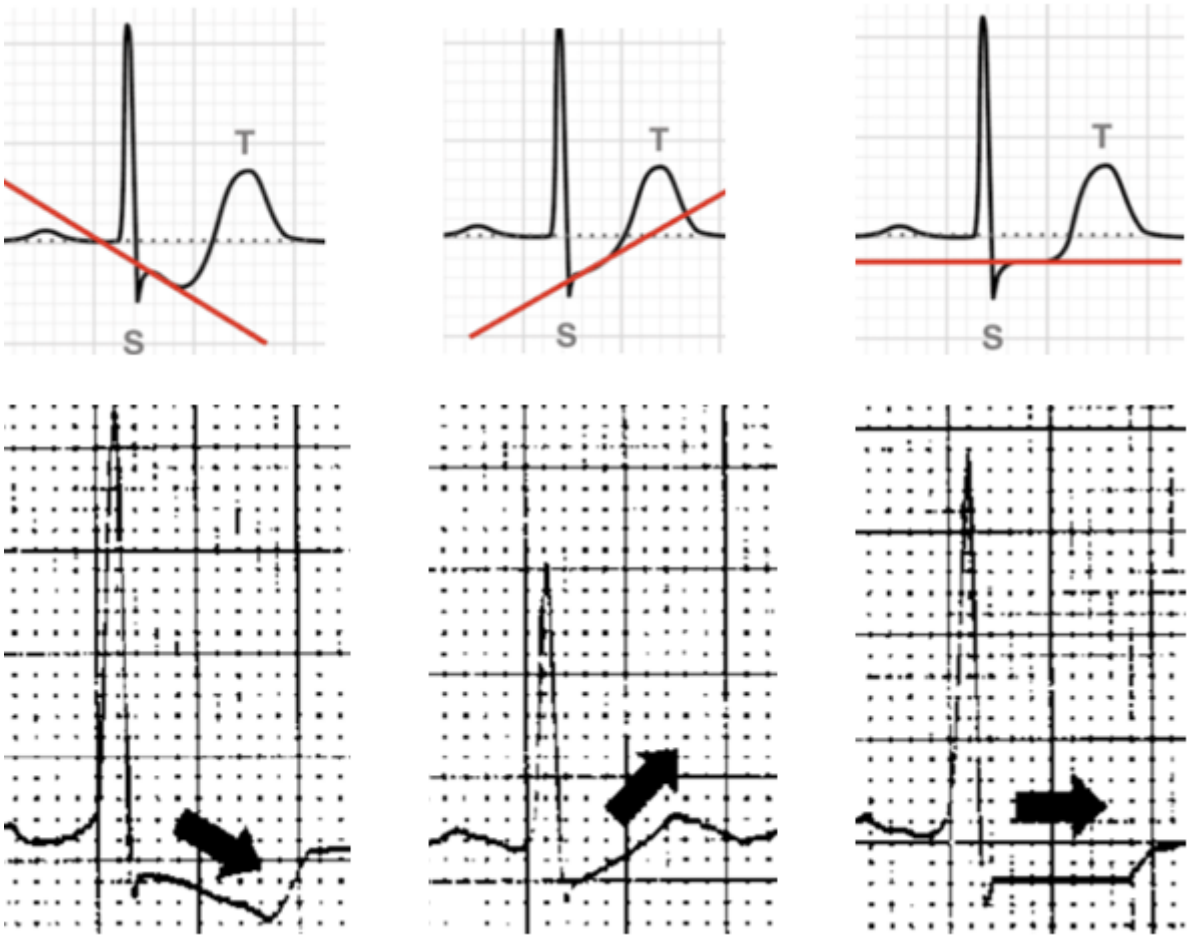
ST depression can be either downsloping, upsloping or horizontal (see figure below)

New horizontal or downsloping ST-depression ≥ 0.5 mm at the J-point in ≥ 2 contiguous leads with prominent R waves or R/S ratio >1indicate myocardial ischemia (according to the 2007 Task Force Criteria).

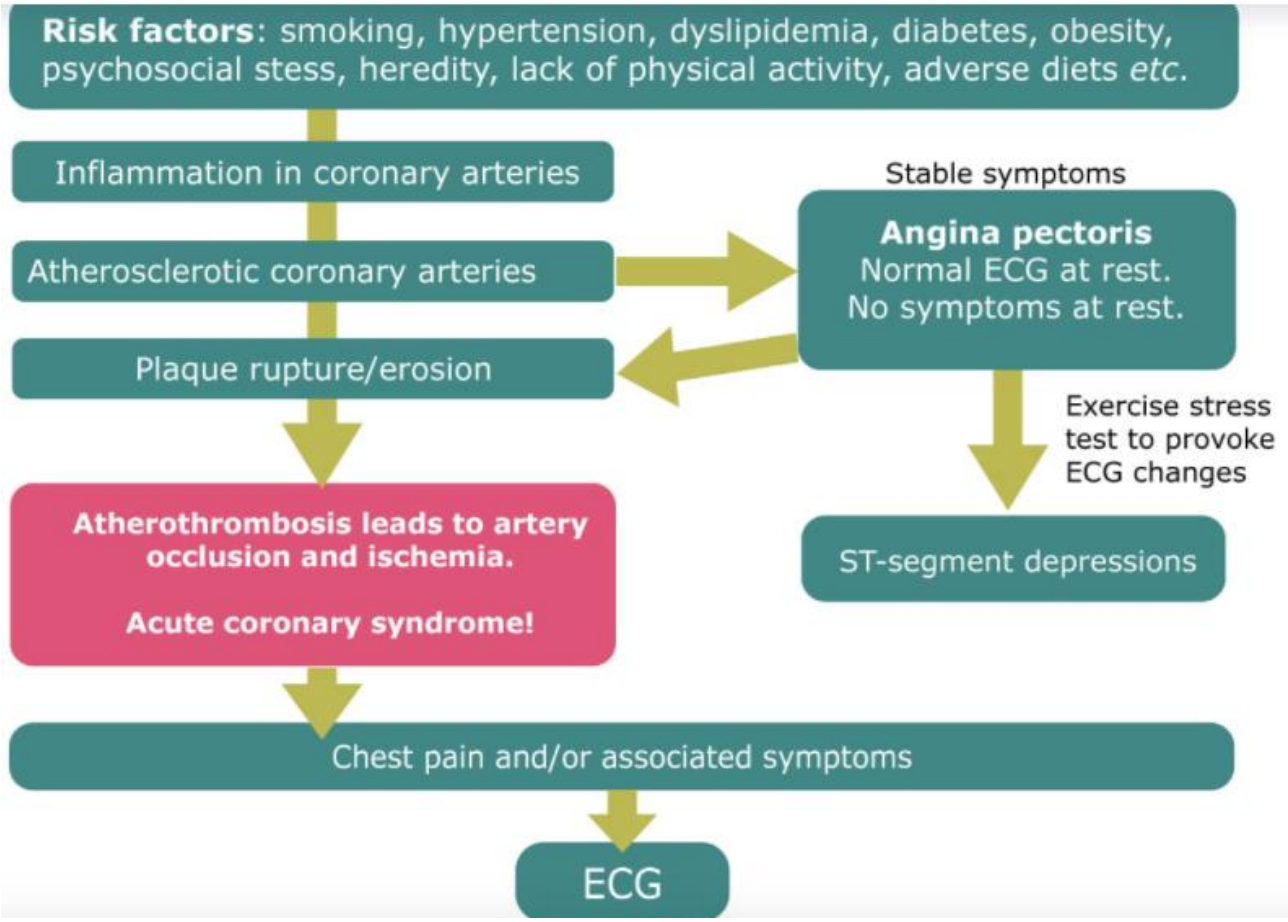
ST depression ≥ 1 mm is more specific and conveys a worse prognosis.

ST depression ≥ 2 mm in ≥ 3 leads is associated with a high probability of NSTEMI and predicts significant mortality (35% mortality at 30 days).

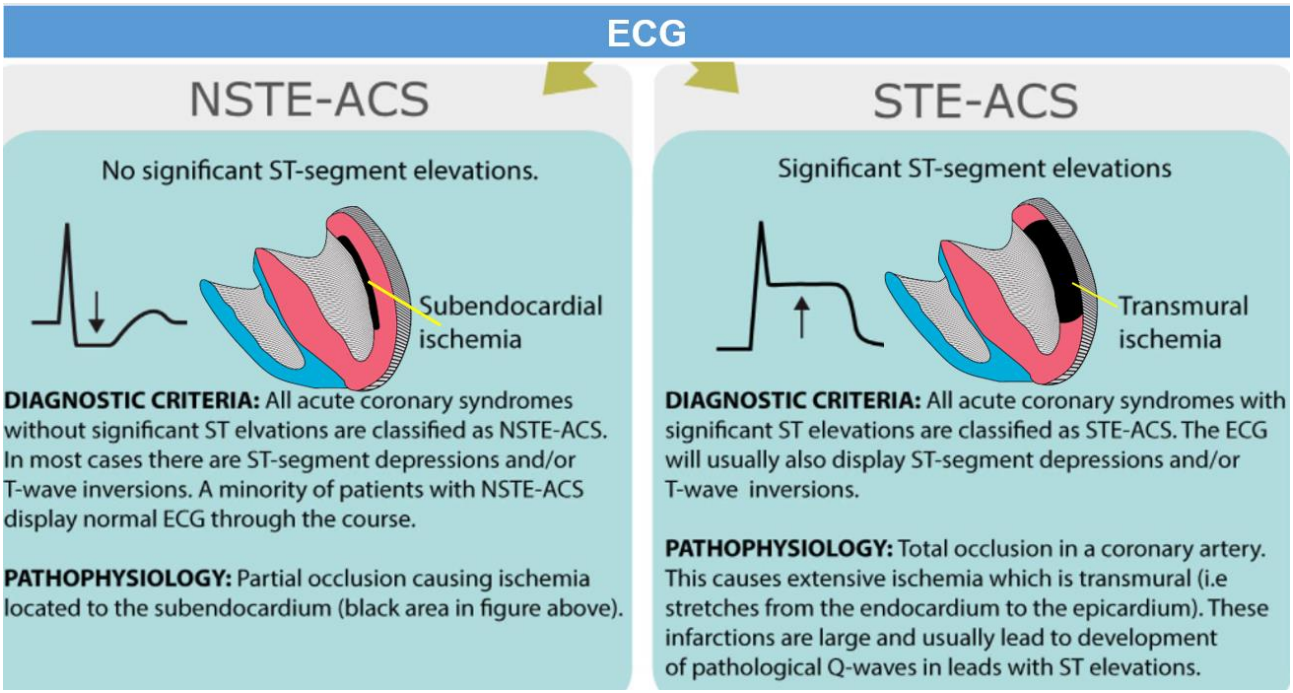
Upsloping ST depression is non-specific for myocardial ischemia.



Down sloping and horizontal ST depression are more specific for sub-endocardial ischemia (*George J. Tayor, MD, 150 Practice ECGs: Interpretation and Review, ISBN – 13: 978-1-4051-0483-8*)



Subendocardial ischemia (NSTE-AVS/NSTEMI)



The ST-vector becomes directed towards the back in subendocardial ischemia. The precis angle will vary depending on the location and size of the ischemic area. No ECG leads has an exploring electrode in front of the

ST-vector, which dis why no ST elevations appear, Instead, leads which detect the ST vector will display ST-segment depression (this vector will head away from all exploring electrodes).

The T-wave vector may also be directed towards the back, which yields negative T-waves in the leads located in front of the explorer electrode.

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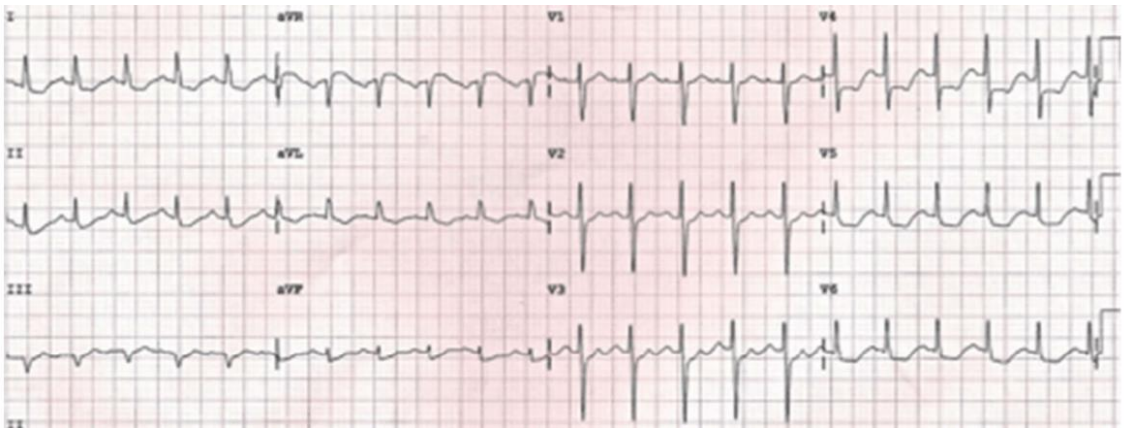
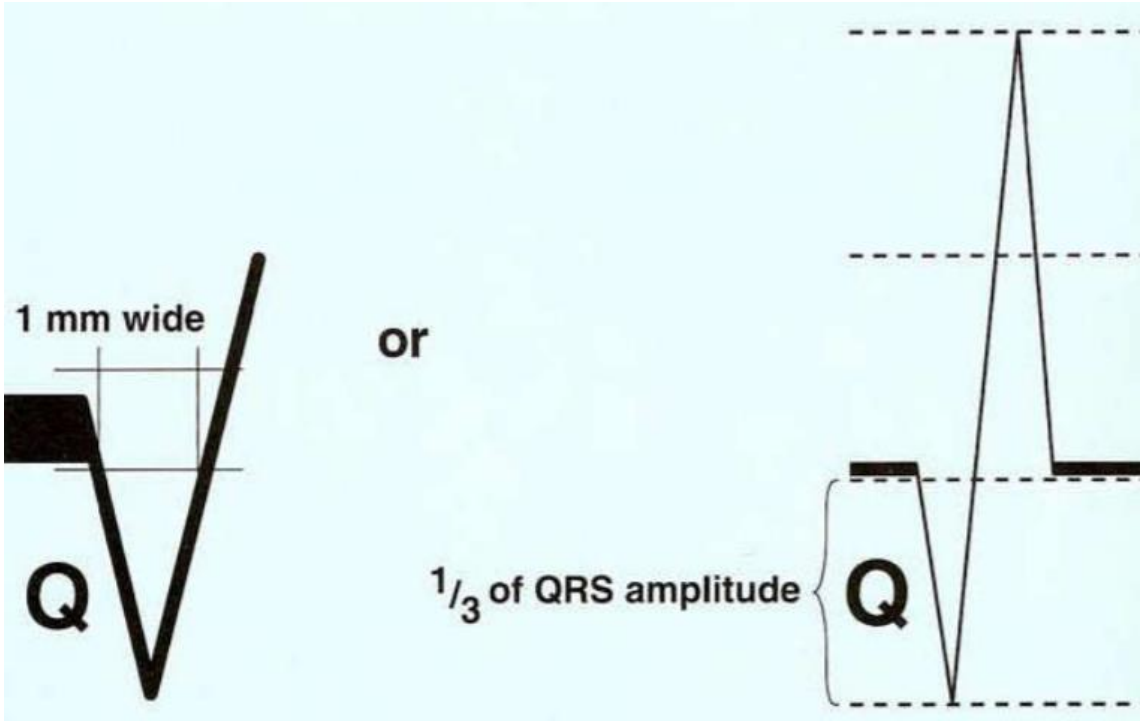
Example

Horizontal ST/T segment depression in V4-V6



Significant Q wave



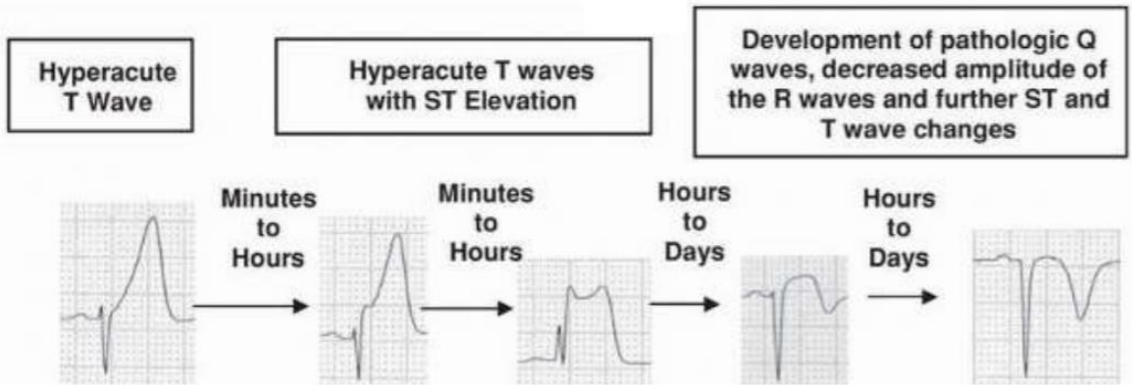
ECG changes associated with prior myocardial infraction (in the absence of LBBB and LVH)

Any Q wave in leads V_2-V_3 > 0.02 s or QS complex in leads V_2-V_3.
Q wave ≥ 0.03 s and ≥ 1 mm deep or QS complex in leads I, II, aVL, aVF or V_4-V_6 in any two leads of a contiguous lead grouping (I, aVL; V_1-V_6; II, III, aVF).[a]

Fourth universal definition of myocardial infarction, EHJ (2018) 00,1-33

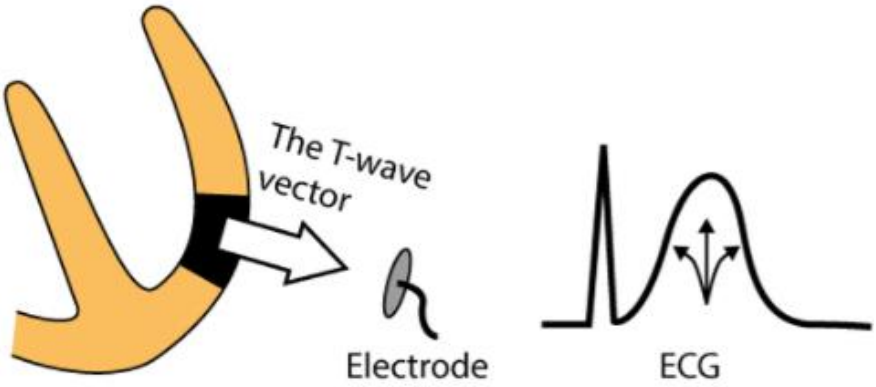
STEMI - timing of ECG change Hyper-acute T wave with ST elevation Decrease R wave and develop Q wave

Minute to hour (s) Hours to day



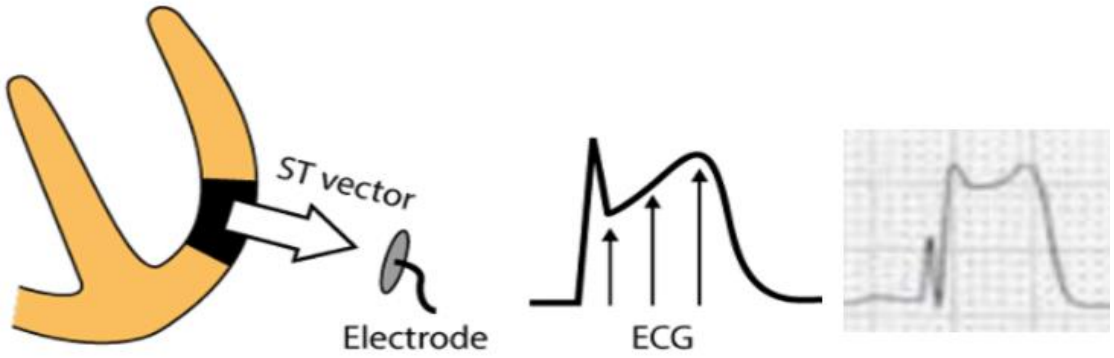
Bayes de Luna, The 12-lead ECG in ST elevation myocardial infraction, ISBN-13: 978-1-4051-5786-5

Hyperacute T wave



In the hyperacute phase of transmural ischemia (the first few minutes the T wave vector becomes amplified and it is directed from the endocardium to the epicardium in the ischemic area. This appears as hyperacute T-wave vector. Hyperacute T-waves only persist for a few minutes, whereafter the J-point (and entire ST – segment) will became elevated.

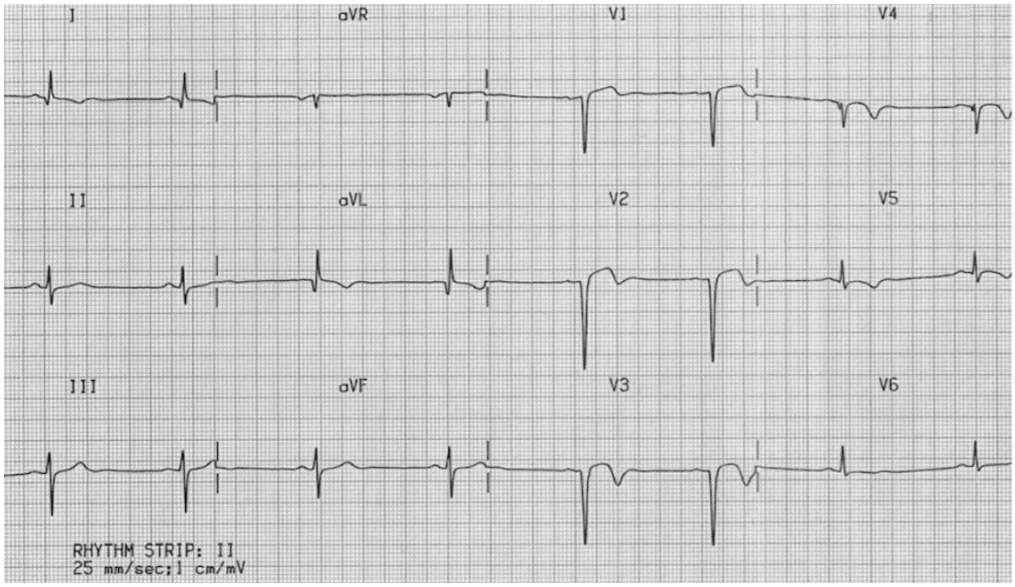
En la fase hiperaguda de la isquemia transmural (los primeros minutos el vector de onda T se amplifica y se dirige desde el endocardio hacia el epicardio en el área isquémica. Aparece como vector de onda T hiperaguda. Las ondas T hiperaguda solo persisten durante un tiempo). pocos minutos, después de lo cual el punto J (y todo el segmento ST) se elevará.



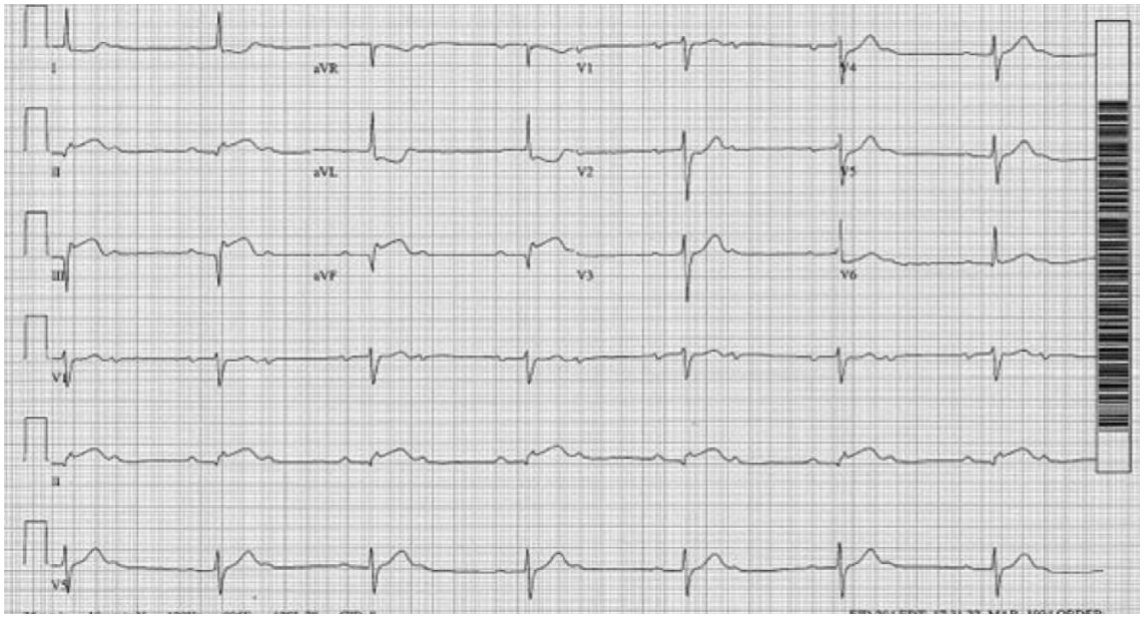
The ST-vector in transmural ischemia will also be directed form the endocardium to the epicardium in the ischemic area. This causes ST-segment elevations in leads with exploring electrodes in front of the ST vector. Leads with opposite angle of observation will instead who ST-segment derpressions, which are simply mirrow images of the ST-segmente elevations. Such ST-segment depressions are referred to as " reciprocal ST-segment depression".

El vector ST en la isquemia transmural también se dirigirá desde el endocardio al epicardio en el área isquémica. Esto provoca elevaciones del segmento ST en las derivaciones con electrodos exploradores frente al vector ST. Los conductores con ángulos de observación opuestos serán, en cambio, derpresiones del segmento ST, que son simplemente imágenes en espejo de las elevaciones del segmento ST. Estas depresiones del segmento ST se denominan "depresión recíproca del segmento ST".

ECG; LV aneurysm



Challenging ECG(s) in Coronary Artery Disease



Answer

♣ 2:1 AV block ♣ ST-segment elevation with Q waves in the inferior leads with reciprocal changes in leads I and aVL

♣ Diagnosis; Acute inferior infarction with 2:1 AV block

Association of inferior wall MI

Heart block (any degree)

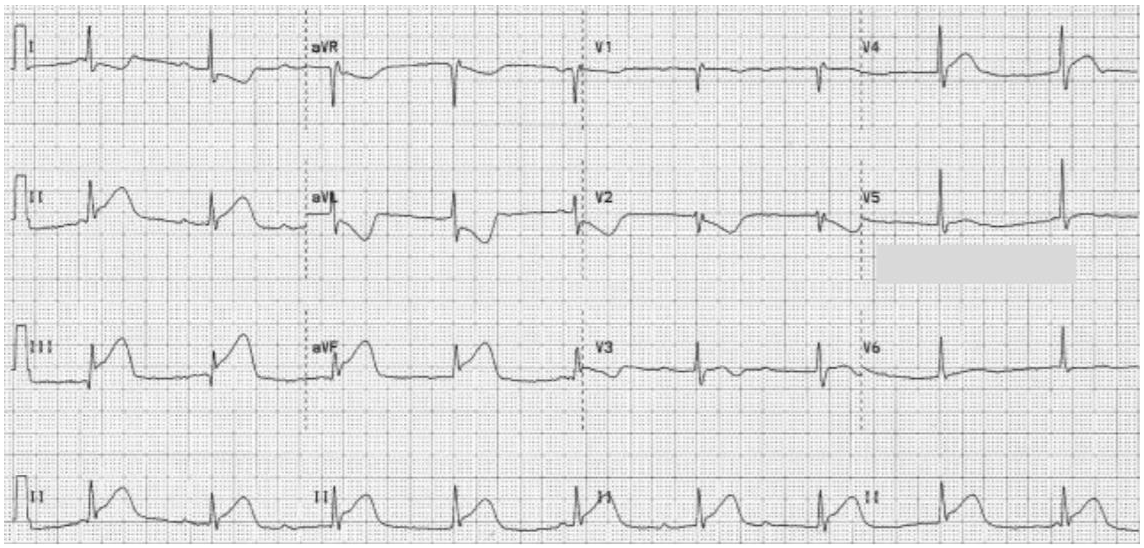
Sinus node disease

Lateral wall MI

RV infarction

Mechanical complication; acute mitral regurgitation

Inferior wall MI with complete heart block



Cardiac arrhythmia in Thailand ACS registry

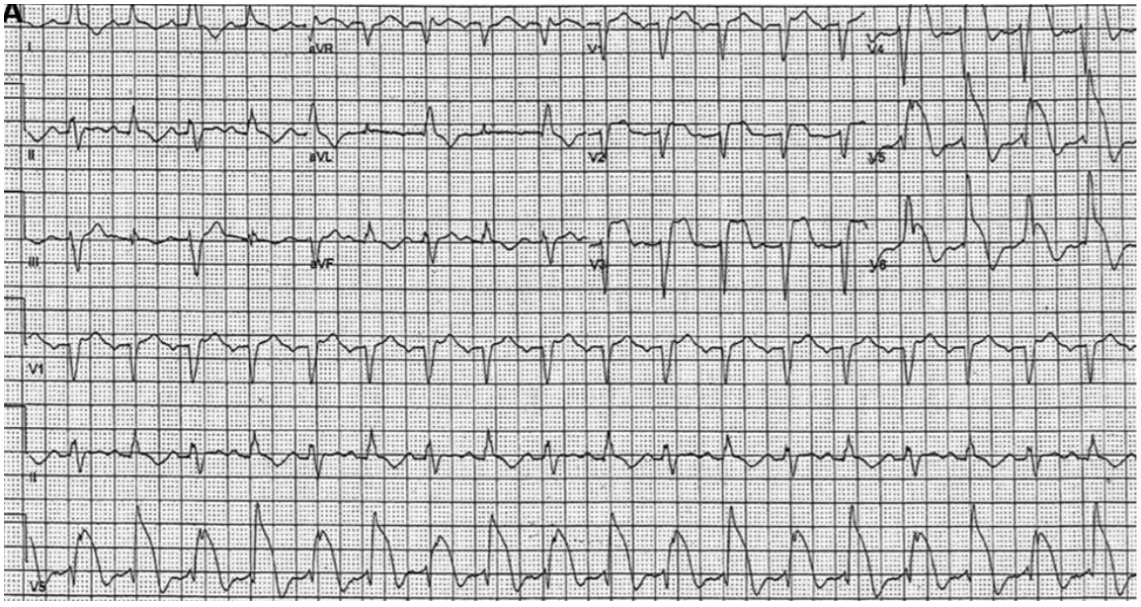
Overall serious arrhythmic complications (sustained VT/VF and 3rdAV block) in Thai registry were 16.6%

♣ Sustained VT/VF was 11.4%

♣ Incidence of serious arrhythmic complication were 29.1% in STEMI, 10.6% in NSTEMI and 3.2% in unstable angina

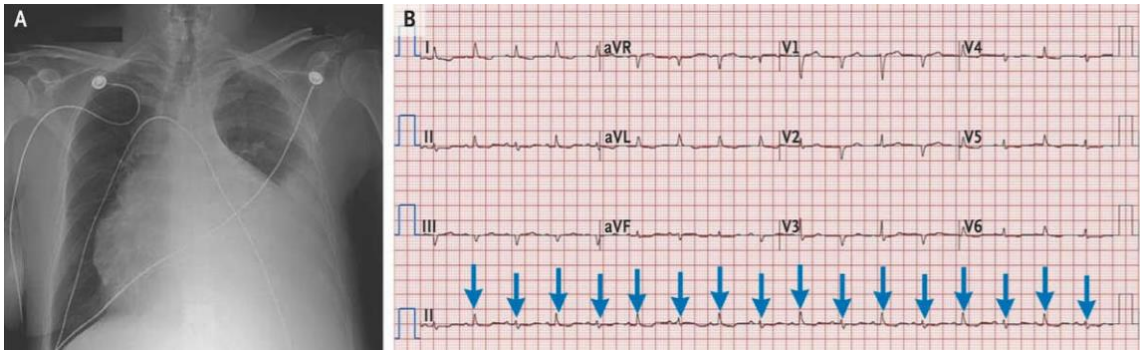
♣ Both VT/VF and AV block were associated with increased in-hospital mortality

♣ CHF, current smoking and cardiac troponin elevation were strong predictors to develop VT/VF and AV block and arrhythmic death

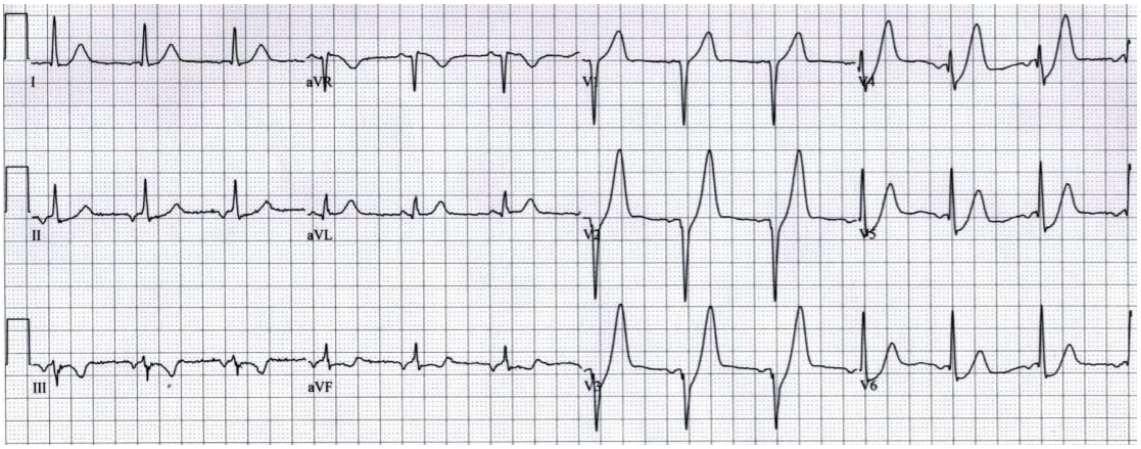


Extensive ST elevation myocardial infarction ♣ Electrical alternans ♣ Cardiac tamponade

Electrical alternans finding in cardiac tamponade

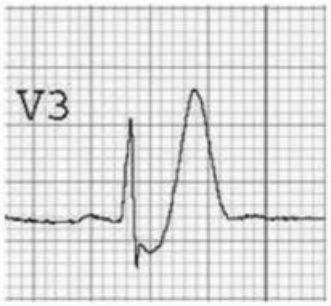


N Engl J Med 2015; 373:e10



Which is the ECG diagnosis?

These ST and T waves abnormalities are known as de Winter´s T-waves



de Winter's T wave

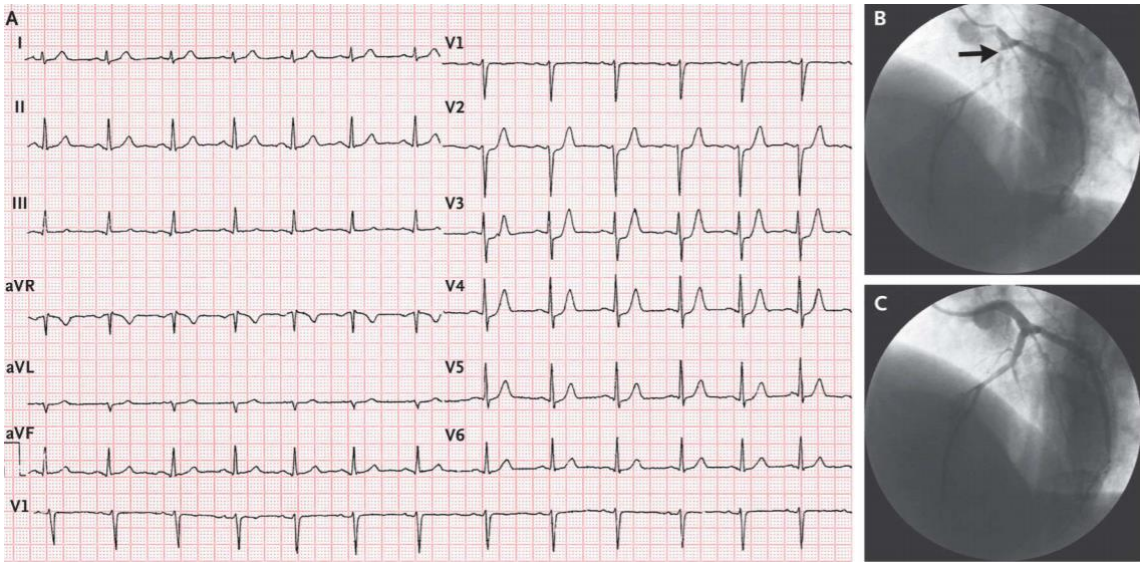
de Winter's T wave

This ECG finding:

- Is specific for left anterior descending artery (LAD) occlusion.
- Represents ~2% of LAD occlusions.
- May persist until the culprit artery is opened (making it a STEMI equivalent) or may evolve into an anterior STEMI

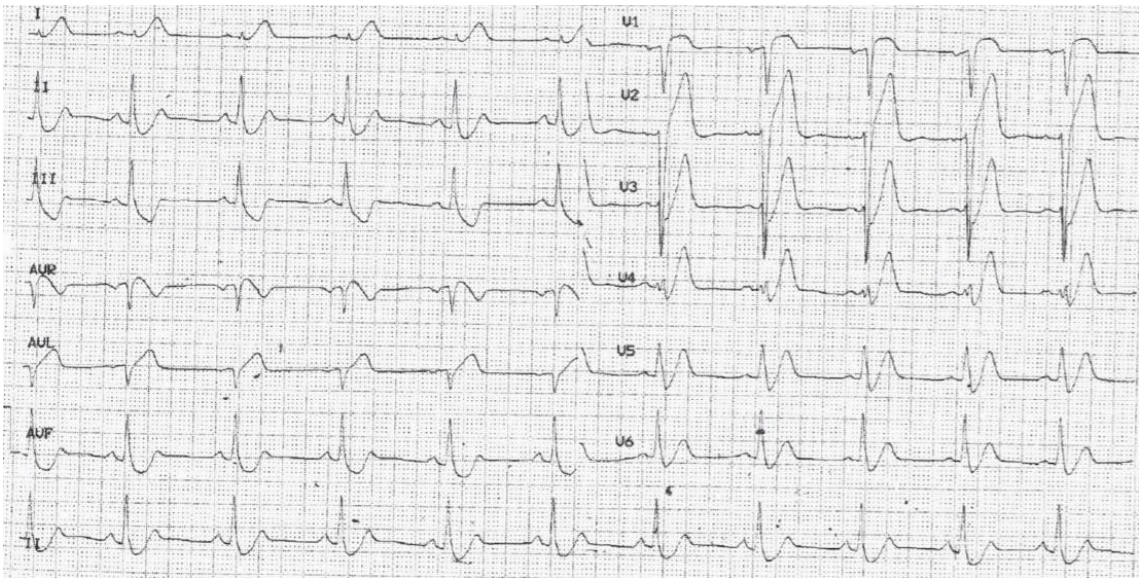
- Ectopic atrial rhythm: inverted P waves in II, III, aVF
- Rate 75 bpm
- Normal axis: +30 degrees, QRS complexes upright in leads I + II
- Normal intervals
- 1mm ST-segment elevation in aVR
- Upsloping ST-segment depression in V2-V6
- Tall, prominent, symmetric T waves throughout the precordial leads

de Winter pattern – associated with proximal LAD occlusion



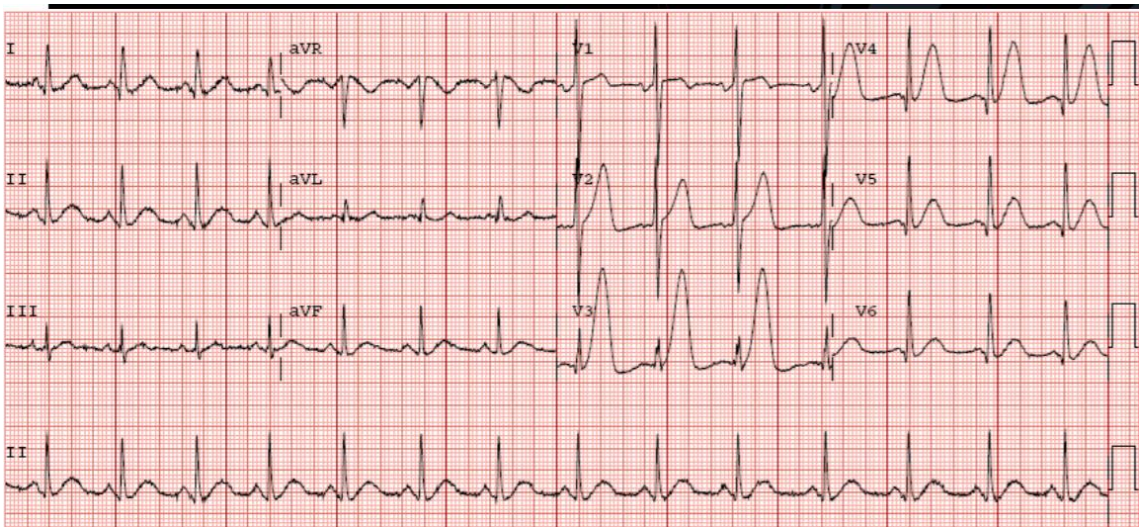
Yun-Tao Zhao, M.D., Ph.D., and Yen-Shu Huang, M.D.ECG Pattern Associated with Left Anterior Descending Coronary Artery Occlusion N Engl J Med 2018; 378:e22 DOI: 10.1056/NEJMicm1714059

Upslope ST depression and hyper-acute T wave



Proximal LAD occlusion

Hyperacute T wave; early sign of acute MI



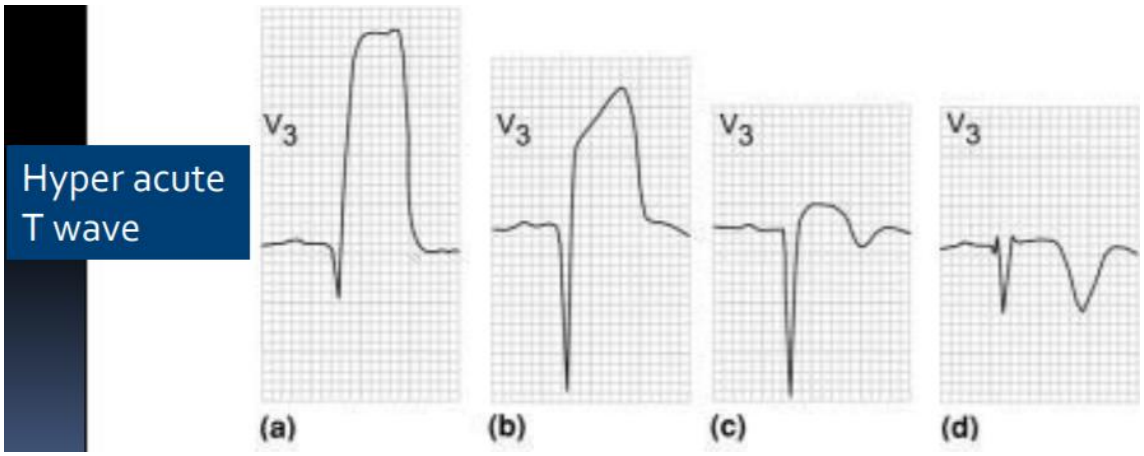
Hyperacute T-wave versus normal T-wave

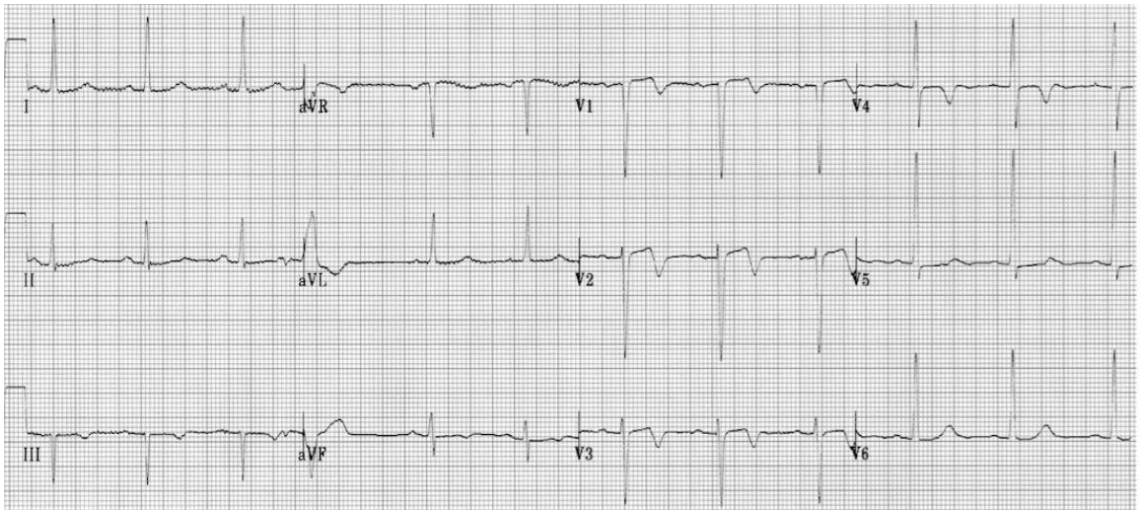
Hyperacute T-wave	Normal T-wave
Usually >8-9 mm	Usually, 5-7 mm
Symmetric	Asymmetric

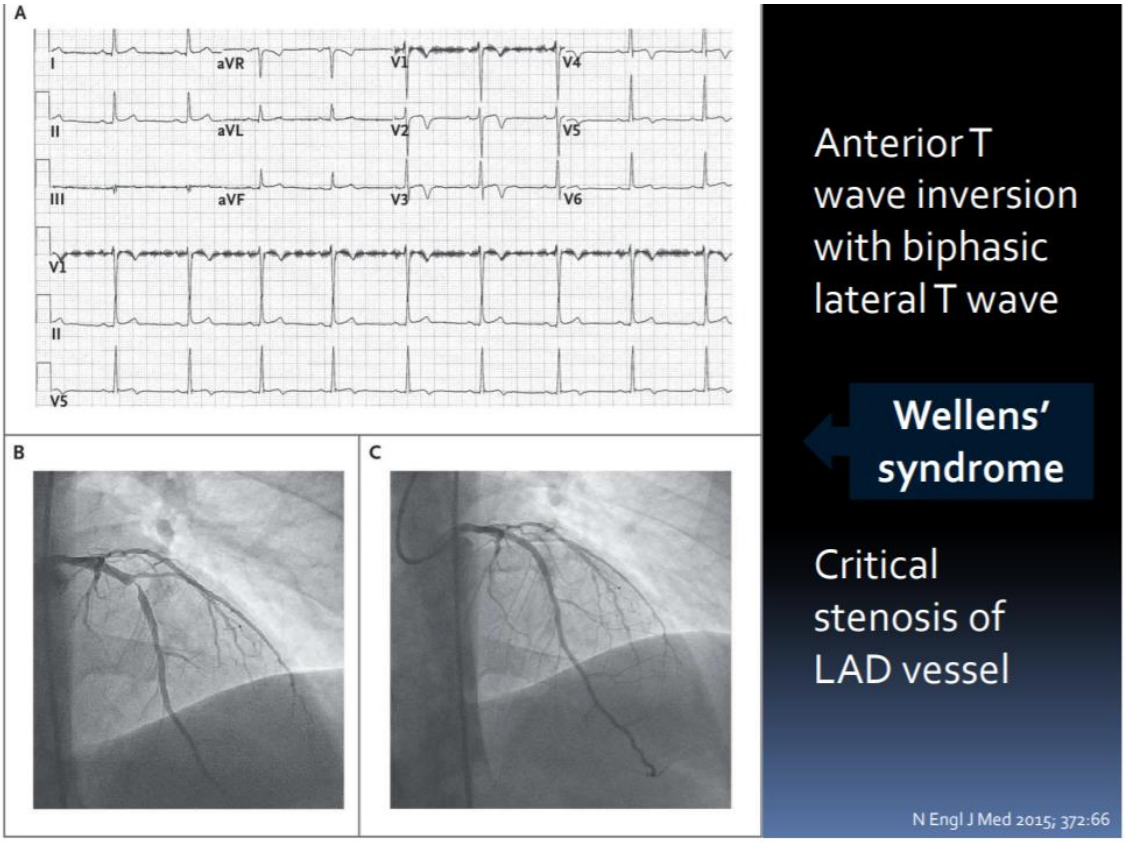
Transient presentation	Static presentation
Narrow or wide base shape	

Evolution of QRS and ST/T morphologies in STEMI due to occlusion of LAD

Few minutes 1 hour 1 day 1 week

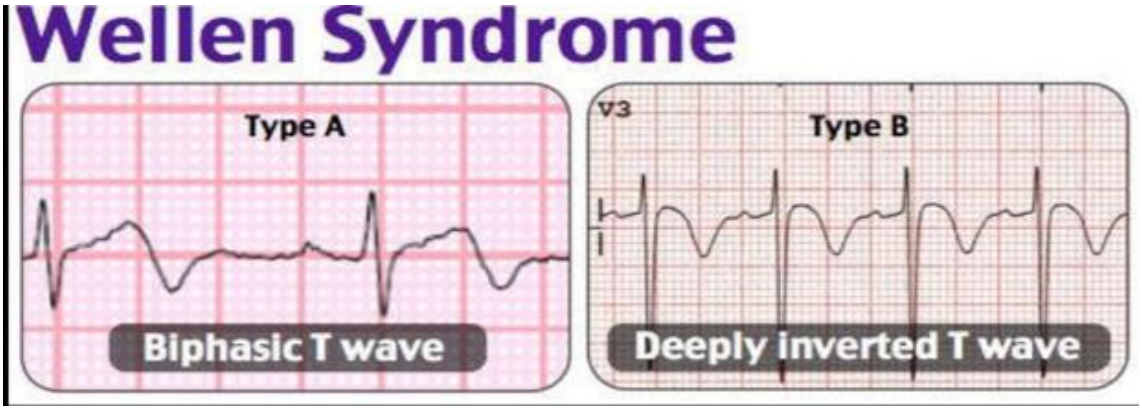






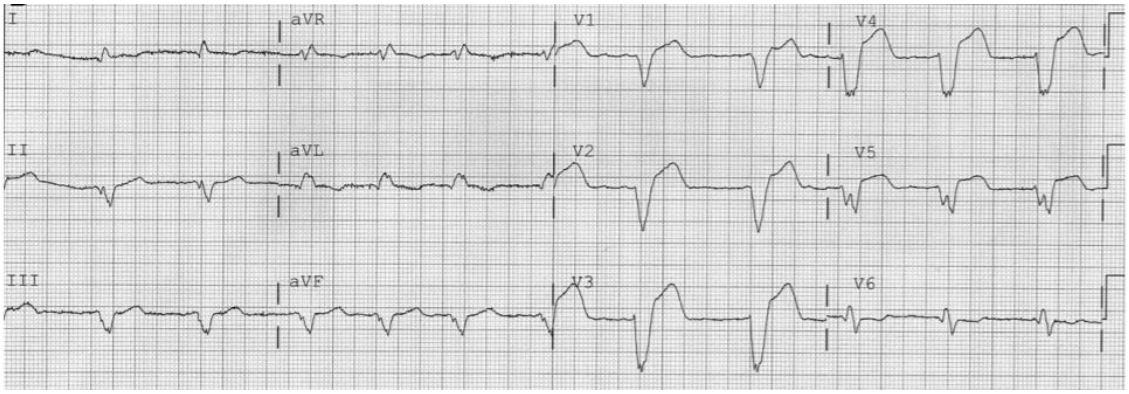
Wellens Syndrome

- Type A Biphasic T-wave
- Type B Deeply Inverted T-wave



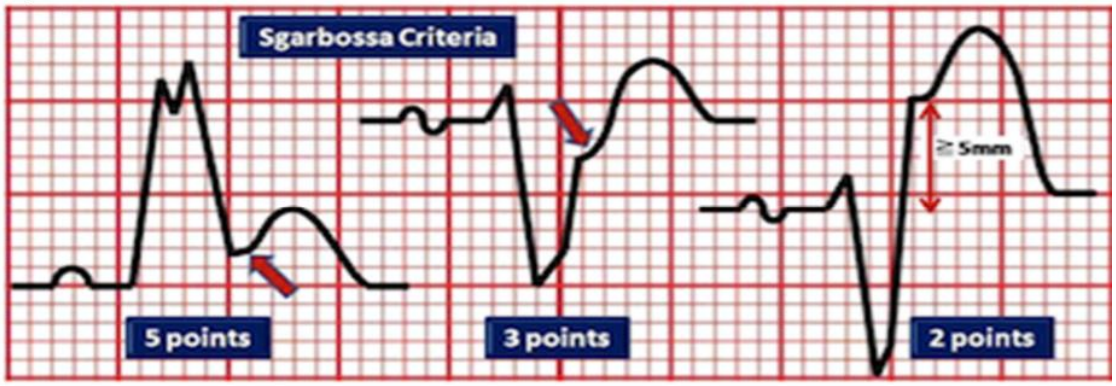
- Highly specific for a critical stenosis of the LADA
- May be pain free at presentation
- Normal or minimal elevated troponin level
- Required immediate Percutaneous Coronary Intervention (PCI)

Acute STEMI with LBBB



Acute MI in LBBB

Sgarbossa criteria (1996)



Sgarbossa ECG Criteria for LBBB	
Concordant STE ≥1mm	5 points
STD ≥1mm in V1 – V3	3 points
Discordant STE ≥5mm	2 points

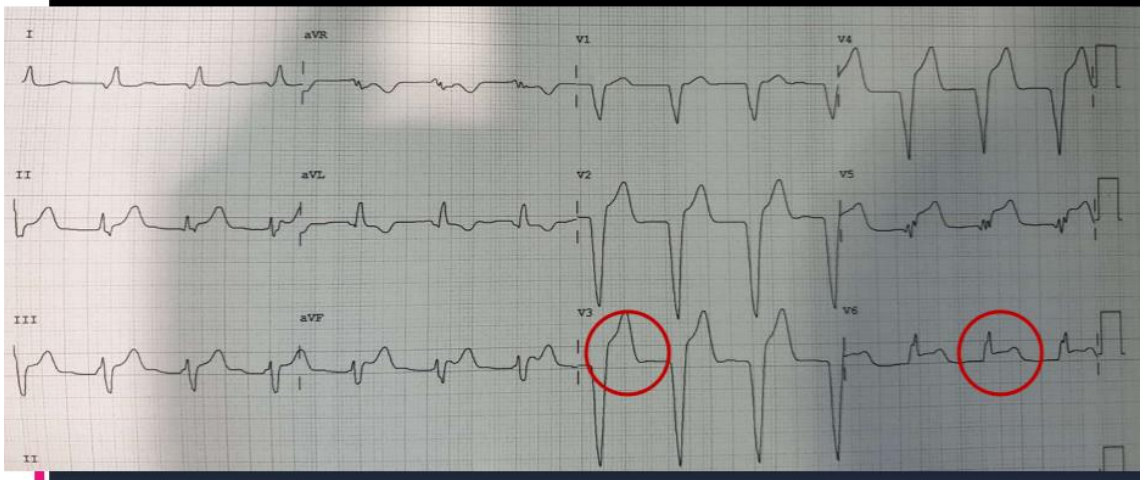
Sgarbossa criteria (1996)

Criterion	Odds Ratio (95% CI)	Score
ST-segment elevation ≥1 mm and concordant with QRS complex	25.2 (11.6–54.7)	5
ST-segment depression ≥1 mm in lead V_1, V_2, or V_3	6.0 (1.9–19.3)	3
ST-segment elevation ≥5 mm and discordant with QRS complex	4.3 (1.8–10.6)	2

Validate for index score ≥ 3

N Engl J Med 1996;334:481-7

Sgarbossa criteria



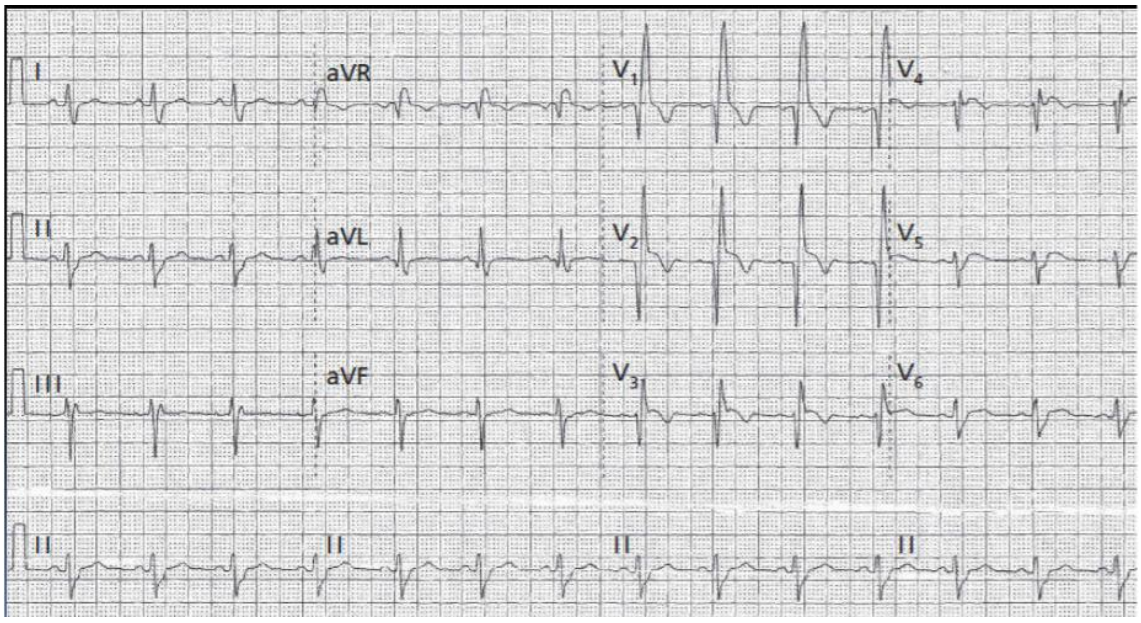
Sgarbossa score = 5 + 2

ACC/AHA 2013 STEMI Guideline for presumably new LBBB

- New or presumably new LBBB at presentation occurs infrequently, may interfere with ST-elevation analysis, and should not be considered diagnostic of acute myocardial infarction (MI) in isolation

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction , circulation , 2013 ; 127:e32-e425

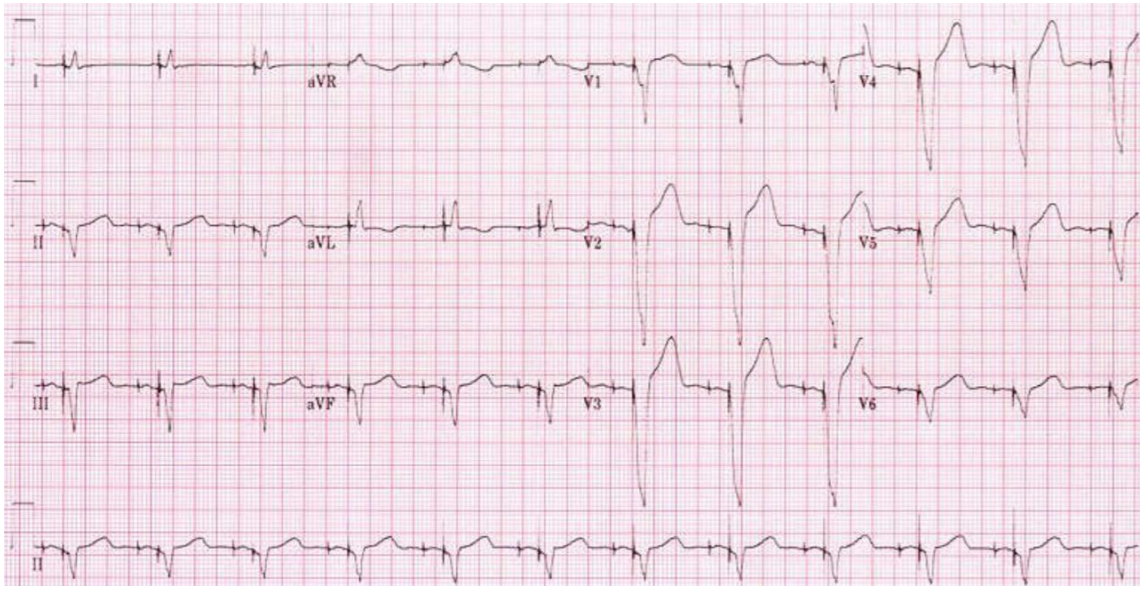
Acute MI in RBBB



Acute MI in RBBB

- Patients with MI and RBBB have a poor prognosis
- May be difficult to detected trans-mural ischemia in patients with chest pain and RBBB
- Primary PCI should be considered when persist ischemic symptoms

Patient with chest pain



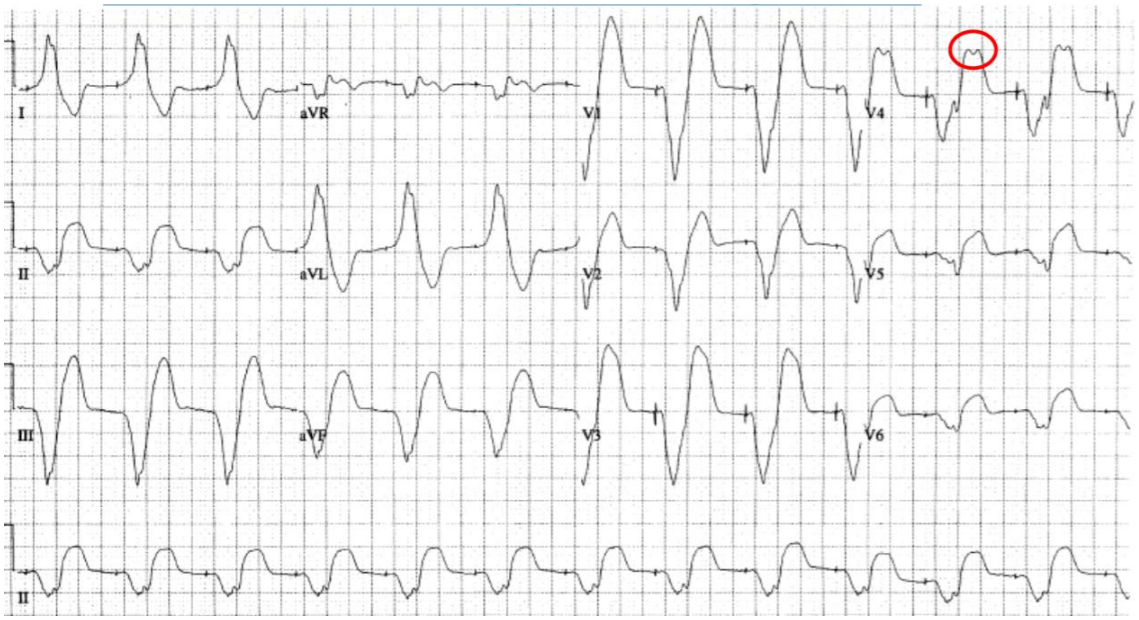
Acute MI in pace rhythm

Difficult to interpretation of ST – segment changes ♣ Reprogramming the pacemaker – evaluation intrinsic heart rhythm ♣ Sgarbossa criteria – less specific

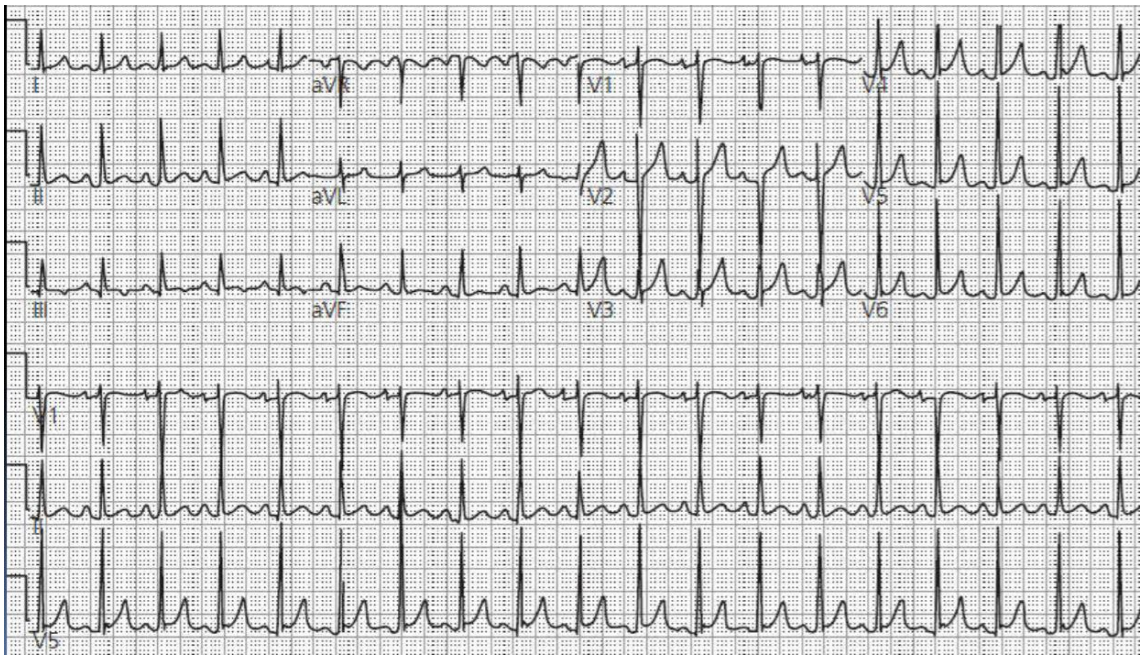
Ventricular paced rhythm

During RV pacing, the ECG also shows LBBB and the above rules also apply for the diagnosis of myocardial infarction during pacing; however, they are less specific

Acute MI in pace rhythm



Marked ST segment elevation and absent R waves in lead V1-V6 ¬ Notching of the upstroke of the QRS complex (Cabrera ‘s sign) is noted in V4.



Which is te diagnosis?

Answer

ECG in pericarditis

♣ Diffuse widespread ST/T elevation

♣ Not in a pattern seen with myocardial infarction

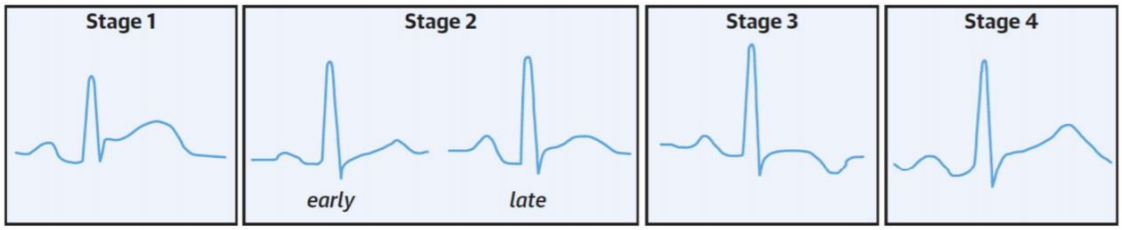
♣ PR depression (especially in lead II)

♣ 4 stages of ECG finding.

Stage	*ECG findings*
1	ST elevation, PR depression
2	ST segments return to baseline. There may be diffuse T wave flattening
3	T wave inversion
4	Normalization of ECG

George A. Stouffer, MD , Pracical ECG interpretation , clues to heart disease in young adults , ISBN : 9781405179287

ECG change in 4 stages of pericarditis



Juan Guido Chiabrando , MD , Management of acute and recurrent pericarditis , JACC , Vol 75, No 1 , 2020

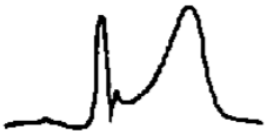
ST segment elevation: pericarditis versus Ischemia

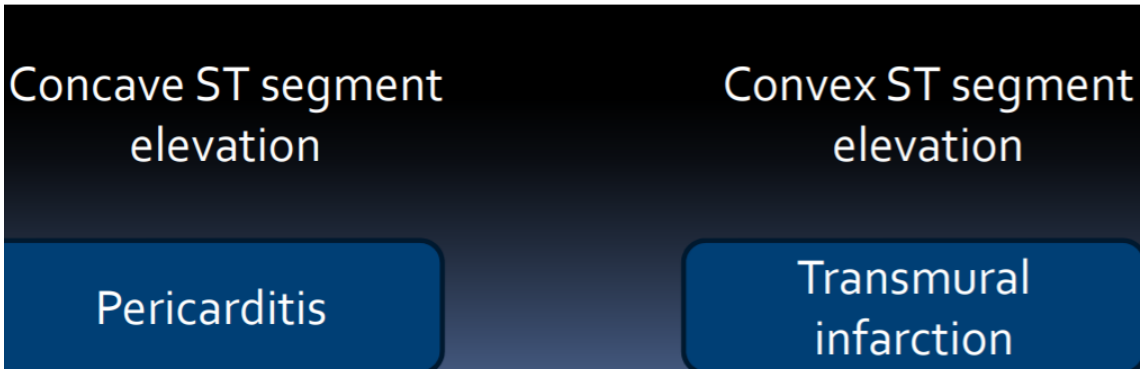
	Pericarditis	Ischemia
Distribution	Global (multiple vascular distributions)	Regional (one vascular distribution)
Reciprocal ST depression	Absent	May be present
ST segment shape	Normal (upwardly concave)	Ischemic (upwardly convex)
PR depression	Present	Absent
Timing of T inversion	T's invert after ST's become isoelectric	T's invert while the ST's are still elevated

	Coronary artery disease (STEMI)	Pericarditis
Number of involved leads	Less (segmentary)	Major (diffuse) and extensive
Intensity of the phenomena	Major	Lesser
Reciprocal effect or mirror image	Frequently present	Absent, except aVR
ST segment elevation convex upward or horizontal	Frequently. In the initial phases is possibly concave upward.	Absent, always concave to the top
PR segment depression	Possible if atrial infarction	Only in viral pericarditis
STSE III > II	Characteristic when present	Absent
Pleuritic positional pain	Rare, but possible	Characteristic

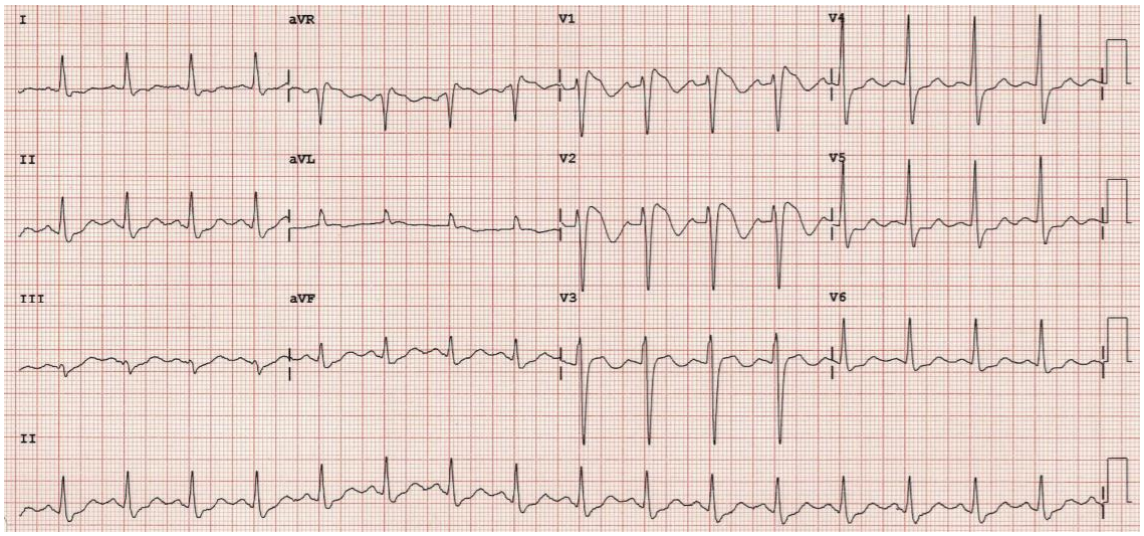
George J. Tayor , MD , 150 Practice ECGs: Interpretation and Review , ISBN – 13: 978-1-4051-0483-8

Patients with ST Segment Elevation

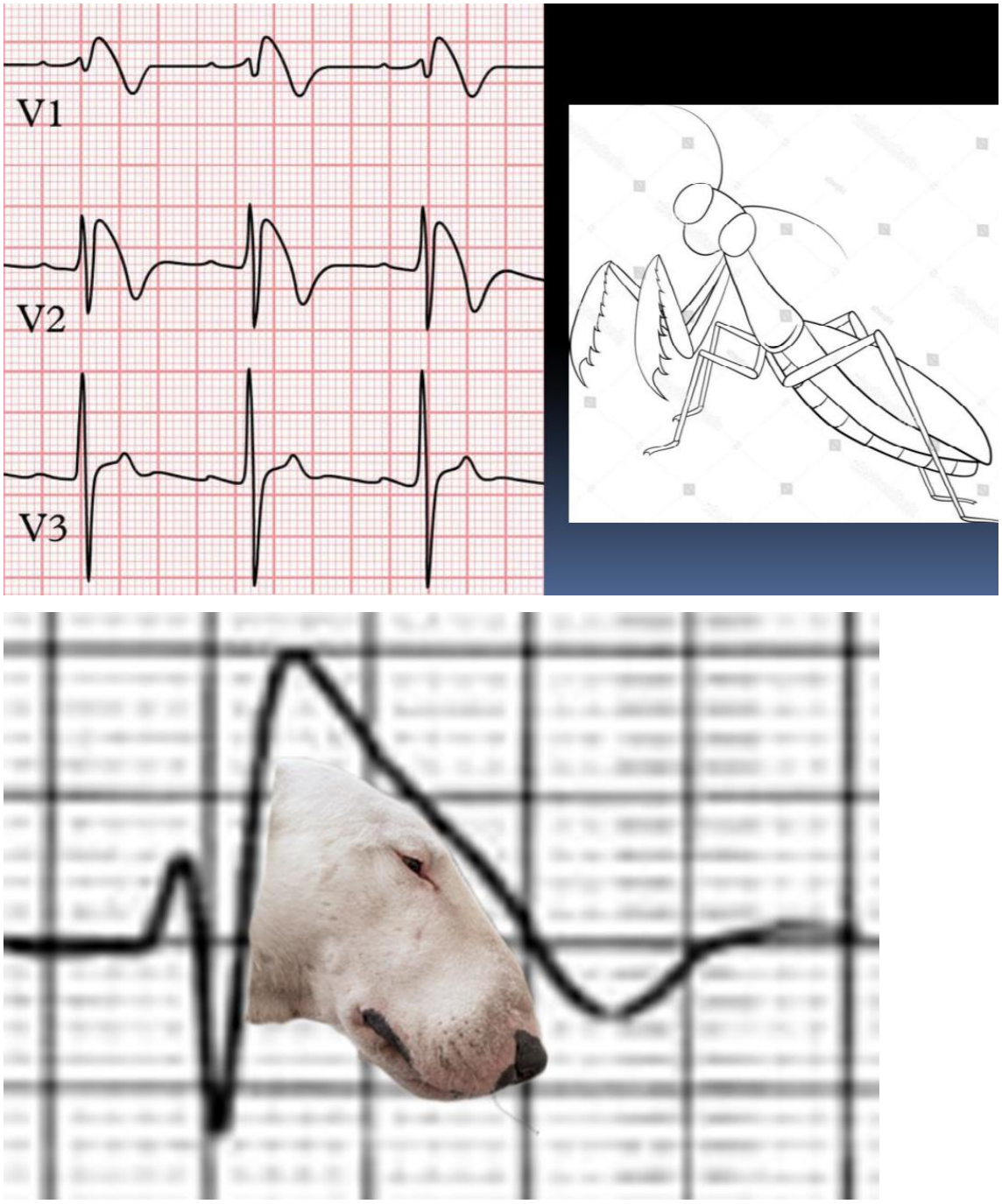




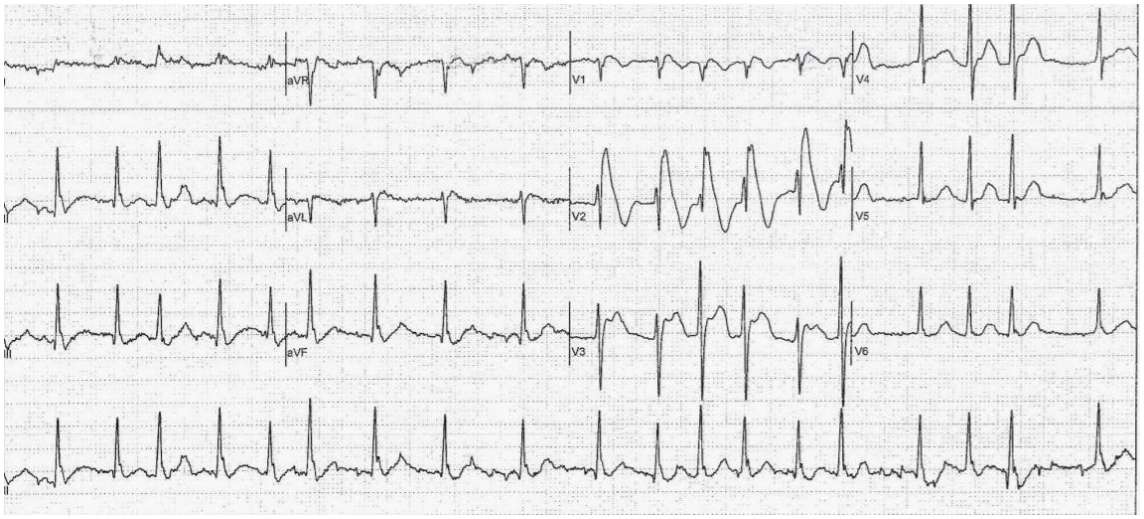
George J. Tayor, MD, 150 Practice ECGs: Interpretation and Review, ISBN – 13: 978-1-4051-0483-8



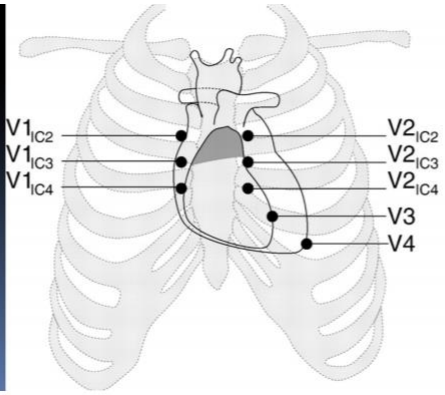
Grasshopper – leg/ pierna de Saltamontes –/ perna de Gafanhoto

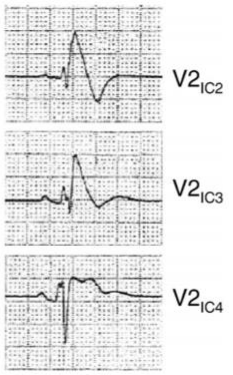


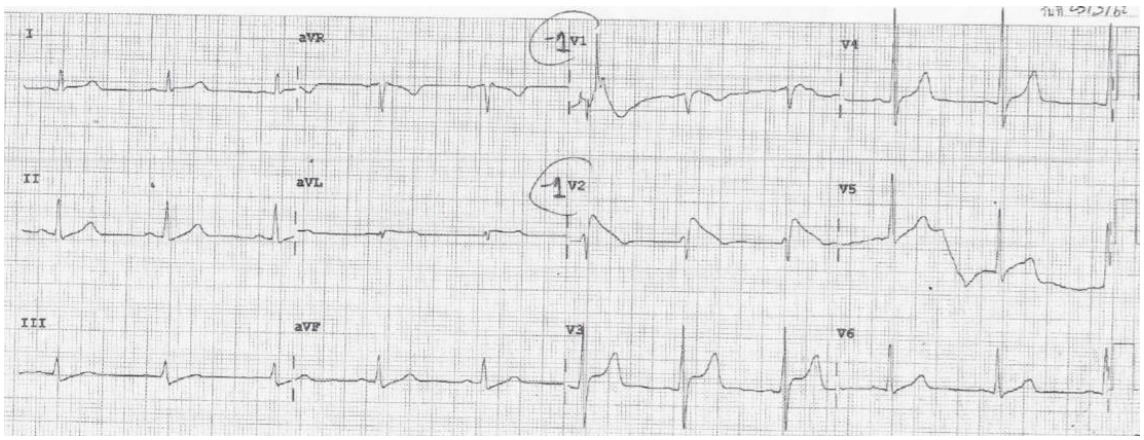
Type 1 Brugada pattern resembling the skull of a bull terrier.

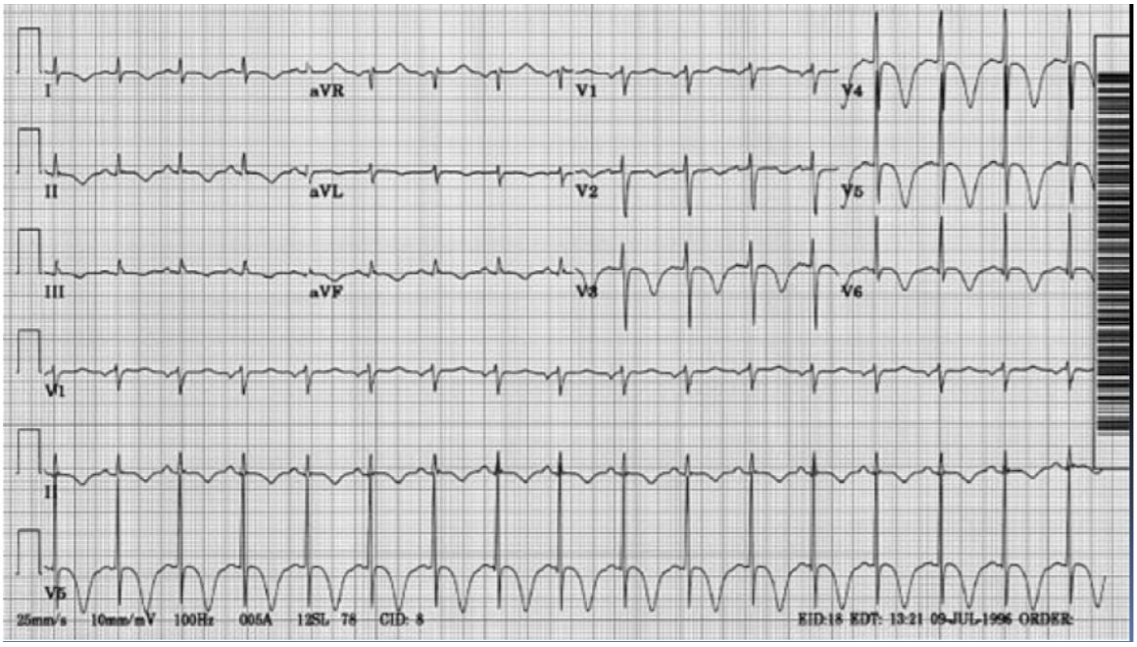


Modified Brugada leads



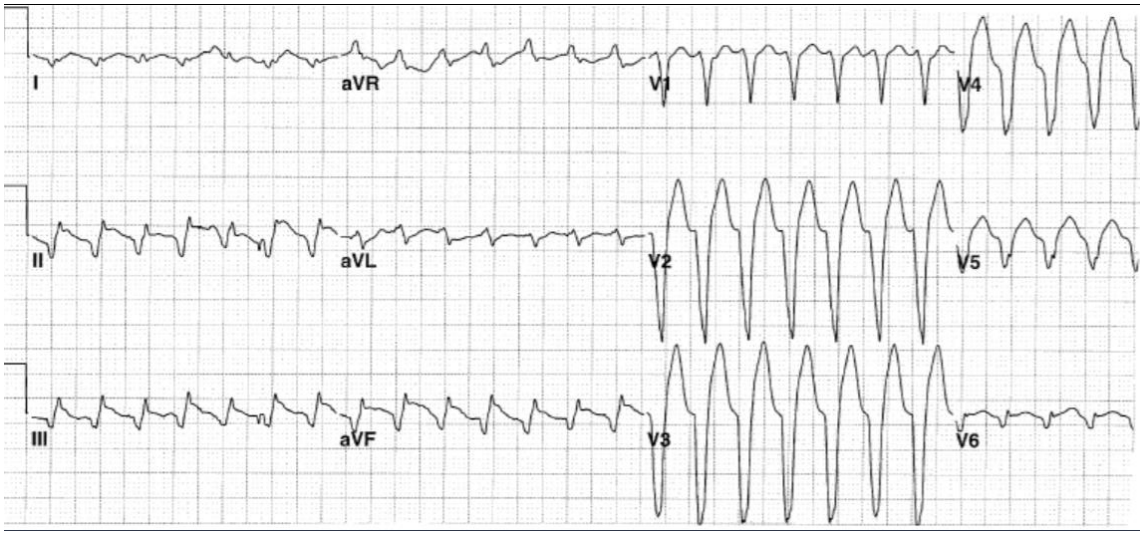






Answer

Sinus tachycardia ♣ generalized T-wave inversion ♣ The T waves are symmetric, deep, and have a long QT interval. Major CNS event such as a subarachnoid or intraventricular hemorrhage.



Answer

Ventricular tachycardia ♣ Wide QRS complex tachycardia Abnormal impulse from ventricular tissue No P wave before QRS complex Life – threatening condition.

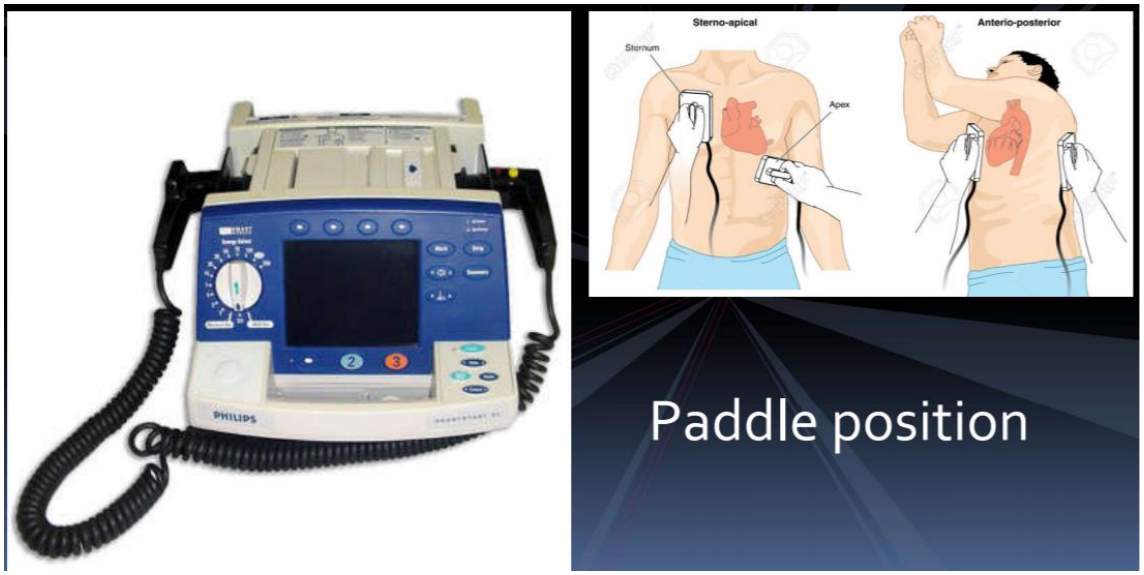
Treatment of VT ♣ Initial treatment ¬Hemodynamic evaluation ⎫

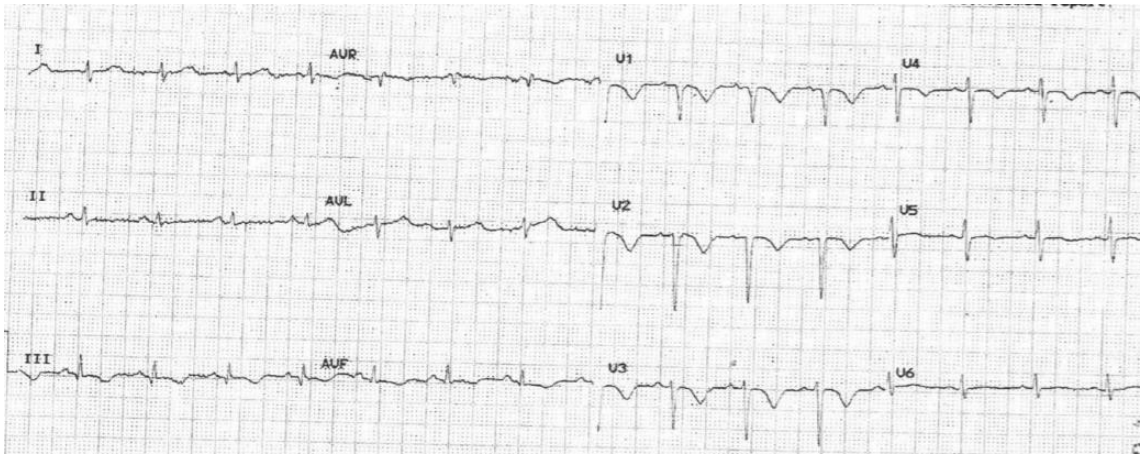
Stable hemodynamic; antiarrhythmic drugs

Unstable hemodynamic; electrical cardioversion

Pulseless VT; CPR with ACLS and defibrillation Antiarrhythmic drug ; amiodarone IV or lidocaine IV

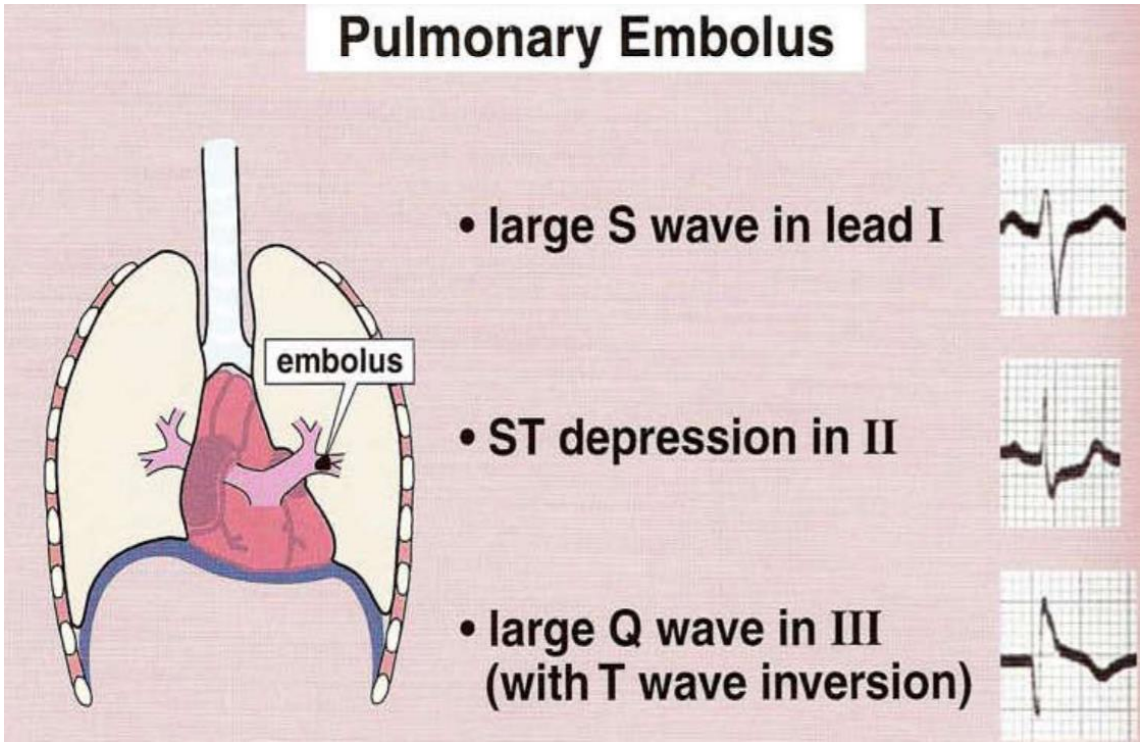
Initial treatment Electrical cardioversion

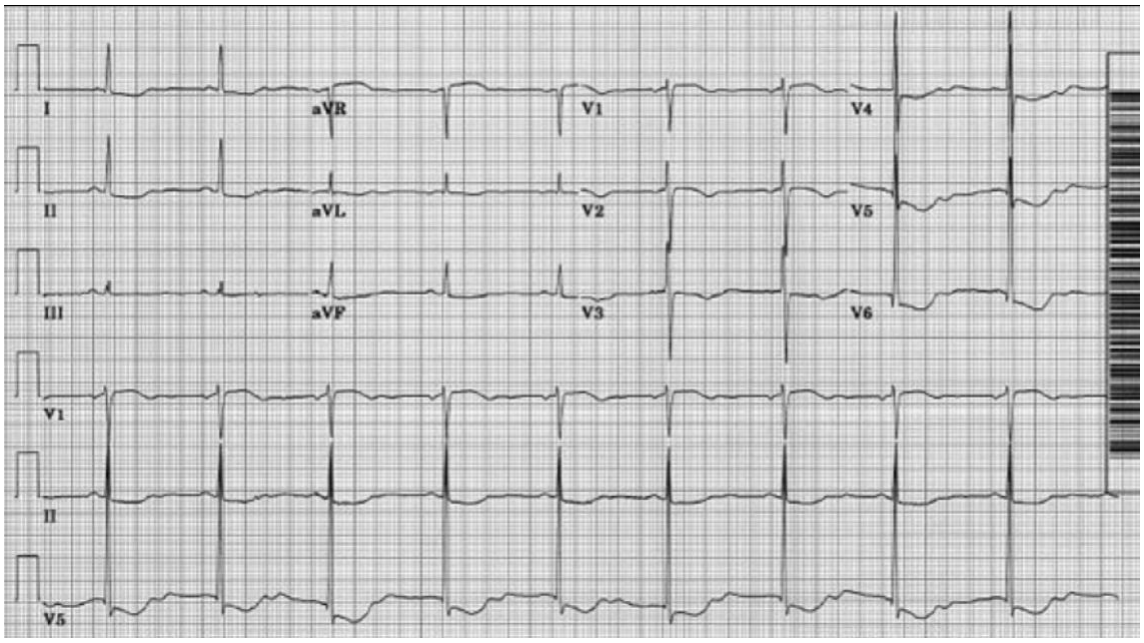




Clinical acute pulmonary embolism.

ECG diagnosis: large S wave in I, ST depression in II, large Q wave in III (The McGinn-White Sign is the S1Q3T3 pattern seen on the ECG in the setting of acute pulmonary embolism or other causes of acute right heart strain), delayed transition zone (V6). The QRS transition zone refers to where the QRS complex switches from being mostly negative to mostly positive, from the point of view of the chest leads, V1 through V6, which “view” the heart through the horizontal plane.





Answer

Sinus bradycardia ♣ Prolongation of the QT interval ♣ ST-segment depression, T-wave flattening, and TU fusion with prominent U waves in the lateral precordial leads ♣ Hypokalemia

Standard medical therapy for any patient presenting with suspected NSTEMI/STEMI

includes

Oxygen therapy when appropriate,

Nitrate administration unless contraindicated,

Analgesic therapy with morphine,

β-adrenergic blockers within 24 hours,

Antiplatelet therapy with ASA and a P2Y12 inhibitor. **(. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. J Am Coll Cardiol 2014;64:e139–228**.)

Management of NSTEMI includes ischemia-guided therapy or medical management. Invasive coronary intervention is not recommended unless the patient presents with life-threatening high-risk characteristics **(. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. J Am Coll Cardiol 2014;64:e139–228**.) (see Table below).

Strategy selection for patients with NSTEMI

Strategy	Risk Indicators
Immediate invasive (within 2 h)	Refractory angina Signs or symptoms of HF or new or worsening mitral regurgitation Hemodynamic instability Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy Sustained VT or VF
Early invasive (within 24 h)	None of the abovementioned, but GRACE risk score >140 Temporal change in troponin New or presumably new ST depression
Delayed invasive (within 25–72 h)	None of the abovementioned but diabetes mellitus Renal insufficiency (GFR <60 mL/min/1.73 m^2) Reduced LV systolic function (EF <0.40) Early postinfarction angina PCI within 6 mo Prior coronary artery bypass grafting GRACE risk score of 109–140: TIMI score ≥2
Ischemia-guided strategy	Low-risk score (eg, TIMI [0 or 1], GRACE [109]) Low-risk troponin-negative female patients Patient or clinician preference in the absence of high-risk features

In STEMI, early reperfusion therapy with PCI is the mainstay of therapy. (**O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. Circulation 2013;127: E362–425. Available at: https://www.heart.org/idc/groups/heart-public/@wcm/@mwa/documents/downloadable/ucm_458913.pdf.)**

Fibrinolytic therapy may be the preferred reperfusion therapy for STEMI in non-PCI capable facilities where FMC-to-device cannot be achieved within the recommended time window of 120 minutes. (**O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. Circulation 2013;127: E362–425. Available at: https://www.heart.org/idc/groups/heart-public/@wcm/@mwa/documents/downloadable/ucm_458913.pdf.)**

CABG is only considered a first-line strategy for STEMI in cases of cardiogenic shock.12 (**O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. Circulation 2013;127: E362–425. Available at: https://www.heart.org/idc/groups/heart-public/@wcm/@mwa/documents/downloadable/ucm_458913.pdf.)**
Prevention of CAD resulting NSTEMI/STEMI should play a large part in practice. Optimal blood pressure, physical activity, cholesterol, diet, weight, tobacco use, and blood glucose levels are associated with lower risk of cardiovascular disease and a decline in the NSTEMI/STEMI.
https://www.ccit.go.th/saveheart/document/2562/ECG%20in%20CAD%20%E0%B8%AA%E0%B9%88%E0%B8%87%20slide.pdf

Case presentation

The patient is a 69-year-old white male with onset of typical chest pain 7 days ago which worsened on the day of admission.

Risk factors: Advanced age and cigarette smoking. There was no history of hypertension, dyslipidemia, or diabetes.

Physical examination: BP = 130/90 mmHg; dyspneic, regular heart rhythm with a fourth heart sound (S4), split second sound (S2), and warm limbs with symmetrical pulses.

He was in Killip Class II with rales in both lung bases.

The admission ECG is illustrated in Figure 1.

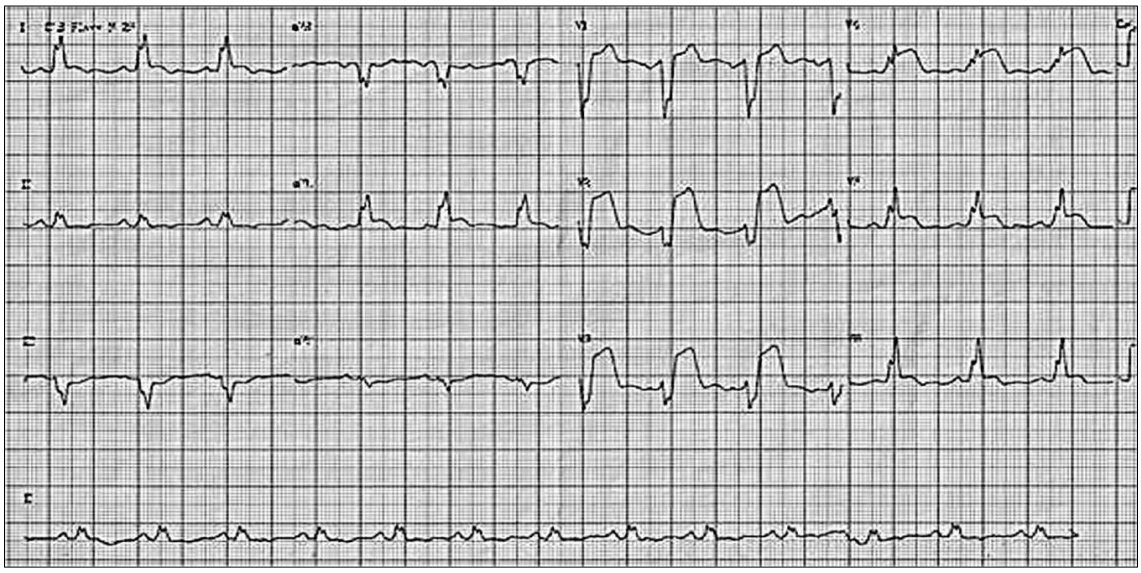


Figure 1. Electrocardiographic findings: sinus rhythm, HR: 83 bpm, PR interval ≥120 ms, QRS axis 10°, QRS duration >120 ms, predominantly negative QRS complexes (rS) in the right precordial leads (V1, V2 and V3), and monophasic notched R waves in leads I, aVL, V5 and V6. ST segment elevation indicative of anterolateral transmural injury present in leads V1-V6, I and aVL. Marked ST segment elevation (>5 mm) present in V2-V3. There is a decrease in the QRS/ST-T ratio in V2 and V3. (In the presence of uncomplicated CLBBB, this ratio is usually 2:1 or 3:1 in V2) (Figure 2). In CLBBB associated with acute myocardial infarction (AMI), the ratio of QRS/ST-T voltages is closer to 1:1 as in this case (Schamroth, 1975). Finally there is concordant ST segment elevation in the same direction as QRS in leads I, aVL, V5 and V6, a finding not seen in uncomplicated CLBBB (Figure 3).

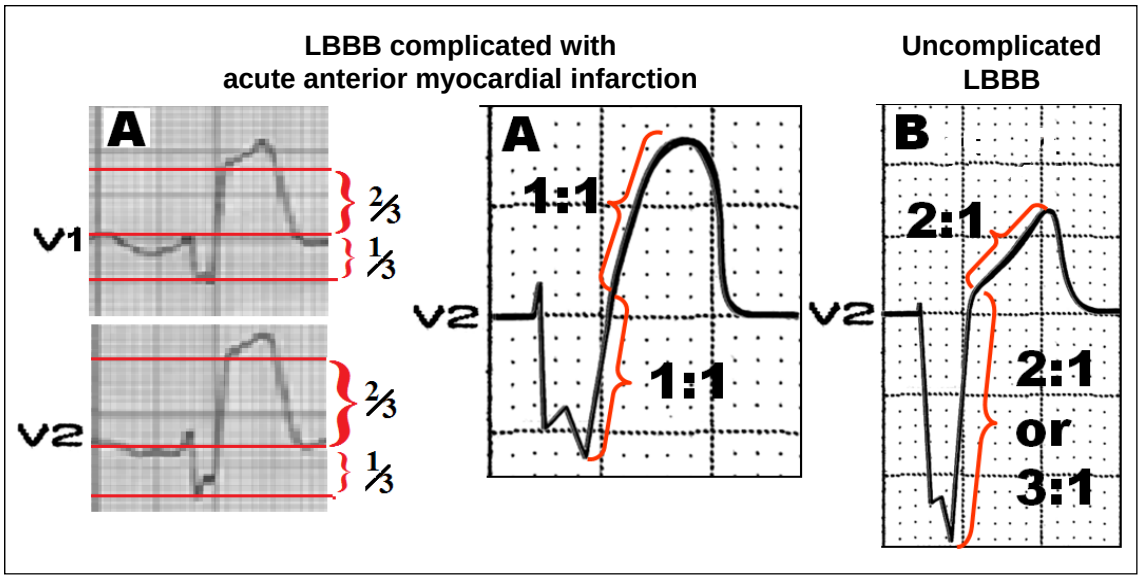


Figure 2. In Figure 2A, a decrease in the QRS/ST-T ratio is observed in V1 and V2; this ratio is <1:1 This is an important electrocardiographic sign of CLBBB complicated with anterior wall infarction (1). A ratio ≤1:1 is due to reduced QRS voltage resulting from the infarcted myocardium. In Figure 2B, the V2 lead is shown in uncomplicated CLBBB. In this case, the QRS/ST-T width ratio in V2 is more typically 2:1 to 3:1.

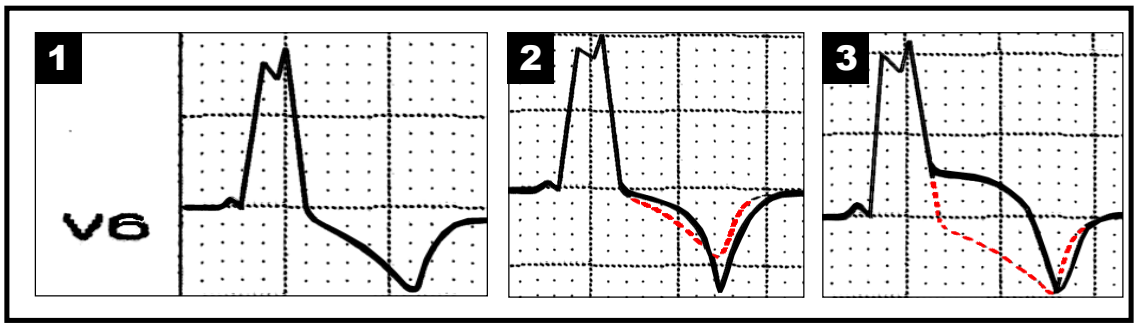


Figure 3. Figure 3 shows the left precordial lead V6 in uncomplicated CLBBB (1) and CLBBB associated with transmural ischemia [65] [66]. Figure 3-3 is similar to leads I, aVL, V5-V6, in the present case illustrated above in Figure 1. The red dotted line in Figure 3B and 3C refers to the normal repolarization in uncomplicated CLBBB noted in Figure 3-1.

ECG features in uncomplicated CLBBB in precordial leads

Ventricular depolarization: In the presence of uncomplicated CLBBB, monophasic and frequently notched R waves are observed in the left leads I, aVL, V5 and V6 with a ventricular activation time (intrinsicoid deflection) in leads I and

V6 ≥50 ms. There may be an initial small q wave in I and aVL but never in V5 and V6.

Possible Rs or RS patterns are found in V5 and V6 which may indicate late transition association with right ventricular enlargement, left anterior fascicular block, or an electrically inactive area in the LV free wall. In this latter case the final S wave is usually wide (≥4 ms) and notched (so called Q wave equivalent).

In the early years of electrocardiography Frank Wilson suggested that the S waves in lead V6 in patients with LV free wall infarction and CLBBB were due to the V6 electrode capturing the intracavitary potential of this ventricle; it was called the “electrical window of Wilson”. Later, with the application of vectorcardiography, it was determined that the appearance of S wave in these patients was due to the rightward shift of the afferent limb of the QRS loop in the orthogonal Z plane and not the intracavitary potential. This hypothesis is reinforced by the fact that the S wave appears wider (>40 ms) and notched.

Ventricular repolarization: In uncomplicated CLBBB the J point and ST segments are directed opposite to the deflection of the QRS. In leads with positive QRS complexes (I, aVL, V6) the J point is depressed and the ST segment has upward convexity followed by an asymmetric negative T wave with the initial descending portion being slow and the final ascending part being rapid.

This pattern is secondary to the alteration in the sequence of ventricular depolarization caused by the left bundle branch block. The axes of the QRS and ST/T are parallel with opposite directions in a degree close to +180°. In other words, these are alterations secondary to ventricular repolarization with wide QRS-ST-T angle; however the ventricular gradient remains normal. The normal QRS and ST/T pattern in lead V6 in uncomplicated CLBBB is shown in Figure 4.

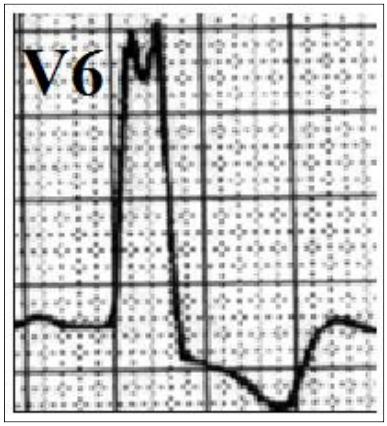


Figure 4. In the right precordial leads in patients with uncomplicated CLBBB, as well as in patients with right ventricular pacing, the QRS complex is totally (QS) or predominantly negative (rS) and ventricular repolarization is characterized by J point and ST segment elevation of upper concavity followed by asymmetrical positive T waves (appropriate discordance) (Figure 5).

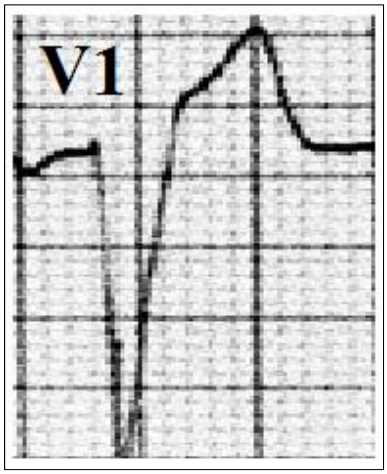


Figure 5. In summary: Uncomplicated CLBBB is characterized by the presence of “appropriate” discordance between ST segments and T waves relative to the QRS polarity. Thus, ST segment elevation with upper concavity is observed, followed by positive and asymmetrical T wave with slow ascending ramp and more rapid descending ramp in precordial leads with complexes of the rS or QS type (right precordial leads); ST segment depression of upper convexity followed by asymmetrical negative T wave with slower descending ramp than the ascending one in the left leads I, aVL, V5 and V6. They are “secondary” changes in ventricular repolarization due to changes in the sequence of depolarization with a wide QRS/ST-T angle but with normal ventricular gradient. This gradient is defined as the algebraic sum (or net difference) of the QRS area and the T area of the ECG.

Electrocardiographic characteristics of CLBBB associated with acute MI

CLBBB with ischemic T waves may be characterized by symmetrical limbs resembling “seagull wings” as illustrated in Figure 3-2. In the present case, however, CLBBB complicated with acute antero-apical infarction is characterized

by ST segment elevation with upper convexity in leads I, aVL, and V5-6 as illustrated in Figure 3-3.

Patients with suspected acute coronary syndrome and acute myocardial infarction (AMI) who present with CLBBB represent a particular diagnostic and therapeutic challenge because both intraventricular conduction disorders and infarction affect the first portions of the QRS complex (Q wave). Although current guidelines recommend early reperfusion therapy for patients with new CLBBB, or when the CLBBB is not known to have previously existed, only a minority of patients with CLBBB are finally diagnosed with AMI and many will not have an occluded culprit artery diagnosed in the catheterization laboratory. This approach to treatment may lead to a significant number of patients vulnerable to the risks of fibrinolytic therapy without the probability of benefit. Also there are unnecessary risks and costs of catheterization due to false positive AMI diagnoses. Therefore, alternative strategies are needed to identify AMI in clinically stable patients with CLBBB that do not have ECG findings highly specific to ST segment elevation MI.

Generally, in patients with uncomplicated CLBBB the presence of ST segment elevation in the right precordial leads V1-V3 is a normal consequence of the abnormal sequence of ventricular depolarization which results in an obligatory change in the sequence of ventricular repolarization. The presence of ST segment elevation matching the positive QRS polarity in the left leads I, aVL, V5 and V6 in the admitting ECG in this case (Figure 1) is abnormal. This is also illustrated in Figure 3-3 and in Figure 6.

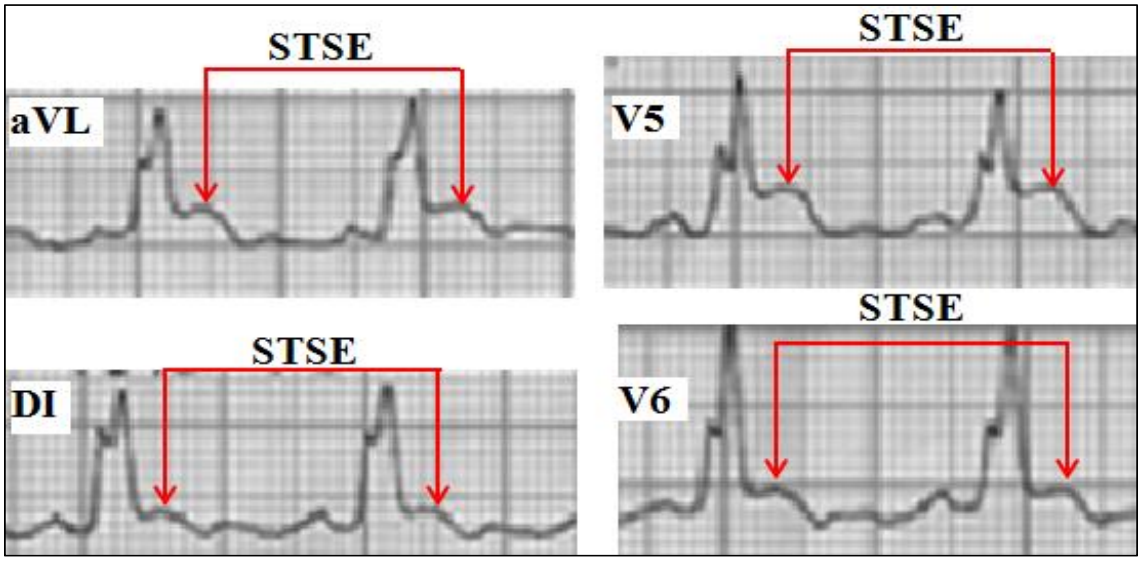


Figure 6. Figure 6 shows ST elevation in left leads I, aVL, V5 and V6 matching the preceding QRS complex. Additionally, the ST segment is upwardly convex. This aspect is always abnormal. Also, the very unusual mismatching ST segment elevation (>5 mm) in the right precordial leads may indicate the presence of AMI.

In 1996 Sgarbossa et al [66] [65] published an ECG scoring system derived from data obtained in the GUSTO study (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) published in 1993 with the aim of assessing the changes in ventricular repolarization in patients with AMI in the presence of *de novo* CLBBB. The following three criteria were included in the score.

- Criterion A: ST elevation ≥1 mm in leads with positive QRS complexes (inappropriate concordance): 5 points. This criterion is most specific for the diagnosis of infarction. Figure 7A.
- Criterion B: ST segment depression ≥1 mm in the leads with predominantly negative QRS complexes, V1-V2-V3 (inappropriate concordance): 3 points. This is the least specific criterion. Figure 7B.
- Criterion C: ST segment elevation ≥5 mm in the leads with predominantly (rS) or completely negative (QS) QRS complexes (V1, V2 or V3) (inappropriate discordance): 2 points.

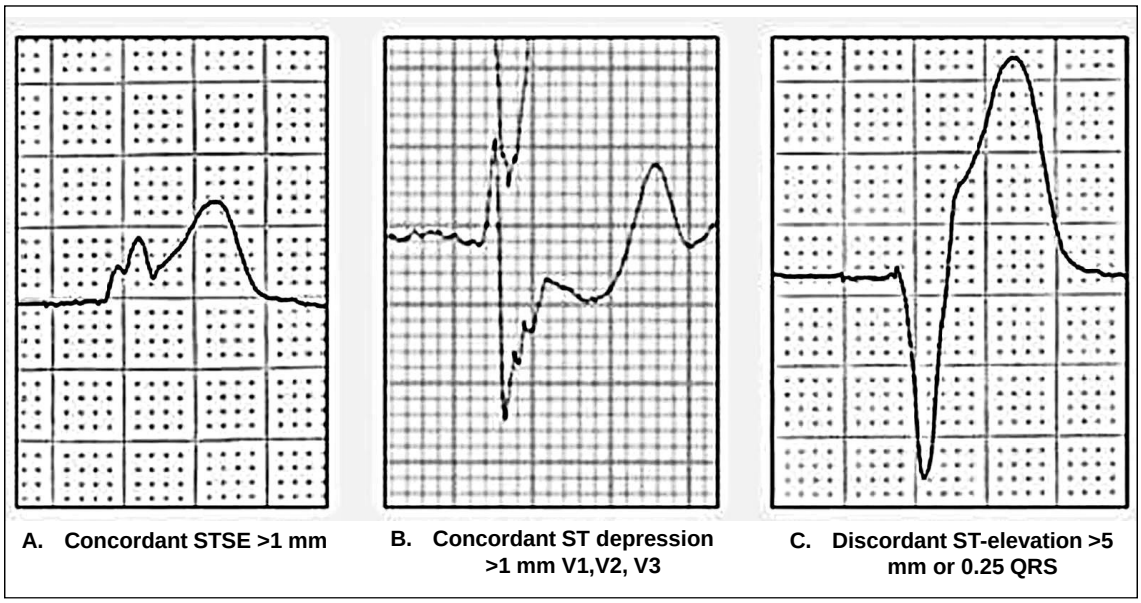


Figure 7. Sgarbossa's CriteriaMI.

A score of ≥3 points is highly predictive of STEMI and has a high specificity (90%), but a low sensitivity.

The new 2013 STEMI guidelines have made a significant change withdrawing the previous recommendations for early reperfusion therapy in patients with suspicion of ischemia and new or supposedly new CLBBB. The new guidelines do not acknowledge that some patients with suspicion of ischemia and CLBBB have MI, and sparing reperfusion therapy in them could be fatal.

The Sgarbossa ECG criteria are the most validated tool to help in the diagnosis of AMI in the presence of CLBBB. A Sgarbossa score of ≥3 has an excellent specificity (98%) and positive predictive value for acute coronary occlusion confirmed by angiography. Thus, Cai et al [67] have proposed a new diagnostic algorithm and triage strategy adding the Sgarbossa criteria to quickly identify those patients with chest pain and new or supposedly new CLBBB who have an acute coronary occlusion. This is a high risk population in whom urgent reperfusion therapy would not be applied according to the 2013 guideline. This new algorithm may also significantly reduce the inappropriate use of the catheterization lab and prevent inappropriate fibrinolytic treatments as recommended by the 2004 AMI guidelines.

The algorithm by Cai Q et al [67] for patients with suspicion of AMI and *de novo* CLBBB is illustrated in following fluxogram bellow

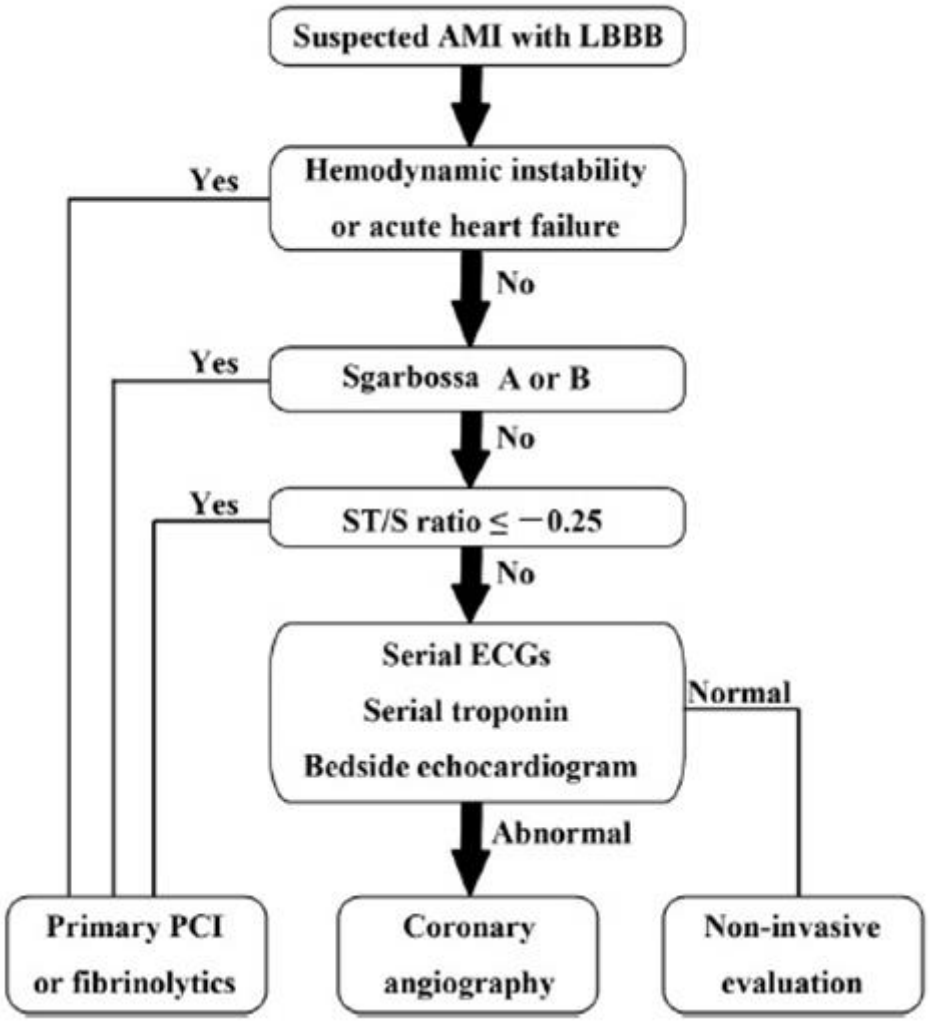


Figure 8. Fluxogram.

In a systematic review and meta-analysis made by Tabas et al [68], the Sgarbossa scoring system revealed that a score ≥3, which represents ≥1 mm of matching elevation of the ST segment or ≥1 mm of matching depression of ST segment from V1 to V3, is useful for the diagnosis of AMI in patients with CLBBB in the ECG. Also, the Sgarbossa score proved to have a good to excellent interobserver variability [69].

A score of 2, representing 5 mm or more of a mismatching ST shift, proved to have less accurate positive probability. The Sgarbossa score of 0 was not useful in ruling out AMI. The great drawback of the Sgarbossa criteria for the diagnosis of AMI in the presence of CLBBB is its low sensitivity (approximately 20%) according to the recently published meta-analysis.

Criterion C, ≥5 mm discordant ST segment elevation in the right precordial leads, is problematic as a criterion because it may be found in patients with CLBBB who do not have AMI, especially when very deep S waves are present in leads V1-V3. Smith et al [70] suggested that it would be more rational to analyze the proportionality between ST segment elevation and S wave depth (ST/S).

According to these authors, the discordance should be proportional to QRS amplitude. The substitution of the measurement of absolute discordant ST segment elevation ≥5 mm in the right precordial leads by an ST/S ratio ≤0.25 significantly improved the diagnostic utility for recognizing acute myocardial infarction. This new criterion is based on the electrophysiological principle that repolarization voltages are always proportional to depolarization voltages. Figure 9 shows an example of this new substitute for the C criterion of Sgarbossa.

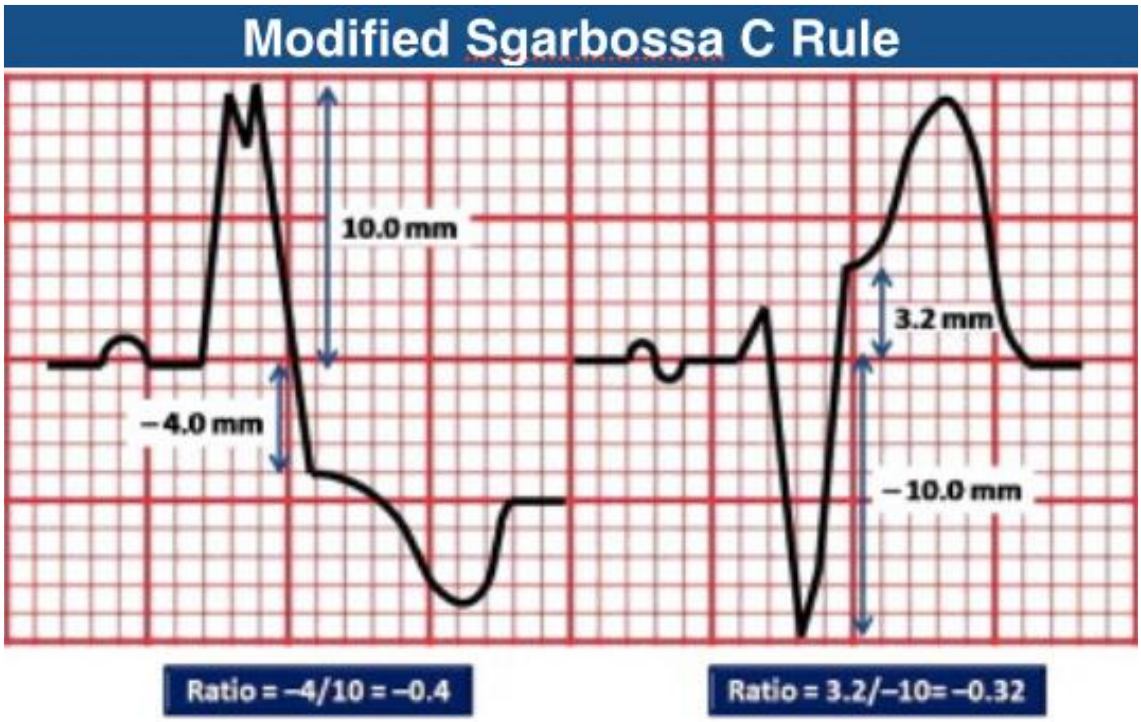


Figure 9. ECG.

Figure 10 illustrates this new criterion in a patient with CLBBB who has an AMI due to total occlusion of the left anterior descending coronary artery.

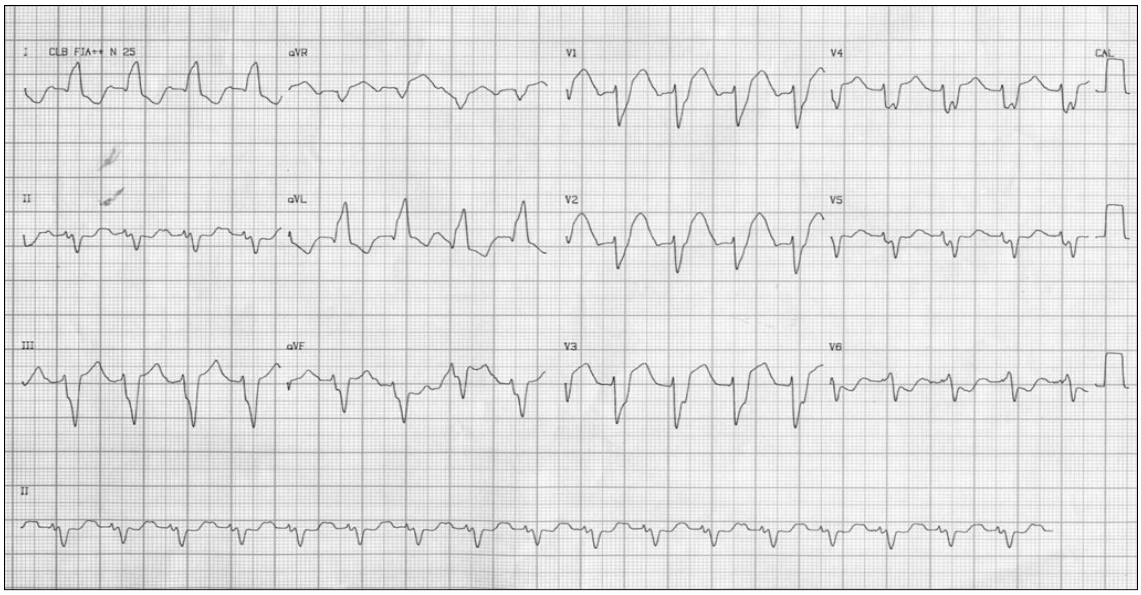


Figure 10. Electrocardiographic diagnosis: Sinus tachycardia, heart rate 115 bpm, extreme left axis QRS in the frontal plane (-60°), QRS duration >120 ms, qR in I and aVL, decrease in QRS/ST-T ratio in V1 and V2 (close to 1/1). This is an electrocardiographic sign of CLBBB complicated with acute anterior wall infarction. ST segment with upper convexity in the right precordial leads (normal: upwardly concave). A notch of 50 ms is present in the ascending ramp of the S wave in V3 and V4 (Cabrera's sign), and the ST/S ratio in lead V2 is < -0.25.

Studies have indicated that the presence of concordant elevation (Sgarbossa criterion #1) is related to AMI with a culprit artery in 71.4% of the cases. It was also observed that when concordant ST segment elevation is absent, CLBBB is not related to acute coronary occlusion. CLBBB without concordant ST segment elevation should not be a criterion for the activation of the catheterization lab for reperfusion therapy.

In the example in Figure 11, the presence of concordant ST segment elevation is seen in lead II and the ST/S ratio >0.2 in leads III and aVF. Coronary angiography revealed total occlusion of the right coronary artery treated by primary angioplasty.

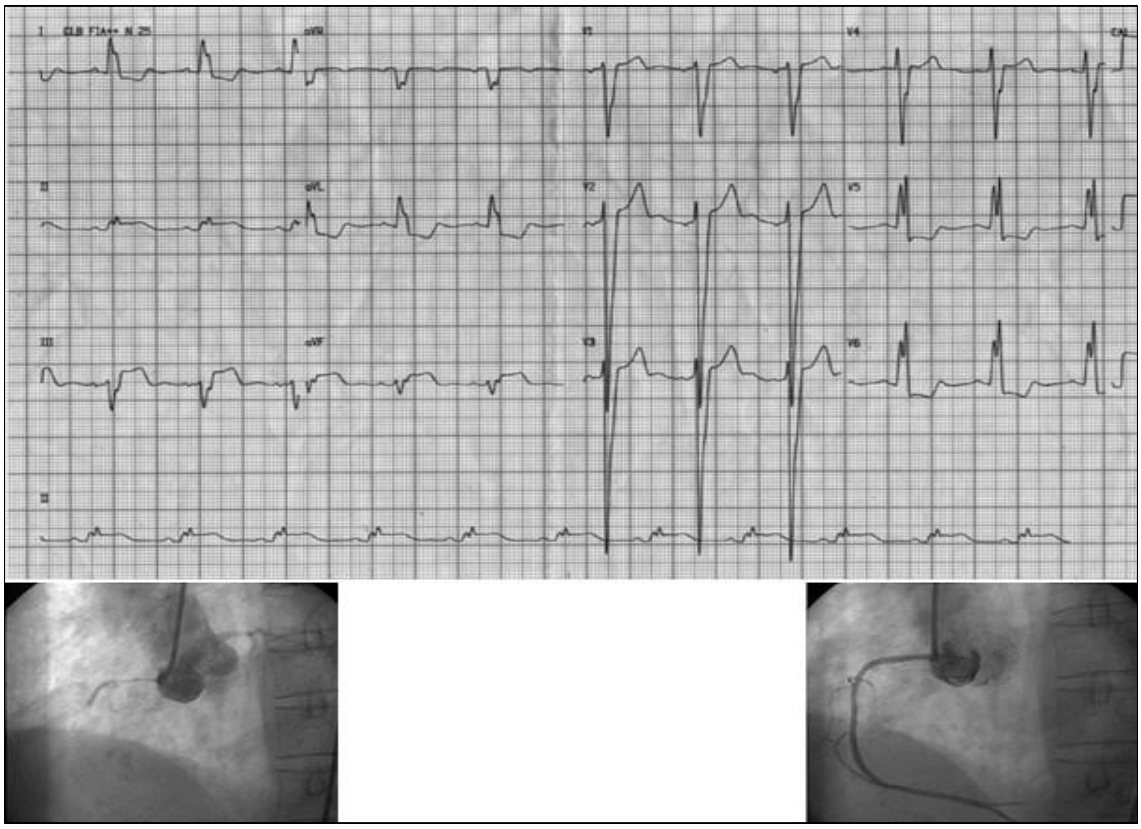


Figure 11. ECG diagnosis: Sinus rhythm, HR 75 bpm, QRS axis -5°, typical CLBBB pattern. ST segment elevation is present in III, II and aVF; ST segment elevation is greater in III than in II, indicating that the injury vector points to +120°, which suggests proximal occlusion of the right coronary artery. There is concomitant ST segment depression in I and aVL and in the left precordial leads because the injury vector moves away from the left superior and apical region of the LV.

Sørensen et al [71] assessed ECGs and mortality in a pre-hospital cohort of 4905 consecutive patients suspected of having AMI. CLBBB was considered to be present when QRS duration ≥ 120 ms associated to classical morphological criteria. Both mortality and angiographic data were measured from a database. The whole population was divided into four groups: with or without AMI and with or without CLBBB. Mortality was evaluated by the Kaplan-Meier analysis and compared to the log-rank statistical analysis. The presence of AMI was diagnosed in 954 patients, from whom 118 also had CLBBB. From 3951 patients without AMI, 436 had CLBBB.

The patients with AMI and CLBBB underwent revascularization less frequently than those patients with AMI without CLBBB (24 vs. 54%, $p<0.001$).

AMI with CLBBB was considered as *de novo* in 43 patients; and among them only 2 underwent primary angioplasty. One-year mortality was 47.2% in the group of patients with AMI+CLBBB, 17.5% in patients with AMI without CLBBB, 20.8% in those with CLBBB without AMI, and 8.6% in patients without AMI or CLBBB (log-rank<0.001) respectively. From the patients with AMI and CLBBB, only 25% underwent revascularization and only a few were referred to emergency primary angioplasty. The approach of improving triage and pre-hospital identification of patients at high risk with CLBBB and chest pain may improve the result.

Al-Faleh et al [72] validated Sgarbossa's criteria prospectively in a large population. These authors verified that patients with Sgarbossa score ≥ 4 presented a greater mortality when compared to those with score below 3. The authors concluded that these criteria constitute a simple approach and a practice that optimizes risk-benefit and improves the therapeutic approach.

The guidelines recommend urgent reperfusion for patients with new CLBBB (nLBBB), similar to patients with STEMI without nLBBB. However, the comparison between both groups of patients is limited. Both groups were compared by Yeo et al [73] in regard to clinical characteristics, type of treatment, and results. In general, patients with nLBBB had a greater percentage of co-morbidities in comparison to those with STEMI without this conduction disorder. In comparison to patients with STEMI, those with nLBBB were less likely to receiving reperfusion therapy in the acute phase (primary percutaneous coronary intervention - PCI) (93.9% vs. 48.3%, p<0.0001) and had a greater percentage of door-to-balloon time ≤ 90 minutes (76.8% vs. 34.5%, p<0.0001). Mortality rates were greater for the patients with nLBBB in comparison to those with STEMI without nLBBB (13.3% vs. 5.6%, p<0.0001). After multivariate adjustment, the patients with nLBBB were not associated with an increased risk of in-hospital mortality. The authors concluded that the patients with nLBBB presented a greater percentage of co-morbidities and were less prone to receiving reperfusion therapy (PCI) in the acute phase. In spite of these differences, adjusted mortality rates were similar between patients with nLBBB and those with STEMI.

In the following sequence, two cases of nLBBB complicated with inferior and anterior infarction in the acute phase are illustrated.

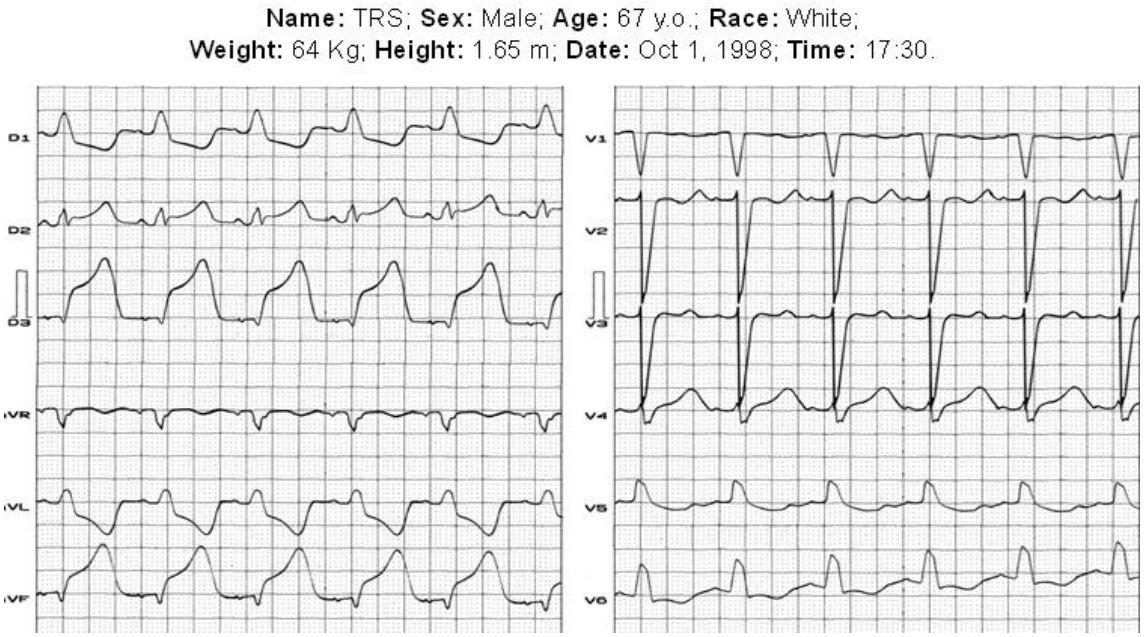


Figure 12. Clinical diagnosis: Acute inferior wall myocardial infarction (AMI) associated with nLBBB evolving after 5 hours. ECG diagnosis: nLBBB + ST segment elevation in III, aVF and II. Pardee's complex are noted in the inferior wall leads. Typical ECG findings of CLBBB associated with acute inferior wall MI are seen in leads III and aVF resembling monophasic action potentials (Pardee's complex). ST segment elevation in III>II indicates that the injury vector points to +120° and indicates proximal occlusion of the right coronary artery.

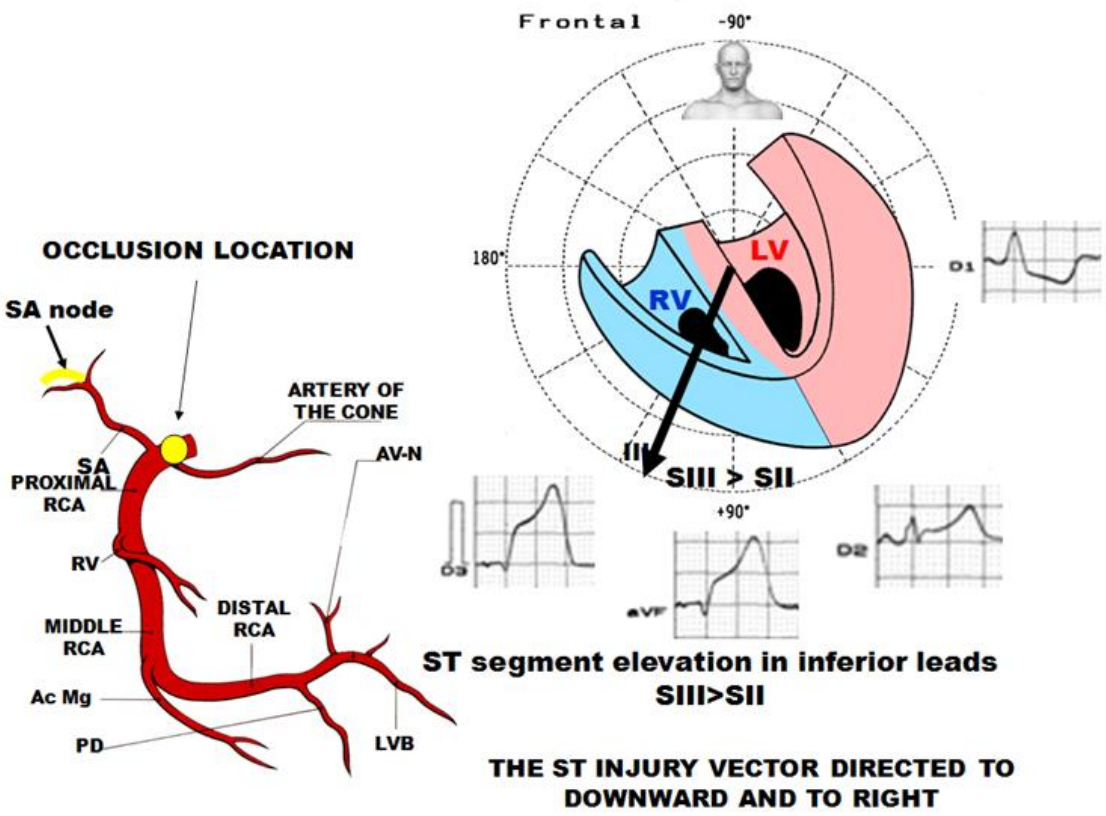


Figure 13. Figure.

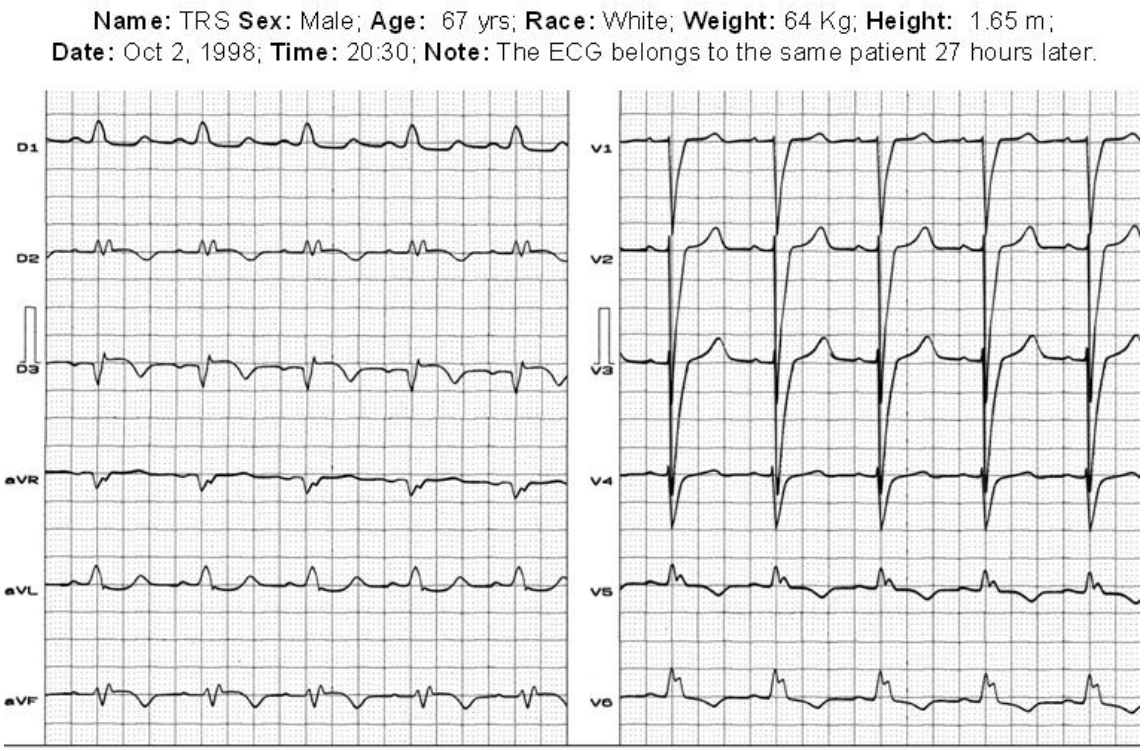


Figure 14. Clinical diagnosis: Inferior subepicardial ischemia. ECG diagnosis: Q wave of necrosis, only visible in lead III. Inferior subepicardial ischemia. A decrease in R waves voltage is seen in V5-V6, which indicates additional involvement in the LV apical region.

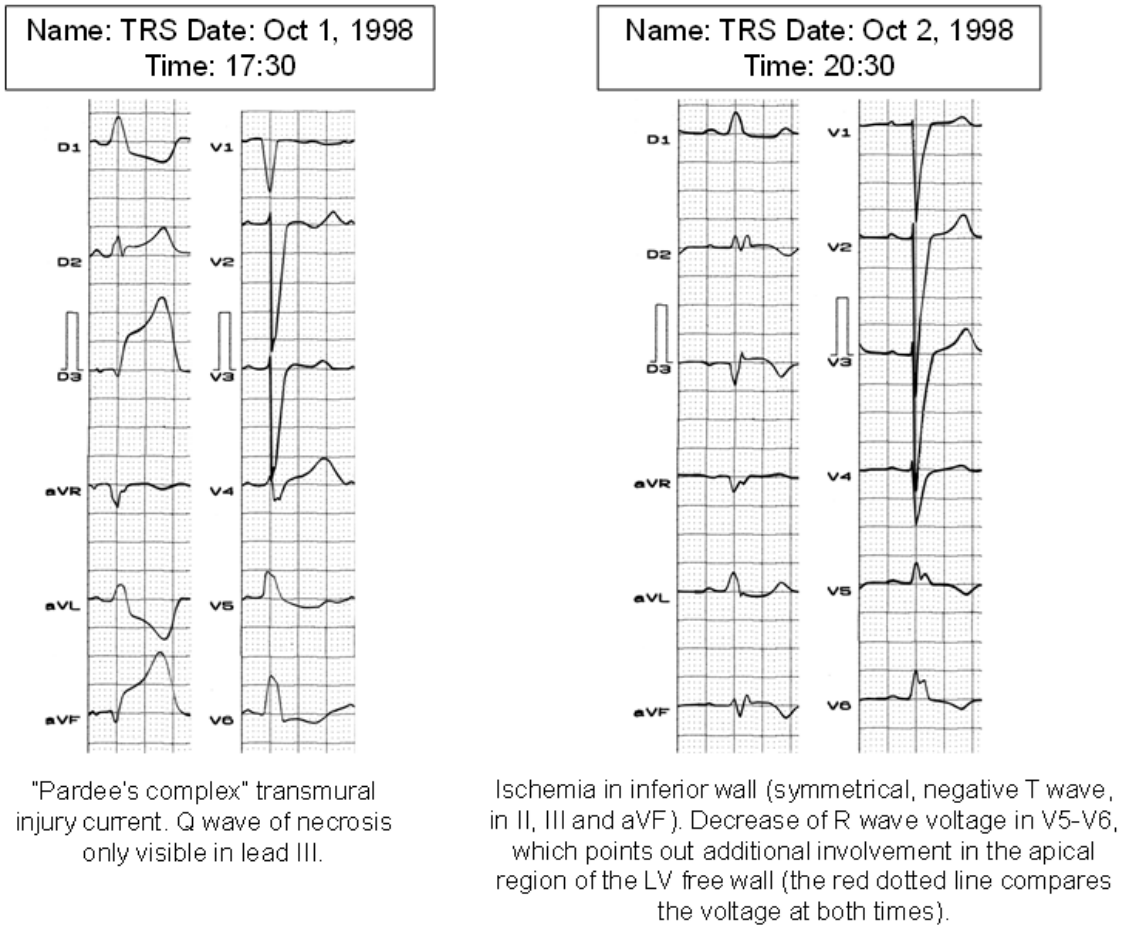


Figure 15. Figure.

The tracing in Figure 16 shows an example of a patient with anterior wall infarction complicated by CLBBB.

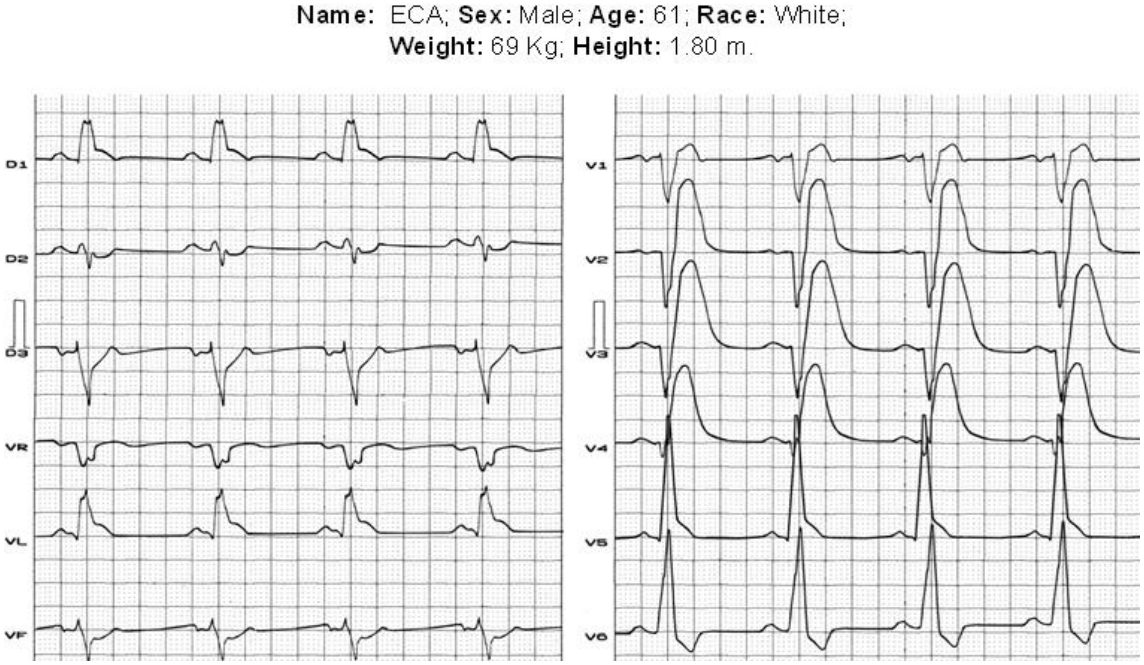


Figure 16. Clinical diagnosis: Hypertension, type II diabetes mellitus, acute myocardial infarction. ECG diagnosis: nLBBB associated with anterolateral wall MI. A qR pattern in leads I and aVL is present with significant transmural anterolateral injury current. ST segment elevation with upper convexity matching the QRS complex in lead I and aVL is present. The QRS/ST-T ratio = or <1 (normal 2:1 or 3:1) (see Figure 17).

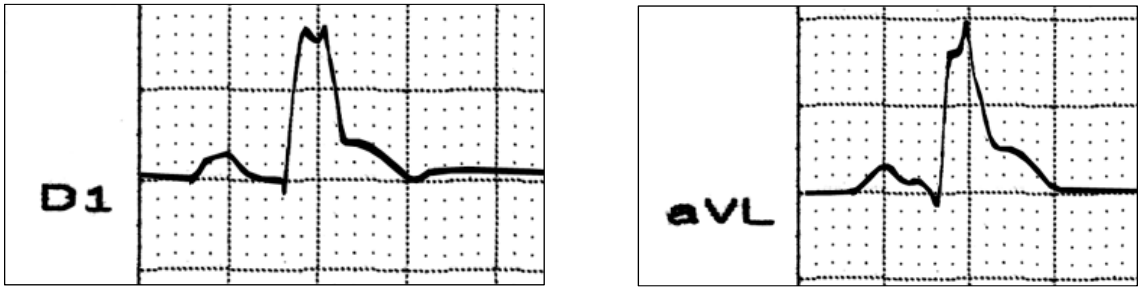


Figure 17. Transmural injury current is illustrated in the high lateral wall concordant with QRS, a finding that is always abnormal.

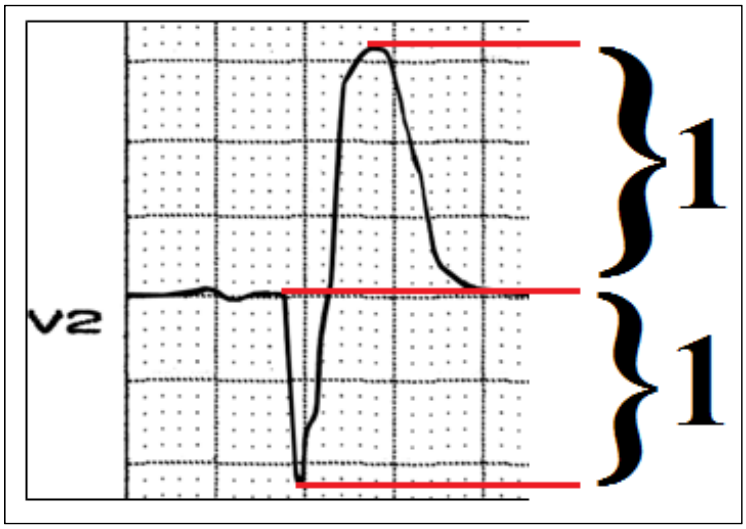


Figure 18. QRS/ST-T ratio = or <1 (normal 2:1 or 3:1).

Case report number 2 - Uremic Pericarditis Resembling Acute Myocardial Infarction

Case Presentation

MAR is a 70 yr old woman with long-standing hypertension treated with an angiotensin converting enzyme inhibitor (ACEI). She was admitted to the emergency department with symptoms of progressive dyspnea on exertion that

had worsened over the past 20 days. She was found to be in severe respiratory failure. She had a past history of left nephrectomy for uncertain reasons. On physical examination she appeared very dyspneic with a blood pressure of 160/80 mmHg, heart rate of 115 bpm, and with some premature beats. Laboratory assessment revealed low peripheral oxyhemoglobin saturation (SpO2 86%; normal SpO2 95-100% breathing room air at sea level), and high serum potassium (K^+ 6.2 mEq/L). Her initial ECG revealed peaked T waves consistent with hyperkalemia (hyperpotassemia).

Initial management:

I) Oral tracheal intubation with mechanical ventilation (OTI/MV).

II) Intravenous administration of: 10 ml calcium gluconate (to stabilize the myocardial membrane), sodium bicarbonate (1 mEq/Kg, IV bolus), and regular insulin with glucose (10 U IV + 50 gr of glucose). After these measures, the T wave abnormalities in the ECG improved.

The patient subsequently developed intense chest pain of uncertain etiology, and serial ECGs, illustrated in Figures 4 and 5, were obtained. The abnormalities observed in these tracings were initially interpreted as an ST Elevation Myocardial Infarction (STEMI). ECG diagnosis of STEMI requires the presence of >1.0 mm ST segment elevation in at least two contiguous ECG leads in the frontal plane or lateral precordial leads (V4-5), >2.0 mm in the right precordial leads (V1-3), or presumably new complete left bundle branch block. Because of her ECG findings she immediately underwent coronary angiography that revealed normal coronary arteries.

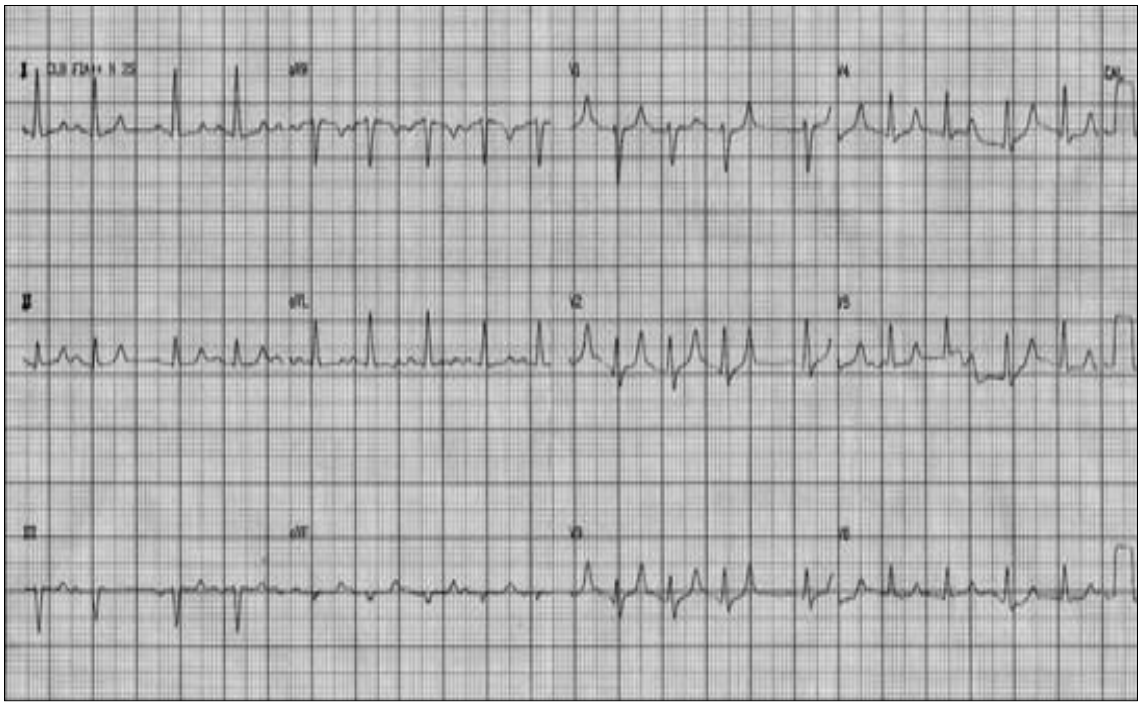


Figure 19. ECG diagnosis: Sinus tachycardia with peaked, symmetrical T waves with narrow base (desert-tent or Eiffel tower-like T waves). These are the earliest repolarization abnormalities when serum potassium levels exceed >5.5mEq/L.

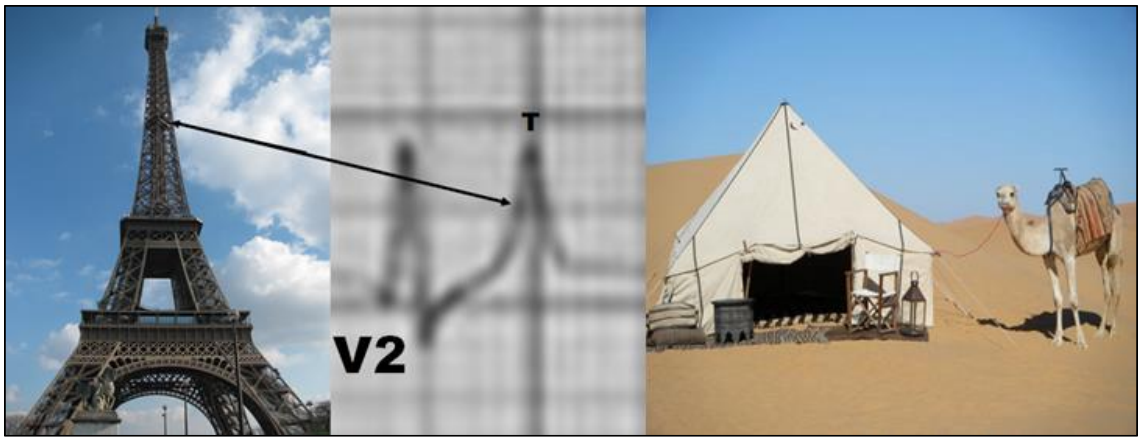


Figure 20. Tall, peaked/pointed/thin T waves resembling a desert tent or Eiffel Tower.

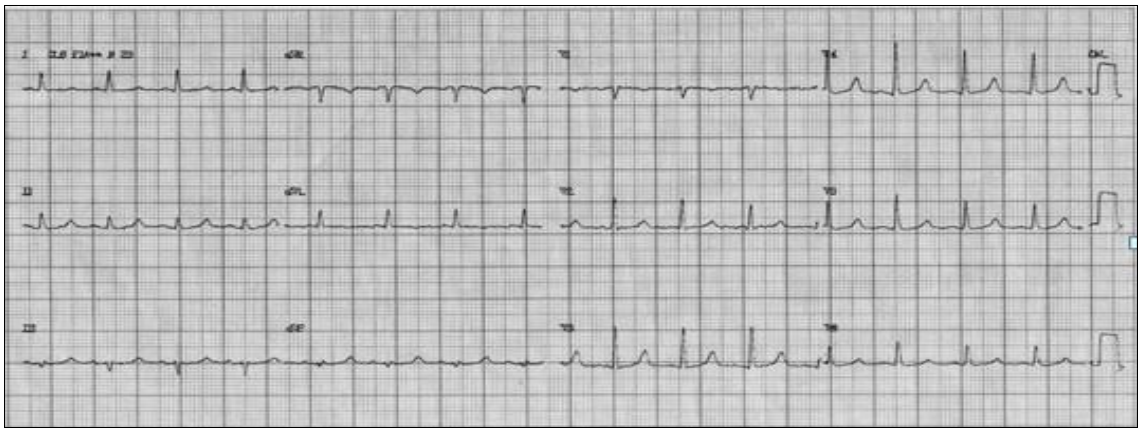


Figure 21. There is regression of the T wave abnormalities after initiating the treatment.

Table describes ECG abnormalities at various serum potassium levels.

Serum potassium level	**Electrocardiographic patterns found**
K^+ > 5.5 mEq/L and < 6.5 mEq/L: Mild hyperkalemia	Repolarization abnormalities: tall, symmetrical and narrow-based T waves resembling a desert tent or the Eiffel tower. Usually this is the earliest sign of hyperkalemia.
K^+ > 6.5 mEq/L and < 7.0 mEq/L: Moderate hyperkalemia	Progressive paralysis of the atria muscle cells results in widening and flattening of P waves due to slow interatrial conduction with eventual disappearance of the P wave. Sinus rhythm, however, is maintained through interatrial conduction pathways (sino-ventricular rhythm). First degree AV block may be present. Decrease in R wave voltage, prolonged QRS duration, and ST segment changes resembling acute myocardial injury, dialyzable injury current or Brugada phenocopy may be seen.
K^+ > 7.0 mEq/L and < 7.5 mEq/L or	Dromotropic alterations and bradycardia: QRS widening with bizarre morphology, high degree AV block, junctional or ventricular escape rhythms, pseudo CLBBB, CRBBB, fascicular blocks, sinus

Severe hyperkalemia	bradycardia, or atrial fibrillation with slow heart rate response. Wide QRS-T complexes resembling sine waves usually seen in more severe hyperkalemia sometimes occur.
K^+ > 8.0 mEq/L and < 9.0 mEq/L Severe hyperkalemia	Decrease in R wave voltage, prominent S waves, diffuse QRS complex widening resembling CLBBB or CRBBB; extreme SAQRS shifts in the FP suggesting LAFB or LPFB. QRS complex widening is differentiated from true bundle branch blocks where the delay is more in the final or mid-final QRS, while in hyperkalemia the delay is always more diffuse. In the late phase the QRS complex merges with the T wave resulting in a smooth, diphasic sine wave appearance with QT interval prolongation. The intensification of ST segment depression or elevation, known as a dialyzable injury current, may eventually resemble the type 1 Brugada pattern or acute anteroseptal STEMI with absence of R waves from V_1 through V_4 and marked ST segment elevation (transmural injury current).
K^+ > 9.0 mEq/L Extreme hyperkalemia	Wide QRS complexes, sino-ventricular rhythm (absence of P waves), irregular rhythm, pseudo-AF, very wide and bizarre QRS complexes, ventricular tachycardia, ventricular fibrillation, and asystole when potassium concentrations exceed 12 - 14 mEq/L.

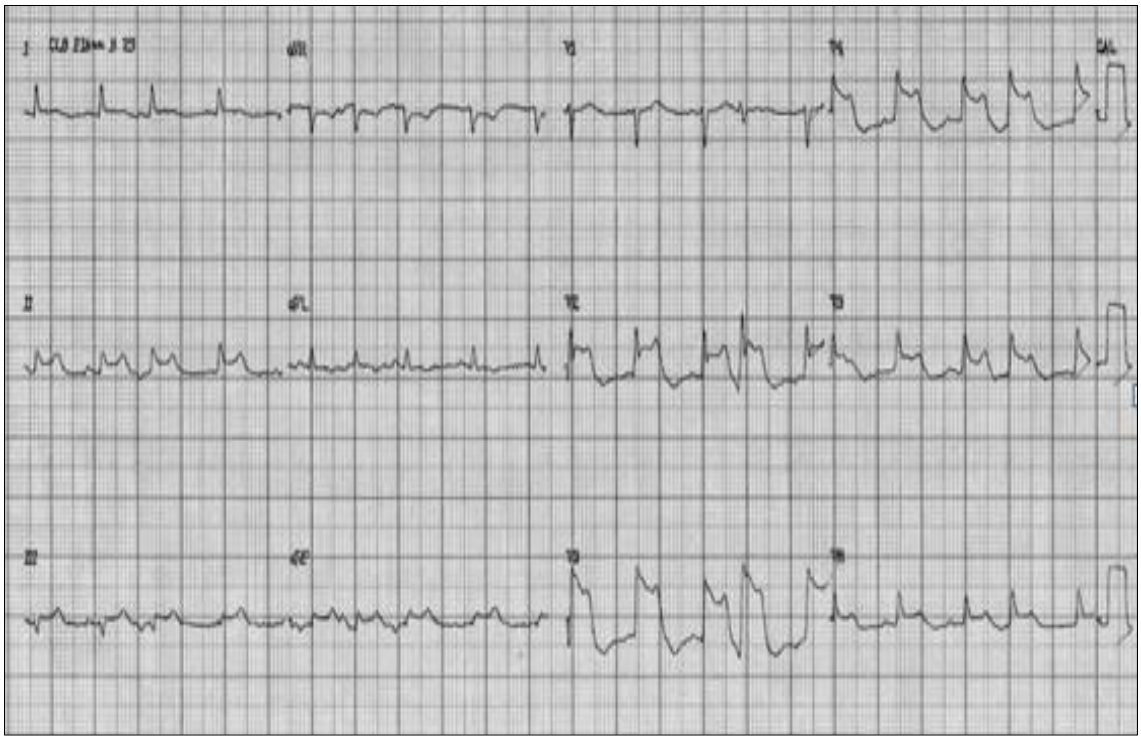


Figure 22. Diffuse concave upwards ST segment elevation with PR segment elevation in lead aVR and premature atrial complexes (during chest pain episode).

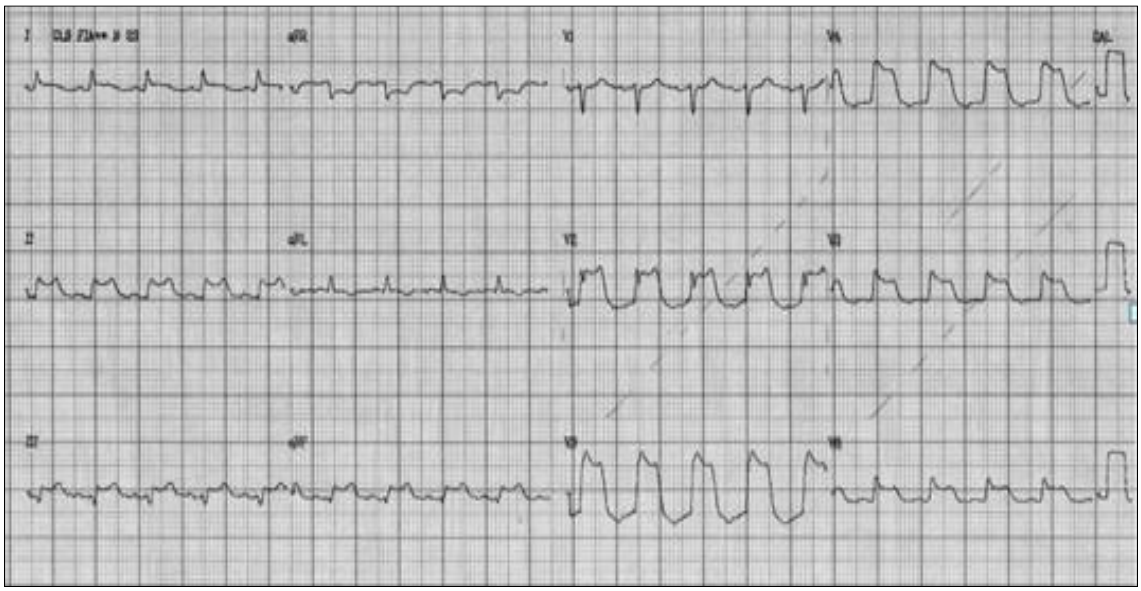


Figure 23. Marked concave upwards ST segment elevation more prominent from V2 through V6, II and III with PR segment elevation in aVR (during chest pain). This pattern in the mid precordial leads resembles an intracellular monophasic action potential (a single polarity) and can be mistakenly diagnosed as an acute STEMI. The combined appearance of ST elevation in both anterior and inferior leads along with PR segment shifts opposite to P polarity may also be suspicious

of stage I acute pericarditis [74 75]. The typical pattern in acute pericarditis is diffuse ST segment elevation in I, II, aVL, aVF and from V3 to V6. ST segment depression is always seen in lead aVR, frequently in V1, and occasionally in V2 [76, 77].

After the cardiac catheterization the patient's precordial pain persisted and radiated into the trapezius muscle region; it improved when sitting up, and it worsened when lying down. On physical examination a triphasic pericardial friction rub was audible along with a tachycardia that was exacerbated when sitting up and leaning forward.

The lab tests were suggestive of acute and chronic renal failure (CRF): metabolic acidosis, hyperkalemia and hypocalcemia.

pH: 7.04; PO2: 126; PCO2: 14; K: 7.0 mEq/L; HCO3: 3.8 mEq/L; Glucose: 134 mg/dL; BUN: 475 mg/dL; Cr: 18.9 mg/dL; Ca: 0.4 mg/dL; Hgb: 6.4 mg/dL; Tp: 0.13 g/dL; CK-MB: 14.1.

ECG changes in chronic renal failure reflecting both hyperkalemia and hypocalcemia include prolonged ST segments often with QT prolongation (hypocalcemia) as well as peaked, symmetrical T waves (hyperkalemia).

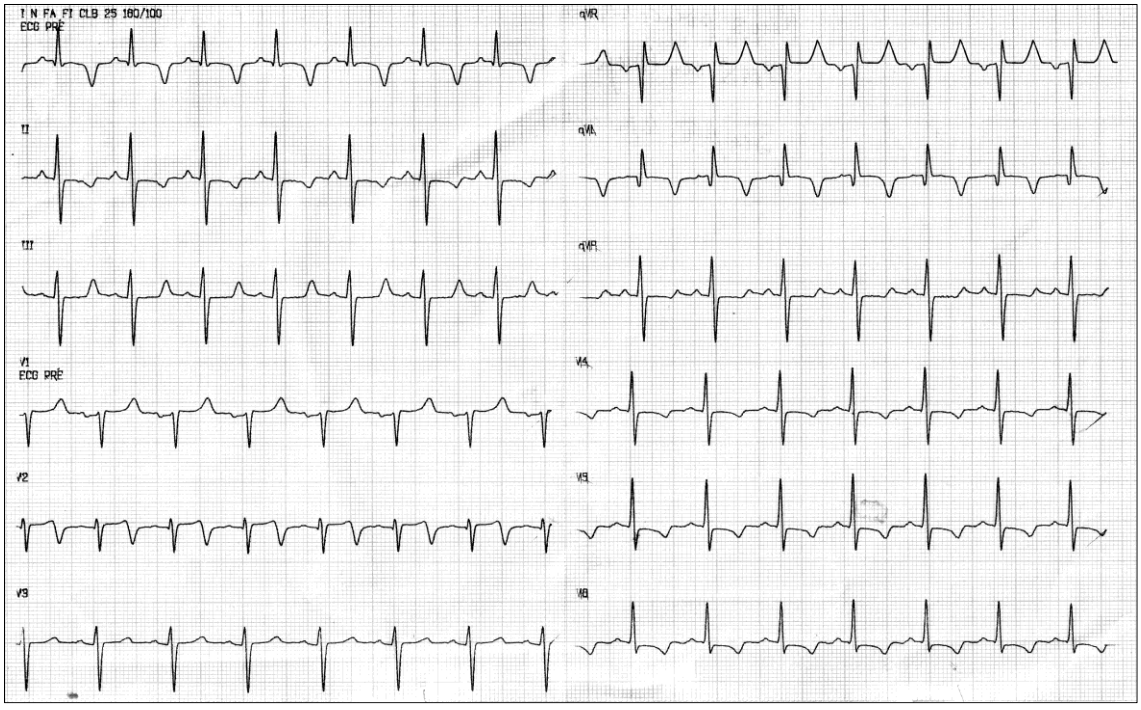


Figure 24. Clinical diagnosis: 47 yr old man with polycystic kidney disease and chronic renal failure (Creatinine 7.0 mg/dL) treated with dialysis for hyperkalemia

and hypocalcemia. ECG diagnosis: Prolonged ST segments, peaked, symmetrical T waves, and QT prolongation.

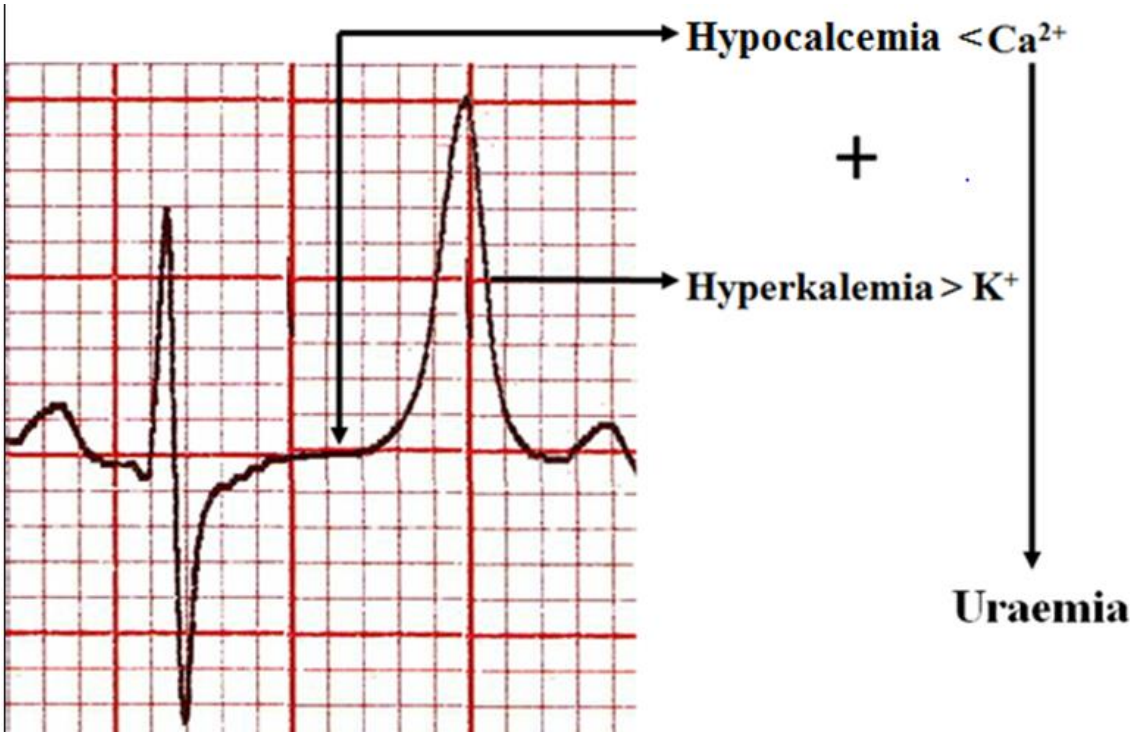


Figure 25. The lead shows typical prolonged ST segment (hypocalcemia) associated with a tall, symmetrical T wave with a narrow base (hyperkalemia). The patient (MAR) underwent hemodialysis with progressive improvement. After 1 week there was regression of ST segment elevation and new diffuse T wave inversion indicating Stage III ECG evolution of pericarditis. At this time the pericardial rub had disappeared.

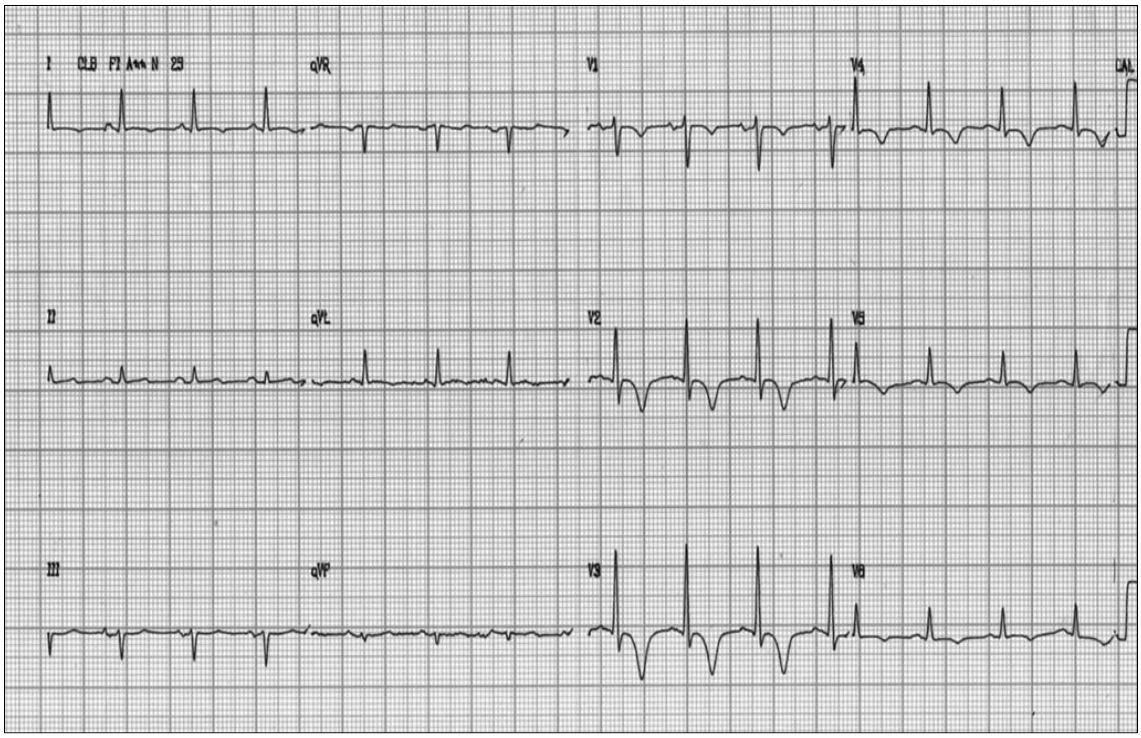


Figure 26. There is resolution of ST segment changes and widespread inversion of T waves indicating Stage III pattern of acute pericarditis.

Acute pericarditis is an inflammatory disease of the pericardium with multiple causes. It is the most common form of pericardial disease presenting to the emergency department, and it is often mistakenly diagnosed as an ACS (as in the present case).

The real incidence is not known; however in individuals who are not immunosuppressed 90% of cases have a viral or idiopathic etiology [78] [79].

Acute pericarditis is found in approximately 5% of the patients admitted in the ER for chest pain not due to acute myocardial infarction. It occurs more frequently in men between age 20 and 50 years.

Potential etiologies of acute pericarditis include infection, acute myocardial infarction, medications, chest wall trauma, and systemic diseases such as rheumatoid arthritis and chronic renal failure. However, most often diagnostic evaluations are inconclusive.

Possible etiologies of pericarditis.

I. Infectious:
   - Viral: infectious being most frequent.
   - Bacterial including tuberculosis.
   - Fungal.

- Parasitic.

II. Autoimmune and collagen vascular diseases:
    - Lupus (systemic lupus erythematosus)
    - Scleroderma
    - Dermatomyositis
    - Rheumatoid arthritis
    - Polyarteritis nodosa
    - Ankylosing spondylitis
    - Reiter's syndrome
    - Familial mediterranean fever.

III. Autoimmune processes:
    - Acute polyarticular arthritis or rheumatic fever.
    - Post-cardiotomy syndrome.
    - Post-myocardial infarction syndrome.
    - Chronic autoimmune pericarditis.

IV. Processes in organs adjacent to the pericardium:
    - After acute myocardial infarction
    - Myocarditis
    - Aortic aneurysm
    - Pulmonary infarction
    - Pneumonia
    - Esophageal diseases
    - Hydro-pericardium in CHF
    - Paraneoplastic

V. Metabolic:
    - Uremia (as in the present case) is a frequent cause. It is observed in 8% of patients with chronic or acute renal failure. It relates to the degree of azotemia with BUN levels usually >60 mg/dL. (The reference value for those older than 60 years is 8-23 mg/dL). Pericarditis is often related to inadequate dialysis or fluid overload.
    - Myxedema
    - Addison's disease
    - Diabetic ketoacidosis

- Severe hyperlipidemia.

VI. Gestational:

- Pregnant women (very rare).

VII. Trauma:

- *Direct injuries of the pericardium:* direct penetrating injuries, esophageal perforations, foreign bodies.
- *Indirect injuries of the pericardium:* irradiation, non-penetrating injuries.

VIII. Neoplastic:

- *Primary Tumors:* rare.
- *Secondary tumors:* metastasis of breast, lungs, stomach, colon cancer, sarcoma, lymphoma, leukemia, etc.

IX. Idiopathic: Up to 50% of the cases in some series.

X. Diagnosis

- The diagnosis is based on a history of pleuritic chest pain and the presence of a pericardial rub (present in 85% of the cases) [80]. Typical ECG changes are characterized by diffuse and widespread concave upwards ST segment elevation often mistakenly confused with STEMI [78 81 82]. At least 2 of 4 criteria are necessary for diagnosis: pleuritic chest pain, pericardial friction rub, diffuse concave upwards ST segment elevation, and pericardial effusion [83 84].
- Fever is present in approximately 46% of the cases, and 40% have a recent history of respiratory infection. Classically, the pleuritic chest pain is relieved by leaning forward in a sitting position and worsened in a supine position; it often radiates to the inter-scapular region because the trapezius muscle and the pericardium have the same sensory innervation [85, 86]. Pain may be minimal or absent in patients with pericarditis due to uremia, neoplasm, tuberculosis, or radiation therapy.

XI. Physical examination

- A pericardial rub is virtually 100% specific for the diagnosis; however, sensitivity is variable (16-85%) depending on the frequency of auscultation and etiology [78 82]. The rub is best heard at end-expiration with the diaphragm of the stethoscope placed in the low left sternal

border while the patient is sitting forward. Erb's point is the ideal location to hear the rub.

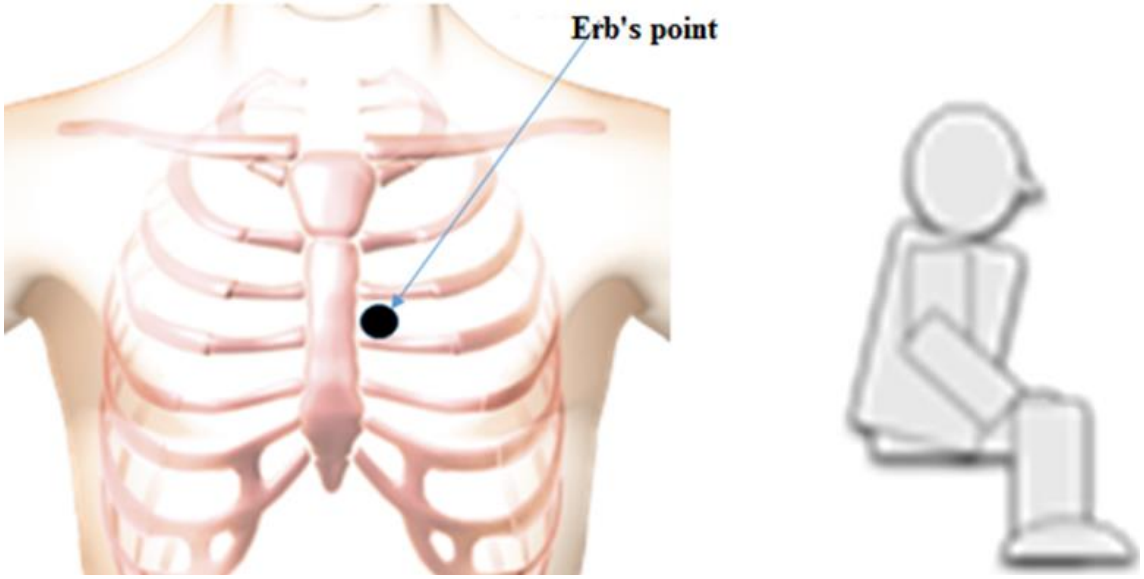


Figure 27. Location of Erb's point and the proper position for pericardial rub auscultation. The pericardial friction rub has three components that correlate with the phases of the cardiac cycle: a systolic component, an early diastolic and a late diastolic component (triphasic). Often not all three components are audible in a given patient at any particular time.

In patients with uremic pericarditis with autonomous nervous system impairment the heart rate may remain non-tachycardic even in the presence of tamponade, fever, hypotension and anemia [87].

Laboratory data

Acute phase inflammatory markers including sedimentation rate, leukocytosis and C-reactive protein (CPR) are elevated in approximately 75% of the patients. Increase in cardiac troponins (TnI) is indicative of myocardial involvement or myopericarditis [88] [89].

Other tests to confirm the etiology should include thyroid function, rheumatologic tests, renal function, and blood cultures when suspicious of bacterial infection. In the presence of a large pericardial effusion, histological

analysis and immunohistochemistry of the pericardial fluid should be done to rule out TB (adenosine deaminase) or neoplasia [89].

In patients that do not respond to therapy after a week, other etiologies should be pursued to rule out autoimmune disease and HIV.

Electrocardiography

The electrocardiographic alterations in pericarditis involve PR segments, ST segments and rhythm according to the time course of pericarditis. The ECG can be normal in approximately 6% of cases. In acute pericarditis the ECG changes evolve over four serial stages [90] [91].

Stage I: concave upwards ST segment elevation in multiple leads except aVR and V1 where ST depression may occur; symmetrical and peaked T waves with narrow base and mild increase in voltage; and PR segment depression (except in aVR, where there is PR segment elevation). These alterations are observed in more than 80% of the cases [91] [92].

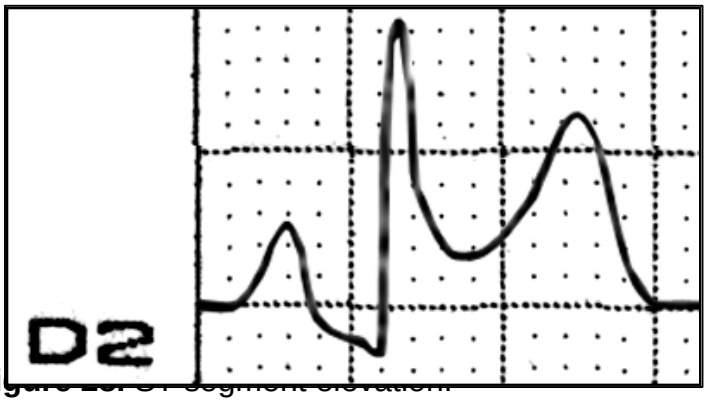


Figure 2. ST segment elevation.

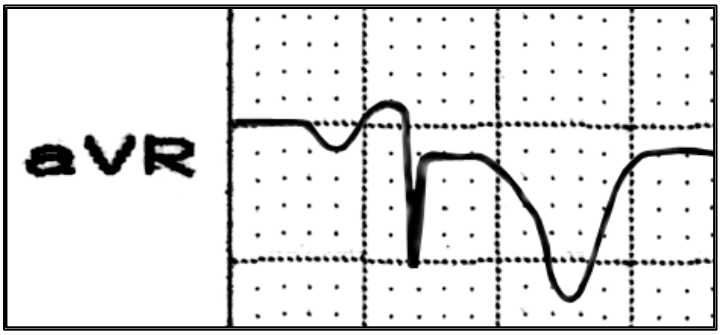


Figure 29. Reciprocal alterations in aVR.

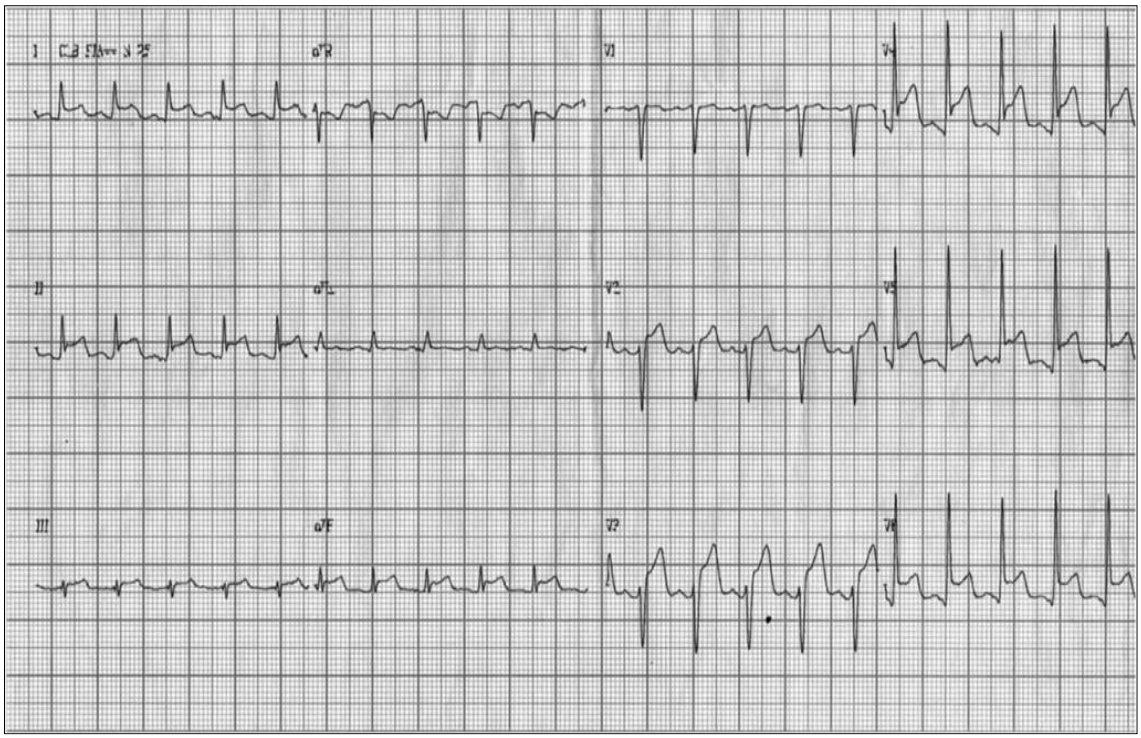


Figure 30. Stage 1 of acute pericarditis. Diffuse concave upwards ST segment elevation and PR segment elevation is shown in aVR.

Another useful ECG finding in Stage I acute pericarditis is Spodik's sign [93], the slightly downward sloping TP segment best seen in lead II as illustrated by the black arrow in Figure 31.

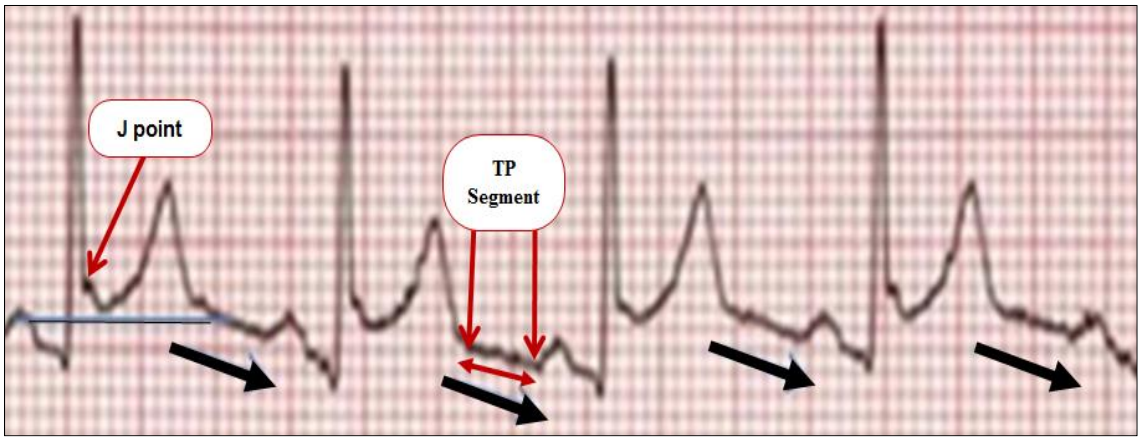


Figure 31. Lead II shows Spodik's sign characterized by downward TP segment, indicated by the black arrows.

Table modified from [94] lists the differential diagnosis of ST segment elevation.

Table - Main causes of ST segment elevation
Acute Myocardial infarction
Acute myocarditis
Acute pericarditis
Takotsubo cardiomyopathy or stress-induced (apical ballooning) cardiomyopathy
Left ventricular hypertrophy
Left ventricular aneurism
Hypertrophic Cardiomyopathy
Acute aortic dissection
Pulmonary embolism
Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia
Left Bundle Branch Block
Hyperkalemia

Post electrical cardioversion
Ventricular paced rhythm
Vasospastic or Prinzmetal´s angina
Brugada Syndrome
Benign Early repolarization pattern
Inferolateral Early Repolarization (ER)
Idiopathic ventricular fibrillation
Congenital Short QT syndrome
Hypothermic J-wave
Hypercalcemia
Acute cerebral hemorrhage. J-wave in acute nervous system injuries; i.e. subarachnoid hemorrhage. cardiac arrest, etc.
Dysfunction of the cervical sympathetic system

Stage II: Reversion of ST and PR segments shifts along with T wave flattening (after some days).

Stage III: Diffuse T wave inversion resembling myocardial ischemia. Absence of Q waves indicative of myocardial necrosis is a useful clue to differentiate this stage of pericarditis from the diagnosis of myocardial infarction.

Stage IV: T wave abnormalities resolve to more normal morphology; this may take weeks to months after the onset of acute pericarditis.

Other ECG alterations: Alterations in rhythm may occur during any stage and include sinus tachycardia and various atrial arrhythmias [95].

In the presence of pericardial effusion the most typical finding is low QRS voltage [96] which improves after pericardiocentesis. In the setting of pericardial tamponade electrical alternans of QRS voltage may be seen. Low QRS voltage is defined as complexes of less than 5 mm (0.5 mV) in the frontal plane leads and

less than 10 mm in the precordial leads. QRS alternans is the beat by beat variation in axis, amplitude and/or morphology.

Low voltage may also be present in other diseases including emphysema, infiltrative myocardial disease, and pneumothorax. After pericardial drainage the QRS voltage does not normalize immediately, suggesting a continued inflammatory process. Electrical alternans is the result of the heart moving around in a large effusion. This pattern is more visible in the precordial leads. Isolated QRS alternans is not specific to pericardial effusion, but the presence of *both* P and QRS alternans is pathognomonic.

The most frequent type of alternans involves only the QRS. When P, QRS, and T waves are included it is called total alternans and is observed in case of cardiac tamponade. Beck's triad (jugular vein distention, hypotension and muffled sounds) is a feature of cardiac tamponade.

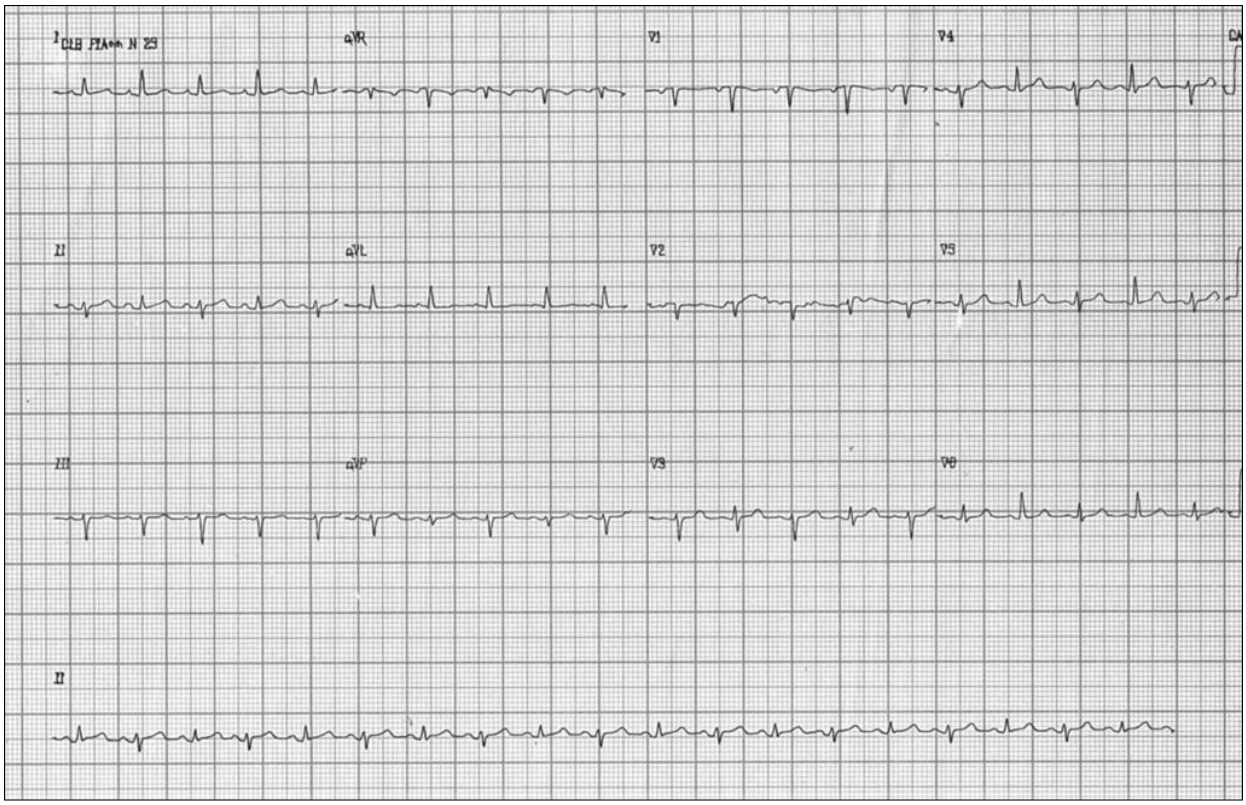


Figure 32. Patient with TB pericarditis and cardiac tamponade. ECG shows low, diffuse voltage and QRS electrical alternans.

Differential diagnosis of pericarditis

	Early repolarization syndrome	**Acute pericarditis in early stage/stage I**

ST/T ratio in V6	<0.25	Variable.
T wave	Always wide, positive and persistent. Greater voltage.	It decreases its width in hours. Less voltage. Only increased in the early stage.
ST	Significant elevation only in precordial leads. Reciprocal depression only in aVR.	Diffuse elevation in multiple leads. There may be reciprocal depression in aVR.
Response to exercise	Frequent return of ST to the baseline. T wave may normalize.	No change in ST segment elevation.
Hyperventilation	The polarity of T may be modified.	It does not modify the polarity of T.
Presentation	Stable.	Transient.
HR	Frequent bradycardia.	Frequent tachycardia.
Clinical	Asymptomatic.	Symptomatic.
Age range	20 to 40 years.	Predominance 40 or more years.

The electrocardiographic features of early repolarization that help in the differentiation with acute pericarditis in stage I include:

- Slow heart rate: bradycardia.
- QRS electrical axis, ST segment and T wave pointing in the same direction in the frontal plane.
- Frequent deep and narrow Q waves followed by R waves with great voltage in the left precordial leads.
- Notch or slurring in the downward slope of R.
- Sudden change in precordial QRS transition.

- J point and ST segment elevation; usually J <2 mm (it may exceptionally be >5 mm) with upper concavity in intermediate and left leads, and sometimes in inferior leads, followed by wide and positive T wave;
- Before sympathetic stimulus and sympathomimetic drugs, J point and ST segment elevation is observed.
- Absence of reciprocal or mirror image, except in aVR.
- Pseudo-symmetrical T waves with great width and polarity matching their corresponding QRS complexes.

	STE-ACS /STEMI	**Acute pericarditis**
Number of involved leads	Segmentary and located	Greater (diffuse) and extensive
Intensity of phenomena	Greater	Lower
Reciprocal or mirror effect	When present, it occurs in several leads	Only in aVR [97].
QRS complex prolongation	Yes	No
QT interval shortening in leads with ST segment elevation.	Yes	No
QT dispersion [98]	Greater	Lower

Chest X-rays

A chest X-ray is mandatory in all patients with suspicion of pericarditis. The presence of cardiomegaly occurs only when there is more than 200 ml of fluid in

the pericardial sac with the cardiac outline acquiring a globular shape (Figure 33, a patient with purulent pericarditis).

The chest X-ray may also be of great help in identifying the etiology by showing concomitant pulmonary infection or masses in the mediastinum. This tool has a moderate sensitivity (70%) but low specificity (41%) for the diagnosis of pericardial effusion [99].

The presence of pericardial calcification (Figure 34) strongly suggests constrictive pericarditis, although it is only present in 25% of these patients [100].

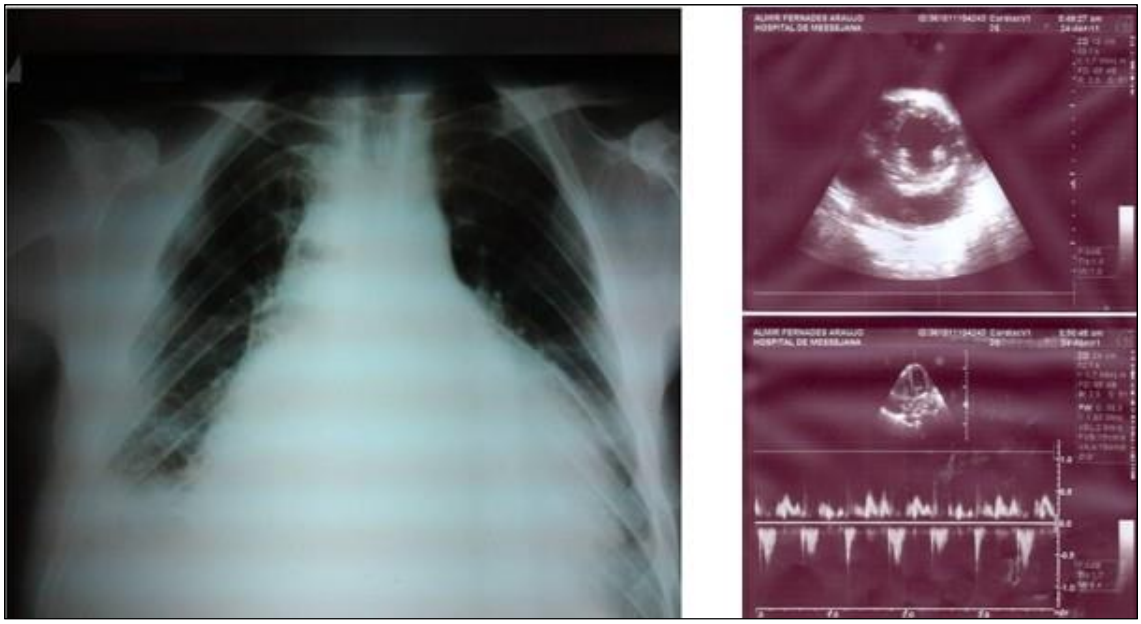


Figure 33. X-rays shows globular increase of the cardiac area with pleural effusion at the right. Echo showing pericardial effusion.

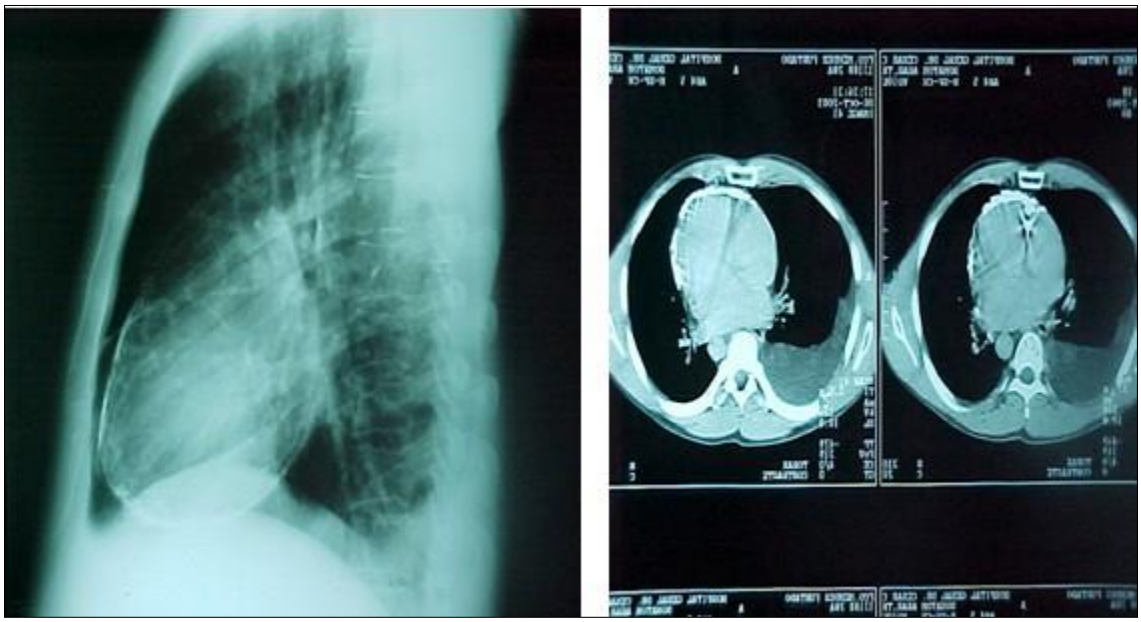


Figure 34. Typical pericardial calcification in the chest X-rays, confirmed by CT.

Echocardiogram

Cardiac ultrasound should be performed in all cases of suspected pericarditis to assess the presence of pericardial effusion [76, 77]. The echocardiogram may offer clues to the etiology as it allows characterizing the nature of the liquid (transudate or exudate) and verifying if there is fibrin (as in TB) or calcium.

The collapse of the RA is the most sensitive sign of tamponade; however collapse of the RV is more specific. Doppler may also indicate the echocardiographic expression of a paradoxical pulse.

CT and NMR

Computerized tomography and nuclear magnetic resonance are two advanced imaging modalities that more accurately evaluate the pericardium.

They are useful jointly with the echo to better characterize effusion and tamponade. They should not be done in critically ill patients who require immediate treatment. They are especially useful in detecting loculated effusions or when associated with pleural effusions. Pericardial thickening may be evaluated by both methods enabling assessment of chronicity and severity. Density of fluid similar to water suggests transudate; greater than water suggests malignancy, blood or pus [101].

Analysis of pericardial fluid and biopsy

In cases of refractory pericarditis with effusion analysis of the pericardial fluid should be done in order to determine the etiology, although the definitive cause is only obtained in 20% of cases.

Treatment

Most cases of acute pericarditis have a viral etiology and do not need to be hospitalized. They respond very well to therapy with non-steroidal anti-inflammatory drugs (NSAIDs). Complicated patients should be admitted for diagnosis, treatment and for the detection of cardiac tamponade, the most feared complication [102].

High risk indicators include increase in positive troponins, fever above 38°C with leukocytosis, voluminous pericardial effusions with or without cardiac tamponade, immunosuppressed patients, patients on oral anticoagulation, myocardial dysfunction by echo suggesting myopericarditis. These markers indicate the need of hospital admission for etiological evaluation and therapeutic interventions.

NSAIDs should be used in anti-inflammatory doses: acetylsalicylic acid (ASA), 500 to 750 mg every 6 or 8 hours for 7 to 10 days, followed by gradual reduction of 500 mg per week, for three weeks; ibuprofen, 400 to 800 mg every 6 or 8 hours, for 14 days; indomethacin is sometimes used, because it may reduce scar formation. The duration of the treatment with NSAIDs is usually around 14 days and guided by serum levels of C-reactive protein.

Colchicine has been shown in controlled clinical trials to be more effective than NSAIDs in relieving symptoms and preventing recurrence [103] [104] [105] [106]

Colchicine is generally well tolerated, with a low incidence of adverse side effects [107]. A multicenter, double-blind, placebo-controlled and randomized study concluded that colchicine, added to conventional anti-inflammatory treatment, significantly reduced the rate of subsequent recurrences of pericarditis in patients with multiple recurrences. Taken as a whole with the results of other studies, colchicine should be considered a first-line treatment for acute or recurrent pericarditis in the absence of contraindications or specific indications [108]. The dose of colchicine is 0.5 mg BID or 0.5 mg once daily in patients <70 kg for three months during the first event or 6 months in recurrent pericarditis.

The routine use of corticosteroids should be avoided, since it is associated with an increase in the rate of recurrence. They may be considered indicated in the following situations:

- Pericarditis refractory to NSAIDs and colchicine.
- In cases in which the above mentioned drugs are contraindicated.
- Autoimmune etiology or connective tissue diseases.

Prednisone, when used, is dosed at 1 mg/Kg/day for at least 1 month before tapering; there is evidence that a lower dose of 0.5 mg/Kg/day has the same efficacy with fewer side effects or recurrences [109]. To prevent recurrence or reactivation of acute pericarditis, slow weaning and addition of colchicine (1 mg per day) should be done.

Bacterial pericarditis requires pericardial drainage and appropriate antibiotic therapy. TB pericarditis requires a multidrug management approach. If there is a neoplastic etiology, appropriate chemotherapy is required, although there is a high rate of recurrence. The patients with uremic pericarditis require intensive hemodialysis.

Pericardiocentesis and pericardiectomy

Pericardial drainage is mainly indicated in the cases of cardiac tamponade, purulent pericardial effusion, or large symptomatic effusions [89]. Pericardial drainage is made either by percutaneous technique with placement of a drainage catheter or by open surgical drainage (pericardial window). It may also be done using video-assisted pericardioscopy.

Echo guided percutaneous pericardiocentesis decreases complications and increases the likelihood of success [110]. Patients with constrictive pericarditis refractory to clinical treatment should undergo pericardiectomy [76, 77].

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III) Time for a new paradigm shift in myocardial infarction.

Emre K Aslanger 1, H Pendell Meyers 2, Stephen W Smith 3 Time for a new paradigm shift in myocardial infarction. Review Anatol J Cardiol. 2021 Mar;25(3):156-162. doi: 10.5152/AnatolJCardiol.2021.89304.

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Abstract

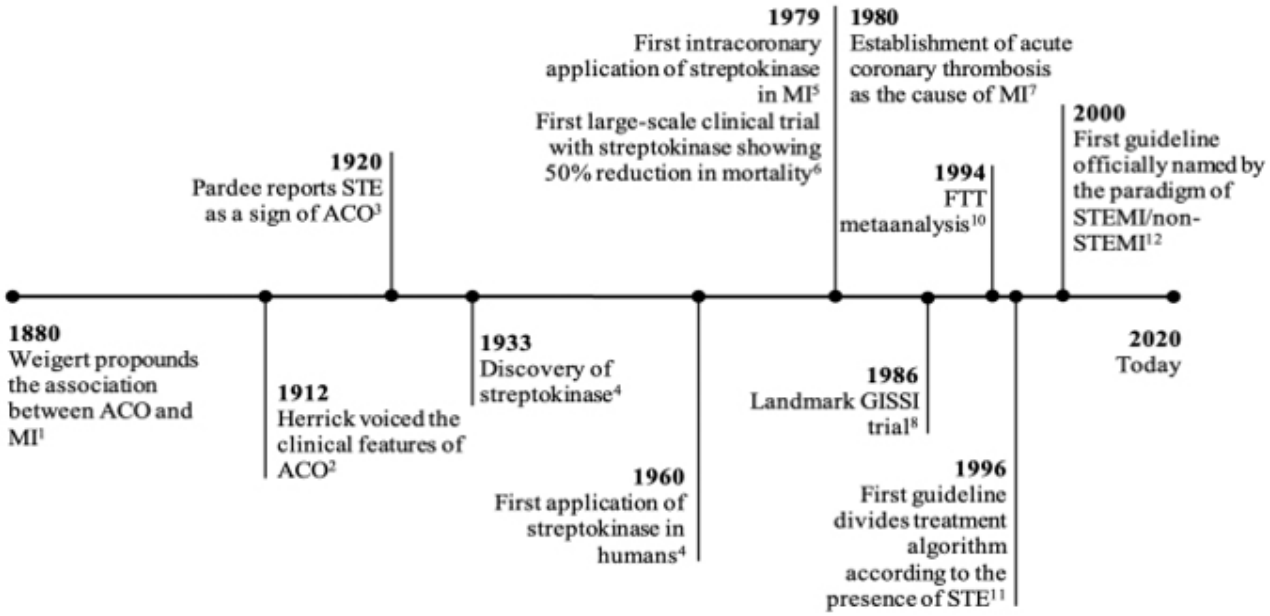
The ST-elevation myocardial infarction (STEMI)/non-STEMI paradigm per the current guidelines has important limitations. It misses a substantial proportion of

acute coronary occlusions (ACO) and results in a significant amount of unnecessary catheterization laboratory activations. It is not widely appreciated how poor is the evidence base for the STEMI criteria; the recommended STEMI cutoffs were not derived by comparing those with ACO with those without and not specifically designed for distinguishing patients who would benefit from emergency reperfusion. This review aimed to discuss the origins, evidence base, and limitations of STEMI/non-STEMI paradigm and to call for a new paradigm shift to the occlusion MI (OMI)/non-OMI.

Introduction

Surveying the history of myocardial infarction, the pre-reperfusion era is the dark ages for today's cardiologists. It may be easy to chuckle at the naivete of the management approach for patients with acute coronary occlusion (ACO) during that era (Fig. 1), and it may seem mysterious that the medical community reacted so slowly to the accumulating evidence (Fig. 2) (1–12). However, the physicians of the past were no less certain that they were providing the best possible treatment options available as are today's clinicians. Therefore, we must ask ourselves if we, too, are unaware of the obvious opportunities for improvement in the management of ACO, and what steps we can take to enact those improvements.

Figure 1



As the historical timeline shows, it has been more than a century since acute myocardial infarction (AMI) was linked to coronary occlusion (1) and half a century since acute thrombosis was blamed as the primary mechanism (7). Since then, it has been of the utmost importance to distinguish patients with ACO or near occlusion, whose myocardium is at imminent risk of irreversible infarction without immediate reperfusion, from those patients with myocardium that is at risk, but not imminently and who can be stabilized with medical therapy. Before the reperfusion era, and even well into that era, the established AMI paradigm used for this differentiation was the Q-wave/non-Q-wave AMI dichotomy (9). As clinicians had little to offer patients for opening acutely occluded arteries, this paradigm was actually used to retrospectively classify patients according to whether their subsequent ECG developed Q-waves, the ominous sign of the irreversible transmural loss of myocardium. However, the term “Q-wave MI” implicitly referred to ACO that clinicians had not been able to intervene upon.

At the end of the last millennium, as a result of large-scale randomized-controlled trials (RCTs) comparing fibrinolytics with placebo, there was a revolutionary paradigm shift from Q-wave MI/non-Q-wave MI to STEMI/non-STEMI (NSTEMI). The seminal Fibrinolytic Therapy Trialists’ (FTT) meta-analysis (10), which pooled data from 58,600 patients who were enrolled in all 9 RCTs of thrombolytics versus placebo of at least 1,000 patients, showed an impressive 3% absolute reduction in short-term mortality. This was an unmatched breakthrough in the

entire history of cardiology, but one critical question was obscured by the elation over that great success. Although patients with ACO were the ones who were most expected to benefit from emergent reperfusion, how did these studies attempt to identify those with ACO from those without? Surprisingly, they did not. Angiography was not employed in these studies, either prior to or after therapy. Instead of enrolling patients with proven ACO, the researchers randomized patients with “suspected AMI” to thrombolytics versus placebo. In general, these were high-risk patients with acute chest pain and with concerning but undefined electrocardiographic (ECG) findings. Overall, the group that received fibrinolytics had a significantly lower mortality. In a post-hoc analysis, the authors compared the effects of fibrinolytics in all patients to the effects in subsets of patients with ST-depression (STD), ST-elevation (STE), and “normal.” Unfortunately, only 4 of the RCTs defined their version of STE, and these 4 had varying cutoffs and methods of measurement, usually not specified. Compared with giving fibrinolytics to all the patients regardless of ECG findings, using an undefined amount of STE as an arbiter of fibrinolytics administration produced an improvement in the number-needed-to-treat for short-term mortality from 56 to 43. Conversely, the subgroups of STD and “normal” ECG showed a non-significant trend to mortality harm. With these findings, the term STEMI became almost synonymous with ACO that necessitates acute reperfusion. Later, after fine-tuning of STE cutoffs by several investigators comparing the normal variant STE to STE in AMI (but, again, without the use of angiography) (13–16), “STEMI criteria” became a guideline-supported central dogma of cardiology (17–19).

At this point, we must ask ourselves the abovementioned foundational question: Are we perhaps unaware of errors in our current approach and thus ignoring opportunities for improvement in the management of ACO? Unfortunately, the answer seems to be yes.

Caveats of the STEMI/NSTEMI paradigm

The STEMI/NSTEMI paradigm is neither sensitive nor specific for the identification of ACO as it was flawed from the start. In the FTT meta-analysis (10), there were undoubtedly many patients with false positive STE (STE due to non-AMI conditions) who received thrombolytics, thus gaining no benefit despite

the risk. Conversely, in the “normal” ECG and STD subgroups, there were doubtless many patients with ACO (including patients with “posterior” AMI, hyperacute T waves, and so on) whose benefit was confounded by those with a normal or STD ECG who did not have ACO (Fig. 3). Overall, without any ECG subgroup analysis, the group that received fibrinolytics had a lower mortality reflecting a high enough prevalence of ACO in the population with STE in whom benefit of administering fibrinolytics overweighs their harm.

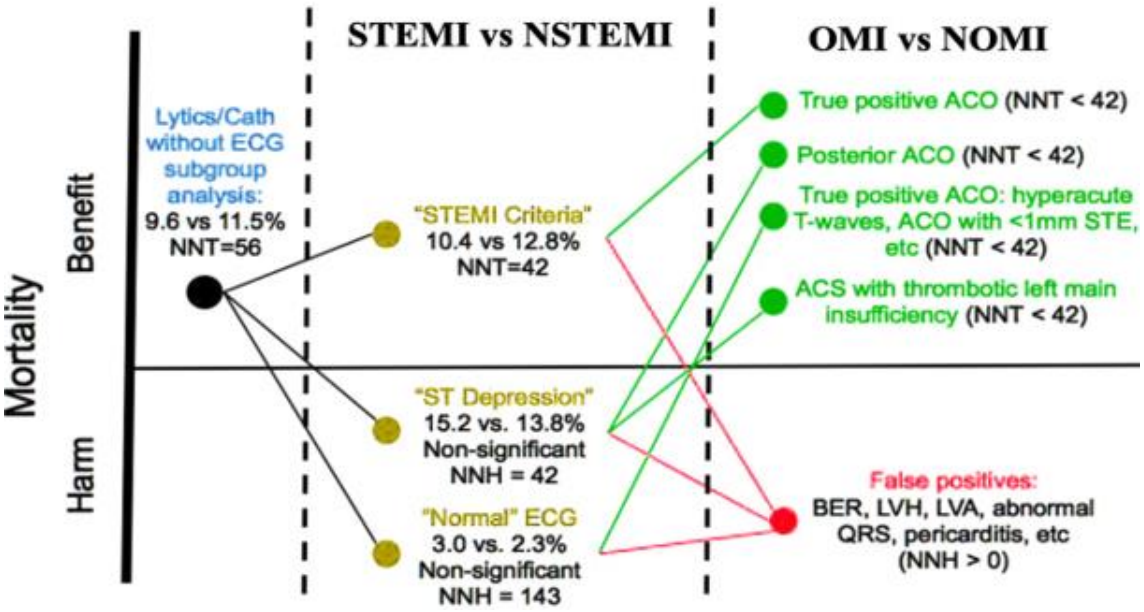


Figure 3

A comparison of ST-segment elevation myocardial infarction/ non-ST-segment elevation myocardial infarction and occlusion myocardial infarction/ non-occlusion myocardial infarction paradigms using the Fibrinolytic Therapy Trialists’ meta-analysis mortality data.

As mentioned above, the STE cutoffs recommended in the 4th universal definition of MI (17) did not originate from these studies; instead, they were derived from studies comparing healthy individuals with those with AMI diagnosed by CK-MB, not by the presence of ACO (13–16). Thus, STEMI criteria were not originally derived or validated for the selection of patients with ACO who would most benefit from fibrinolytics or any other means of reperfusion intervention.

Because “STEMI” inappropriately became the term and concept used in place of ACO before ubiquitous cardiac catheterization was available, no study has ever

questioned the benefit of emergent reperfusion therapies in ACO other than those manifesting the STEMI criteria. In the percutaneous coronary intervention era, STEMI criteria derived from studies of AMI as diagnosed by CK-MB are used, and their limited specificity for ACO cause a substantial amount of false catheterization laboratory activations (20–22). More importantly, the sensitivity is poor, missing at least one-third of the ACO (23–30) with the result that this unfortunate group of patients, labeled as NSTEMI, are deprived of emergent reperfusion therapy, just as they were in the old days of Q-wave/non-Q-wave MI approach. Marti et al. (23) have shown that approximately one-fifth of the patients with ACO had ≥1 mm of STE, including 12.7% of left anterior descending artery occlusions. Schmitt et al. (24) have found that 29% of the patients with ACO did not meet STEMI criteria, with circumflex occlusions being the most missed (50%). In the PARAGON-B trial (27) 27% of the patients with NSTEMI had completely occluded culprit vessels at the time of next day angiography. On average, these patients had a larger infarct size, worse left ventricular function, higher biomarkers, and higher long-term mortality than those of NSTEMI patients with open arteries. In a similar analysis of the TRITON-TIMI-38 (28), 26.2% of the patients with NSTEMI had completely occluded culprit vessels at the time of angiogram. A meta-analysis of 7 studies by Khan et al. (29) have showed that of the 40,777 NSTEMIs, 25.5% had ACO on angiography an average of 24 hours after presentation, and these patients with ACO but without STE had a 1.5 times higher relative risk of mortality compared with those without ACO. Of note, these numbers may underestimate ACO in NSTEMI as a large percentage of total thrombotic occlusions spontaneously reperfuse by the next-day angiogram; unfortunately, many only autolyse after a substantial loss of myocardium. Conversely, the occlusion might have also occurred later than the ECG decision point, but the recognition of this pathologic substrate that leads to ACO in the short term is still an important issue.

Some physicians who are unfamiliar with the source of the STEMI/NSTEMI paradigm might actually believe that patients with ACO but without STE on their ECG do not gain any benefit from reperfusion. Accordingly, many objections to the need for a paradigm change center around studies that purport to show that

early angiography for patients with undifferentiated NSTEMI does not result in better outcomes (31–38). These objections fail to take into account that these studies excluded patients with persistent symptoms, and/or did not actually use very early intervention. In the largest such study, patients with persistent symptoms were excluded, and “early” angiography was at a mean of 16 hours; even so, patients with a GRACE score of >140 did indeed benefit from earlier intervention (31). In studies that did not exclude patients with persistent symptoms, and patients underwent truly early intervention, outcomes were indeed better (36–38). Even if all such trials were free of these methodological issues and had instead shown no benefit, they still would not be applicable to the question of whether the subset of NSTEMIs with ACO benefit from emergent reperfusion because these trials did not report the presence or absence of angiographic ACO, much less the outcomes in these patients.

These findings have 2 important messages with the same implication: We need to reshape our minds to understand that ACO needing reperfusion is clearly not synonymous with STEMI because NSTEMI with unrecognized ACO has higher short and long-term risk of mortality than NSTEMI with an open artery and similar to STEMI (39, 40). In addition, although the current guidelines recommend urgent (<2 hours) invasive evaluation “regardless of ECG or biomarker findings” in patients with persistent pain, hemodynamic compromise, severe heart failure, and/or arrhythmias to identify patients with ACO but without STE (17–19), these clinical parameters did not compensate for the silence of the ECG in the abovementioned studies. Furthermore, it is clear that there is a substantial deviation from the guidelines or there would not be so many occluded arteries in the 24-hour angiogram. It appears that even in the context of a highly observed setting of an RCT, physicians did not identify the patients with ACO among all the patients with undifferentiated chest pain.

STEMI/NSTEMI paradigm focuses only on ST-segment

The term “STEMI” is and has been a major obstacle to improvement. It cognitively inspires us to think that only the ST-segment matters. It leads us to ignore other ECG variables, such as the preceding QRS-complex, the T-wave, or even the morphology of ST-segment itself. However, ACO can be reliably recognized with

the help of many ECG findings other than the STE cutoffs recommended by the 4th universal definition of MI, such as minor STE not fulfilling STEMI criteria (41), STE disproportionate to preceding QRS (42, 43), unusual patterns with contiguous leads showing opposite ST deviations (44, 45), and some patterns not showing STE at all (46, 47). The universal definition does in fact mention that there are other ECG findings of ACO than STE, which supports the argument that the name of ACO-MI should not be STEMI, but rather occlusion MI (OMI).

Furthermore, the differentiation of OMI from non-OMI (NOMI) and from non-cardiac chest pain does not end with the ECG. Not only may OMI have no STE, whatsoever; but OMI may also, in fact, present with a normal ECG (without even any subtle, non-diagnostic findings) and is sometimes only diagnosable by biomarkers, echocardiography (48, 49), or angiography, including CT angiography (50).

STEMI/NSTEMI paradigm does not focus on pathology, instead focuses on the test

The STEMI/NSTEMI paradigm uses a feature (STE) of a test (the ECG) as the name of an underlying pathology which is not accurately diagnosed by the test, which creates the “no false negative paradox.” If there is no “diagnostic” STE, then there is no STEMI (even if there is ACO), and thus there can be no false negative test. Even in the presence of potentially fatal but reversible ACO, a negative test is a true negative for absence of STEMI! This has real consequences. When a patient is admitted with an NSTEMI and has an ACO on the next-day angiogram, that patient still gets a diagnosis of “NSTEMI,” and the admitting physician does not get the feedback of “missed a STEMI” because, by definition, this was not a missed STEMI: the standard of care was followed. However, a great opportunity was missed to diagnose an ACO and save the patient’s myocardium and possibly prevent heart failure and even death.

If we still use a surrogate sign paradigm (STEMI/NSTEMI) which does not accurately reflect the real underlying pathology (ACO), with the result that a large

number of patients under our care helplessly infarct a large amount of myocardium, can we really boast that we have emerged from the dark ages? We should name the disease according to the pathologic substrate itself (ACO-MI, or OMI for short).

STEMI/NSTEMI paradigm is not our best option

Recently, Meyers et al. (51) performed a retrospective case-control study of 808 patients with suspected ACS symptoms and compared the accuracy of STEMI criteria with the structured expert ECG interpretation, which incorporates other findings of OMI, including hyperacute T waves, STD of posterior OMI, STE less than the STEMI criteria cutoffs, and so on. Both the interpreters had significantly higher sensitivity (86% versus 41% and 80% versus 36%) for the detection of OMI using the structured expert interpretation rather than using STEMI criteria, with similar specificity. Patients with STEMI (−) OMI had similar infarct size measured by peak troponin but greater delays to angiography compared with patients with STEMI (+) OMI. The interpreters had 94% agreement for the diagnosis of OMI and kappa value 0.849. A total of 55% of OMIs were correctly diagnosed a median of 1.5 hours earlier by structured expert ECG interpretation than by STEMI criteria.

Another study by Meyers et al. (40) compared the STEMI/NSTEMI with the OMI/NOMI paradigms in 467 consecutive patients with high-risk acute coronary syndrome. Among the 108 patients with OMI, only 60% had any ECG meeting STEMI criteria. Patients with STEMI (−) OMI had similar peak troponins, wall motion abnormalities, and clinical outcomes as the patients with STEMI (+) OMI but were much less likely to receive emergent catheterization (28% versus 76%, $p<0.001$). These data support the notion that patients with STEMI (−) OMI likely represent a missed opportunity under the STEMI/NSTEMI paradigm.

Similarly, the DIagnostic accuracy oF electrocardiogram for acute coronary OCClUsion resuLTing in myocardial infarction (DIFOCCULT) study (39) compared the OMI/NOMI approach with the STEMI/NSTEMI paradigm. This was the largest study specifically designed to challenge 20 years of unquestioned dominance of the STEMI/NSTEMI paradigm. In this study, a set of predefined ECG findings in addition to STEMI criteria were used, and the final outcome was

a composite ACO endpoint. In accordance with the previous observations, over one-fourth of the patients initially classified as having NSTEMI were re-classified by the ECG reviewers as having OMI. This subgroup had a higher frequency of ACO, myocardial damage, and both in-hospital and long-term mortality compared with those of the NOMI group. The OMI/NOMI approach to the ECG had a superior diagnostic accuracy compared with the STEMI/NSTEMI approach in the prediction of both ACO and long-term mortality. Furthermore, early intervention in patients with OMI-predicting ECGs was associated with lower long-term mortality, whereas early intervention increased long-term mortality in patients with NOMI-predicting ECGs.

Conclusion

The STEMI/NSTEMI paradigm shift was a major advancement when it was first proposed but is a major obstacle to advancement in the diagnosis and management of ACO. In recent years, there has been considerable incremental progress in the recognition of ACO by ECG findings other than STE, as well as by the use of other diagnostic tools, such as echocardiography (48, 49), CT angiography (50), and conventional angiography. Future studies are needed to better delineate how these modalities could be incorporated into fast diagnostic pathways in difficult cases. However, if we miss the opportunity to change our current paradigm before the next set of AMI guidelines is released, the failure to implement our current knowledge will cost many lives. Therefore, we call for a new AMI paradigm shift from STEMI/NSTEMI to OMI/NOMI.

HIGHLIGHTS

The STEMI/NSTEMI paradigm fails to diagnose nearly a quarter of acute coronary occlusions.

ECG can detect acute coronary occlusion even when STEMI criteria are not fulfilled.

We think that it is time to replace the STEMI/NSTEMI with a new OMI/NOMI paradigm.

We believe this paradigm shift have the potential of improving the acute management of MI.

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