



Maryland Chapter

AMERICAN COLLEGE OF EMERGENCY PHYSICIANS

Maryland ACEP Chapter Educational Conference & Annual Meeting March 12, 2020

FACULTY: [Sarah B. Dubbs, MD, FAAEM, FACEP](#)

PRESENTATION

Hidden Dangers: Cardiotoxicities of Cancer Drugs

DESCRIPTION

Cancer therapy may be life-prolonging and lifesaving but comes with many adverse effects and toxicities. Cardiotoxicities are a particularly important subset of these toxicities, which often come into play when cancer patients present to the emergency department. This talk highlights considerations in emergency department management for patients who have undergone various cancer therapies.

OBJECTIVES

- Patients with history of being treated with antineoplastic chemotherapy and/or chest radiation are at increased risk of cardiovascular events.
- Immune Checkpoint Inhibitor myocarditis is an increasingly recognized and potentially life-threatening complication of immunotherapy drugs.

DISCLOSURE

No significant financial relationships to disclose.



Hidden Dangers: Cardiotoxicities of Cancer Drugs

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No financial disclosures



CA

A Cancer Journal for Clinicians

Annual Age-Adjusted Cancer Death Rates by Sex, US, 1975 to 2017



7
Cancer Statistics, 2020

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Understanding and Addressing Social Determinants to Advance Cancer Health Equity in the United States: A Blueprint for Practice, Research, and Policy

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The Rapidly Changing Landscape in Mature T-Cell Lymphoma (MTCL): Biology and Management

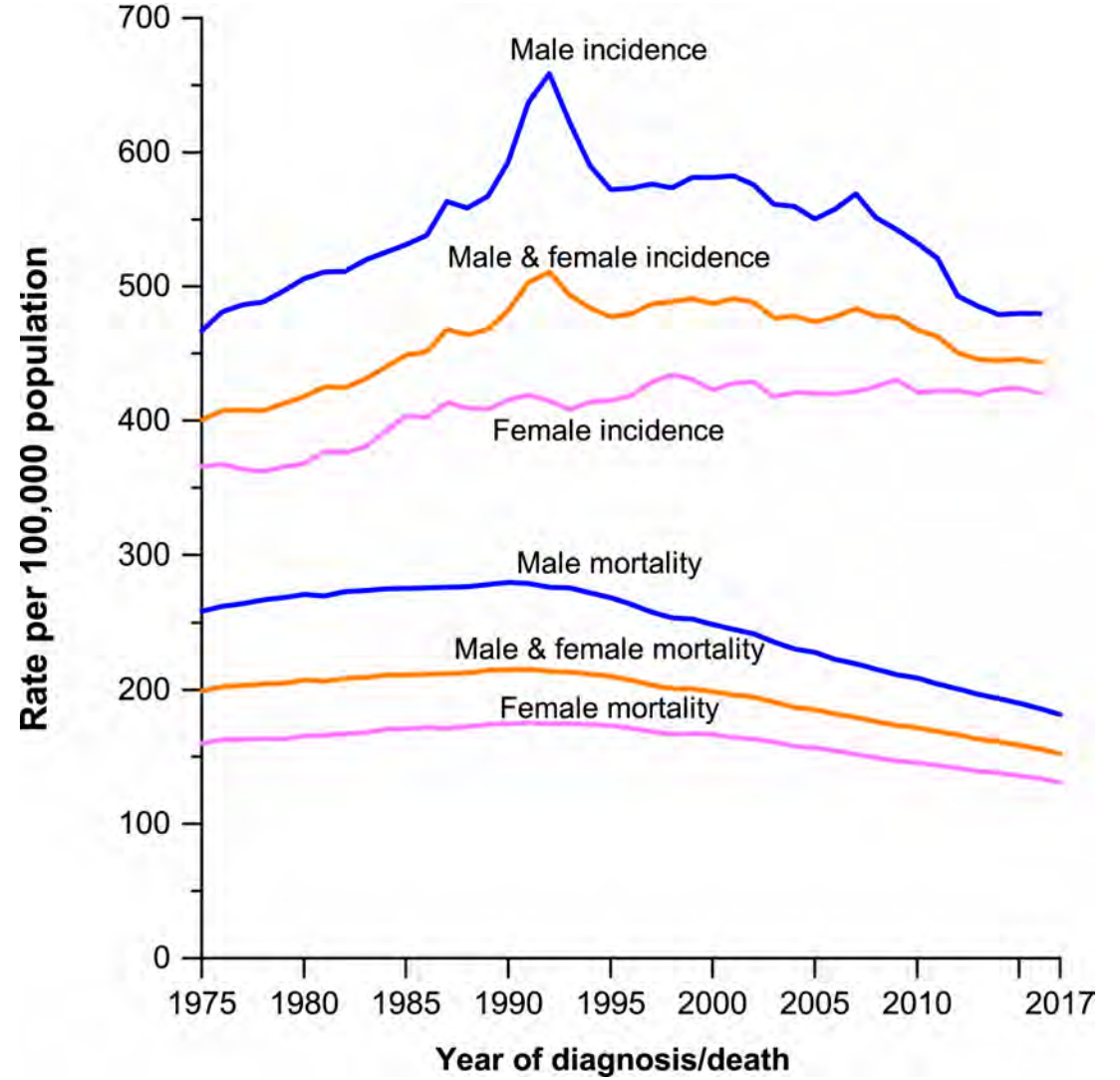


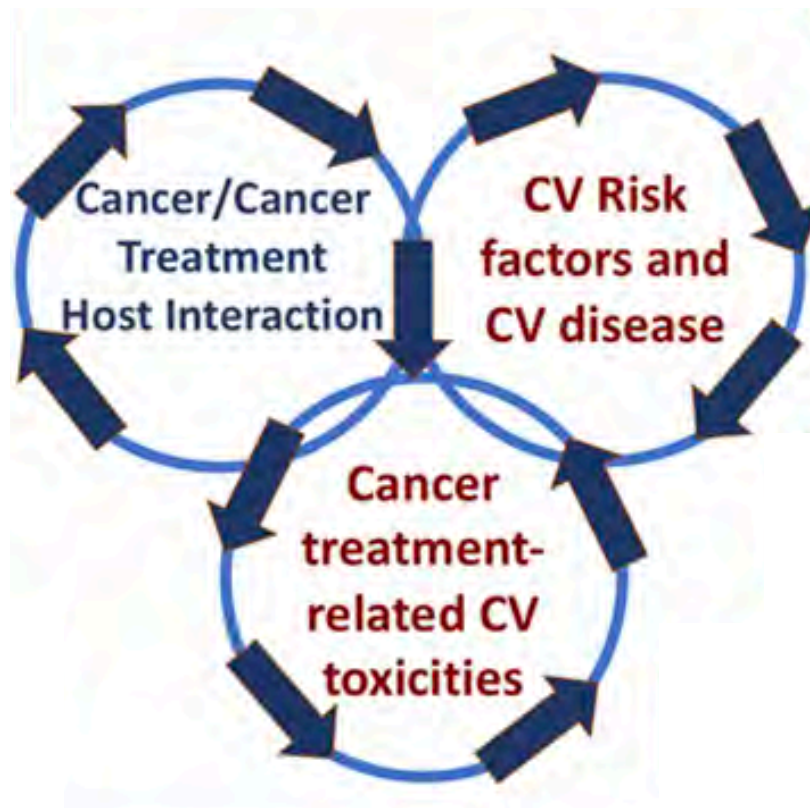
Published for the American Cancer Society by Wiley

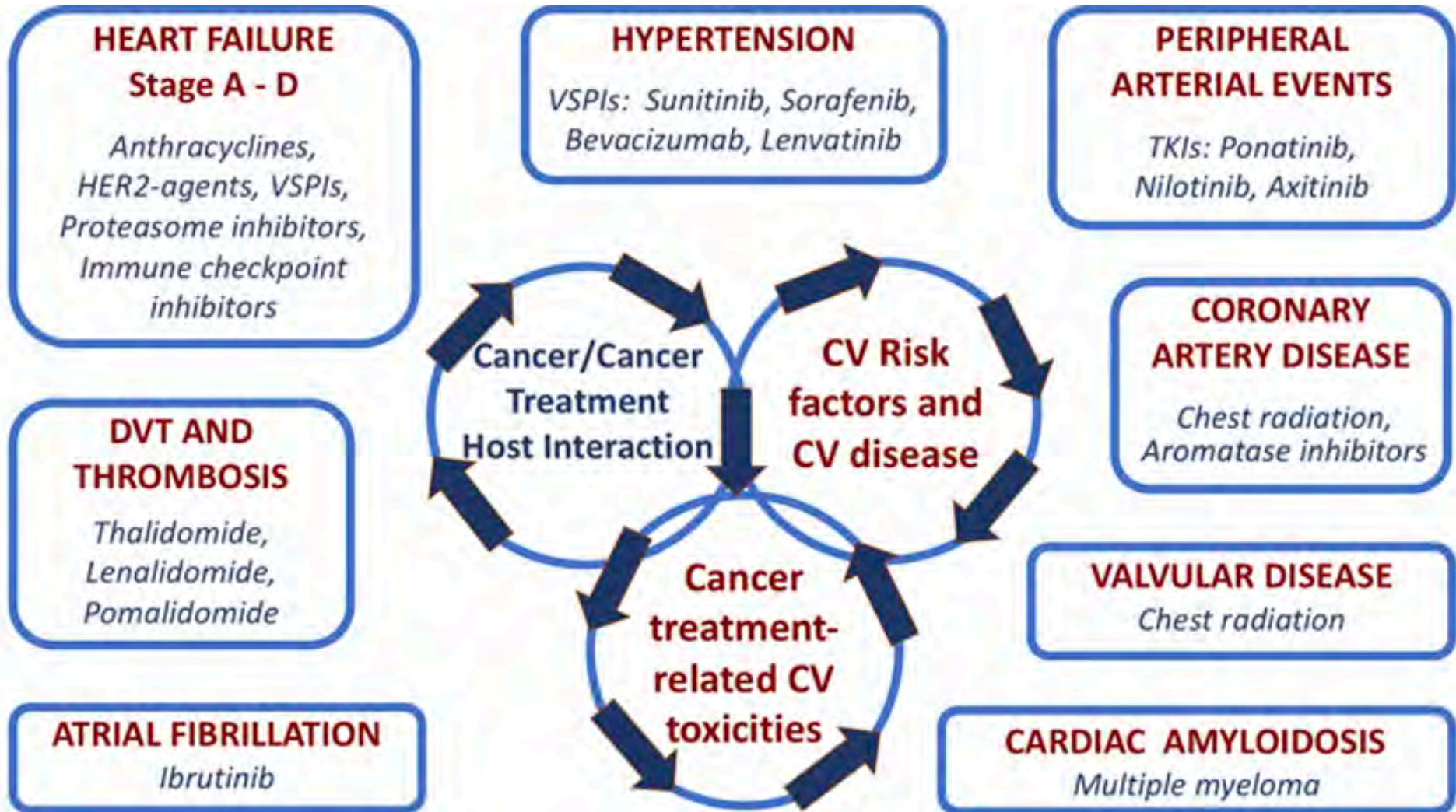
WILEY



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Cancer diagnosis

Cancer treatment

Survivorship



Green, Belinda
MRN: 1234567
45 yo F

CC: "Chest pain and SOB"

Temp: 37.2

HR: 101

RR: 18

BP: 154/78

pO₂: 98% RA

Patient
#1

“Classic” cardiac risk factors

- ◇ Hypertension
- ◇ Hyperlipidemia
- ◇ Diabetes
- ◇ Obesity
- ◇ Smoking
- ◇ Family history

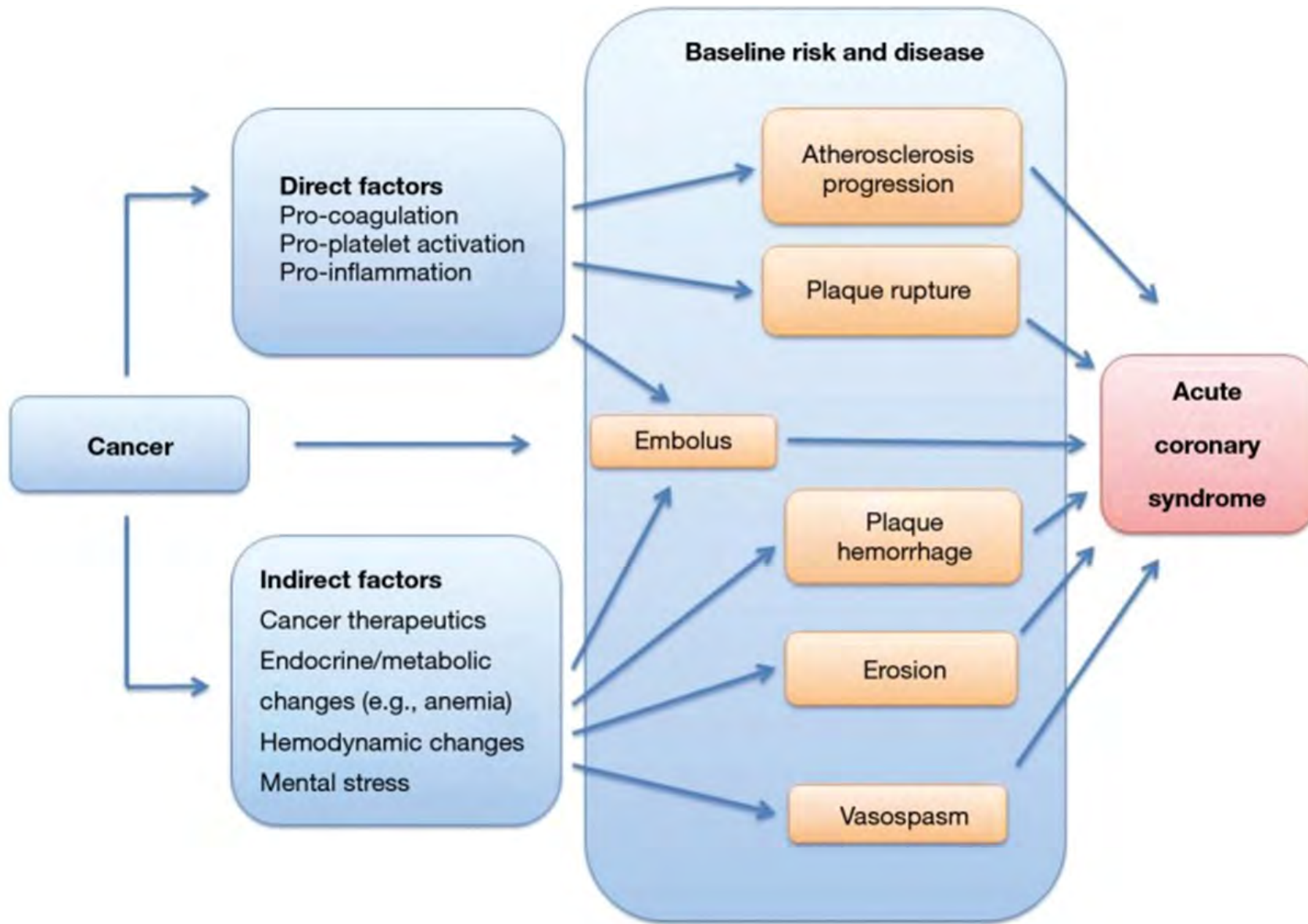
Time to add more?

- ◆ ESRD
- ◆ SLE
- ◆ HIV
- ◆ Marijuana
- ◆ ...CANCER

A perfect storm

- ◆ Antineoplastic agents
- ◆ Chest radiation

- Vasospasm
- Accelerated atherosclerosis
- Endothelial destruction
- Hypercoagulability/thrombosis



Oren O, Herrmann J. Arterial events in cancer patients—the case of acute coronary thrombosis. Vol. 10, Journal of Thoracic Disease. AME Publishing Company; 2018. p. S4367–85.

Special population: Breast Cancer



- ◆ Systematic review of breast cancer survivors showed almost 2x risk of CV death c/w age-matched population (Gernaat et al, 2017)

Table 1. Cancer Treatment and Cardiovascular Adverse Effects

Cancer Treatment	Cardiovascular Adverse Effects
Anthracyclines (eg, doxorubicin, epirubicin)	Left ventricular dysfunction, heart failure, myocarditis, pericarditis, atrial fibrillation, ventricular tachycardia, ventricular fibrillation
Alkylating agents (eg, cisplatin, cyclophosphamide)	Left ventricular dysfunction, heart failure, myocarditis, pericarditis, arterial thrombosis, bradycardia, atrial fibrillation, supraventricular tachycardia
Taxanes (eg, paclitaxel)	Bradycardia, heart block, ventricular ectopy
Antimetabolites (eg, 5-fluorouracil, capecitabine)	Coronary thrombosis, coronary artery spasm, atrial fibrillation, ventricular tachycardia, ventricular fibrillation
Endocrine therapy (eg, tamoxifen, anastrozole, letrozole)	Venous thrombosis, thromboembolism, peripheral atherosclerosis, dysrhythmia, valvular dysfunction, pericarditis, heart failure
HER-2–directed therapies (eg, trastuzumab, pertuzumab)	Left ventricular dysfunction, heart failure
Cyclin-dependent kinase 4/6 inhibitor* (eg, ribociclib)	QTc prolongation
Radiation therapy	Coronary artery disease, cardiomyopathy, valvular disease, pericardial disease, arrhythmias

Mehta LS, et al. Cardiovascular Disease and Breast Cancer: Where These Entities Intersect: A Scientific Statement From the American Heart Association. *Circulation*. 2018 Feb 20;137(8):e30–66.

Special populations: Pediatric Cancer Survivors

- ◆ Childhood Cancer Survivor Study found survivors of childhood cancer had a 15-fold increase in congestive heart failure (CHF), 10-fold increase in CAD, and 9-fold increase in stroke (Armstrong, 2014)
- ◆ Subclinical vascular injury may be present decades after completion of cancer-directed therapy (Brouwer, 2013)



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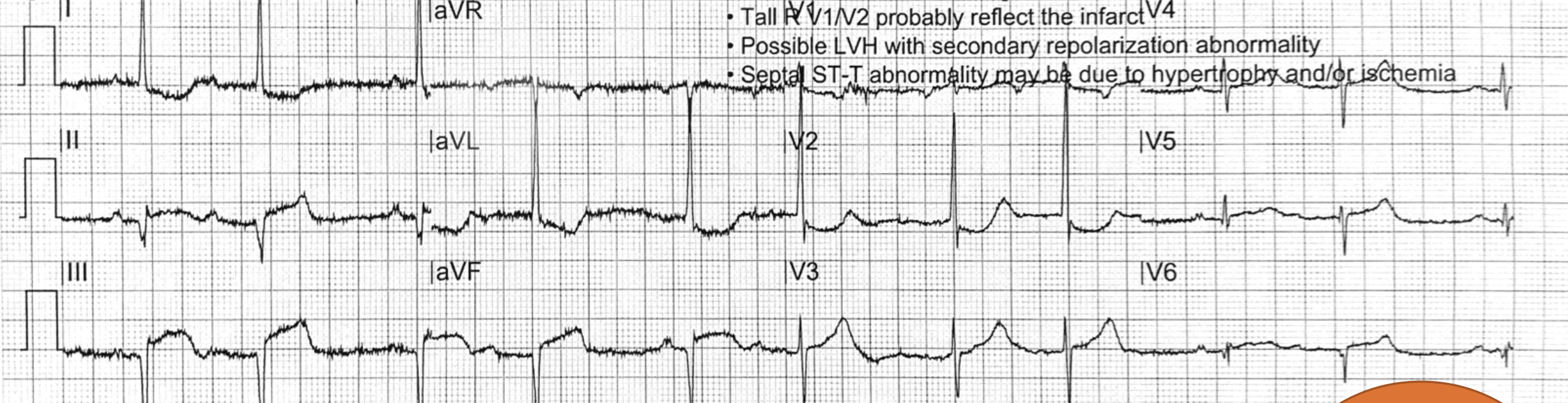
RR: 18

BP: 154/78

pO₂: 98% RA

Patient
#1

Name: 12-Lead 1 HR 64bpm • Abnormal ECG ****Unconfirmed****
 ID: [REDACTED] 16:30:01 • Sinus rhythm with 2nd degree A-V block, Mobitz I (Wenckebach)
 Patient ID: [REDACTED] PR 0.180s QRS 0.070s • Left axis deviation
 Incident ID: [REDACTED] QT/QTc: 0.444s/0.451s • Inferior infarct - age undetermined
 Age: 58 Sex: M P-QRS-T Axes: 86° -43° 114° • Possible lateral infarct - age undetermined
 • Tall R V1/V2 probably reflect the infarct V4
 • Possible LVH with secondary repolarization abnormality
 • Septal ST-T abnormality may be due to hypertrophy and/or ischemia

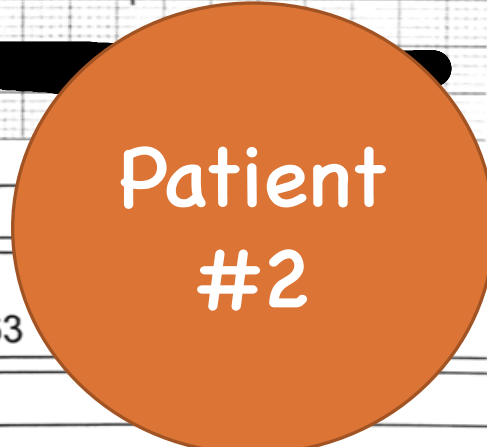


x1.0 .05-150Hz 25mm/sec
 Physio-Control, Inc. Comments: MEDIC 5 BCOFD [REDACTED]

ST measurements are measured at the J point and are expressed in mm.

I	II	III	aVR	aVL	aVF	V1	V2	V3	V4
-1.34	1.46	2.82	-0.05	-2.08	2.14	-0.83	-1.99	0.63	0.63

To ensure printer accuracy, confirm that the calibration markers are 10mm high and the grid squares are 5mm wide.



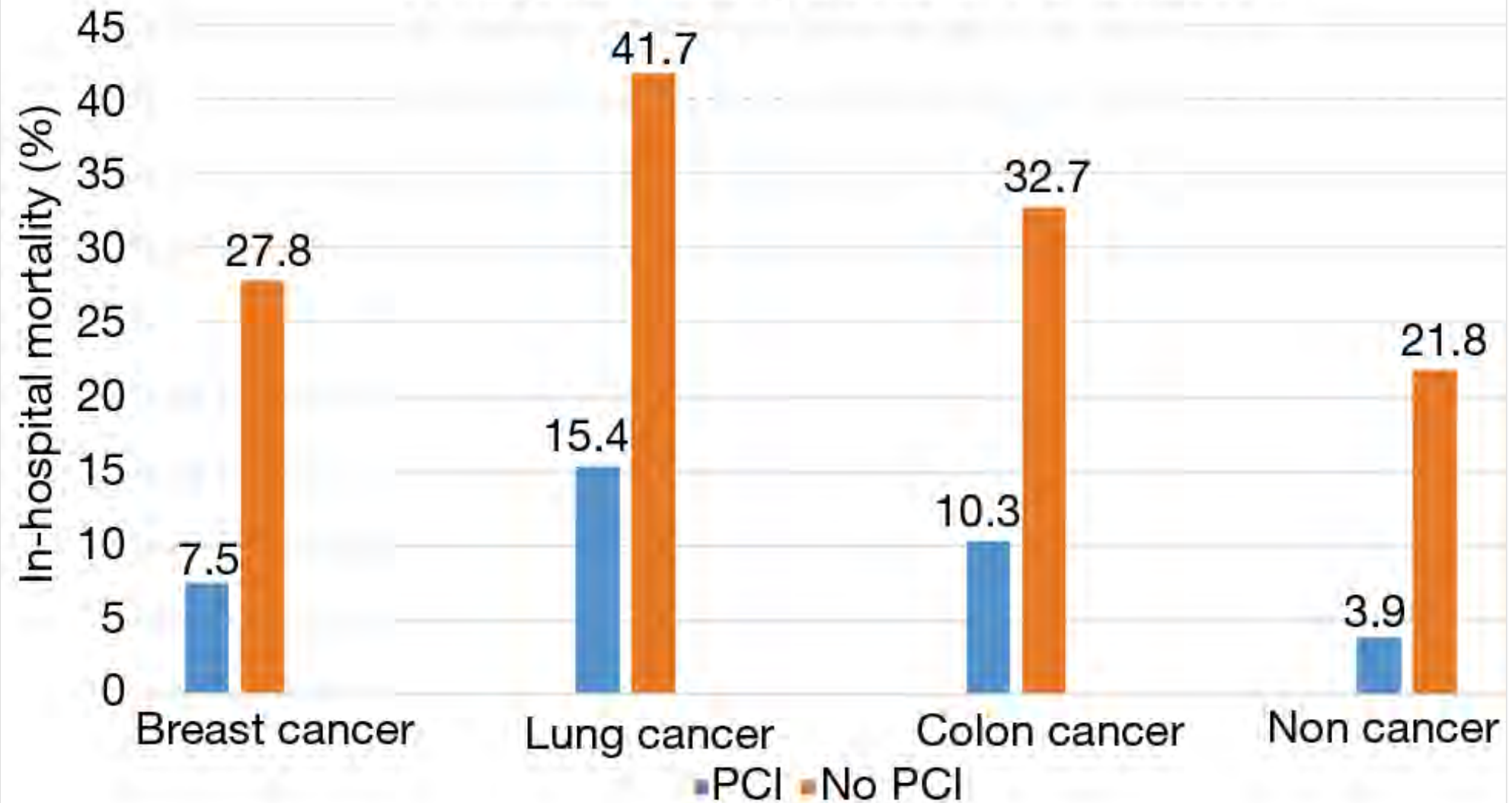
Why the hesitation with PCI?

- ◇ Overall prognosis
- ◇ Dual-antiplatelet therapy vs bleeding risk
- ◇ Malignancy is a key risk factor for early AND late stent thrombosis (Gori, 2019)

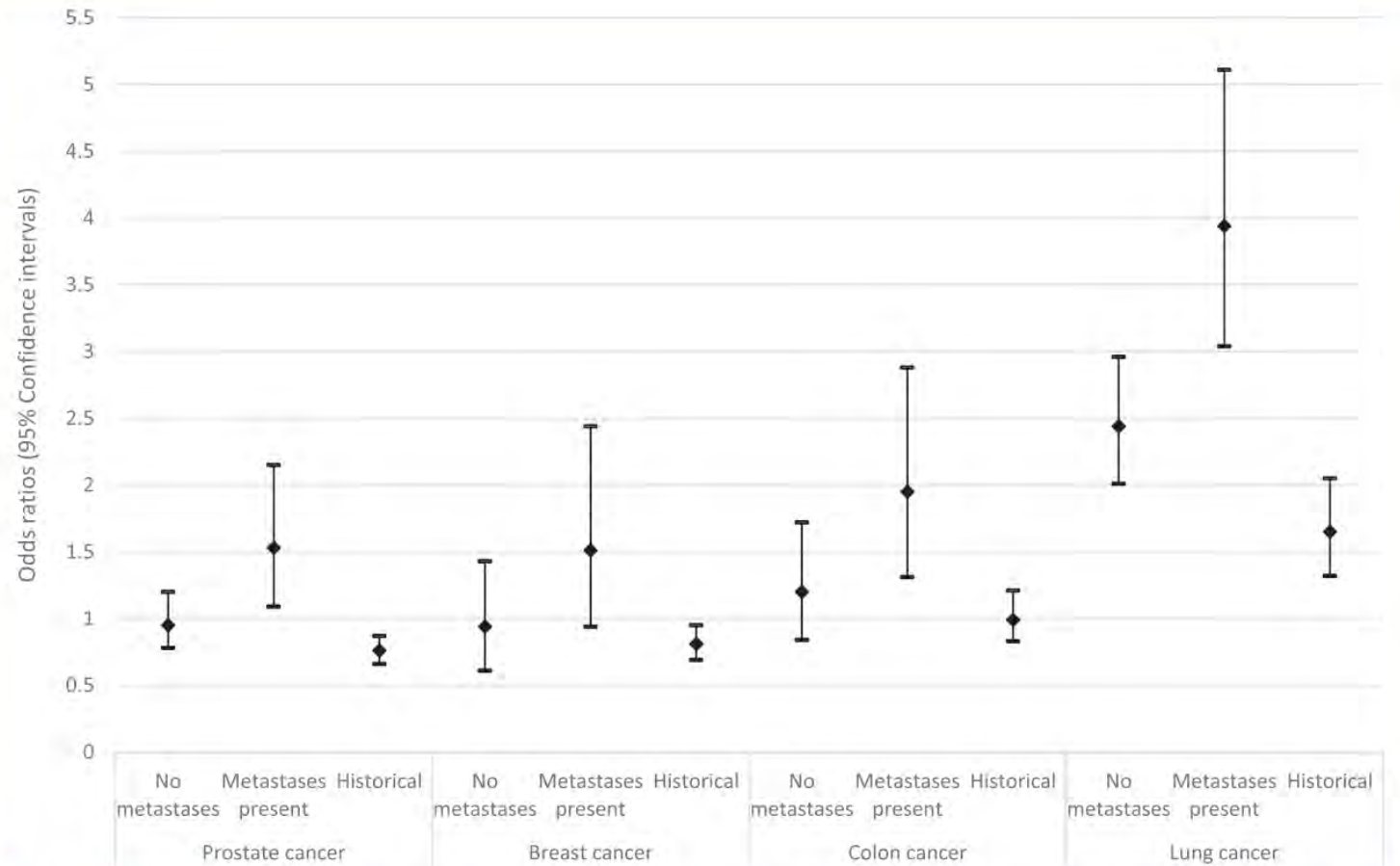
Changing tides with PCI in Cancer Pts with STEMI?

- ◇ Patients with cancer showed greater mortality after STEMI. A cancer diagnosis in the 6 months before primary PCI was strongly associated with early cardiac mortality (Velders, 2013)
- ◇ Cancer history portends worse acute and long-term noncardiac (but not cardiac) mortality (Wang, 2016)
- ◇ Patients with cancer have significantly worse in-hospital mortality compared to those without cancer, partly due to a relatively lower rate of PCI utilization in cancer patients with STEMI (Pothinini 2017)
- ◇ There was no significant difference for in-hospital complications in patients with a history of cancer and those without a history of cancer undergoing primary PCI for STEMI (Jacobs, 2019)

In-hospital mortality based on PCI utilization



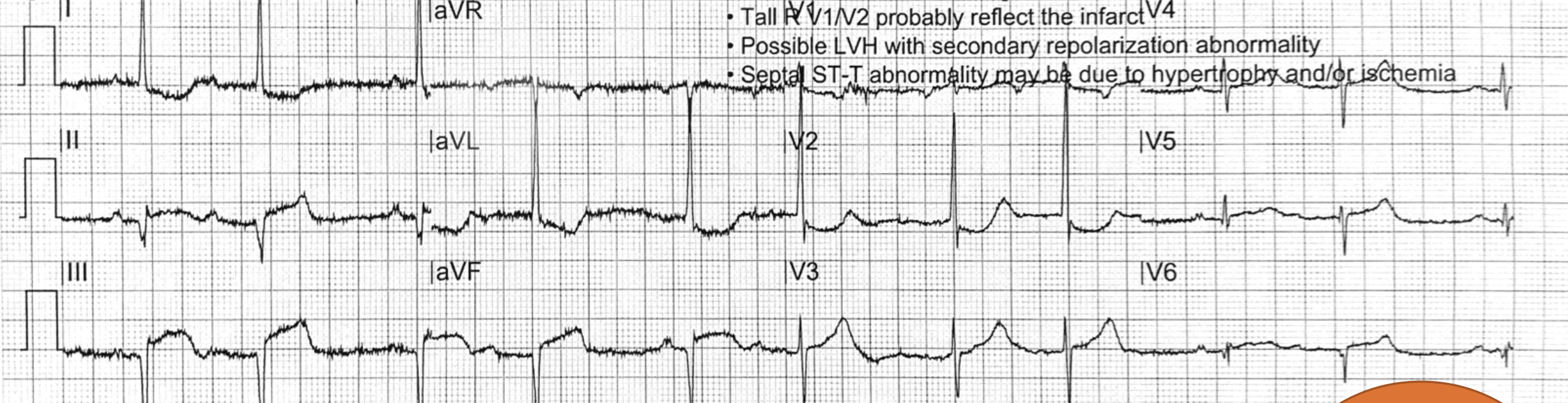
Current vs history of Cancer?



Take home figure The prognostic impact (odds ratio and 95% confidence intervals) of a historical diagnosis of cancer, current cancer with no metastases and current cancer with metastases on in-hospital mortality for prostate, breast, colon, and lung cancer.

Potts JE, Ilescu CA, Lopez Mattei JC, Martinez SC, Holmvang L, Ludman P, et al. Percutaneous coronary intervention in cancer patients: A report of the prevalence and outcomes in the United States. *Eur Heart J.* 2019;40(22):1790-1800A.

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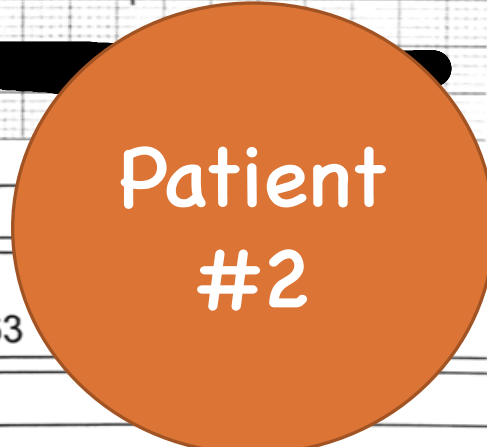


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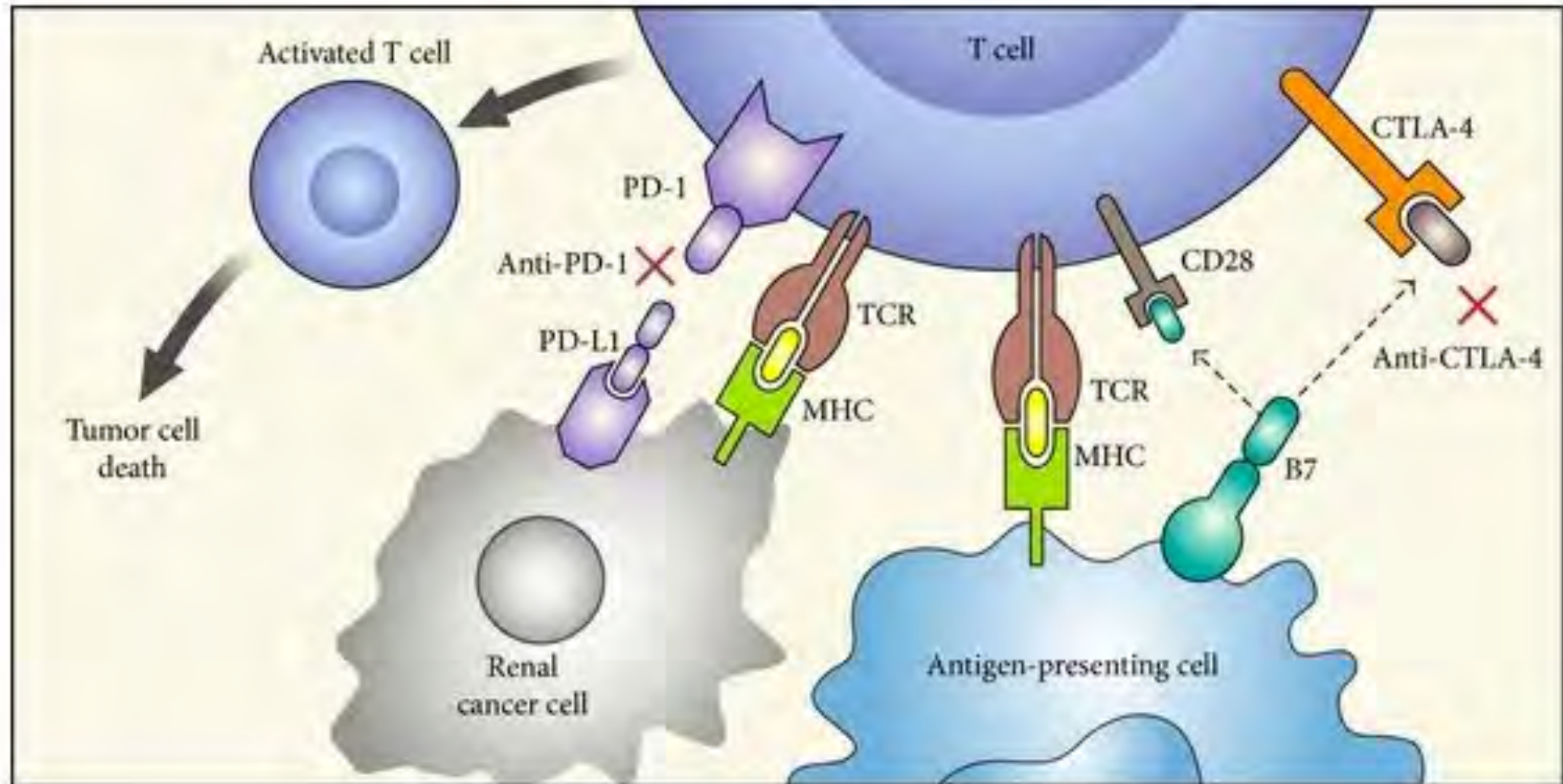
To ensure printer accuracy, confirm that the calibration markers are 10mm high and the grid squares are 5mm wide.





Patient
#3

Immune Checkpoint Inhibitor (ICI) Therapy

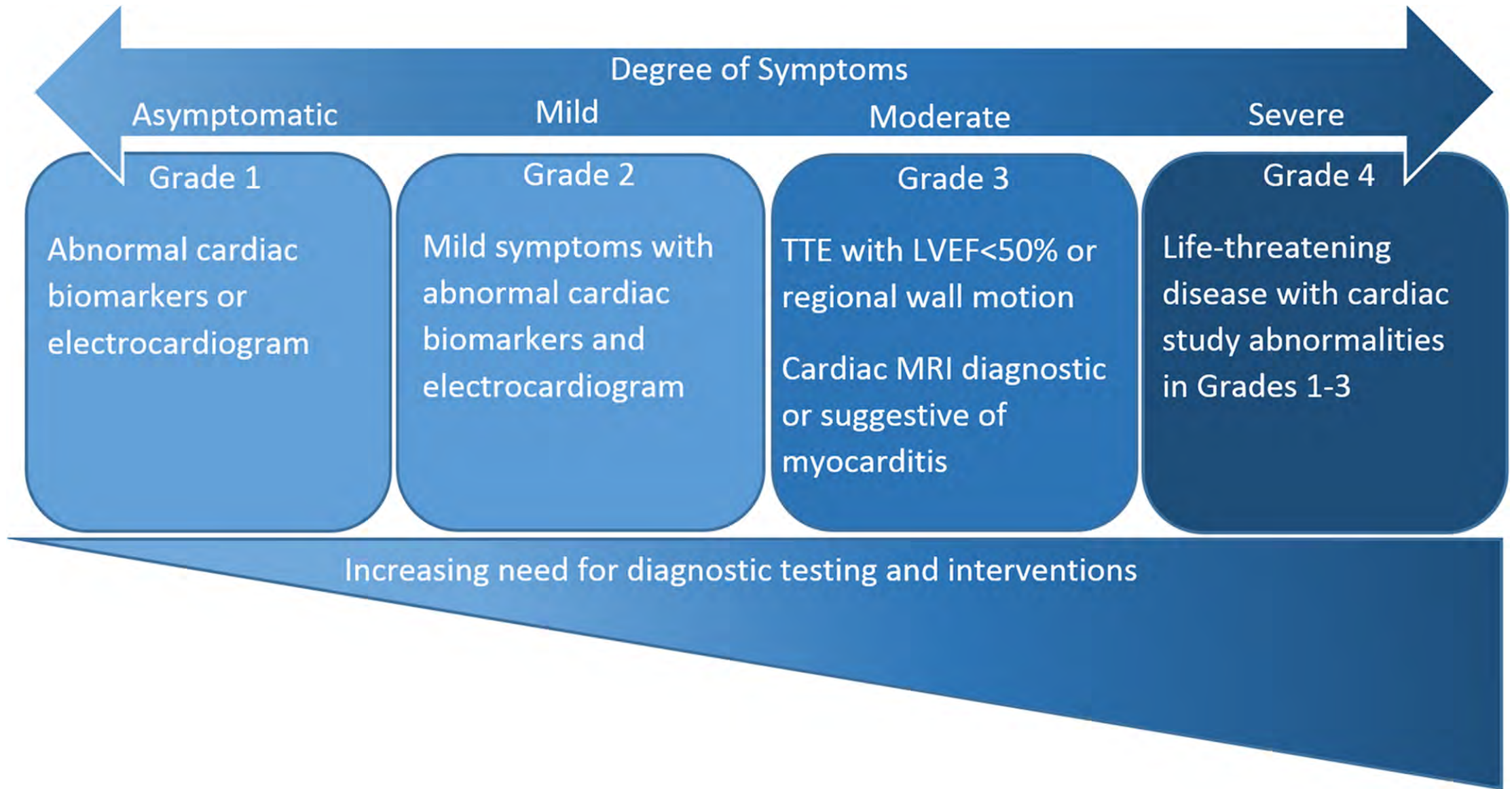


ICI-related cardiotoxicity

- ◇ LV dysfunction, Takotsubo
- ◇ Pericarditis/Pericardial effusion
- ◇ Myocarditis

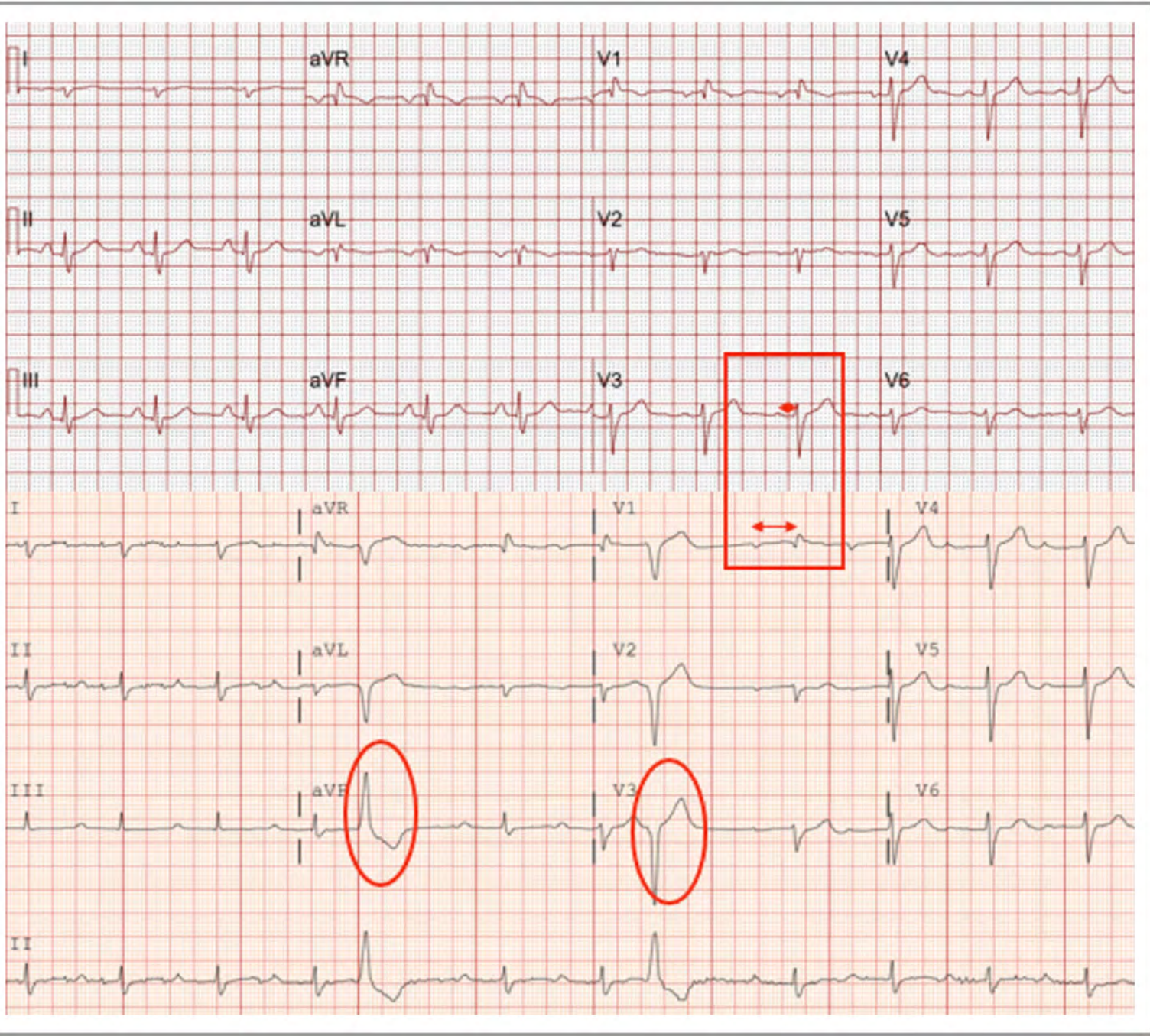
ICI Myocarditis

- ◆ Low incidence (0.04-2.4%) under-recognized/reported
- ◆ Mortality 25-50%
- ◆ Median onset: 34 days (81% within 3 months, longest reported 454 days out) (Mahmood, 2018; Escudier, 2017)
- ◆ Most only received 1-2 doses at onset



Beware: Dysrhythmias

**Any new conduction
abnormality can quickly evolve
into full block!**



Palaskas N,
Lopez-Mattei J,
Durand JB, Iliescu C,
Deswal A. Immune
Checkpoint Inhibitor
Myocarditis:
Pathophysiological
Characteristics,
Diagnosis, and
Treatment. J Am Heart
Assoc [Internet]. 2020
Jan 21;9(2). Available
from:
<https://www.ahajournals.org/doi/10.1161/JAHA.119.013757>

Laboratory

Troponin

- Preferably Troponin I
- Consider Troponin T, CK-MB, Total CK

Natriuretic Peptides

- NT-pro BNP
- BNP

Imaging

Electrocardiogram, 12-lead

Echocardiogram

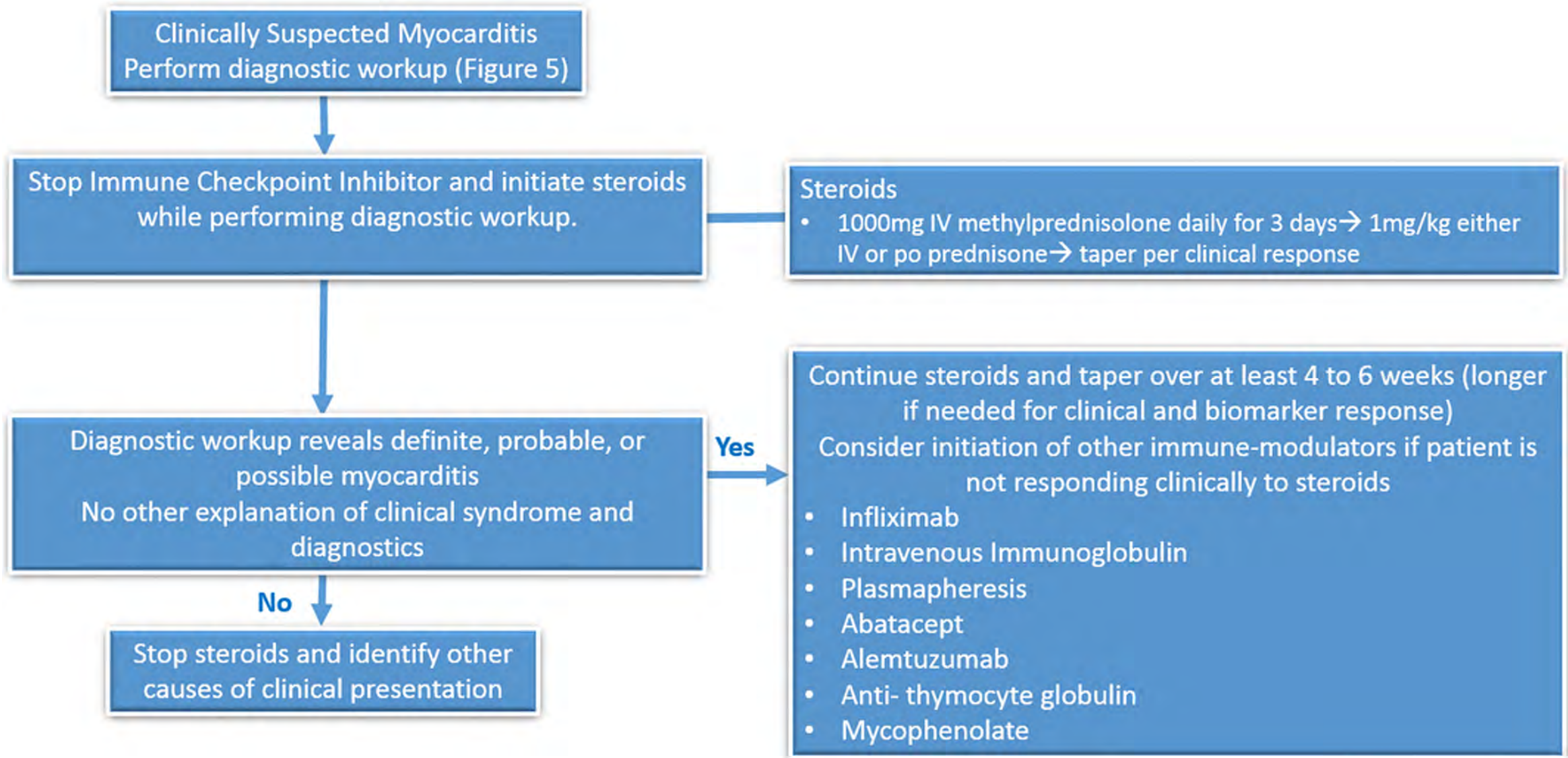
Cardiac Magnetic Resonance

Telemetry Monitoring

Procedures

Endomyocardial Biopsy

Coronary angiography





Patient
#3



Key Points

- ◆ History of cancer/cancer therapy should **ABSOLUTELY** be considered a CV risk factor, and increased risk remains for years after treatment
- ◆ STEMI- decision for PCI is complicated
- ◆ ICI toxicities- save a life by picking up on dysrhythmias early



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