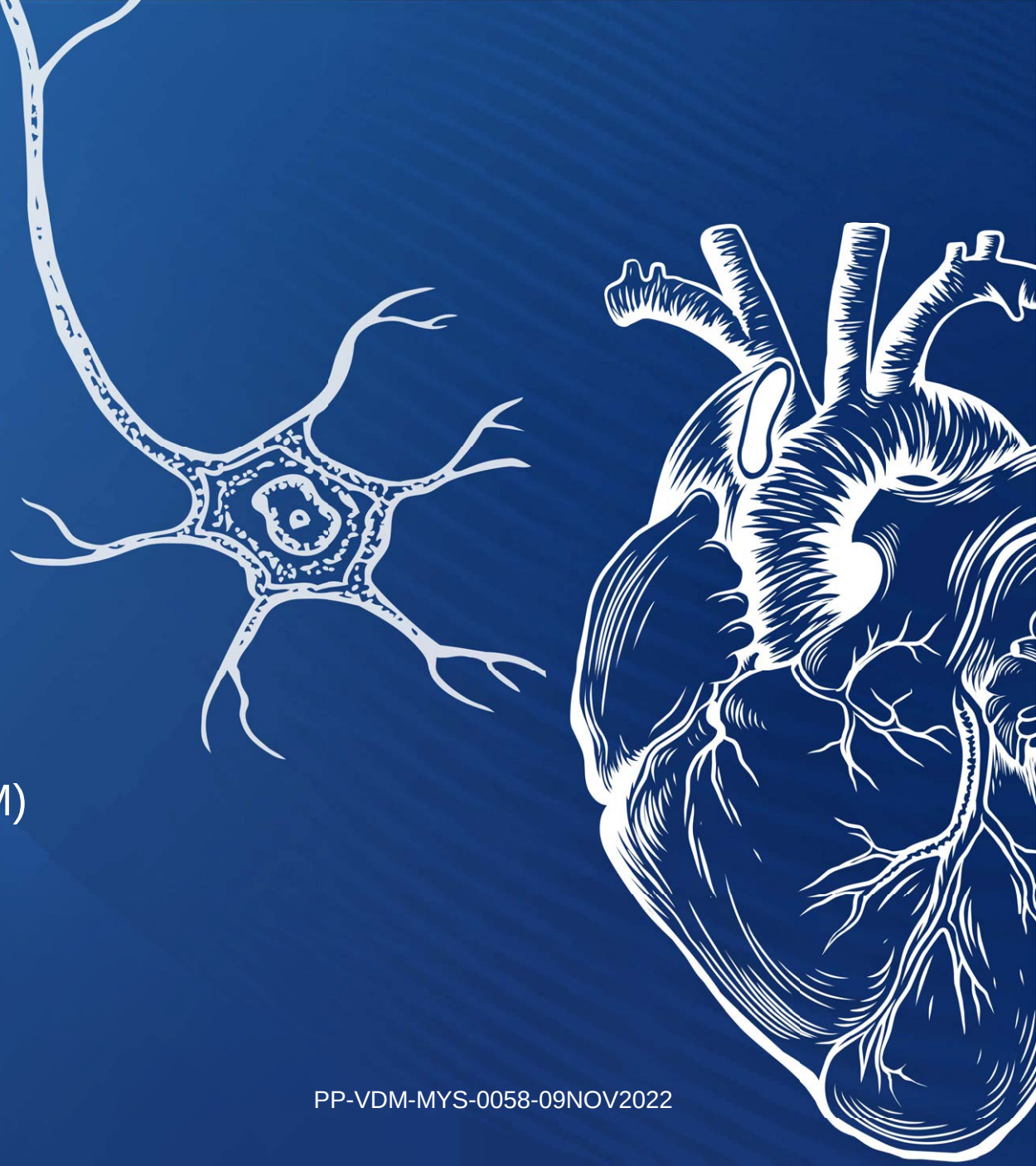
Invasive vs. Non-Invasive Tools for Diagnosis

Transthyretin amyloid cardiomyopathy (ATTR-CM)



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Discover the Tools to Diagnose ATTR-CM

NON-INVASIVE

Nuclear scintigraphy

Nuclear scintigraphy, in combination with testing to rule out AL amyloidosis, can diagnose ATTR-CM with high sensitivity and specificity[1,2]

NON-INVASIVE

Endomyocardial Biopsy (EMB)

EMB requires histology with positive Congo red staining with apple-green birefringence, which is also used to diagnose ATTR-CM[1,3]

Genetic Testing

Genetic testing can also be used in the ATTR-CM diagnostic process[4]

AL, immunoglobulin light chain amyloid fibril protein; ATTR-CM, transthyretin amyloid cardiomyopathy.

References: 1. Gillmore JD, Maurer MS, Falk RH, et al. Nonbiopsy diagnosis of cardiac transthyretin amyloidosis. Circulation. 2016;133(24):2404-2412.doi:10.1161 /CIRCULATIONAHA.116.021612. **2.** Bokhari S, Castano A, Pozniakoff T, Desisle S, Latif F, Maurer MS. 99mTc-Pyrophosphate scintigraphy for differentiating light-chain cardiac amyloidosis from the transthyretin-related familial and senile cardiac amyloidoses. Gire Cardiovasc Imaging. 2013;6(2):195-201. doi:10.1161/CIRCIMAGING.112.000132. **3.** Narotsky DL, Castano A, Weinsaft JW, Bokhari S, Maurer MS. Wild-type transthyretin cardiac amyloidosis: novel insights from advanced imaging. Can J Cardiol. 2016;32(9):1166.e1-1166.e10. doi:10.1016/j.cjca.2016.05.008. **4.** Maurer MS, Elliott P, Comenzo R, Semigran M, Rapezzi C. Addressing common questions encountered in the diagnosis and management of cardiac amyloidosis. Circulation. 2017;135(14):1357-1377. doi:10.1161/CIRCULATIONAHA.116.024438

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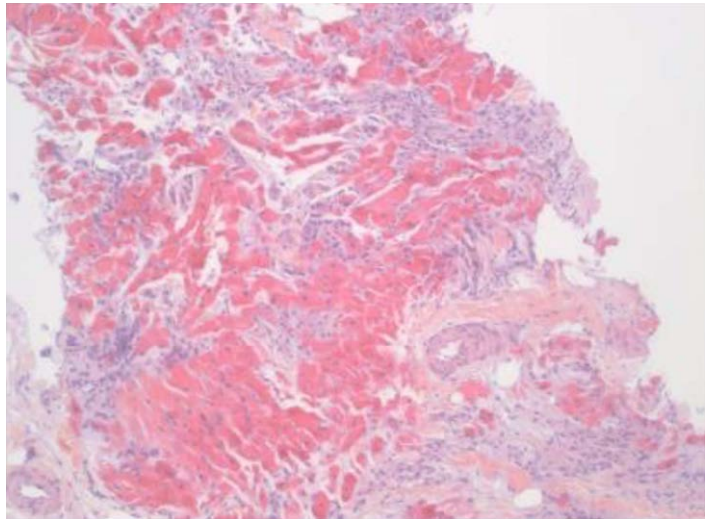
Endomyocardial Biopsy Is An Invasive Approach To Diagnose ATTR-CM[1-3]

- Cardiac tissue biopsy:
  - Documents the extent of amyloid infiltration[1,2]
  - Provides definitive etiologic classification of the amyloidogenic protein[1-3]
  - Achieves a definitive classification to help rule out AL amyloidosis[1]
- Congo red staining with apple-green birefringence under polarized light is indicative of cardiac amyloidosis[3]
- Tissue typing through immunohistochemistry and/or mass spectrometry aids in differential diagnosis between types of ATTR-CM[1]
- Accuracy of biopsy depends on the type of amyloidosis and tissue tested[1]
  - Diagnostic sensitivity of abdominal fat pad is 15% for wtATTR-CM and 45% for hATTR-CM[4]
  - Endomyocardial biopsy is nearly 100% sensitive and specific for ATTR-CM[4]



Illustrative representation of Congo red positive for cardiac amyloid. Image courtesy of Filiale d'Imagerie Cardiovasculaire.

A negative biopsy may not necessarily rule out cardiac amyloidosis, as the distribution of amyloid deposits in the organ biopsied could be patchy and may vary.[5]

ATTR-CM, transthyretin amyloid cardiomyopathy; AL, light chain; wtATTR-CM, wild-type transthyretin amyloid cardiomyopathy; hATTR-CM, hereditary transthyretin amyloid cardiomyopathy.

References: 1. Maurer MS, et al. Circulation. 2017;135:1357-1377. **2.** Gillmore JD, et al. Circulation. 2016;133:2404-2412. **3.** Ruberg FL, Berk JL. Circulation. 2012;126:1286-1300. **4.** Rubin J, Maurer MS. Annu Rev Med. 2020;71:203-219. **5.** Flodrova P, et al. Pathology. 2018;50:261-268.

Genetic counseling and testing are recommended to distinguish between wtATTR-CM and hATTR-CM

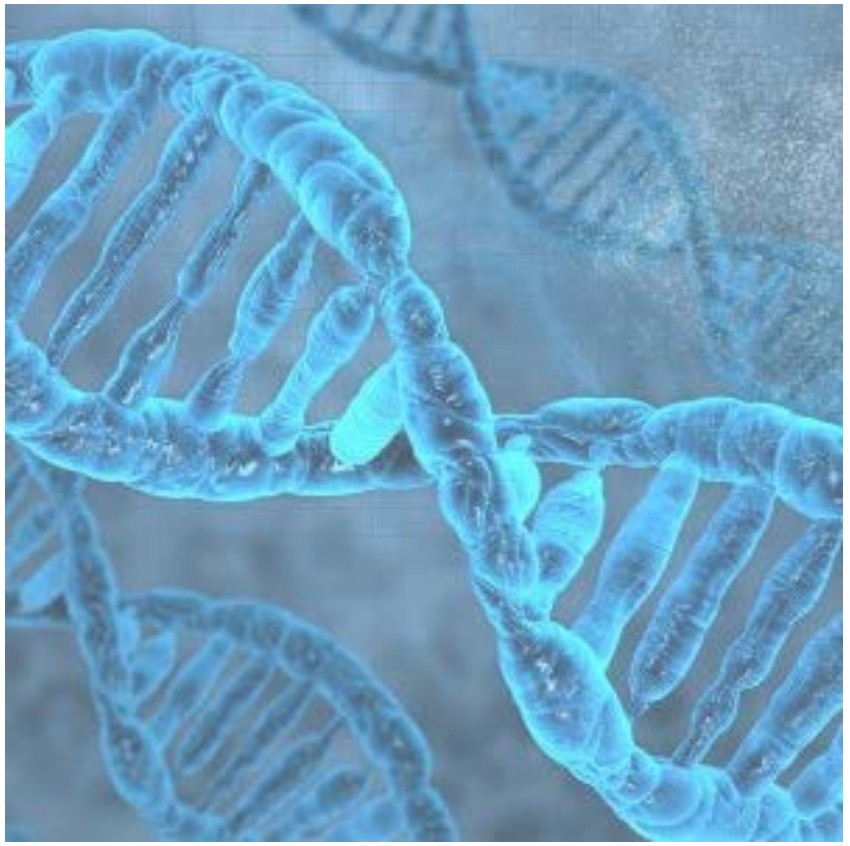
wtATTR-CM and hATTR-CM **cannot be distinguished by clinical profile alone**[1]

Genetic counseling and *TTR* gene sequencing are recommended in all forms of confirmed ATTR-CM[1]

In healthy relatives of patients with hATTR-CM, **pre- and postgenetic test counseling** may be offered[2]

Regularly monitor asymptomatic carriers of hATTR-CM for cardiac involvement[3,4]

Monitoring for hATTR-CM **should begin 10 years before** the established predicted age of onset of symptomatic disease[4]



ATTR-CM, transthyretin amyloid cardiomyopathy; wtATTR-CM, wild-type transthyretin amyloid cardiomyopathy; hATTR-CM, hereditary transthyretin amyloid cardiomyopathy.

References: 1. Maurer MS, et al. Circulation. 2017;135:1357-1377. **2.** Sequeiros J. Orphanet J Rare Dis. 2015;10:20. **3.** Obici L, et al. Curr Opin Neurol. 2016;29(Suppl 1):S27-S35. **4.** Conceição I, et al. Amyloid. 2019;26(1):3-9.

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Transthyretin amyloid cardiomyopathy (ATTR-CM)

For Healthcare Professionals Only

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