CheckRare

Rare and Genetic Disease Network

CME

TTR Amyloidosis

The Undiagnosed Patient (and how to find them)

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TTR Amyloidosis: Epidemiology

> 50,000 worldwide

- ~ 10,000 with FAP
- > 40,000 with FAC
- Assumed to be significantly underdiagnosed

Median age at onset 68 yrs

- Large variance (10th - 90th percentile: 45 - 90 yrs)
- Male: female ration highest in U.S. (4.6)

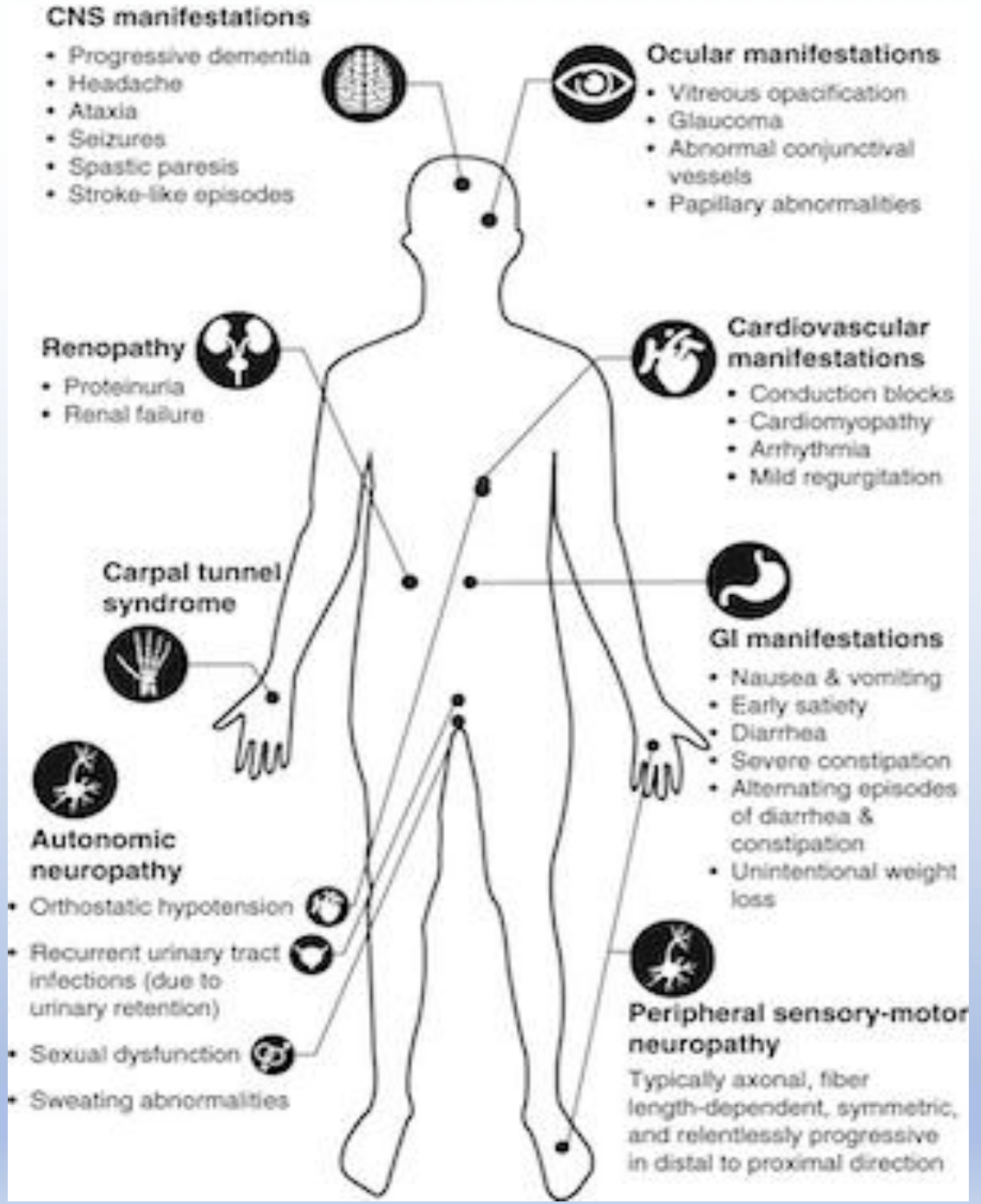
Hawkins P et al. *Ann Med*. 2015;47:625-638; Coelho T et al. Amyloidosis Foundation Physician's Guide. 2008; Ando et al. *Orphanet J Rare Diseases* 2013, 8:31; Gertz MA. *Am J Manag Care*. 2017;23:S107-S112; Coelho T, Maurer M, Suhr O. *CMRO*. 2013; 29:63-76.

TTR Amyloidosis:
The Great Pretender

Multiple Systems Affected

Nonspecific Symptoms

Clinical heterogeneity (even in same families)

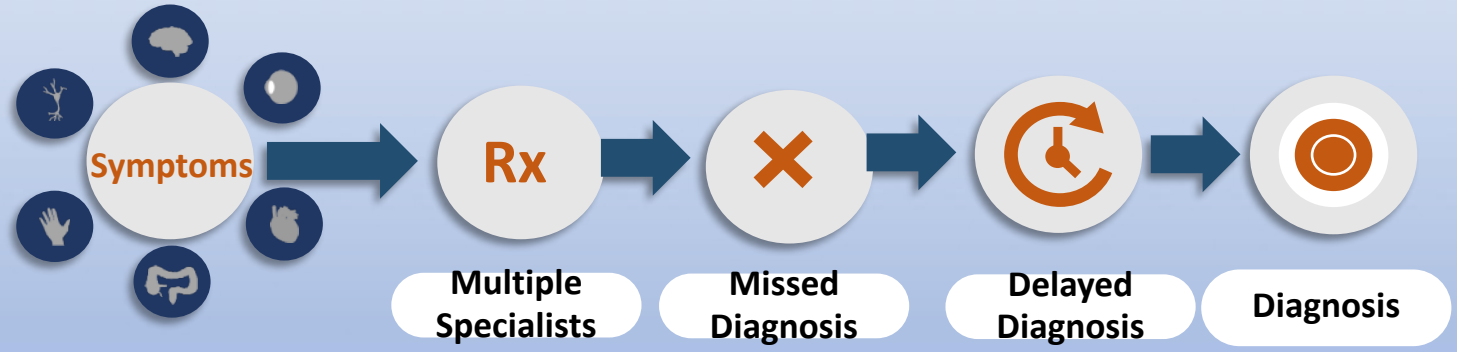


Conceição I, et al. *J Peripher Nerv Syst.* 2016;21(1):5-9;

TTR Amyloidosis: The Great Pretender

45% of patients misdiagnosed initially

- Carpal tunnel syndrome, idiopathic polyneuropathy, ocular herpes, Sjorgrens syndrome, IBS, bronchitis, congestive heart failure, GERD, spinal problems, gastropareses, COPD, NSAID-induced constipation, plantar fasclitis, fibromyalgia
- 2- 4 years (regardless of family history)[1,2]



1. Amyloidosis Foundation. 2. Plante-Bordeneuve V. *Neurology*. 2007; 69(7):693-8

Presenting Symptoms Variability

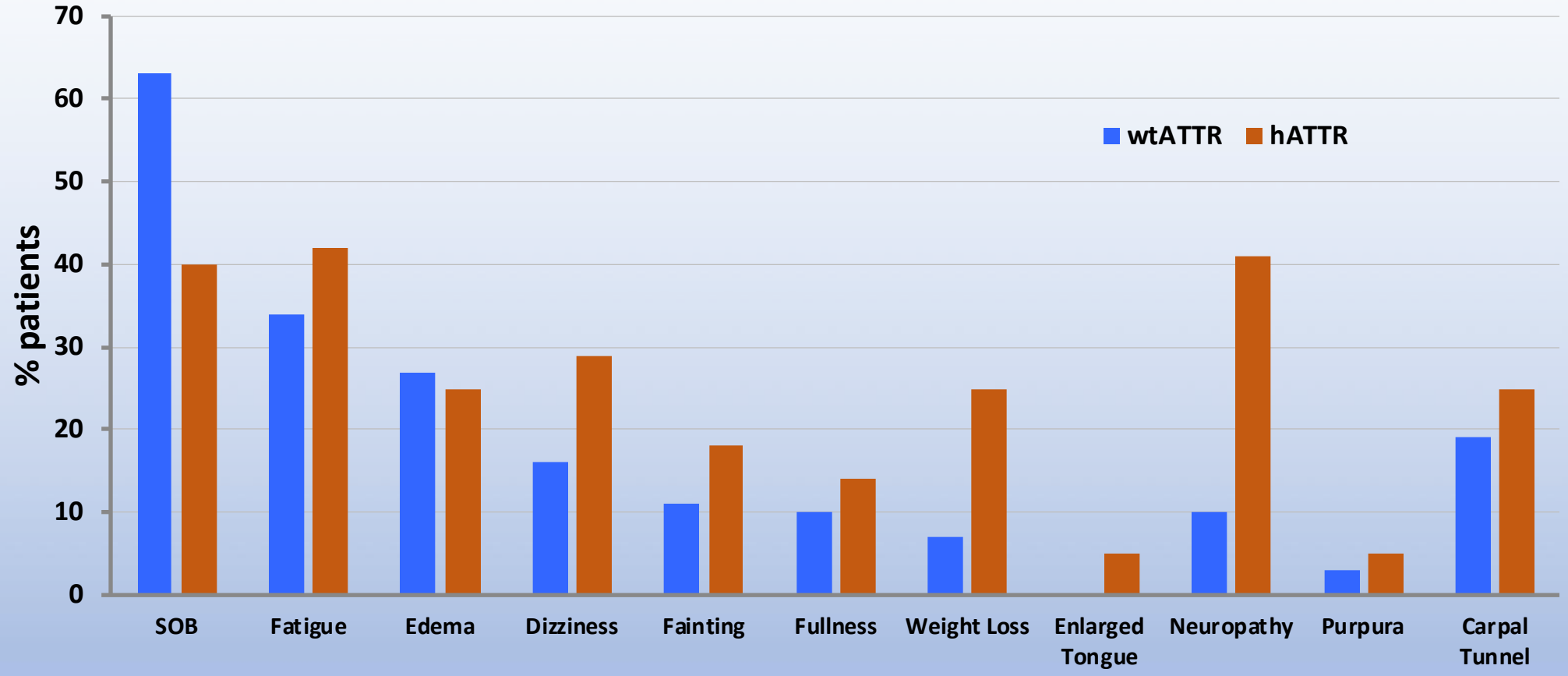


Figure provided by Dr. Gertz

Diagnostic Tests Variability

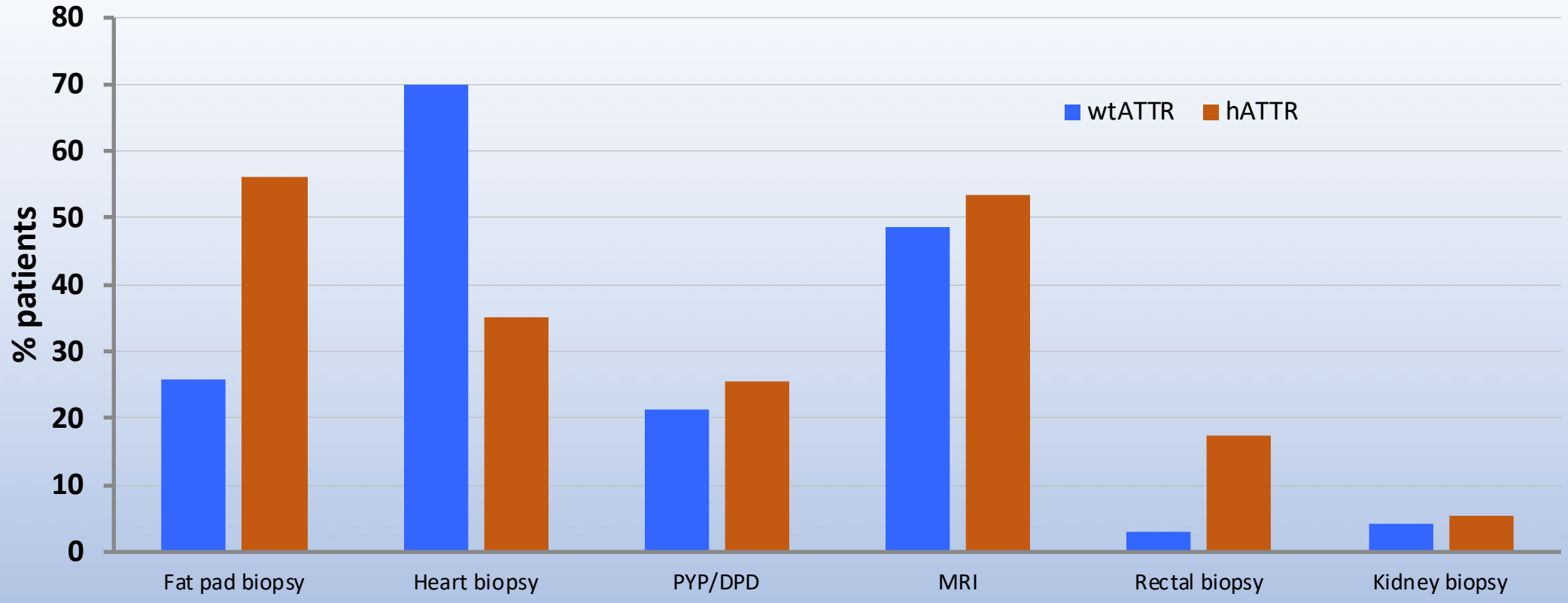


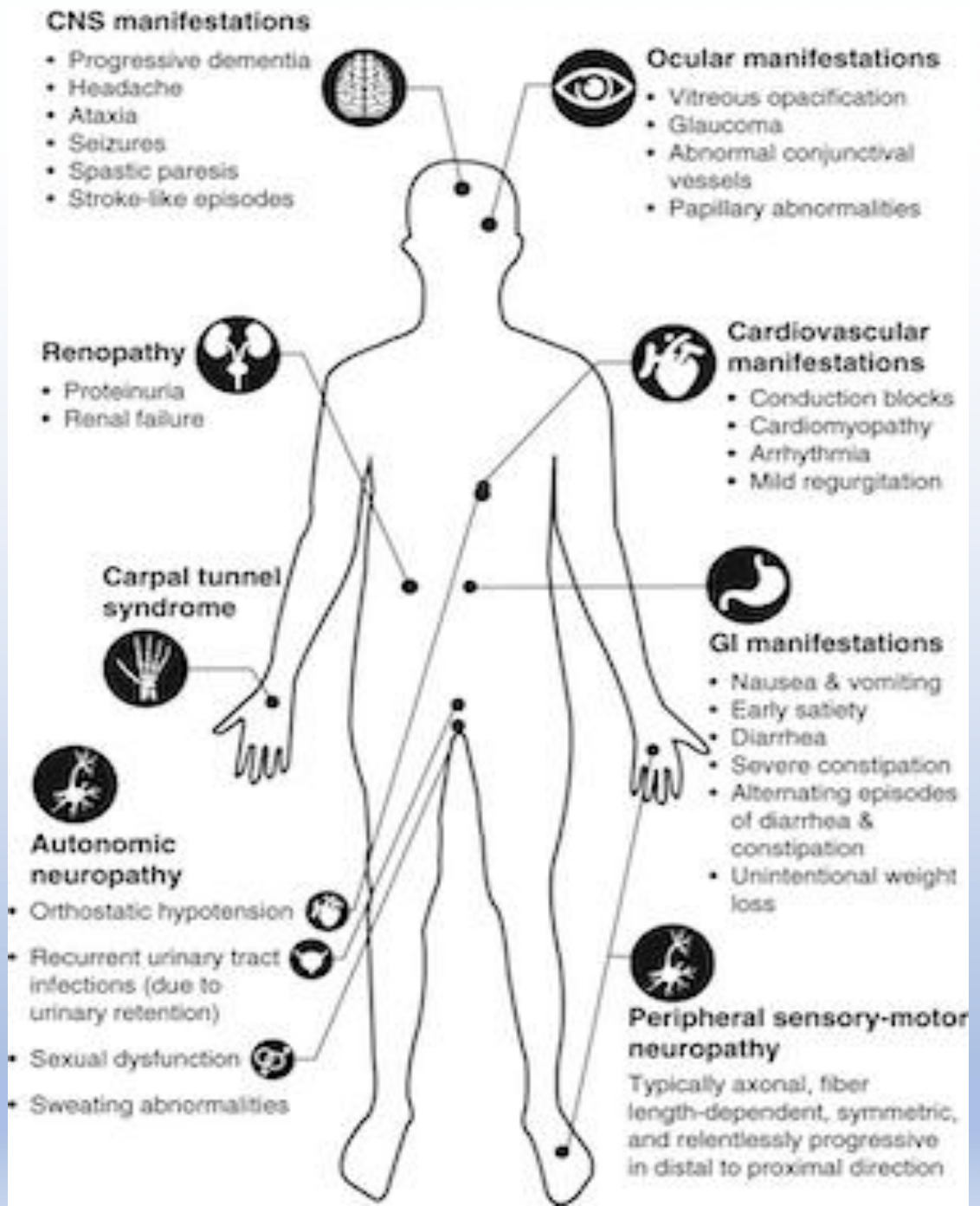
Figure provided by Dr. Gertz

When to Suspect TTR Amyloidosis

Family History

Carpal Tunnel

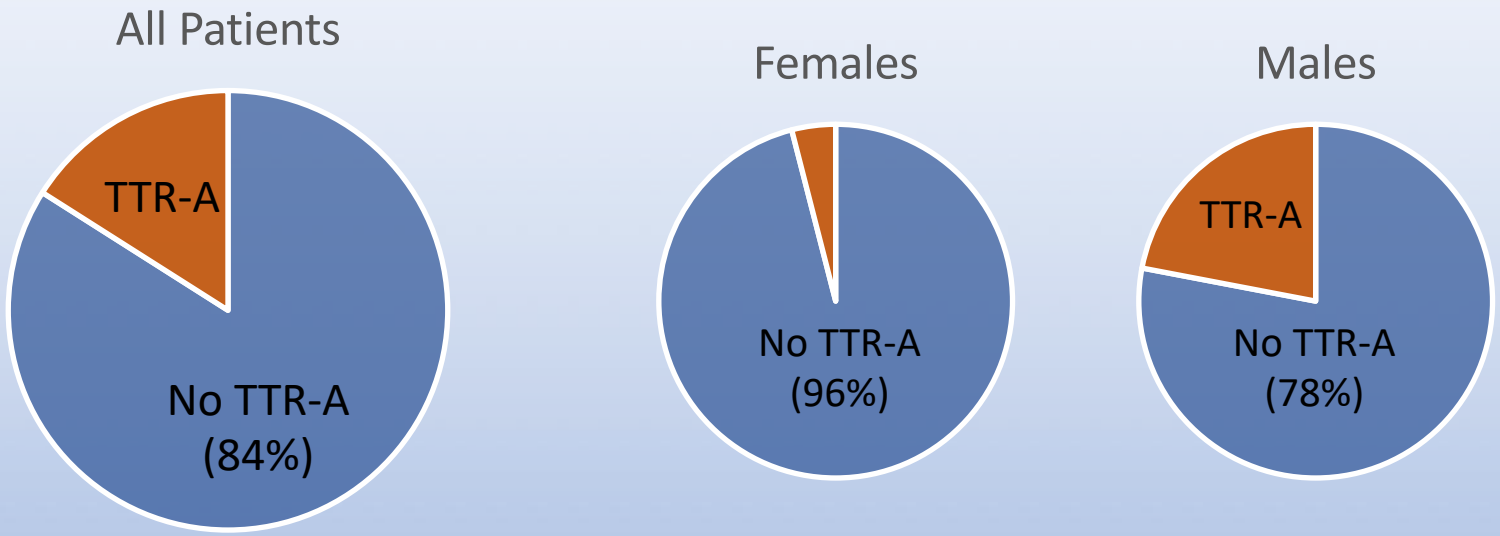
Cardiomyopathies



Conceição et al. *J Peripher Nerv Syst.* 2016;21(1):5-9.

When to Suspect TTR Amyloidosis

Aortic stenosis in elderly (N=151)



Castano et al. *Eur Heart J* 2017;38:2879-87

When to Suspect TTR Amyloidosis

Increased left ventricular wall thickness

- N = 298
- Median Age 62 yrs, 74% male, 23% African origin, median LVWT 18 mm

- **Results**
  - 5% diagnosed TTR-FAC

Damy et al. *Eur Hear J* 2016: 14:1826 – 34.

Red Flags

- Reduction in longitudinal strain with apical sparing
- Discrepancy between left ventricular thickness and QRS voltage
- Atrioventricular block in the presence of increased left ventricular wall thickness
- Echocardiographic hypertrophic phenotype with associated infiltrative features
- Marked extracellular volume expansion, abnormal nulling time for the myocardium or diffuse late gadolinium enhancement on CMR
- Symptoms of polyneuropathy and/or dysautonomia
- History of bilateral carpal tunnel syndrome
- Mild increase in troponin levels on repeated occasions

Wittles et al *JACC* 2019; 7: 709-16