



Sex-Specific Disparities in Diagnostic ECG Interpretation for Myocardial Ischemia

A NARRATIVE REVIEW

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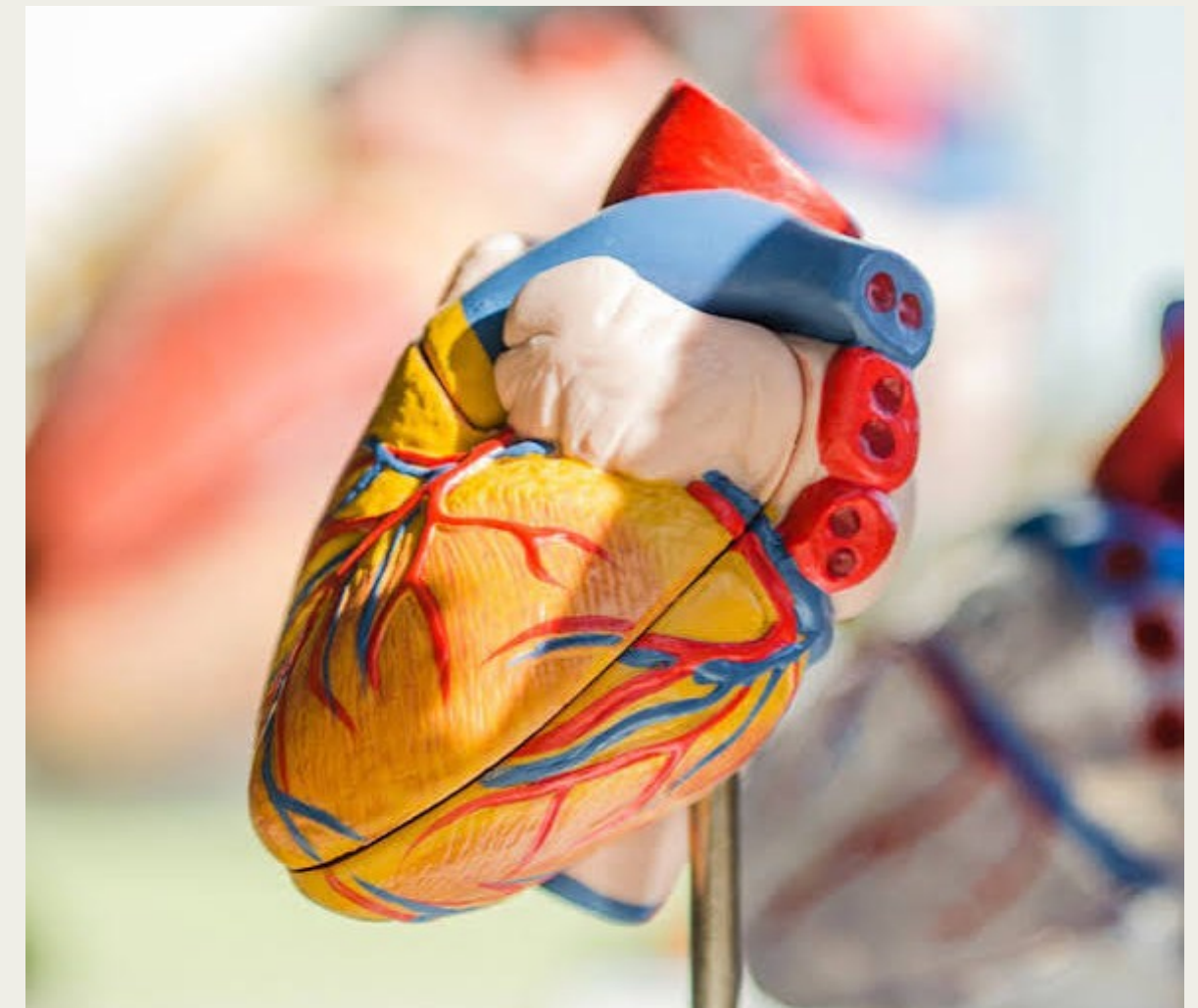
Introduction + Epidemiology



The Problem:

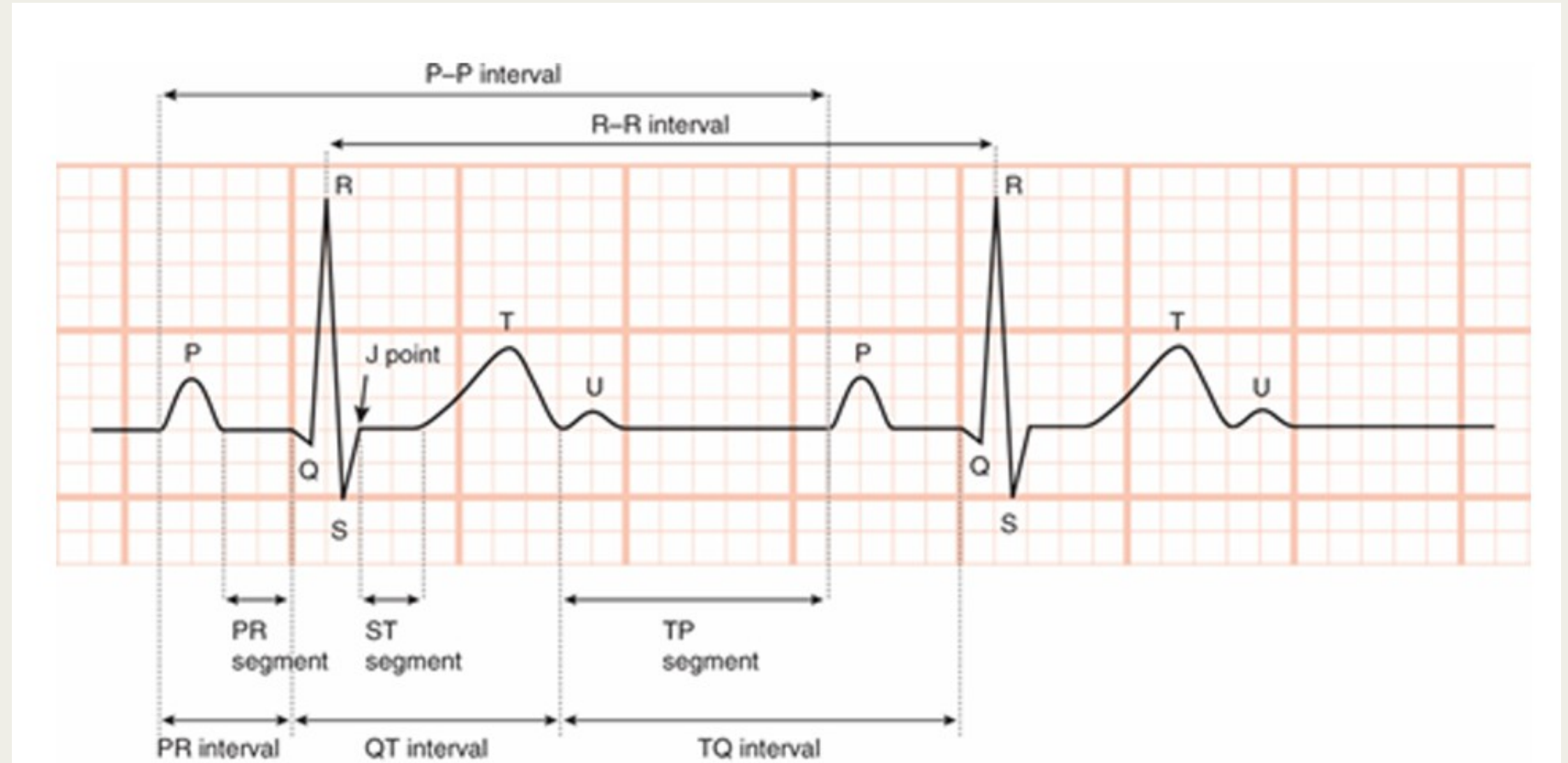
- Cardiovascular disease is the **leading cause of death for women** (**433,000 female fatalities annually in the U.S.**)
- Clinical diagnostic workflows and ECG criteria were **historically calibrated around male physiology**, creating diagnostic delays for women.
- 12-lead ECG is the standard tool used to detect myocardial ischemia
 - Unadjusted ST-segment and QRS thresholds **fail to account for female biophysical signal attenuation**

The Objective: Synthesize how anatomical and electrophysiological sex differences alter ECG waveforms to highlight critical gaps in current clinical practice guidelines



Electrocardiogram Basics

- **QRS Complex:** the electrical depolarization of both ventricles, but it also includes early repolarization
- **J-Point/ST-Segment:** the J point marks the end of depolarization where ST-segment shifts are measured. **Elevation or depression in this segment serves as the primary marker for MI**
- **T-Wave:** represents the repolarization of the heart's ventricles
- **QTc Interval:** measures total ventricular electrical activity corrected for heart rate



Depolarization: the electrical activation of heart cells that tells them to contract

Repolarization: the electrical recovery or recharging of heart muscle cells as they relax to prepare for the next beat

Current Clinical Guidelines

ST-Segment Criteria	Repolarization & QT Limits	Conduction Limits
ST-Elevation (STEMI)	Prolonged QTC Upper Limits	Broad QRS Threshold
≥ 1.0 mm (0.1 mV) in ≥ 2 contiguous leads	Men: >450 ms	One size fits all 120 ms cutoff
Women: ≥ 1.5 mm (0.15 mV)	Women: >460 ms	ST-Depression (NSTEMI)
Men (≥ 40 yrs): ≥ 2.0 mm (0.20 mV)		Horizontal/downsloping ≥ 0.5 mm (0.05 mV) in ≥ 2 contiguous leads
Men (< 40 yrs): ≥ 2.5 mm (0.25 mV)		

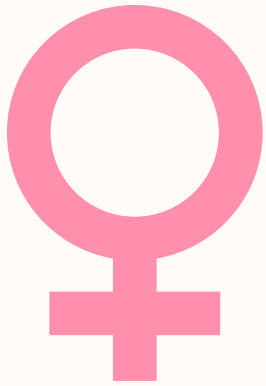
Compiled from the AHA/ACCF/HRS Recommendations for the Standardization and Interpretation of the Electrocardiogram (Part IV: Electrocardiographic Changes Associated With Myocardial Ischemia/Infarction)

PART I:



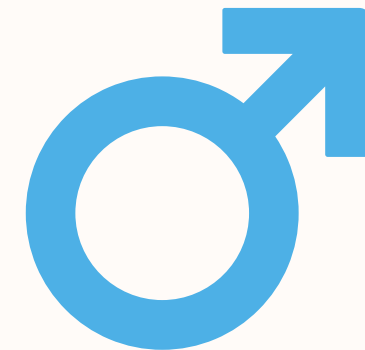
Anatomical & Electrophysiological Sex Differences

Electrophysiological Sex Differences



- **ST Elevation:** flatter/inverted ST Elevation & T-waves in lateral and anterior leads
- **QRS Duration & Voltage:** Shorter in women (approx. 6 ms shorter) and lower in amplitude
- **QT/QTc Interval:** Longer in women by 10-20 ms

- **PQ Interval:** Longer in men starting in young adulthood
- **ST Elevation:** higher baseline ST-elevation levels and taller T-waves
- **Repolarization:** Repolarization is sped up in men



Female vs. Male Cardiac Positions

Compiled from Anatomical basis of sex differences in the electrocardiogram identified by three-dimensional torso-heart imaging reconstruction pipeline

Subpopulation	Superior (z)	Posterior (y)
Healthy Females (N=581)	0.569± 0.033	0.743±0.069
Healthy Males (N=470)	0.544±0.037	0.727±0.071
Healthy Sex Difference	9.6 mm + in females	N/A
Post-MI Females (N=84)	0.565±0.034	0.770±0.069
Post-MI Males (N=341)	0.549±0.036	0.736±0.070
Post-MI Sex Difference	N/A	4.3 mm + in females

Anatomical Position Scale: maps the heart's center onto a relative 0 - 1 scale defined by the subject's outer ECG electrode boundaries (0 = lowest/frontmost, 1 = highest/backmost).

- Female hearts sit significantly more **superiorly and posteriorly** than male hearts in both healthy and post-MI states
- Female hearts shift an **extra 3.1 mm posteriorly post-MI**, alongside a 6.0° more horizontal long axis orientation
- Diaphragmatic elevation from **increased BMI in post-MI females** strongly drives these changes

Key Findings: Female vs. Male Cardiac Positions

Distortion of ECG Vectors

- ECG is a **projection of 3D cardiac electrical activity on a 2D surface**
- Torso depth, breast tissue, and heart position **alter the vector magnitudes** at V 1-6
- Female hearts are positioned more superiorly + posteriorly → **signal attenuation**

QRS Risk Thresholds

- Females require **27% more relative ventricular conduction slowing** than males to reach the standard **120 ms threshold** for broad QRS
- Womens' baseline heart signals travel faster and finish quicker → **one size fits all threshold does not work**

ST Elevation Thresholds

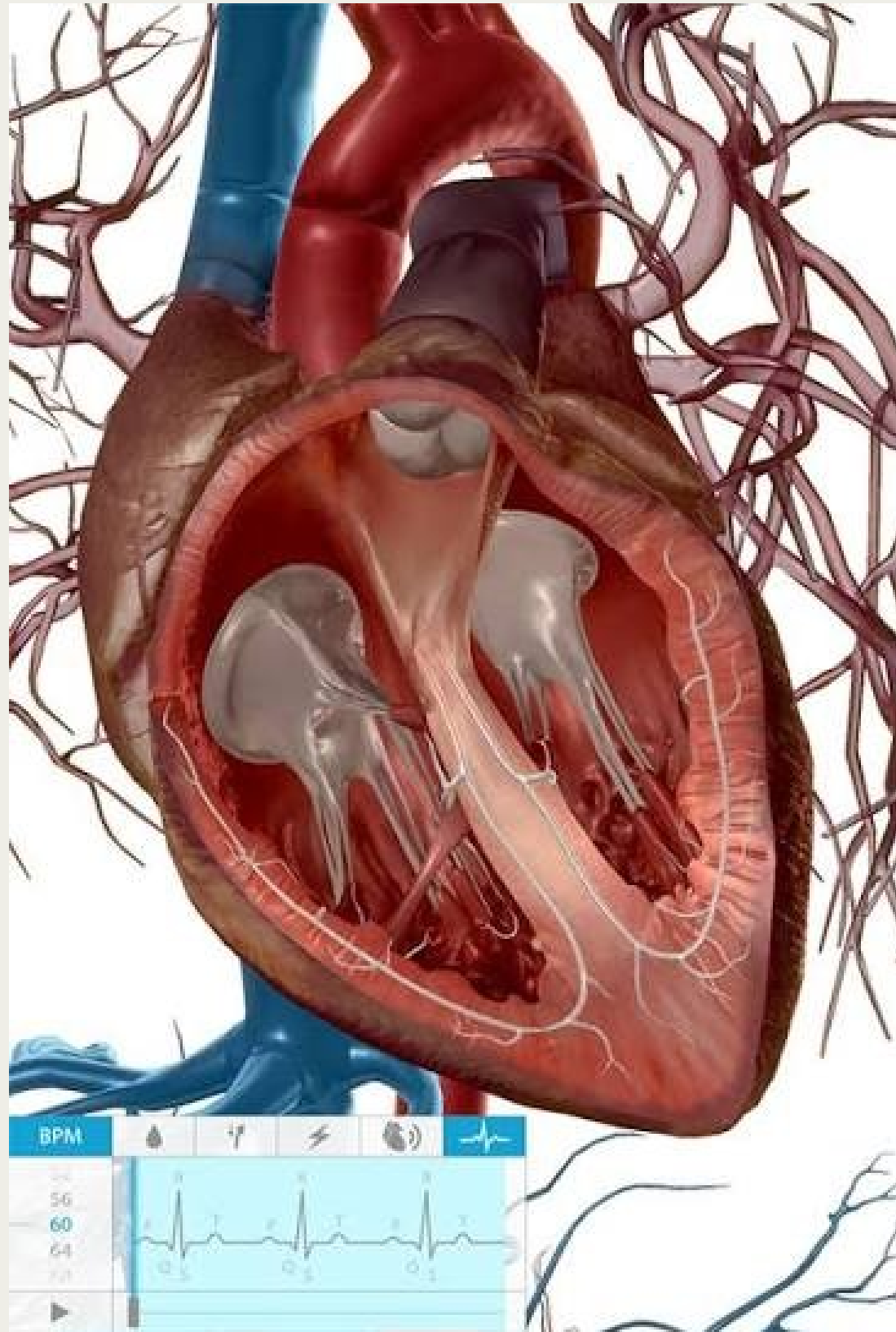
- Men: the male heart sits closer to the chest wall, so a given amount of tissue injury produces a large jump on the surface ECG (2-2.5 mm)
- Women: the female heart sits further back, **same amount of injury would produce a smaller surface jump** (0.8-1.2 mm)

PART II:



Exercise Stress
Testing, Sensitivity,
and Diagnostic
Performance

Diagnostic Sensitivity & Predictive Value by Sex



- ECG sensitivity drops to **51% in women** (and as low as 31%), compared to 67% in men, **lower baseline female voltage hides ischemic ST shifts**
- When female patients present with atypical symptoms, the **PPV of ST-depression drops below 40%**
- Faster female resting heart rates cause T-waves to combine with early ST segments,
 - **Causes false-positive readings**
- **Estrogen** shifts in repolarization cause **non-ischemic ST fluctuations during exertion**

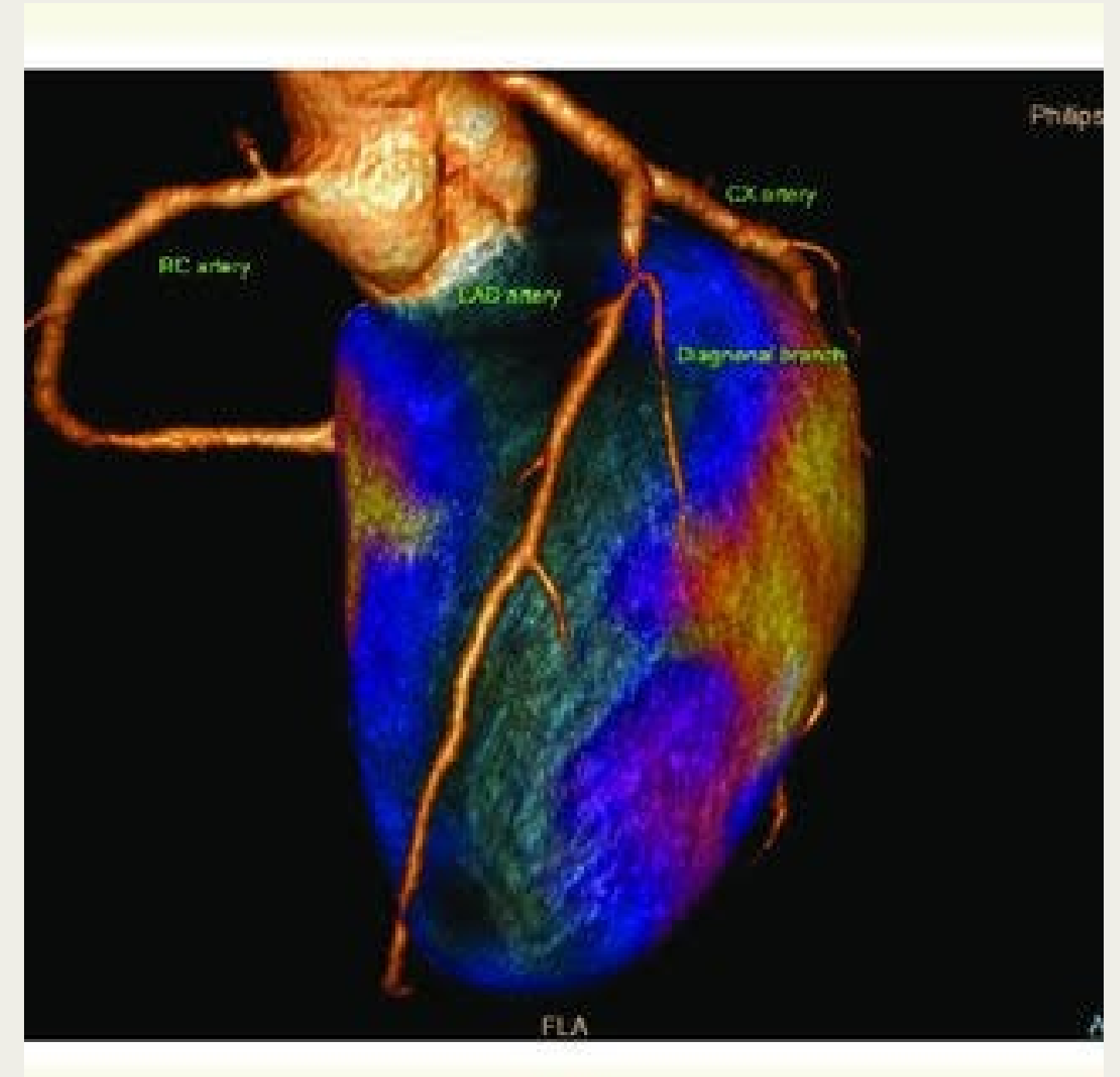
PART III:



Diagnostic Disparities & Missed Ischemia in Clinical Practice

Diagnostic Disparities & Clinical Practice Gaps

- Female heart disease frequently presents as **dyspnea, fatigue, or nausea** rather than exertional chest pain
 - Patients are often **misdiagnosed with anxiety or GI distress**
- Diagnostic delays contribute to a **1.7-times higher in-hospital mortality risk** for female heart attack patients
- Automated **ER algorithms use male-calibrated ST thresholds**,
 - Dismisses lower-amplitude female transmural signals as **non-ischemic**



Health Services Impact and Triage Weight



Health Services Impact

- Delayed diagnosis causes:
 - Preventable **emergency room readmissions**
 - Higher rates of **post-MI heart failure** hospitalizations
 - Increased **long-term healthcare utilization costs**

Clinical Triage Weighting

- CPG algorithms **prioritize classic male exertional angina** over atypical female presentations
- Therefore, **triage protocols must assign equal diagnostic weight to atypical female symptoms when paired with low-amplitude or subtle ST-segment shifts.**

Proposed CPG Addendum (Recommendations)



Visually inspect leads V1-4 for **subtle anterior ST elevations** (ex. 0.8-1.2 mm), to compensate for signal attenuation caused by anatomical differences

Lower broad QRS thresholds for female patients to capture intraventricular delay earlier without the one size fits all 120 ms prolongation

Route female patients with **persistent atypical symptoms and borderline ECGs** directly to non-invasive microvascular imaging to **test for INOCA**

Thank you!

ANY QUESTIONS?



References