Use of Thrombolytics with STEMI

emRIC ECHO
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Presenters

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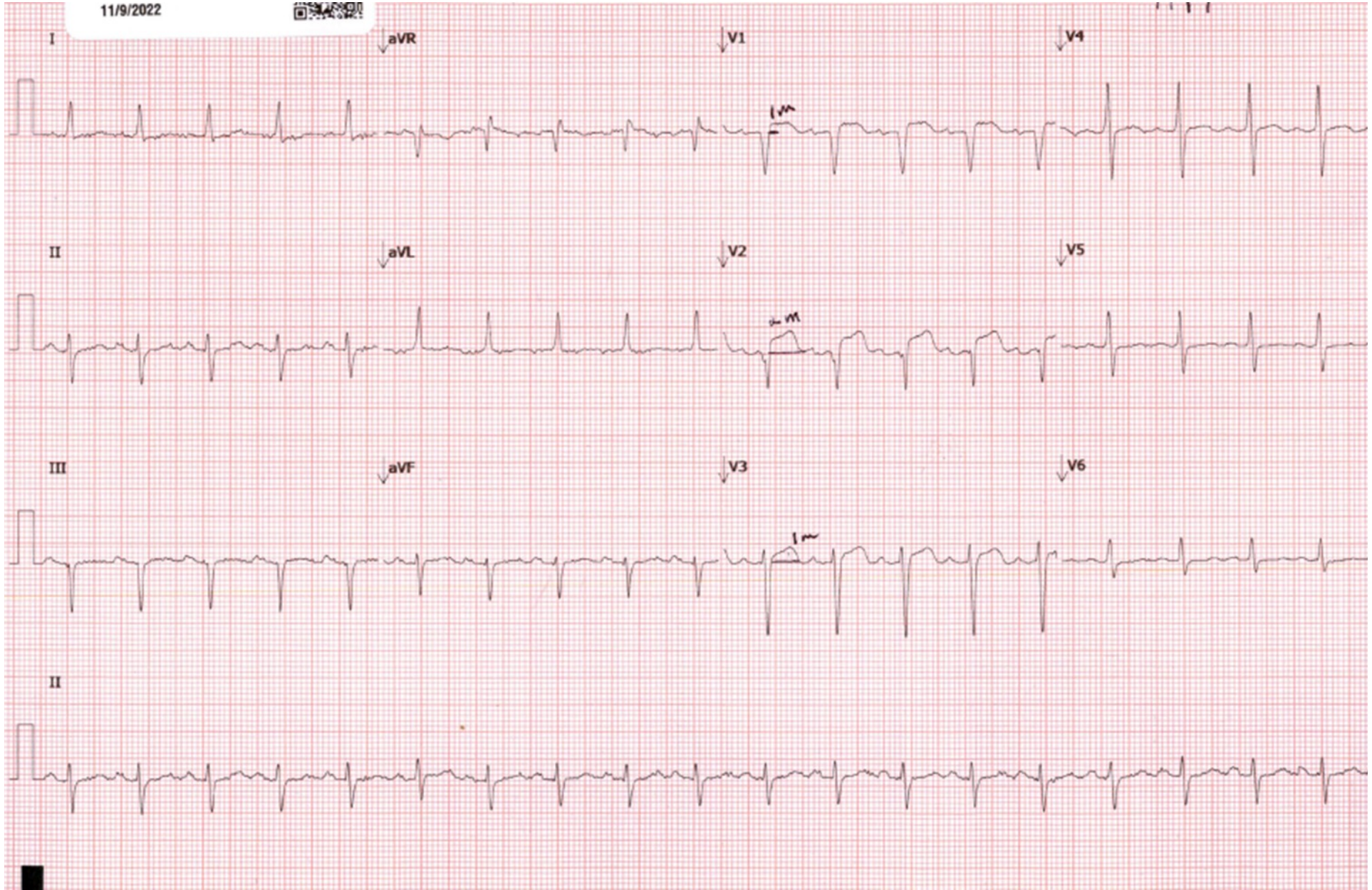
Objectives

- Know thrombolytic agents available for use in STEMI and mechanisms
- Know indications for thrombolytic use in STEMI
- Know absolute and relative contraindications for thrombolytics
- Understand reperfusion rhythms
- Understand post-thrombolytic care
- Understand possible complications and management

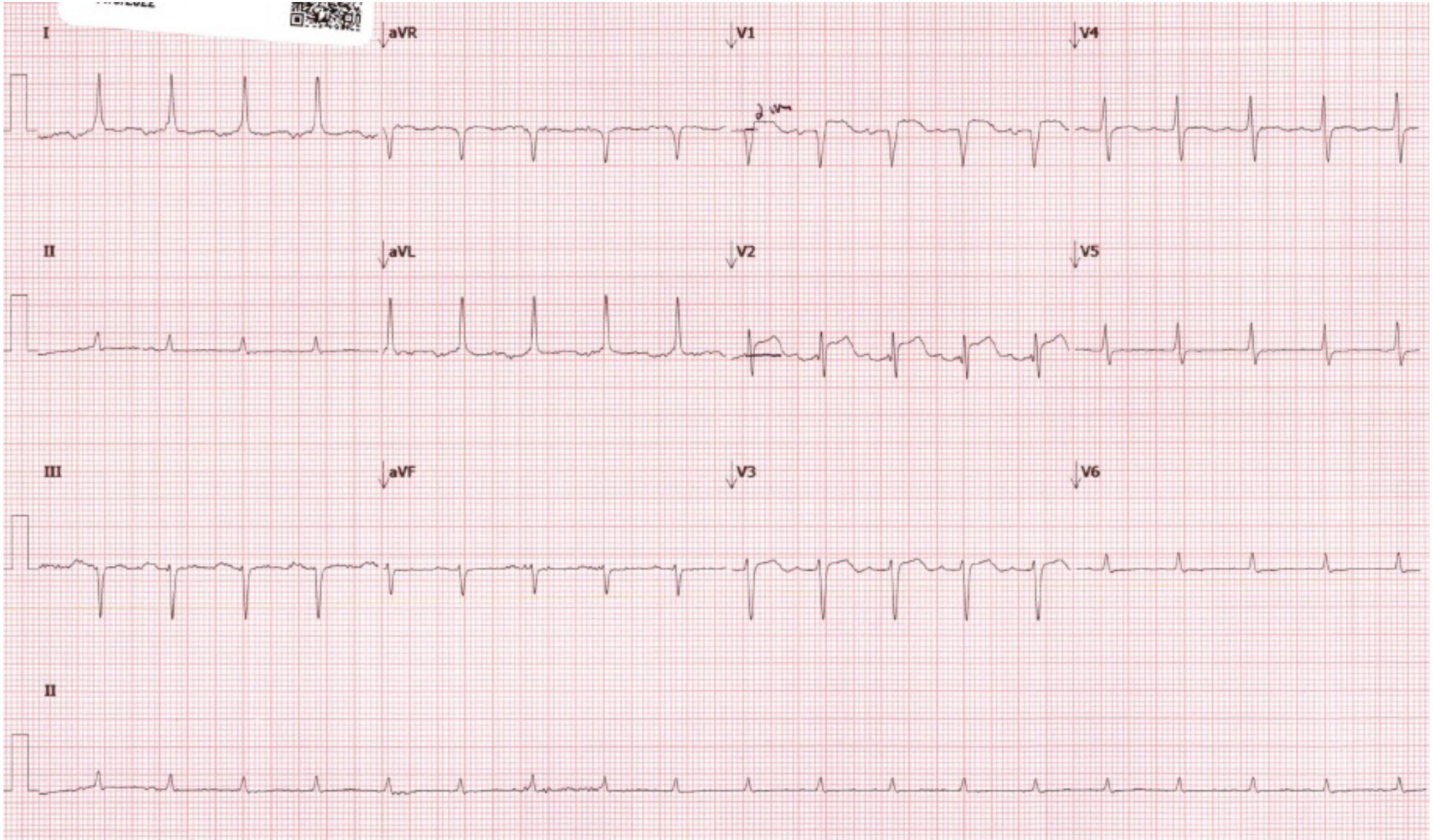
Case #1

- CC: 62M via BLS “not feeling well, high blood pressure”
- HPI:
  - CP x 2 hours, onset on waking, radiates to back
  - No fevers, chills, cough
- PMH: DMII, HTN, HLD, CAD, MI s/p stent
- Meds: ASA, Plavix, Lisinopril taken 1 hour PTA
- PE: BP 195/106, O2:98, HR:118, RR:20, T:98.1

Case #1: ECG #1



Case #1: ECG #2



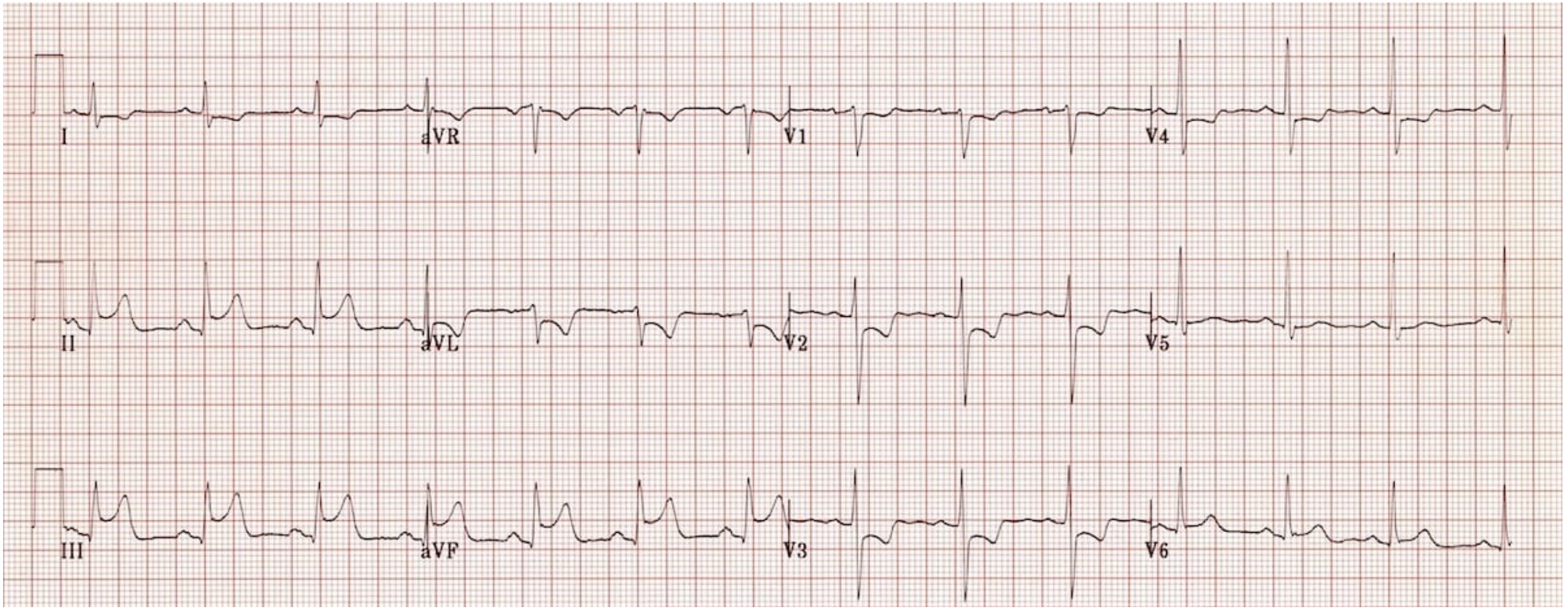
Case #1

- 1702: ED arrival
- 1712: 1st ECG shows STEMI
- 1723: Air Ambulance #1 declines due to weather
- 1728: Air Ambulance #2 declines due to weather
- 1731: ASA 324 mg given
- 1735: CTA: No dissection, No PE
- 1738: Accepted at Tucson Medical Center, Trop 0.52, BNP 2400, PT/INR wnl
- 1805: 2nd ECG done
- 1807: Air Ambulance #3 reports both units are on flights
- 1837: TPA started
- 2010: TPA completed
- 2205: Patient leaves ED in ground ambulance for a 2+ hour transport

Case #2

- 67-year-old male presented with chest pain and SOB
- Stable vital signs
- ECG shows an inferior STEMI
- Snowing outside, helicopters were grounded, and the ground transport was going to be greater than 2 hours

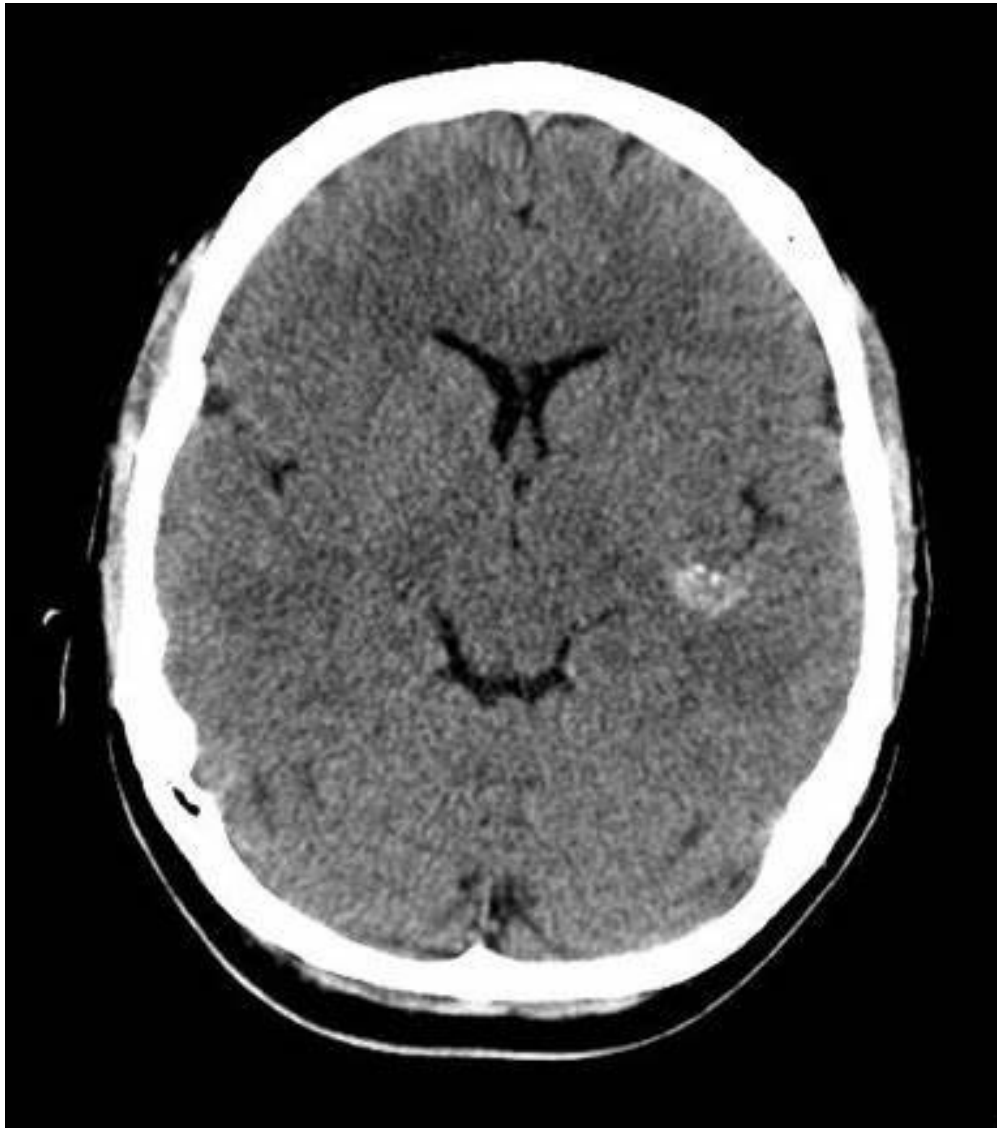
Case #2



Case #2

- Patient given TPA while arrangements made for transfer
- About halfway through TPA infusion, patient started to become confused
- TPA was immediately stopped, and patient sent to CT

Case #2



Case #2

- TPA stopped, avoided any further antiplatelet or anticoagulants
- Elevated head of bed to 30 degrees
- Consulted cardiology and neurosurgery
- Kept SBP less than 140 per recommendations of neurosurgeon
- ECG showed improvement suggesting reperfusion
- Patient's neuro status remained stable. Patient was transferred and did well. Returned to normal neuro status.

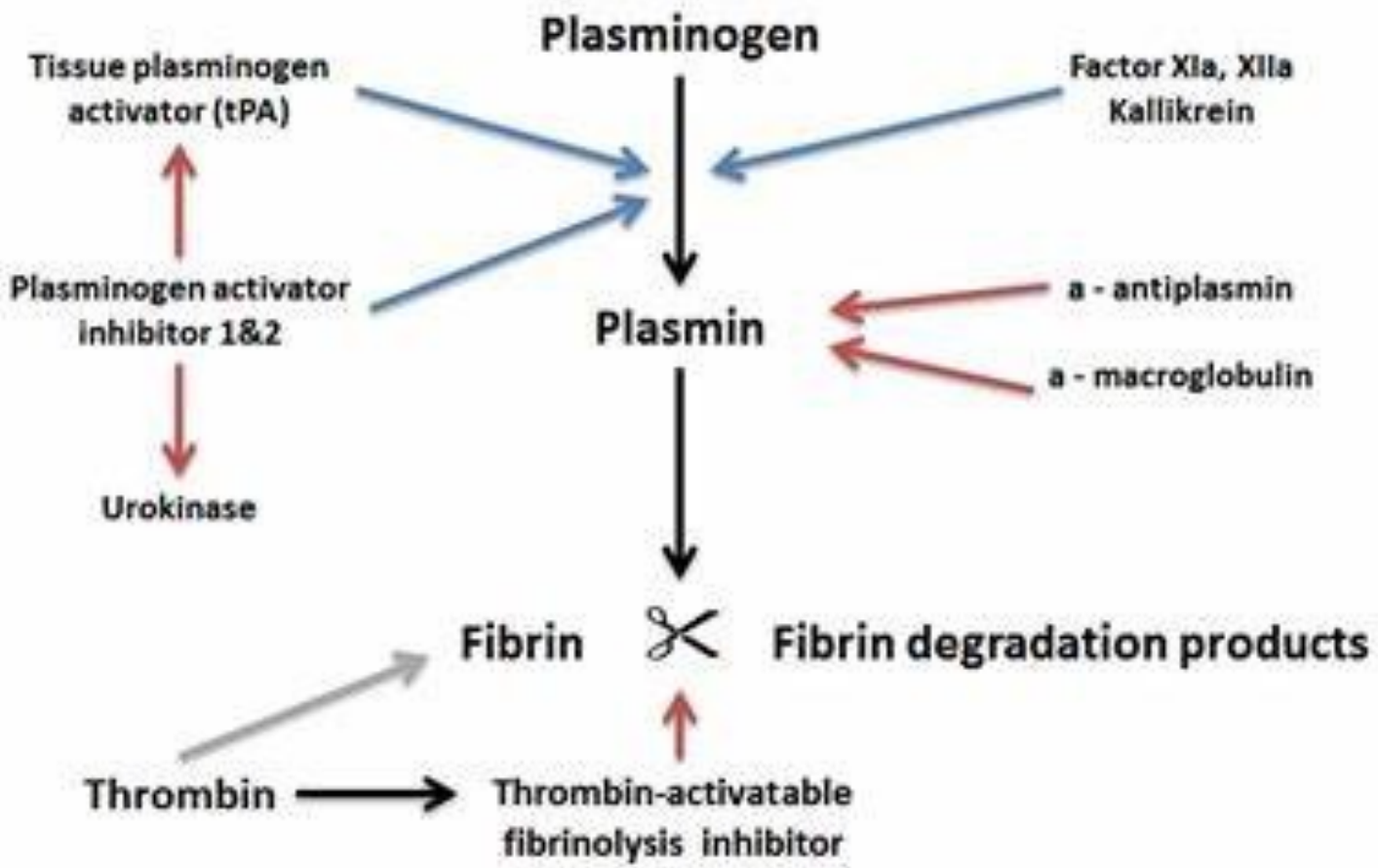
Thrombolytics Available for Use in STEMI

AGENT	DOSAGE
Tenecteplase (TNK)	Weight: • <60 kg: 30 mg IV bolus • 60-69 kg: 35 mg IV bolus • 70-79 kg: 40 mg IV bolus • 80-89 kg: 45 mg IV bolus • ≥90 kg: 50 mg IV bolus
Reteplase (rPA)	• 2 IV boluses of 10 units given 30 min apart
Altiplase (tPA)	Weight ≤67 kg: • First: 15 mg IV bolus • Second: 0.75 mg/kg IV over 30 min (max 50 mg) • Third: 0.5 mg/kg IV over 60 min (max 35 mg) Weight >67 kg: • First: 15 mg IV bolus • Second: 50 mg IV over 30 min • Third: 35 mg IV over 60 min
Streptokinase	• 1.5 million units IV over 60 min

Mechanism of Action

- A thrombus is made from a complex process
- TNK, Alteplase, and Reteplase are fibrin specific in breaking down a thrombus
- Often called fibrinolytic agents
- Thrombolysis and fibrinolysis are interchangeable terms with these meds
- They activate plasminogen to convert to plasmin
- Plasmin breaks fibrin into fibrin degradation products
- These meds will cause fibrin to break down throughout the body

Mechanism of Action



Fibrinolysis (simplified) - Blue arrows denote simulation, red arrows inhibition

Indications

- STEMI
- ED presentation to PCI will exceed 120 minutes
- Symptom duration <12 hours or
- Symptom duration 12-24 hours AND evidence of ongoing ischemia and large area of myocardium is at risk or hemodynamic instability

Absolute Contraindications

- Any history of intracranial hemorrhage
- Ischemic stroke within 3 months
- Intracranial neoplasm or structural cerebral vascular lesion
- Suspected aortic dissection
- Active internal bleeding
- Significant head/face trauma in last 3 months

Relative Contraindications

- Severe hypertension of SBP > 180 mmHg, or DBP > 110 mmHg
- Any history of ischemic stroke
- Major trauma in past 2-4 weeks
- Non-compressible vascular puncture
- Pregnancy
- Active peptic ulcer
- Use of anticoagulants or a bleeding diathesis

Post-Thrombolytic Care

Adjunctive Antithrombotic Therapy to Support Reperfusion With Fibrinolytic Therapy

	COR	LOE
Antiplatelet therapy		
Aspirin		
• 162- to 325-mg loading dose	I	A
• 81- to 325-mg daily maintenance dose (indefinite)	I	A
• 81 mg daily is the preferred maintenance dose	IIa	B
$P2Y_{12}$ receptor inhibitors		
• Clopidogrel:	I	A
• Age ≤75 y: 300-mg loading dose		
• Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding	I	A (14 d) C (up to 1 y)
• Age >75 y: no loading dose, give 75 mg	I	A
• Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding	I	A (14 d) C (up to 1 y)

ACC/AHA STEMI Guidelines. JACC. 2013;61(4).

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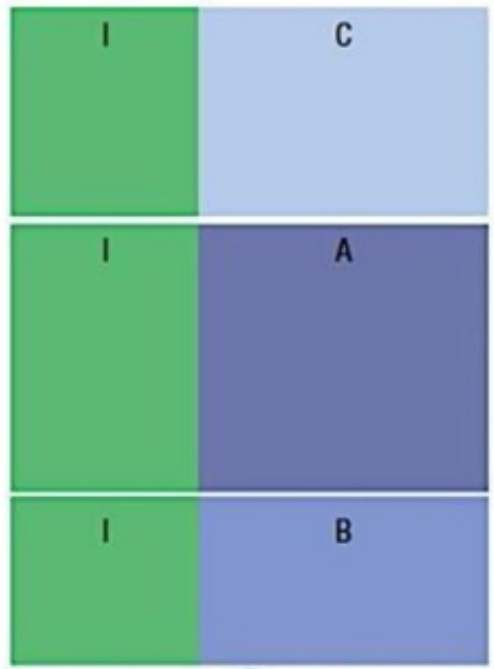
Anticoagulant Therapy to Support Reperfusion With Fibrinolytic Therapy

Anticoagulant therapy

- UFH:
  - Weight-based IV bolus and infusion adjusted to obtain aPTT of 1.5 to 2.0 times control for 48 h or until revascularization. IV bolus of 60 U/kg (maximum 4000 U) followed by an infusion of 12 U/kg/h (maximum 1000 U) initially, adjusted to maintain aPTT at 1.5 to 2.0 times control (approximately 50 to 70 s) for 48 h or until revascularization
- Enoxaparin:
  - If age <75 y: 30-mg IV bolus, followed in 15 min by 1 mg/kg subcutaneously every 12 h (maximum 100 mg for the first 2 doses)
  - If age ≥75 y: no bolus, 0.75 mg/kg subcutaneously every 12 h (maximum 75 mg for the first 2 doses)
  - Regardless of age, if CrCl <30 mL/min: 1 mg/kg subcutaneously every 24 h
  - Duration: For the index hospitalization, up to 8 d or until revascularization
- Fondaparinux:
  - Initial dose 2.5 mg IV, then 2.5 mg subcutaneously daily starting the following day, for the index hospitalization up to 8 d or until revascularization
  - Contraindicated if CrCl <30 mL/min



ACC/AHA STEMI Guidelines. JACC. 2013;61(4).

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Arrhythmias Associated with Coronary Reperfusion

What are Reperfusion Arrhythmias?

- Ventricular or occasionally atrial arrhythmias occurring within 6 hours of start of thrombolysis
- Occur frequently and repetitively
- Are highly specific but poorly sensitive for recanalization of the obstructed artery
- They are a sign of significant reperfusion injury

Mechanisms of Reperfusion Arrhythmias

- Consequence of complex cellular and humoral reactions
- Key role to free oxygen radicals, calcium, thrombin, platelet activating factor and angiotensin II and others
- Enhanced automaticity and triggered activity due to after-depolarizations more common than reentrant phenomena
- Don’t forget the role of electrolyte abnormalities including especially K+, Mg++, Ca++

Incidence of Commonly Observed Reperfusion Arrhythmias

- Accelerated Idioventricular Rhythm (AIVR) 40 – 45 %
- Sinus bradycardia 25 – 30%
- Non-sustained Ventricular Tachycardia 20 – 25 %
- Sustained Ventricular Tachycardia, Ventricular Fibrillation, Polymorphic Ventricular Tachycardia, Heart Block 5 -10%

Accelerated Idioventricular Rhythm (AIVR)

- Regular rhythm of ventricular complexes
- QRS duration > 120 msec.
- Rate 50 – 110 beats per minute (less than 50 bpm is ventricular escape, greater than 110 bpm is Vtach)
- Fusion and capture beats

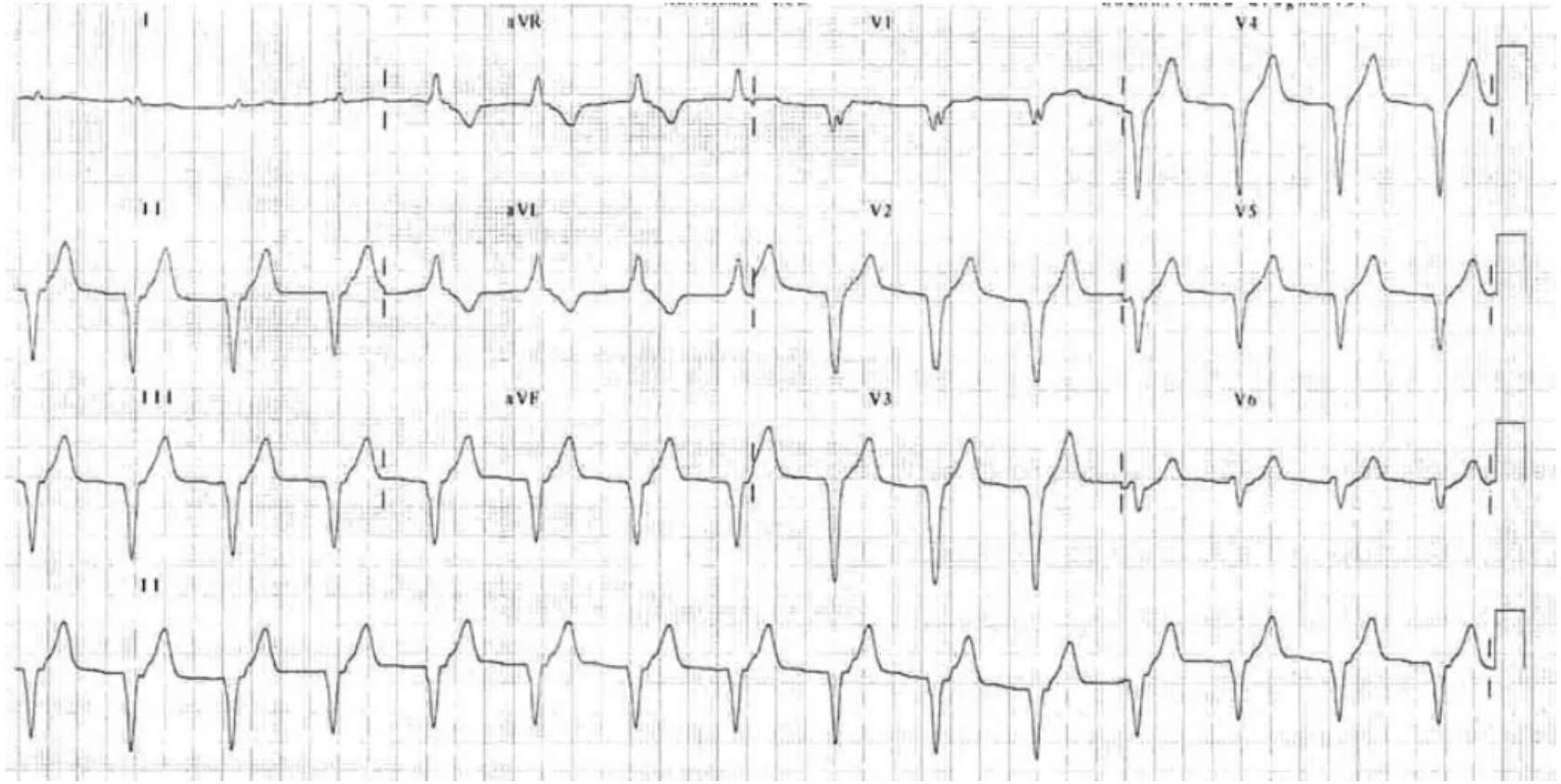
AIVR

Rate 90 BPM and regular

QRS > 120 msec.

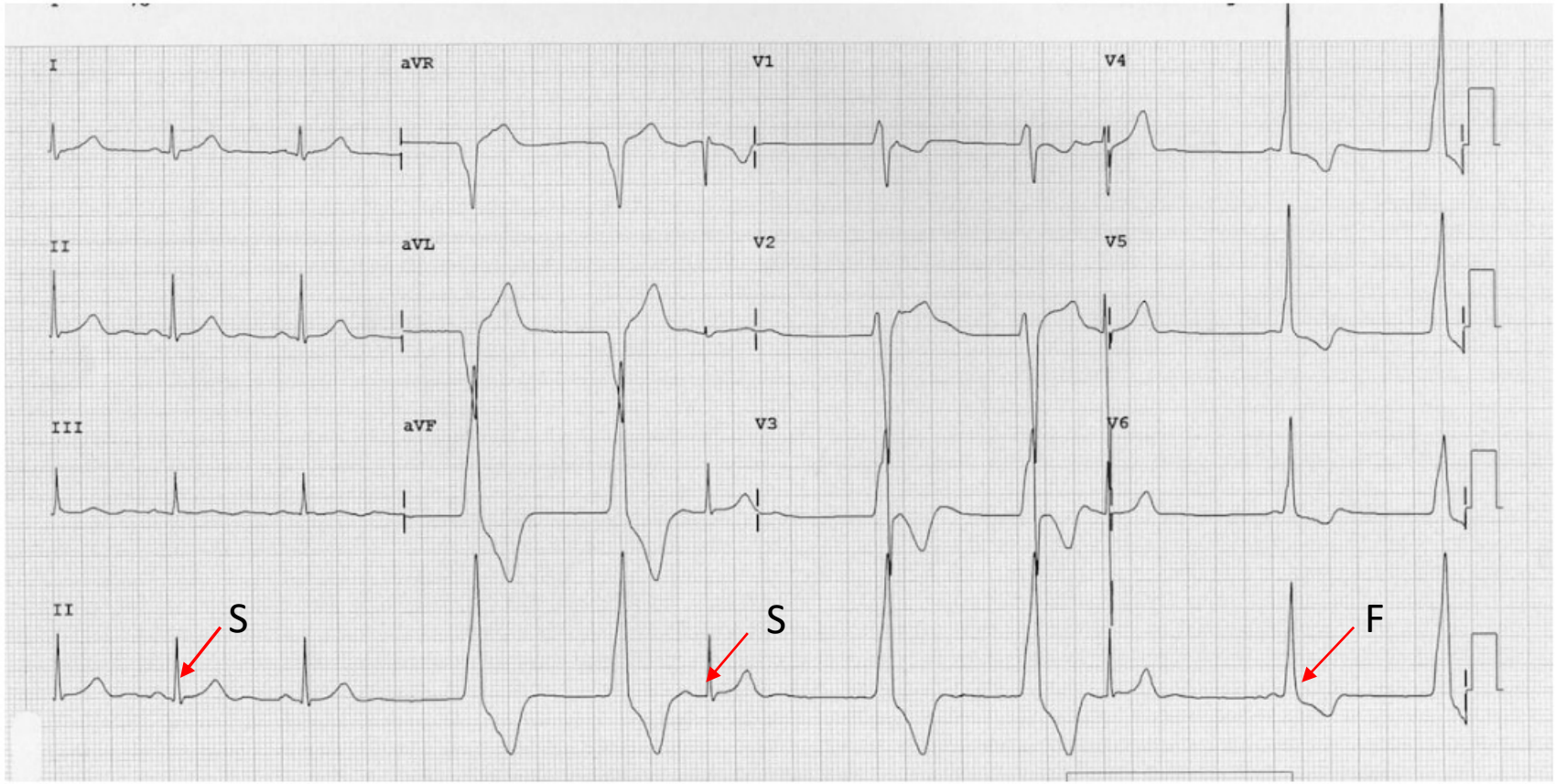
Ventricular origin

No fusion beats



AIVR (isorhythmic)

with sinus capture beats (S)
and fusion beats (F)

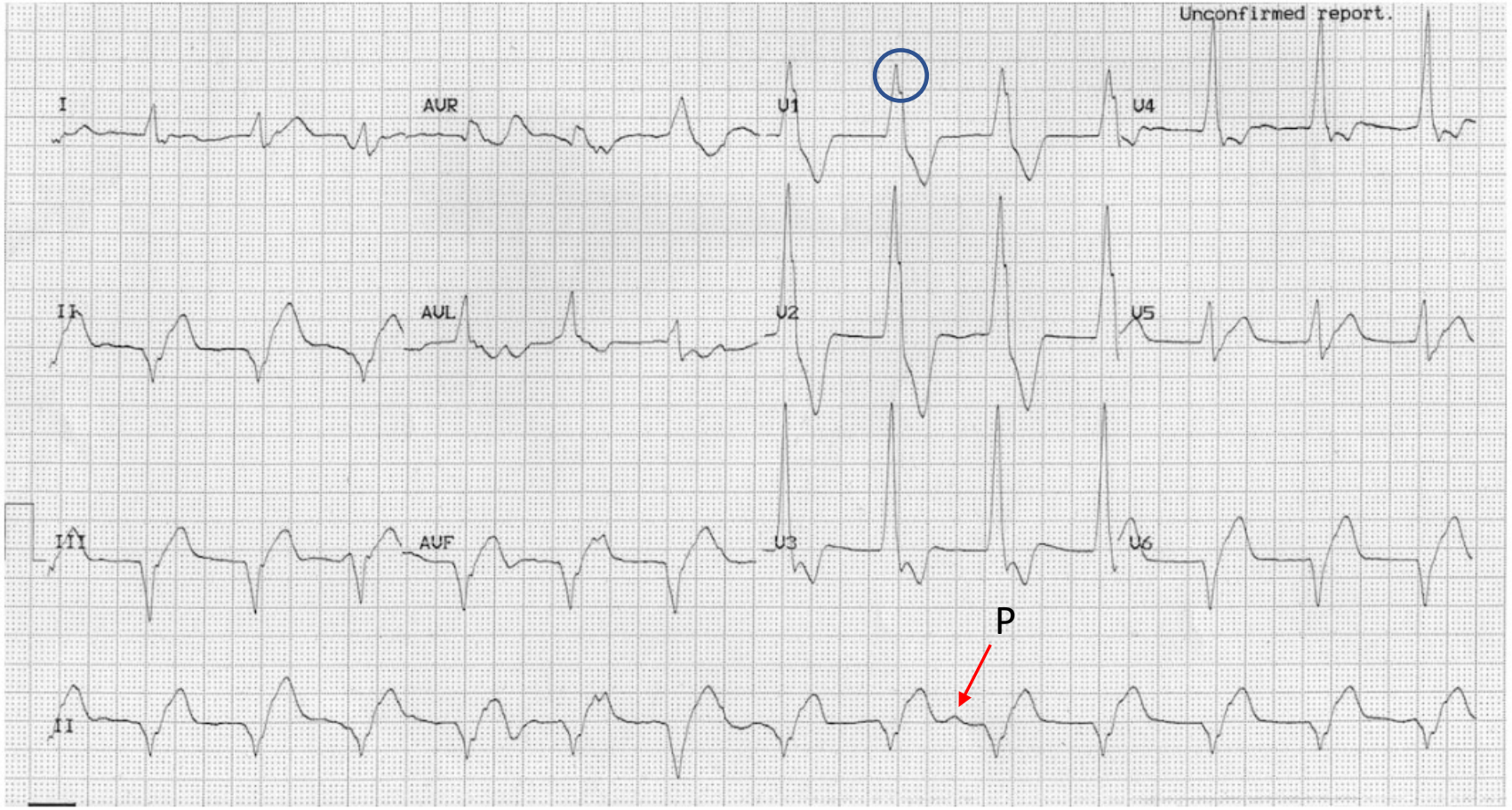


AIVR

Rate 78 bpm

AV dissociation with dissociated

P wave (P)

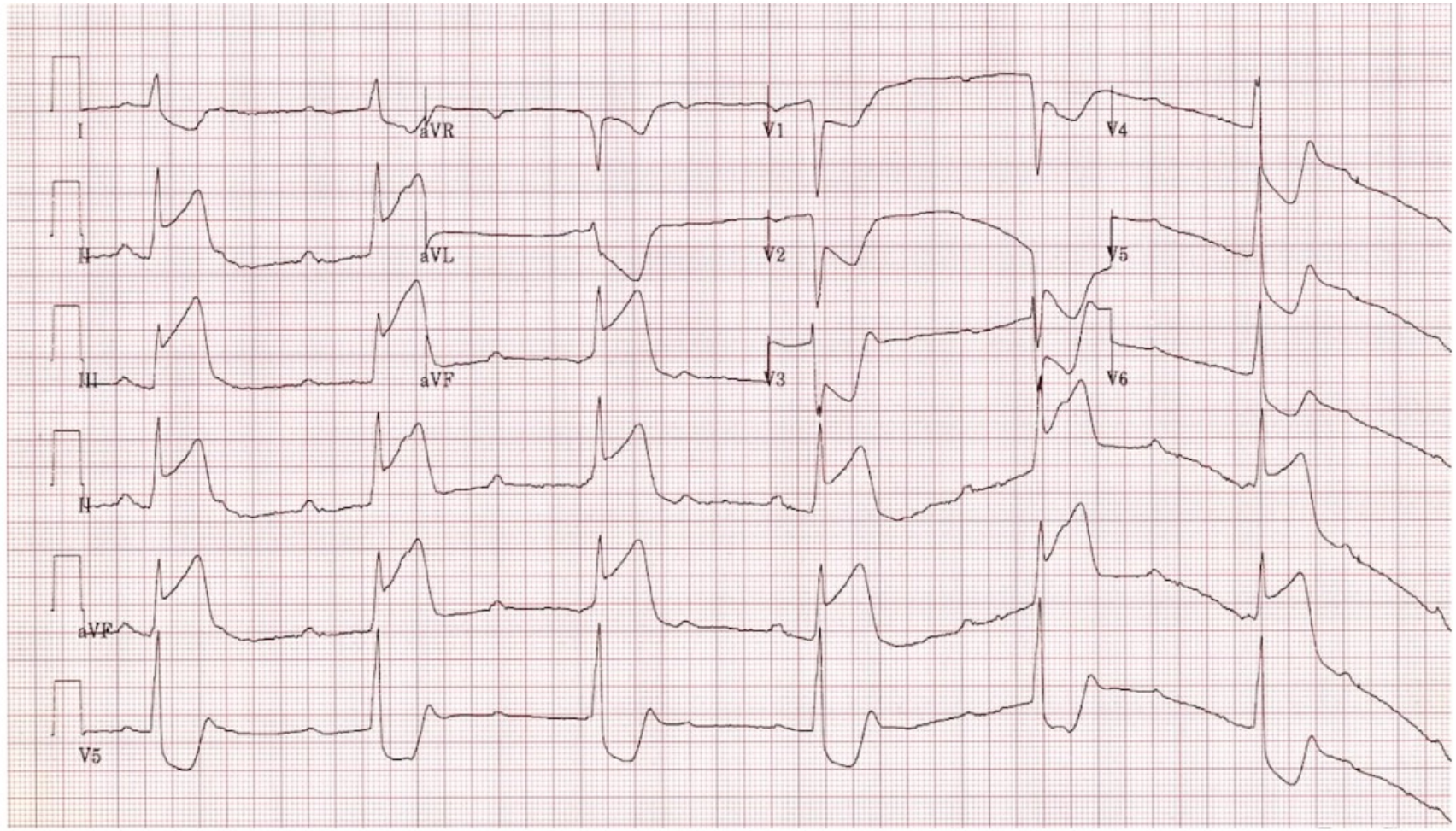


AIVR

- AIVR is almost always a self-limited rhythm
- It is usually associated with hemodynamic stability
- **It should be observed and not treated!**
- **Treatment with drugs such as procainamide and amiodarone may result in asystole**

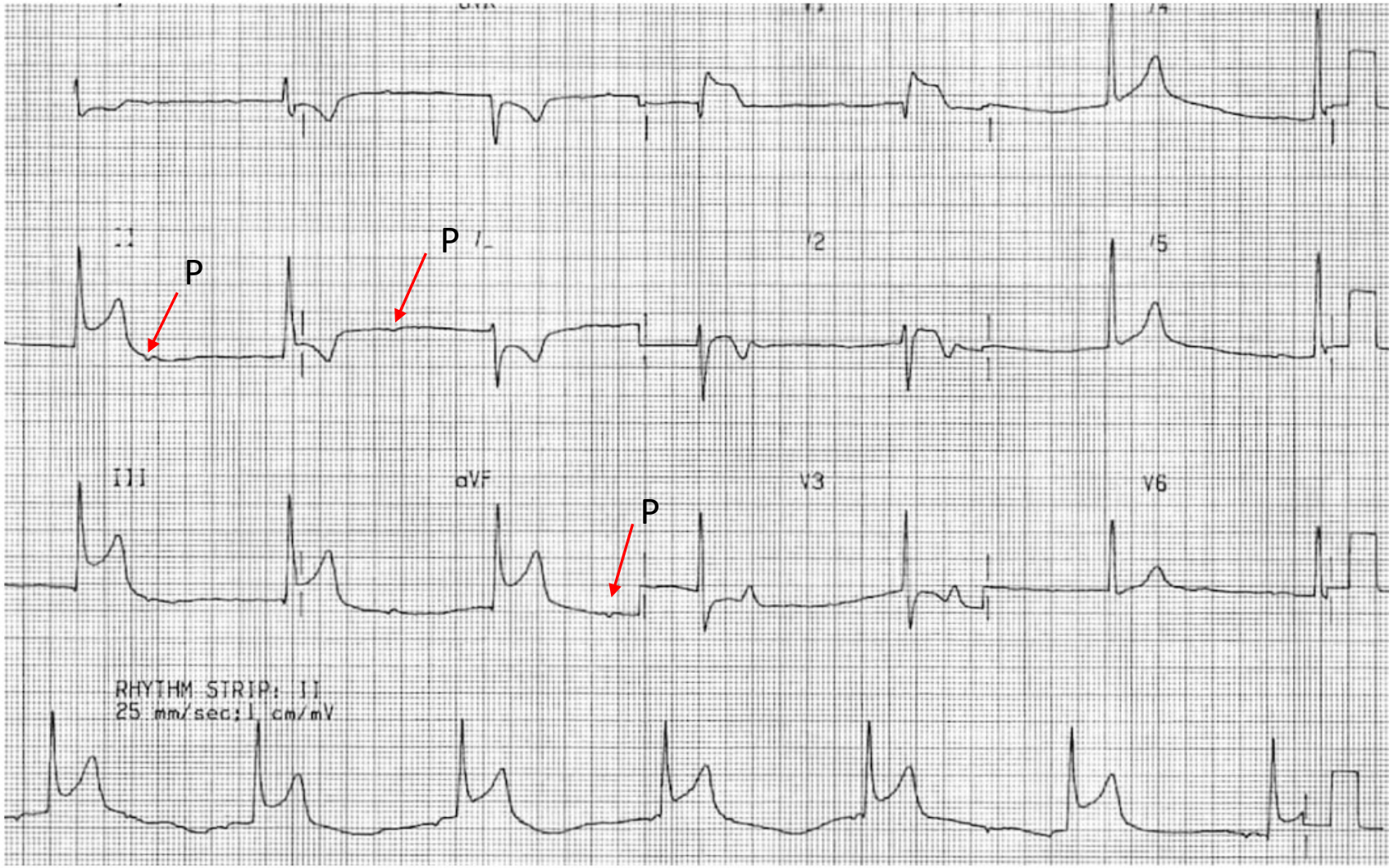
Sinus Bradycardia

- Most often seen in association with inferior STEMI
- May be associated with various degrees of AV block
- May reflect sinus node ischemia or the Bezold-Jarisch reflex
- B-J reflex is vagally mediated and often associated with marked hypotension
- Responds to atropine if hemodynamic instability



- Inferior STEMI with third degree heart block and slow junctional escape rhythm.

Sinus Bradycardia



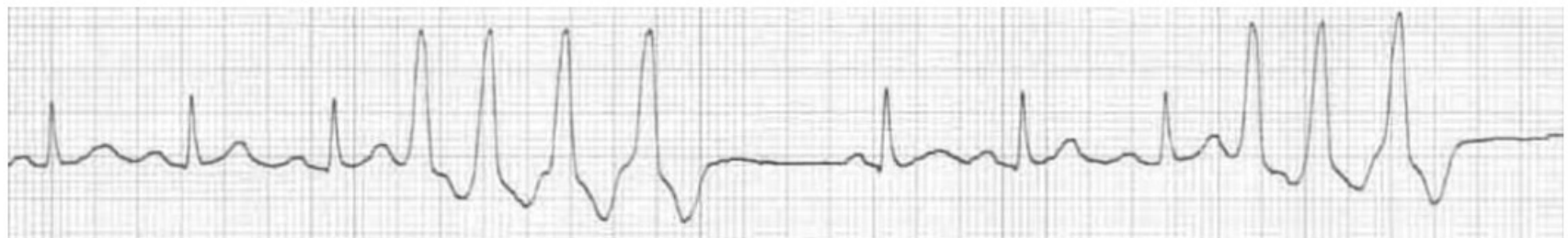
- Inferior STEMI with sinus node dysfunction (either sinus arrest or extreme sinus bradycardia) and a slow junctional

PVC’s and Non-sustained VT

PVCs often occur in repeating patterns:

- **Bigeminy** — every other beat is a PVC
- **Trigeminy** — every third beat is a PVC
- **Quadrigeminy** — every fourth beat is a PVC
- **Couplet** — two consecutive PVCs
- **NSVT** — between three and thirty consecutive PVCs

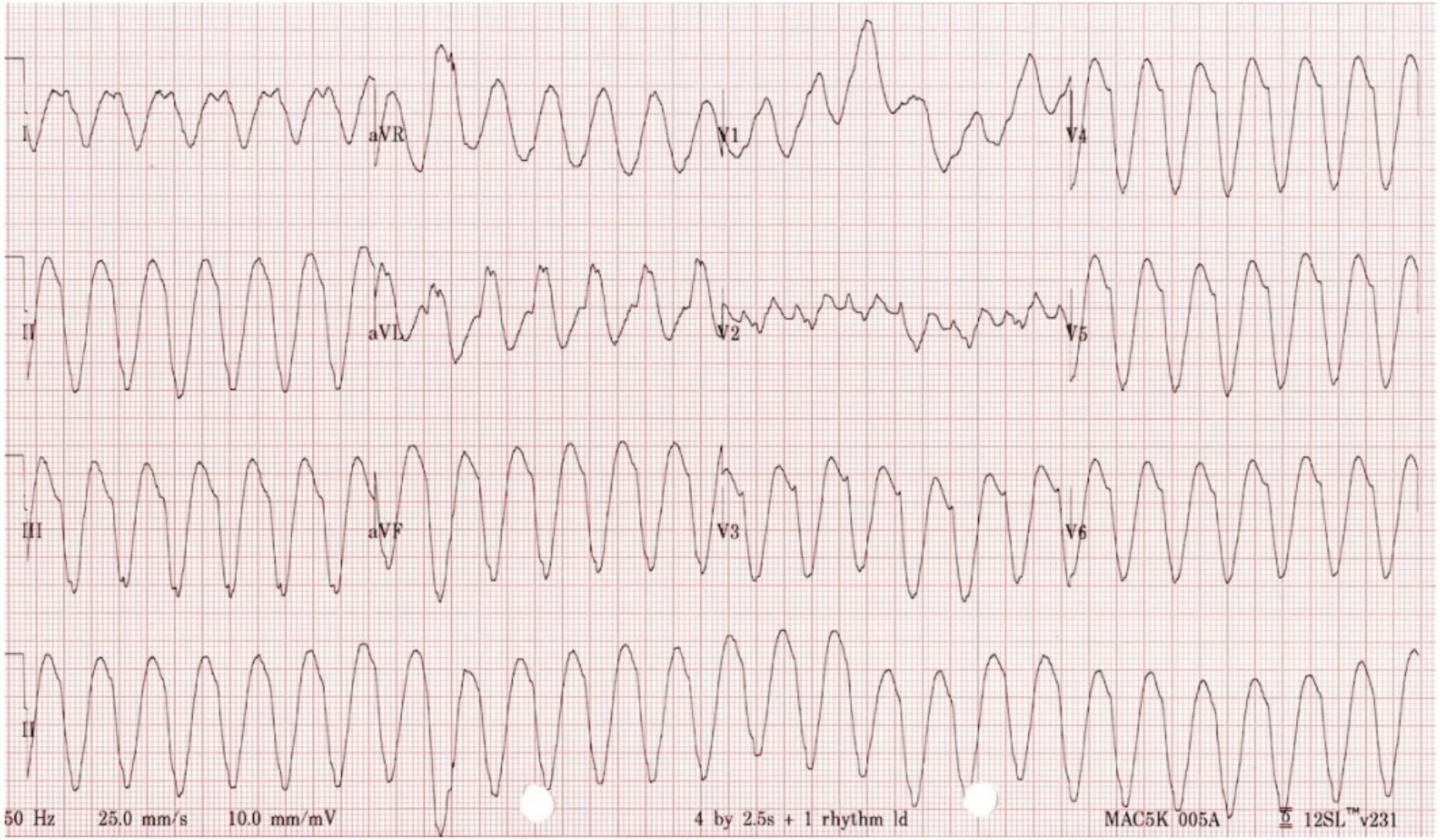
Non-sustained VT (NSVT)



Non-sustained ventricular tachycardia should be observed only

There is no role for “prophylactic” antiarrhythmic therapy

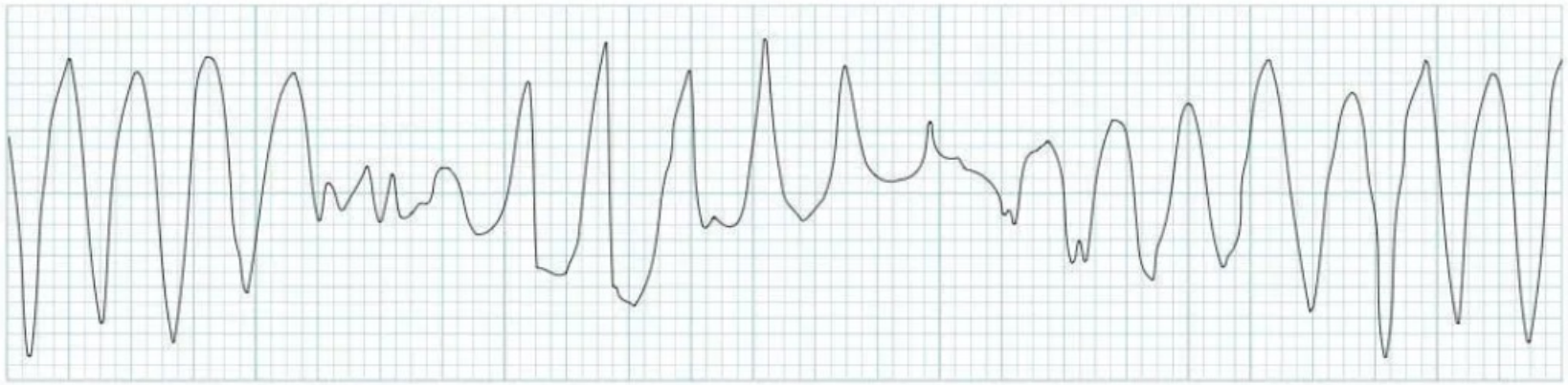
Monomorphic Ventricular Tachycardia



- Although monomorphic ventricular tachycardia may be seen after the start of thrombolytic agents, it is not a typical reperfusion arrhythmia
- It may be managed according to usual protocols depending on hemodynamic stability.
- Electrical cardioversion, if elected, should be synchronized
- Procainamide or amiodarone may be used

Amiodarone: 50 mg IV over 10 mins. then 1mg/min. over 6 hours

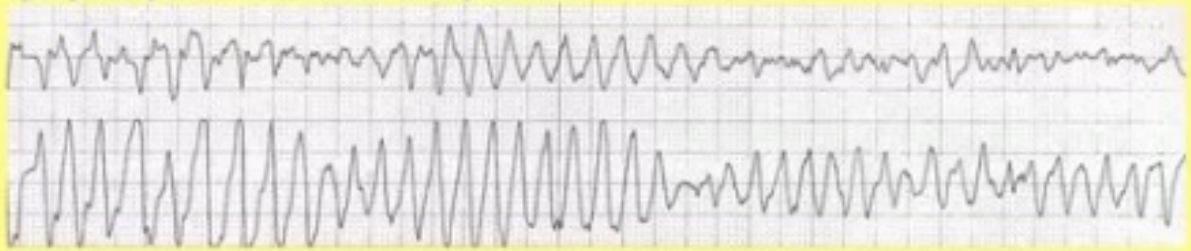
Polymorphic Ventricular Tachycardia



Is this polymorphic ventricular tachycardia
or Torsades de Pointes?

Diagnostic approach to polymorphic ventricular tachycardia

Patient with *polymorphic ventricular tachycardia*



Arrhythmia terminated (e.g. spontaneously or after defibrillation)

Obtain EKG in sinus rhythm: *Is the QT-interval prolonged?*

YES

Torsade de Pointes

NO

THIS IS NOT TORSADE DE POINTES:

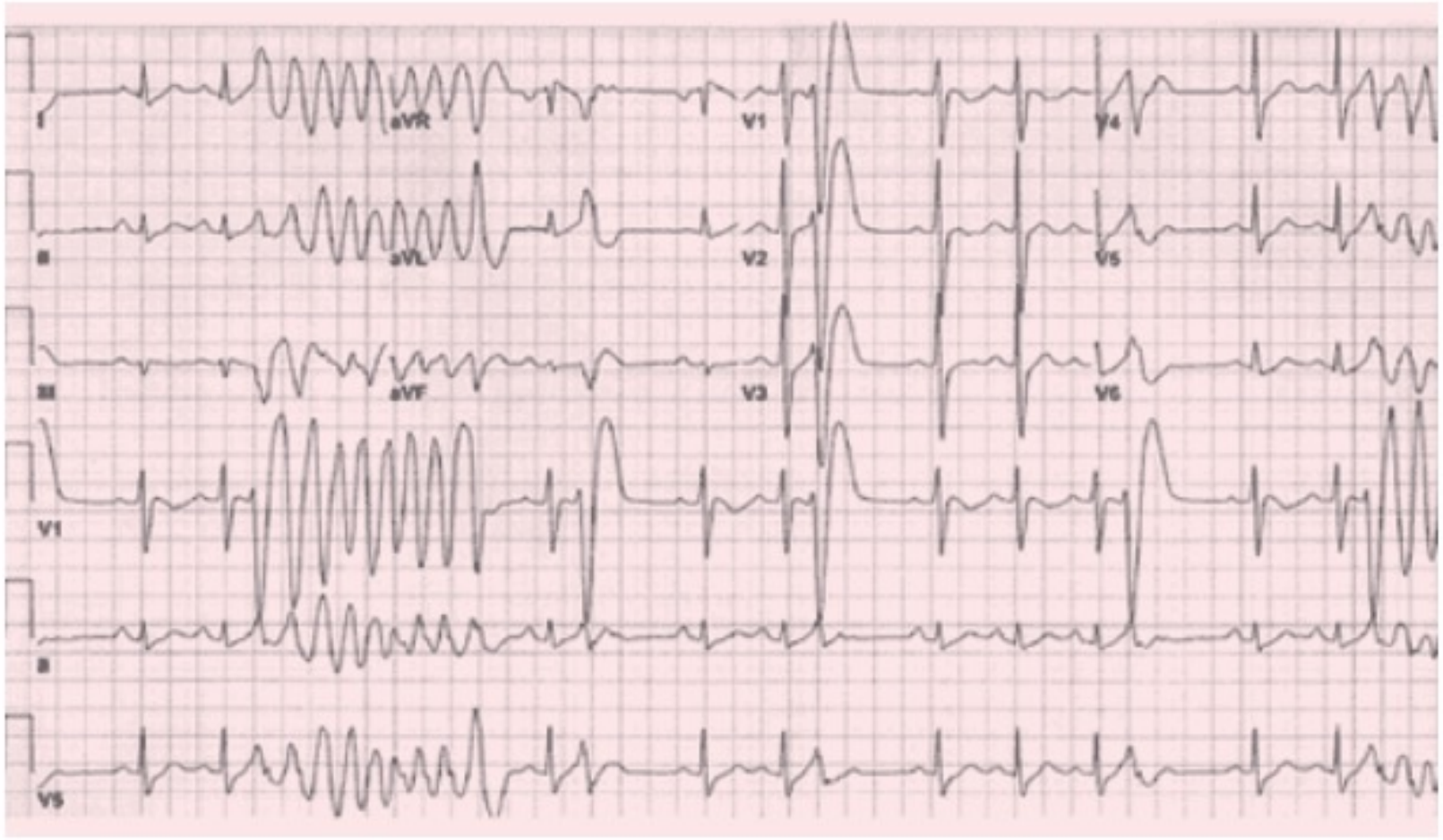
Differential

- Most often acute myocardial ischemia
- Cardiomyopathies, including Takotsubo's
- Idiopathic polymorphic VT, catecholaminergic VT

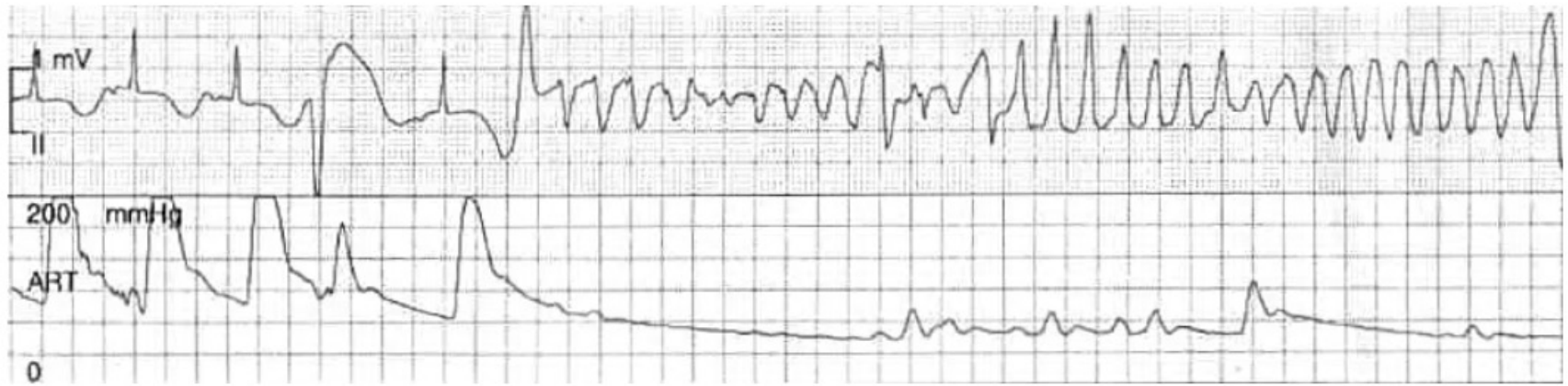
Approach

- Evaluate for ischemia (if ischemic, tx same as monomorphic VT from ischemia).
- Evaluate for cardiomyopathy.
- Beta-blockers or amiodarone may be considered.

Polymorphic Ventricular Tachycardia
Normal QTc

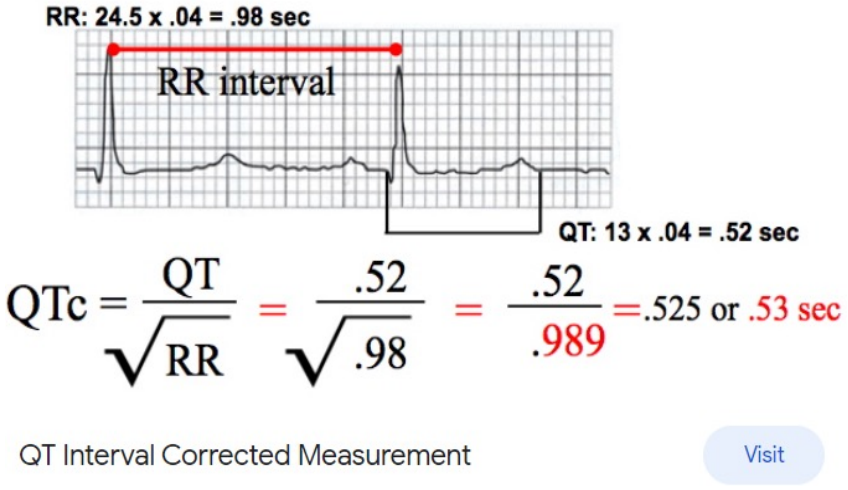


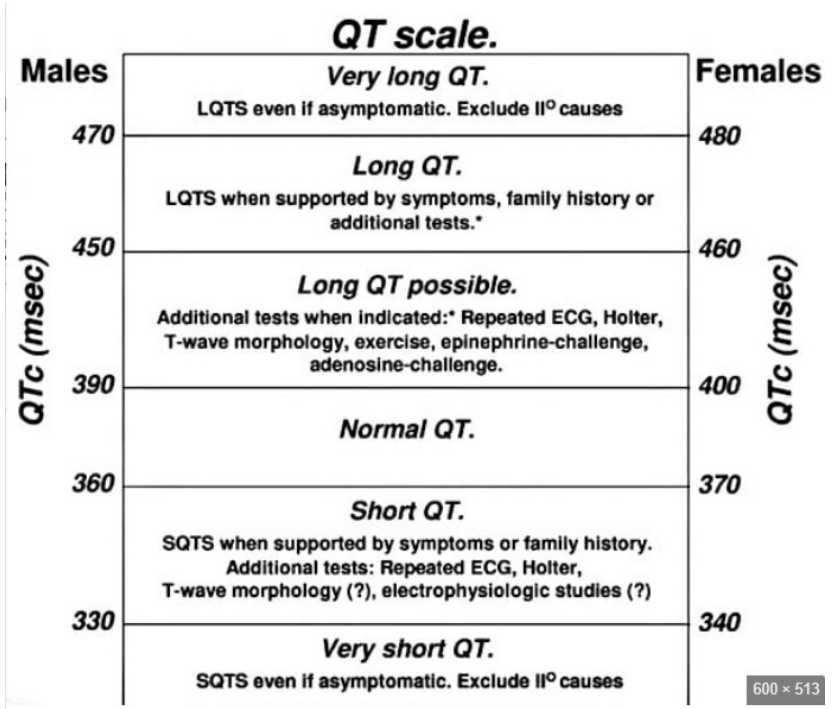
Torsades de Pointes
(a subset of polymorphic VT)
Prolonged QTc



Calculation of Corrected QT interval (QTc)

Method 1.





Method 2.

Most ECG machines calculate it for you…look in the intervals section

In the management of polymorphic VT, measurement of the QTc once the patient is in sinus rhythm (spontaneously or post electrical cardioversion) is the key.

If the QTc is prolonged it is Torsades de Pointes and should be managed with magnesium 2 gm. IV push and antiarrhythmic drugs avoided

If the QTc is normal it can be managed as you would ischemic sustained VT, preferably with amiodarone

Heart block, even if it occurs post thrombolysis, should be managed according to standard protocols

Thanks for your attention!

Complications

- Bleeding (intracranial, GI, GU, retroperitoneal, puncture sites)
- Allergic reaction
- Distal embolization (if there is an unknown thrombus somewhere)

Managing Severe Bleeding

- Stop thrombolytic, anti-platelet agents, and anticoagulants
- Pressure on a venipuncture site or hematoma
- Immediate head CT if concern about intracranial hemorrhage

Managing Severe Intracranial or GI Bleeding

- Paucity of evidence for what to do for intracranial hemorrhage or severe GI bleeding
- AHA recommends giving 10 units of Cryoprecipitate to raise the fibrinogen level
- AHA recommends platelet transfusion if thrombocytopenic or antiplatelets given
- AHA recommends Protamine to reverse Heparin
- Could consider Fresh Frozen Plasma (FFP) if you do not have cryoprecipitate

Take Home Points

- PCI is the best intervention for STEMI if it can be done within 120 minutes
- Thrombolytics do have an 80-85% reperfusion rate
- In many rural areas, if you cannot fly the patient, thrombolytics should be considered early. In some rural areas thrombolytics may always be the first choice because flight times will always exceed 120 minutes
- The sooner you start the thrombolytic, the better. They should be started within 60 minutes of ED arrival if they will be used.

Take Home Points

- TNK (if available) should be your first choice for thrombolytic in STEMI
- Avoid IM injections, arterial punctures and placing central lines unless absolutely necessary for care at your facility
- Do not wait for biomarkers to initiate transfer and thrombolysis (if indicated) in a STEMI patients
- Do not treat reperfusion rhythms

References

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**"Heads, you get a quadruple bypass.
Tails, you take a baby aspirin."**