



Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

# Immune Checkpoint Inhibitor Myocarditis

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#LearnACI

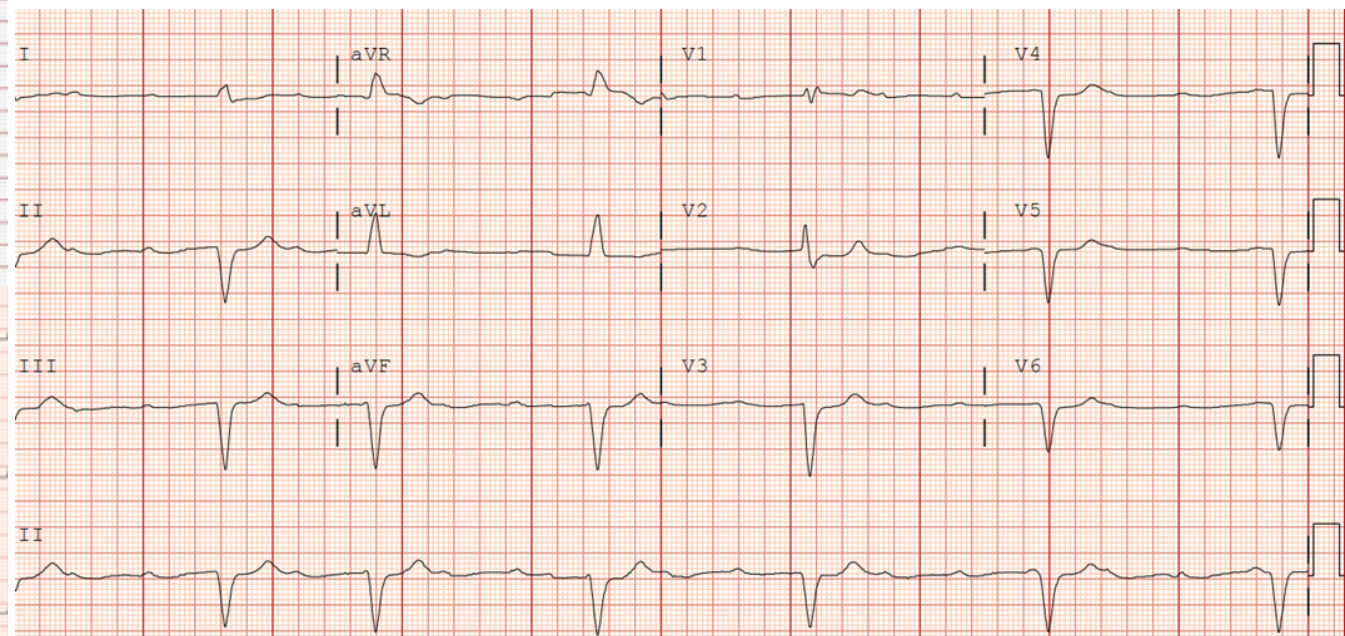
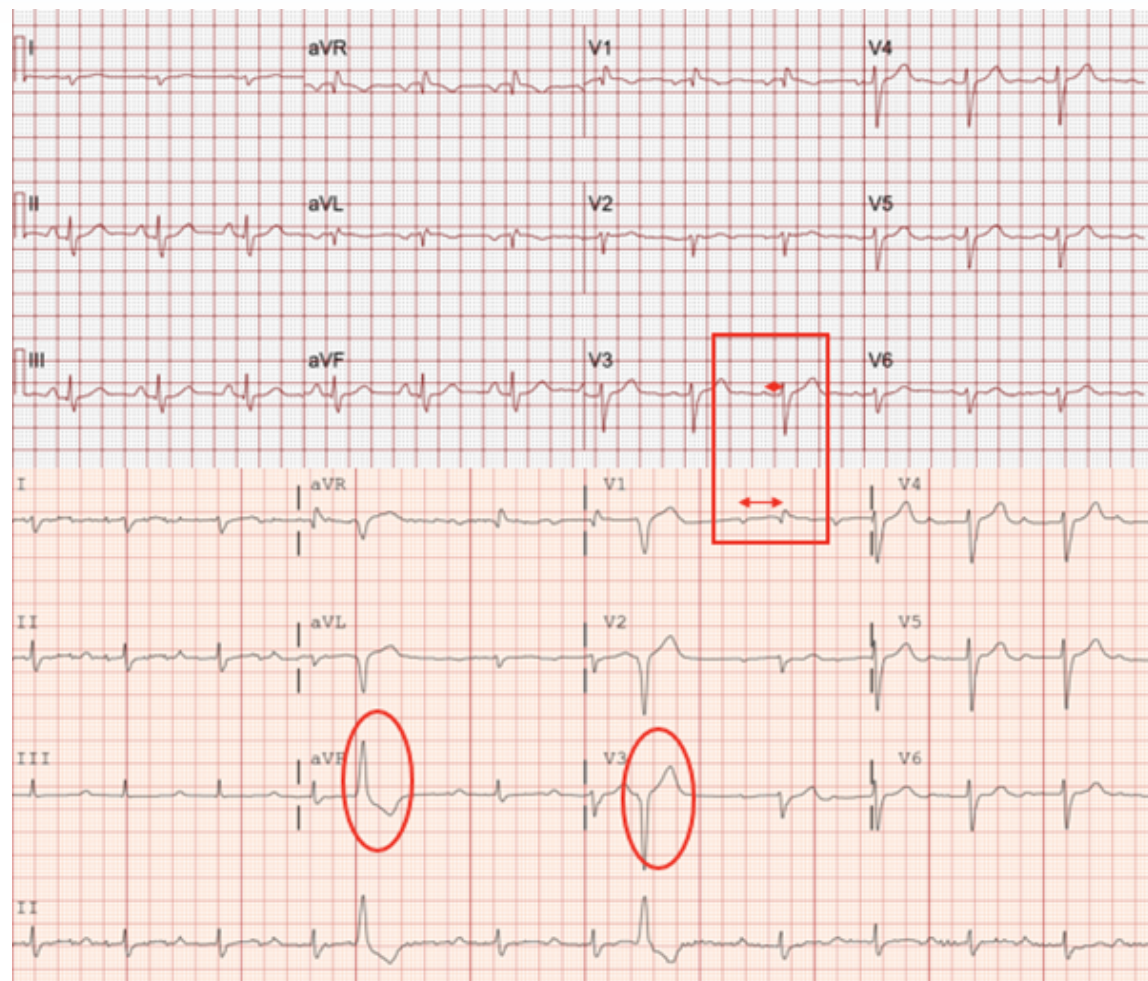
# Disclosures

- Cancer Prevention & Research Institute of Texas, National Institute of Health, Sabin Family Fellowship, Patient Education Resource, Replimmune, Kiniksa
- I will be discussing non-FDA approved indications during my presentation.

# Case Presentation

- 65 year old man with renal cell carcinoma recently started pembrolizumab
- Patient presents with dyspnea 10 days after second dose of pembrolizumab
- No previous cardiovascular disease history
- Previously physically active with good exertional capacity > 4 METs

# Case Presentation

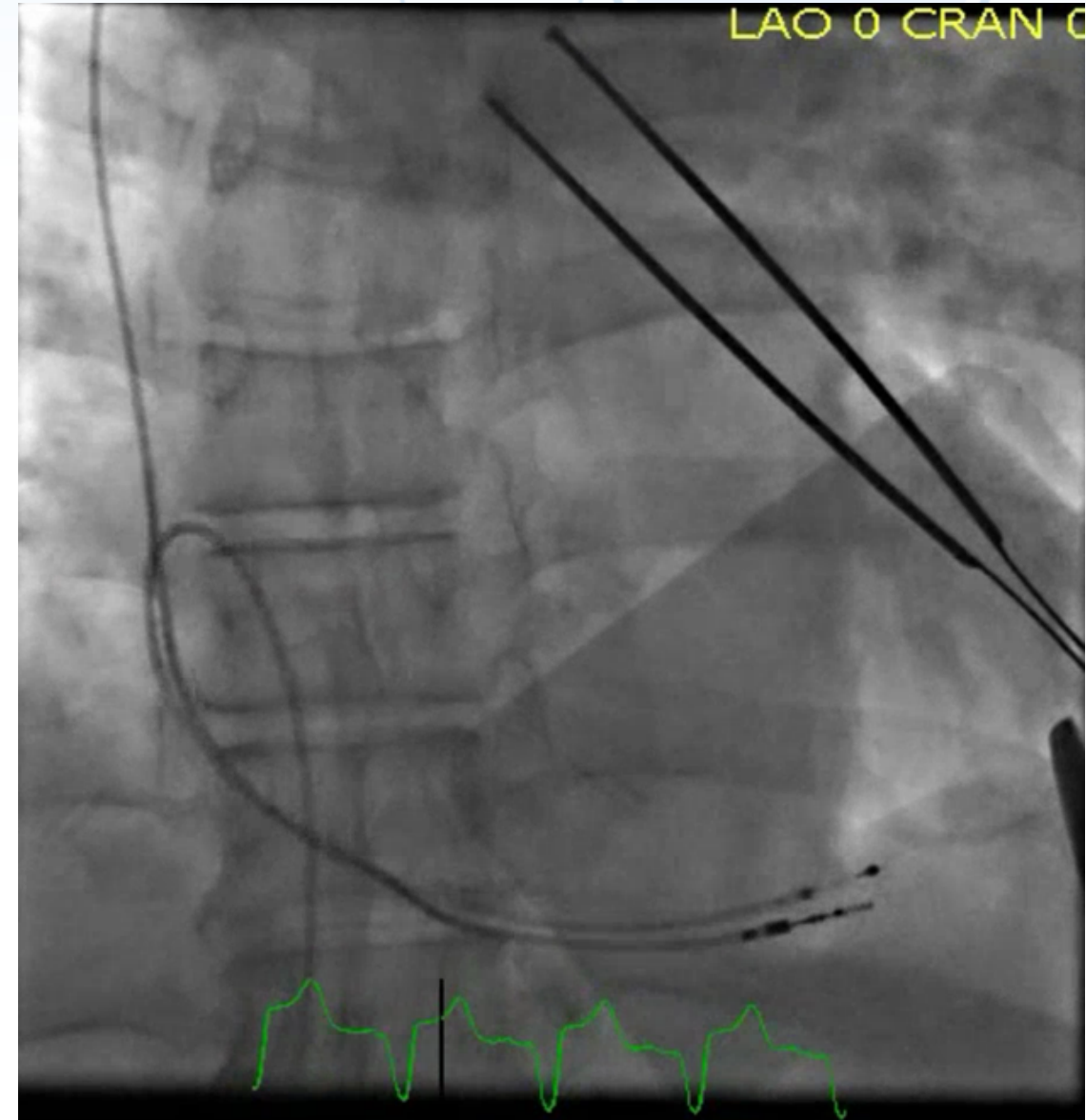


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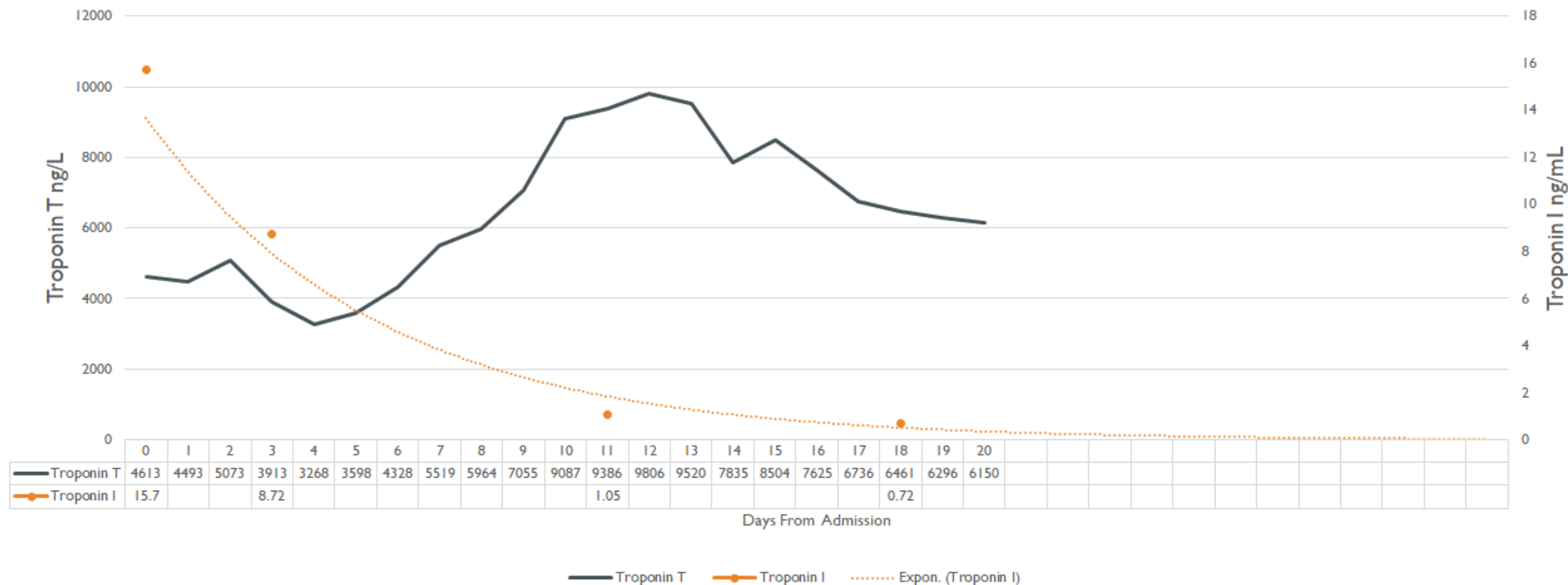


## Internal Fixation Lead

- Allows 4 to 6 weeks of recovery before deciding on permanent pacemaker
- More stable positioning
- Patient can participate in physical therapy
- Time to recover the conduction system



# Troponin T versus Troponin I



# Incidence of Myocarditis

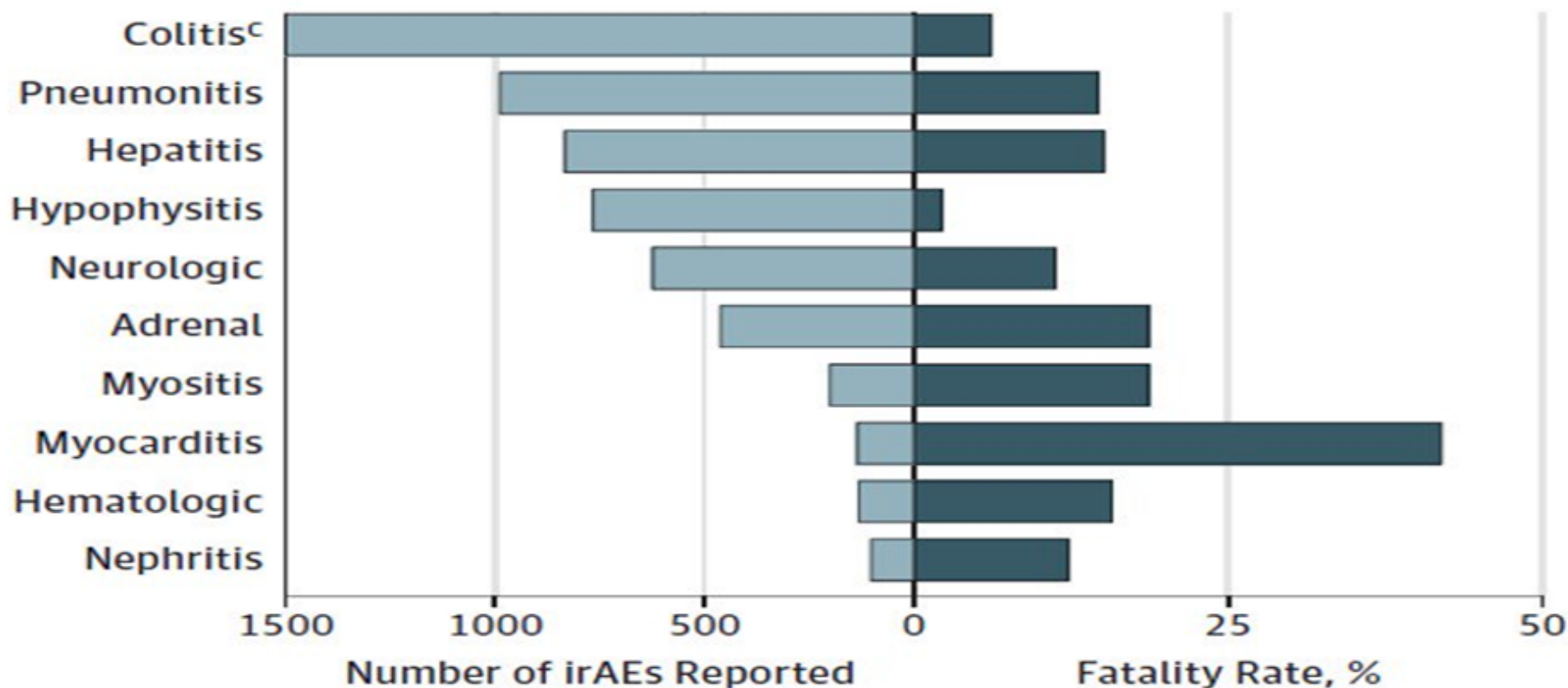
**Table 1. Incidence of Myocarditis and Myositis in Patients Receiving Nivolumab or Ipilimumab plus Nivolumab.**

Characteristic	Nivolumab (N = 17,620)	Nivolumab plus Ipilimumab (N = 2974)
	no. (%)	
Myocarditis		
Any*	10 (0.06)	8 (0.27)
Fatal events	1 (<0.01)	5 (0.17)
Myositis		
Any	27 (0.15)	7 (0.24)
Fatal events	2 (0.01)	1 (0.03)

\* The number of patients with myocarditis includes six patients with concurrent myocarditis and myositis.

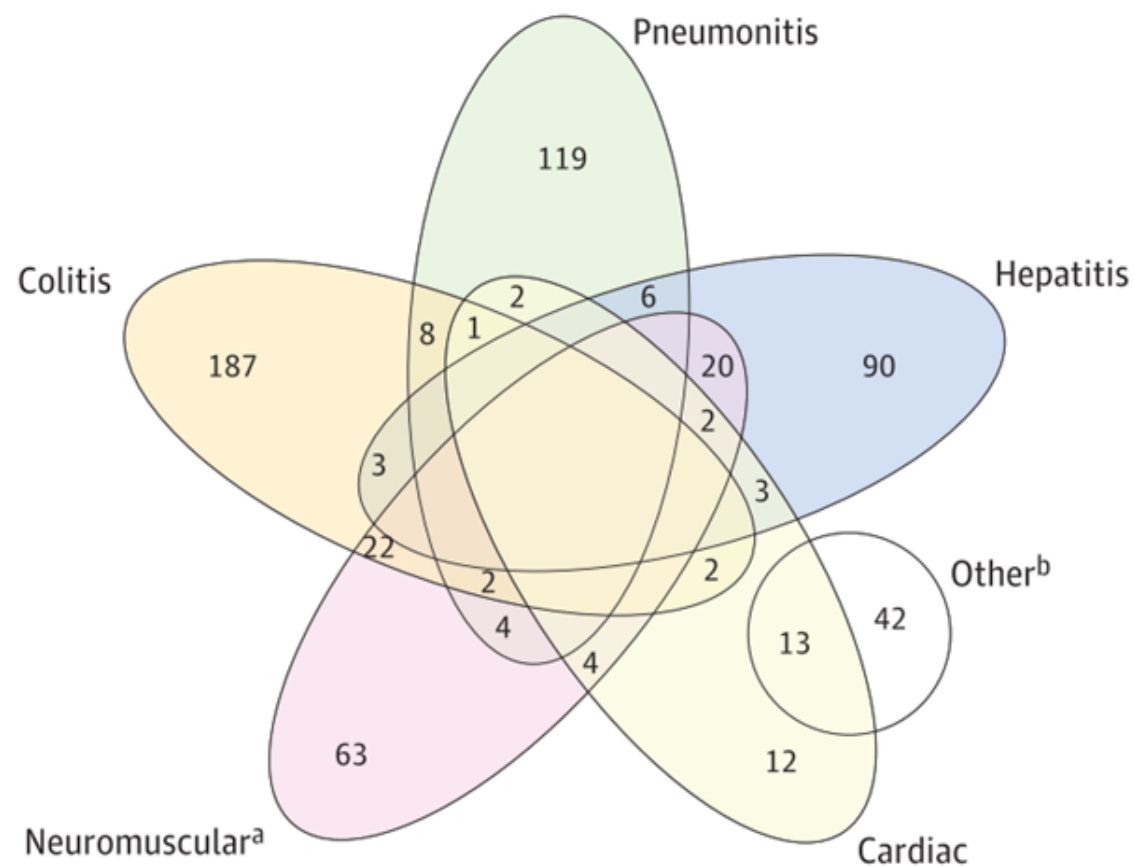
# Mortality of Myocarditis

**C** Cases and fatality rates

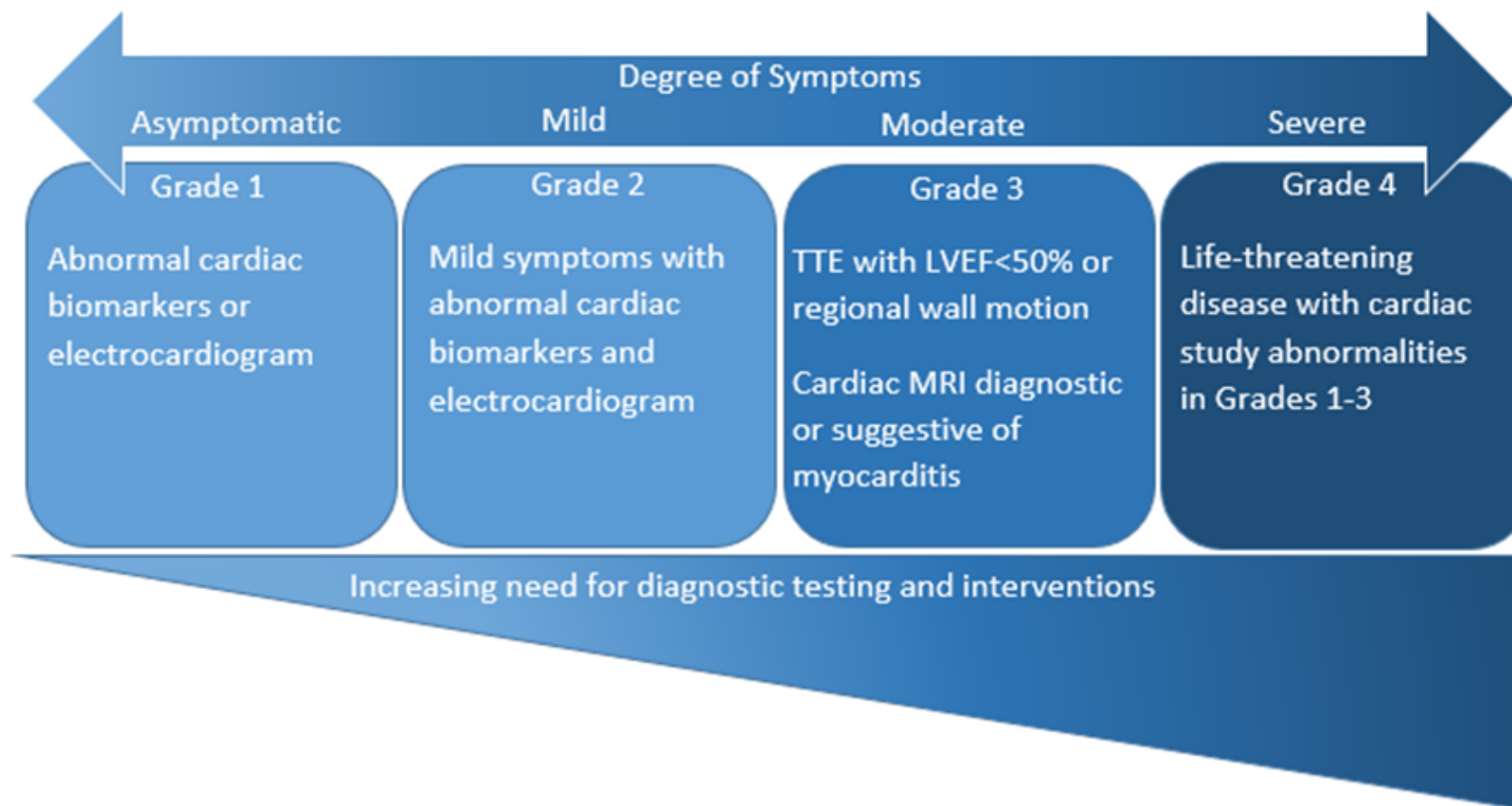




# Concomitant IRAE



# Spectrum of Disease



# Cardiac Biomarkers

- Troponin I is preferred over Troponin T, CK, CKMB<sup>1</sup>
- NTproBNP and BNP are nonspecific markers- especially in cancer patients
- Discharge troponin T above 1.5 ng/mL was associated with worse prognosis and 4-fold increased risk of major adverse cardiovascular events (MACE)<sup>2</sup>
- MACE- cardiovascular death, cardiogenic shock, cardiac arrest, or complete heart block<sup>2</sup>

# EKG/TELEMETRY

- Prolonged PR interval, AV block, ventricular arrhythmias, frequent PVCs, ST depressions, diffuse T wave inversions
- Telemetry monitoring should be performed on admission- monitor for PVC burden, arrhythmias, PR prolongation
- Baseline EKG is not predictive of future events but helpful for comparison if changes occur

# Echocardiography

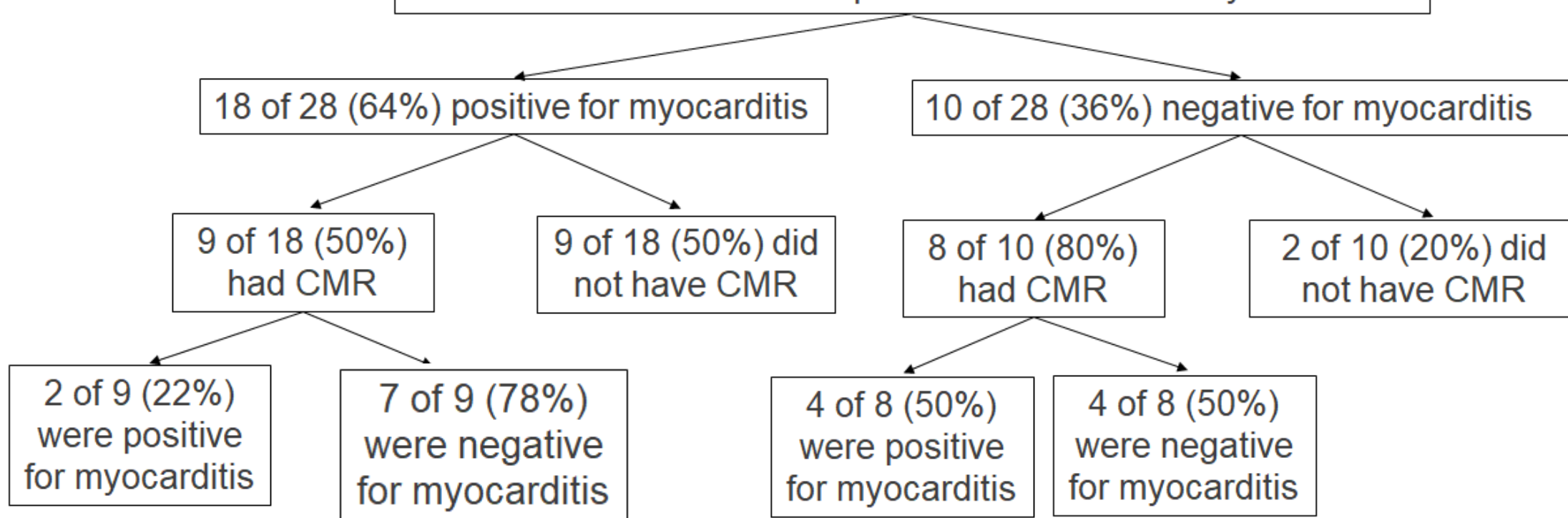
- LV ejection fraction, wall motion abnormalities, pericardial effusion
- Baseline echocardiogram not predictive of events but helpful in comparison
- 51% of ICI Myocarditis have normal LVEF and 38% of these develop MACE

Mahmood SS et al. Myocarditis in Patients Treated With Immune Checkpoint Inhibitors. *Journal of the American College of Cardiology* 2018;71(16):1755-64



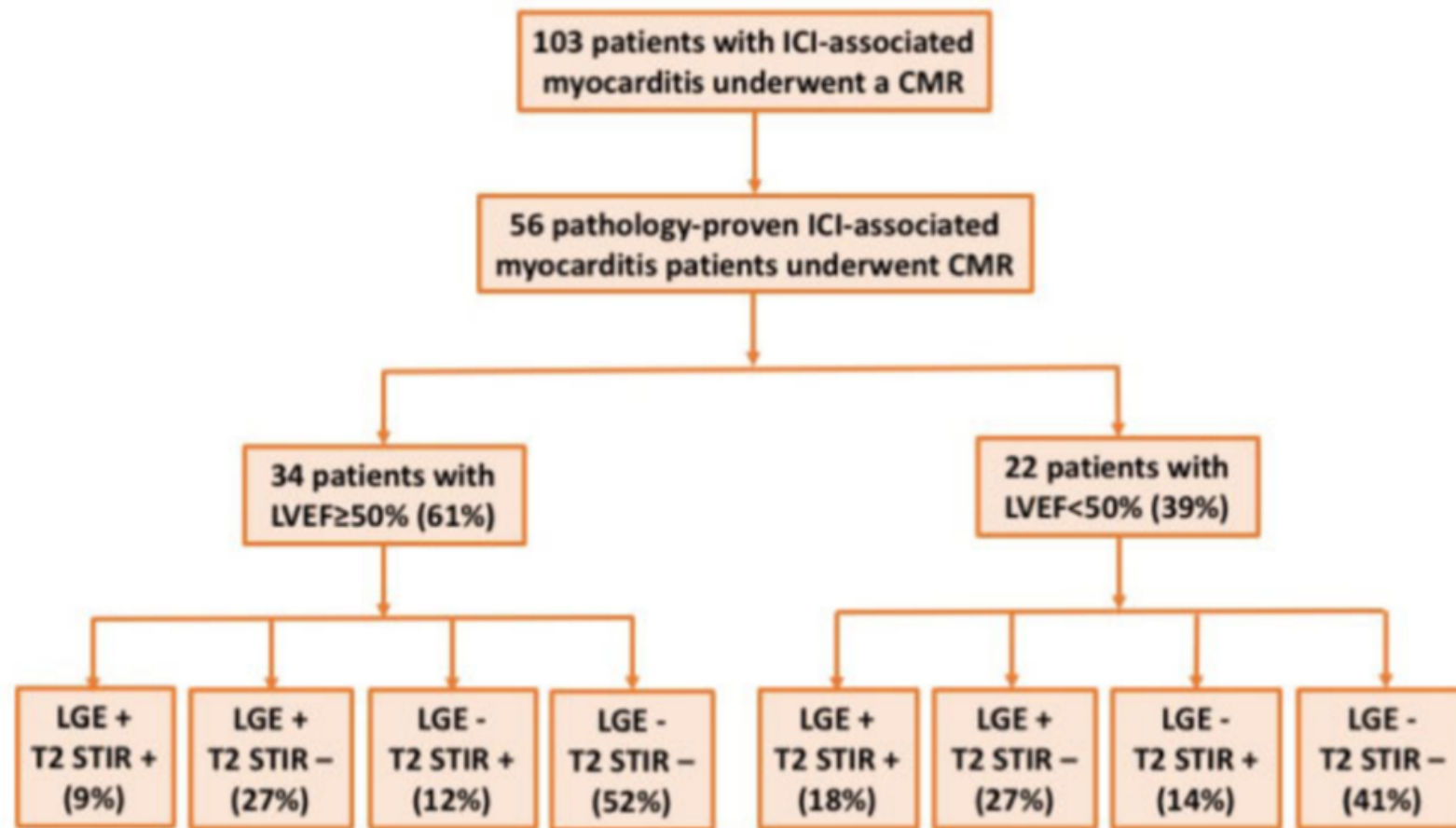
# Cardiac MRI

28 Patients with EMB for suspected ICI associated myocarditis



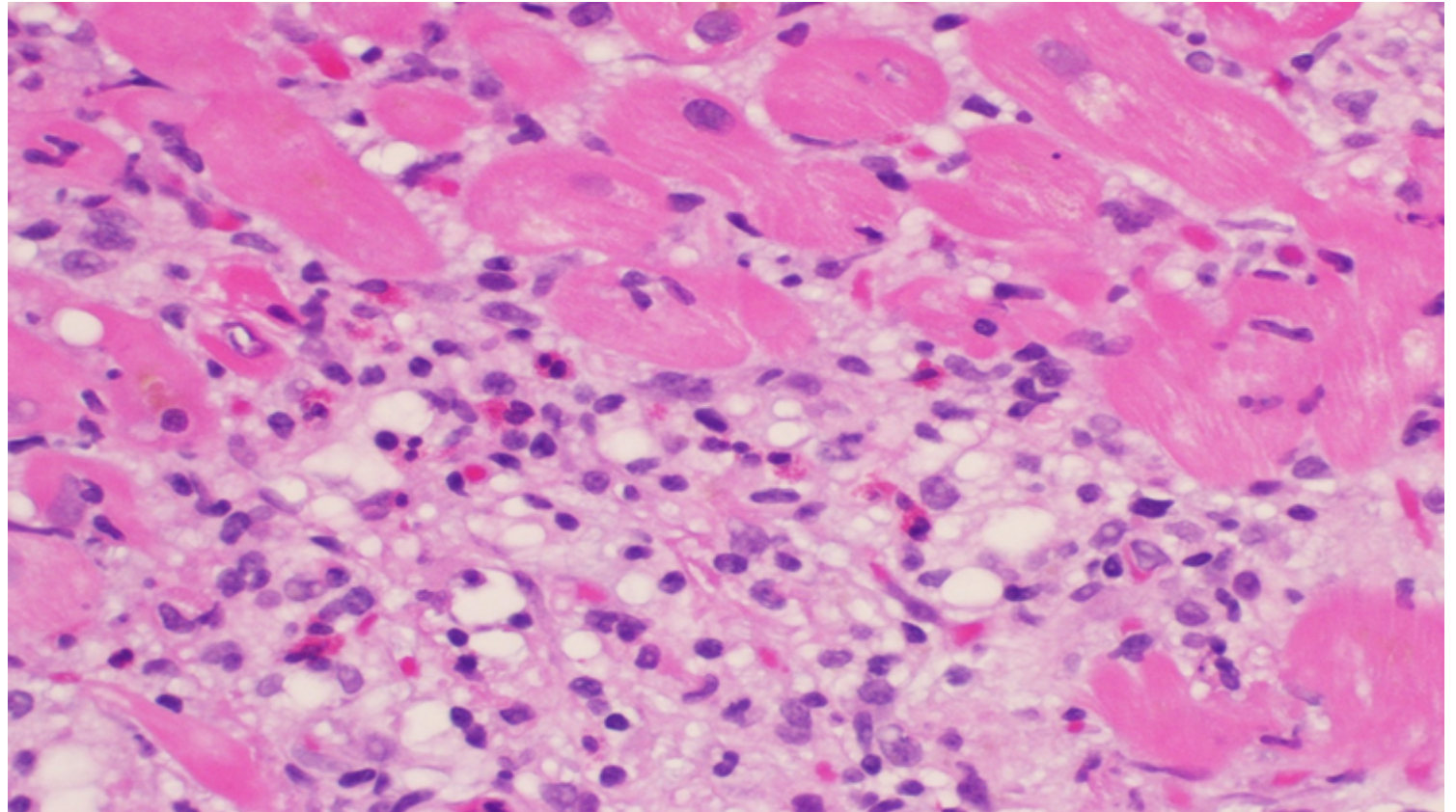
	EMB Positive	EMB Negative	Total
CMR Positive	2 (22%)	4 (50%)	6
CMR Negative	7 (78%)	4 (50%)	11
Total	9	8	17

# Cardiac MRI



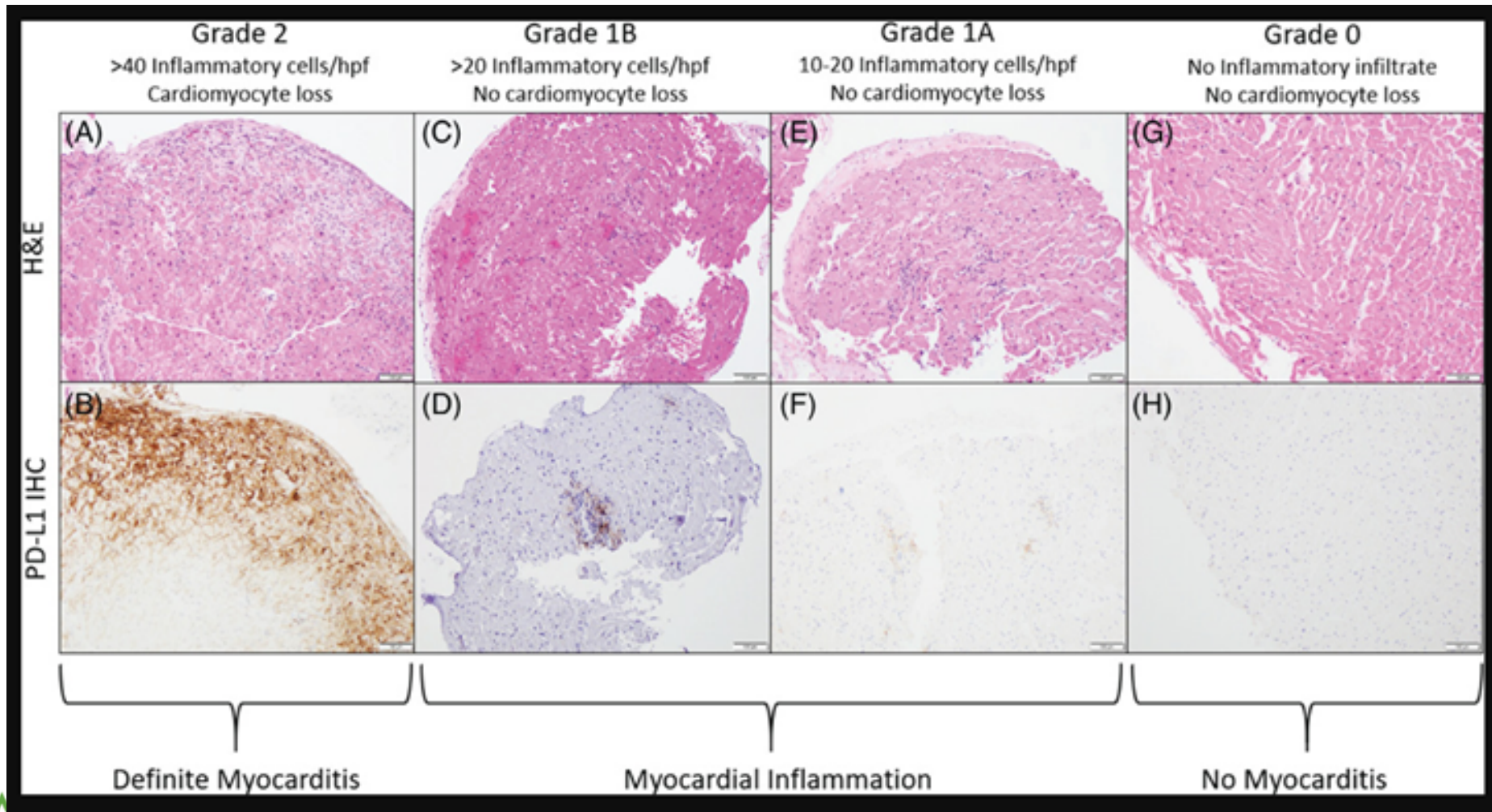
# Endomyocardial Biopsy

- Tissue diagnosis is the gold standard for diagnosing myocarditis
- Uses Dallas Criteria for histologic diagnosis
  - Myocyte Necrosis
  - Inflammatory Infiltrate

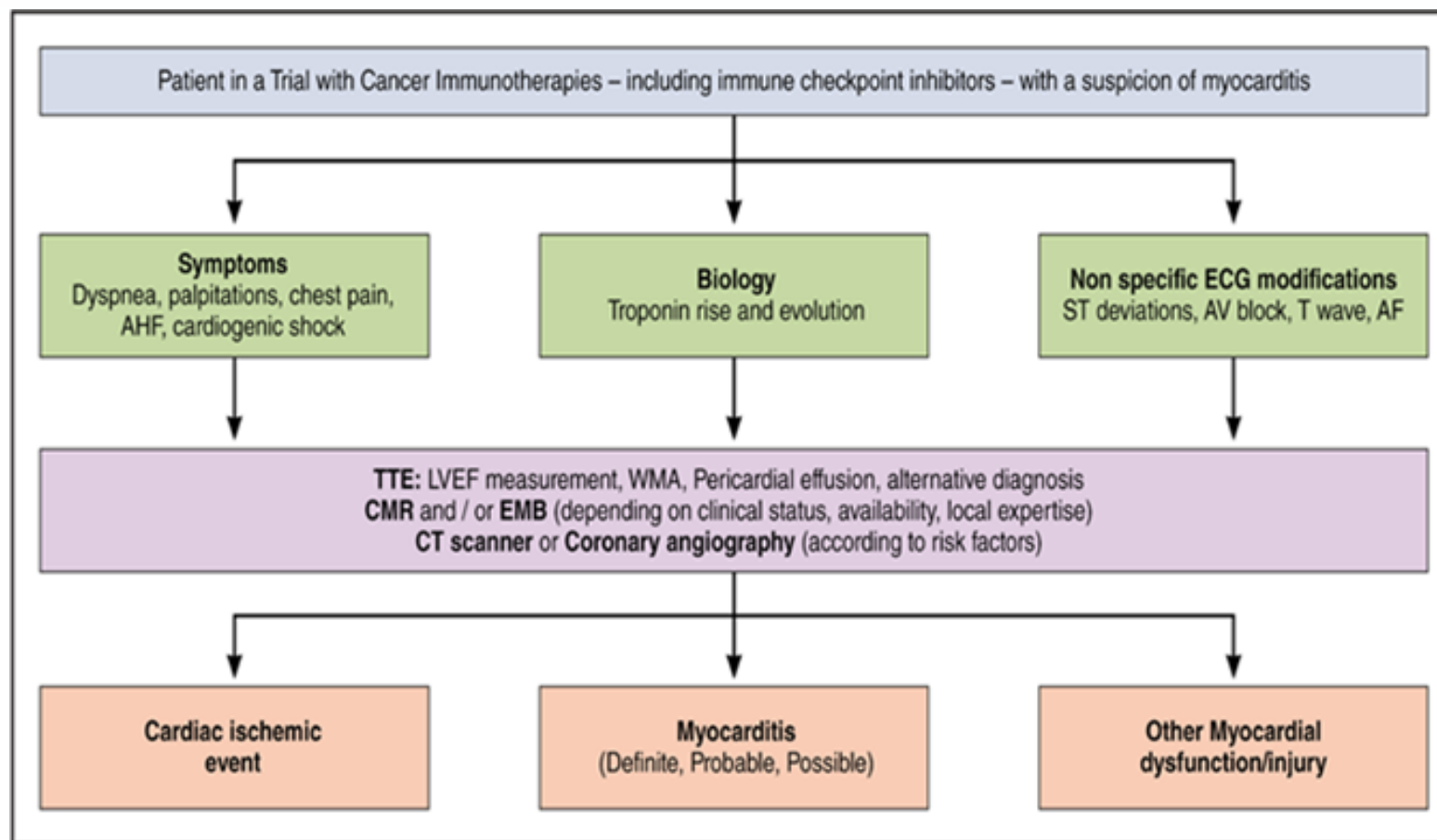




# Endomyocardial Biopsy

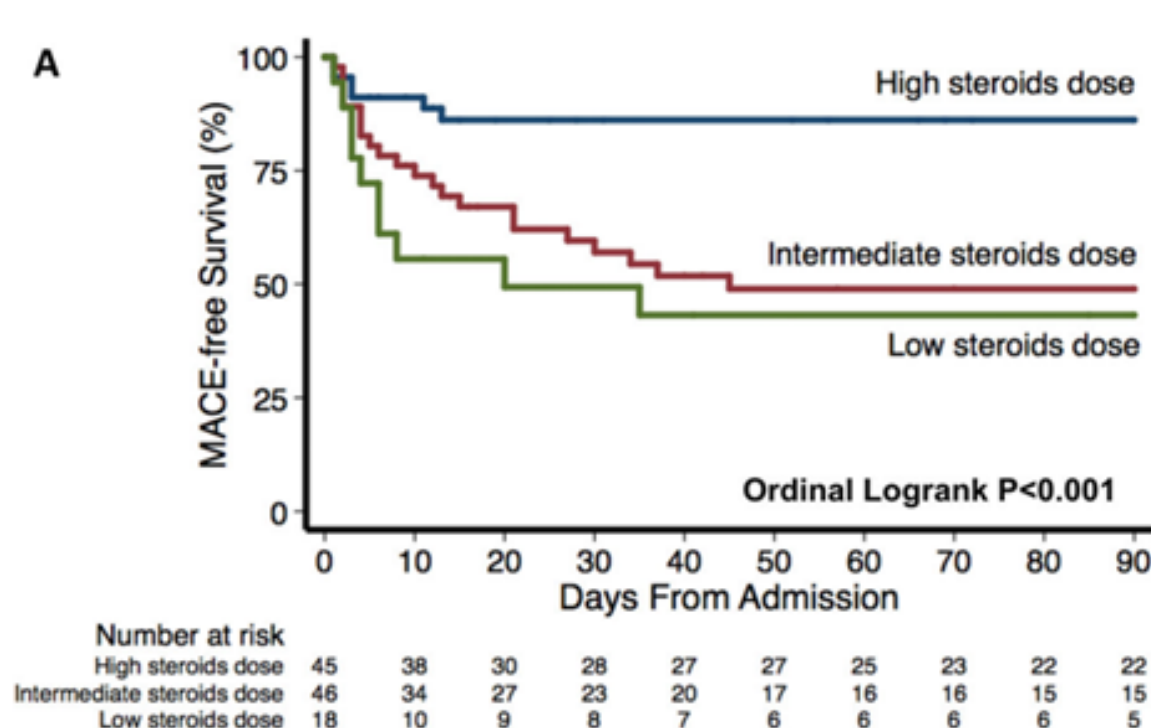
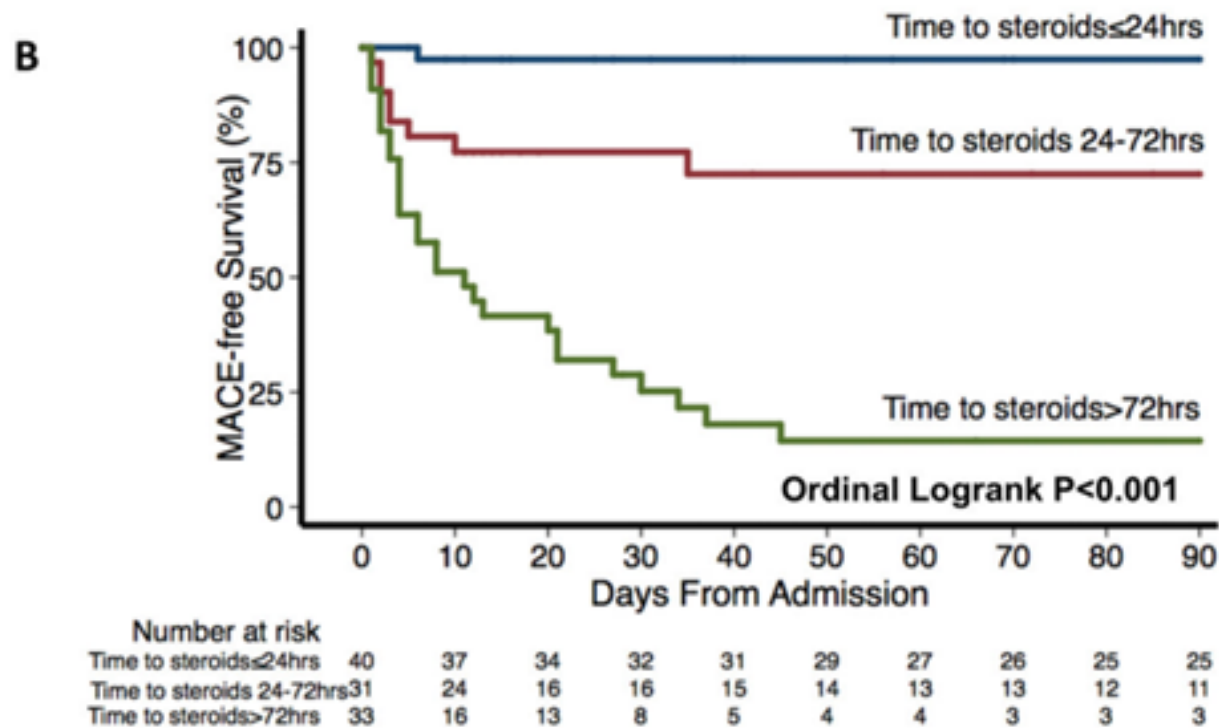


# Diagnosis of ICI myocarditis





# Treatment of ICI myocarditis



Higher initial dose (ie, iv methylprednisolone 1000 mg/d) and earlier initiation of corticosteroids were associated with improved cardiac outcomes with ICI-associated myocarditis.

# Treatment of ICI myocarditis

