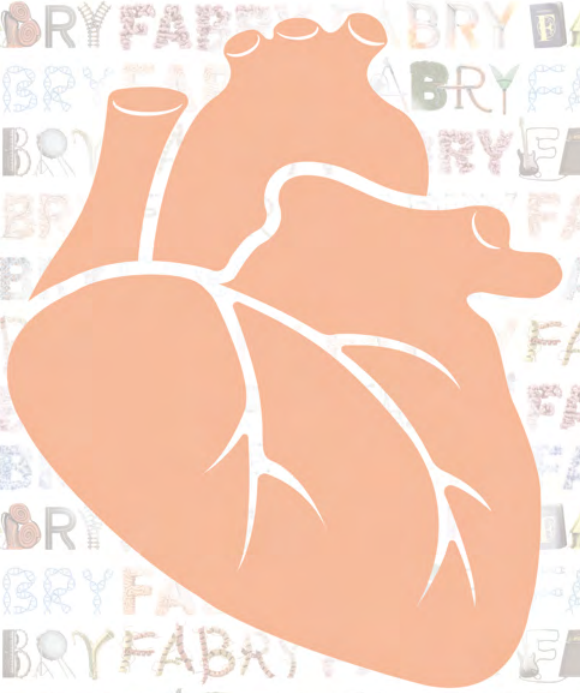


For more information about Fabry disease and disease-related cardiac manifestations,

CLICK HERE

Let's get to the heart of Fabry disease

- Fabry disease is a rare lysosomal disorder affecting both male and female patients. It is caused by variants, also called mutations, in the galactosidase alpha gene (*GLA*), leading to functional deficiency of α-galactosidase A (α-Gal A) in the lysosomes. This allows progressive accumulation of disease-causing substrates, including globotriaosylceramide (GL-3), and a cascade of tissue damage in multiple organs[1]

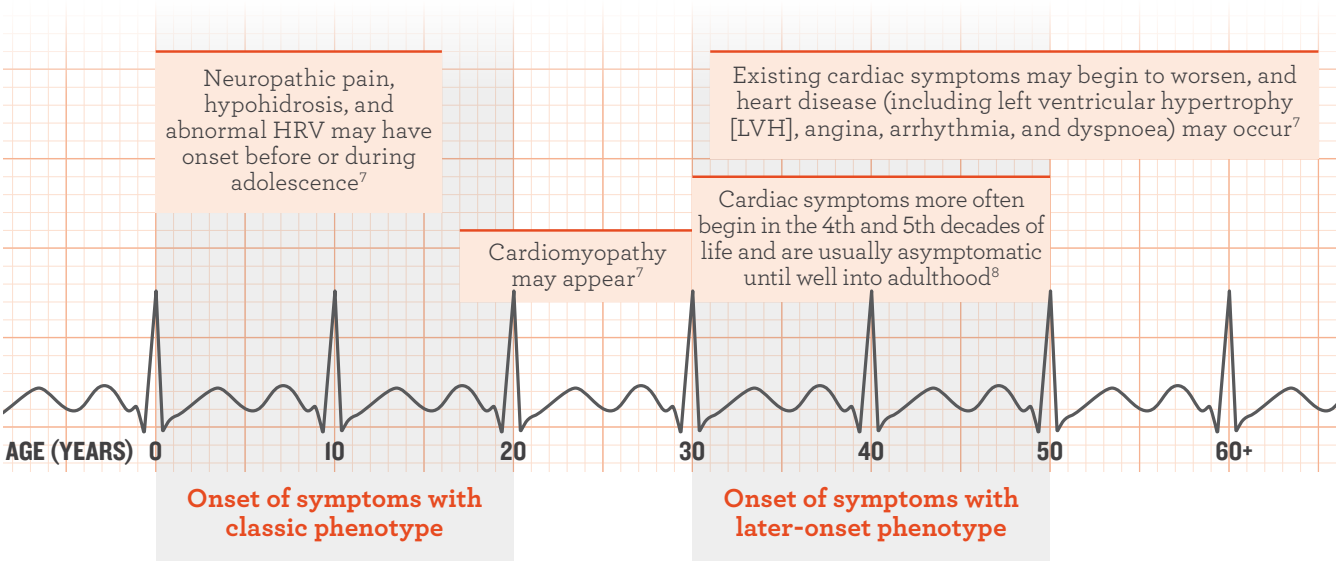
- Cardiovascular disease is the most common cause of death for both men and women with Fabry disease[2]
- In a study by the Fabry Registry, 53% (35/66) of patient deaths were classified as being due to cardiovascular disease[2]

Identifying Fabry disease early is key before irreversible organ damage occurs

Patients with Fabry disease are often categorised as[3,4]:

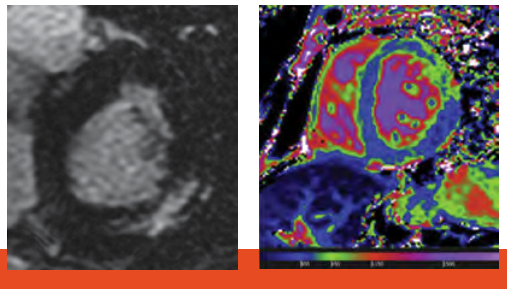
1. Those with the classic phenotype (symptoms tend to manifest during childhood or adolescence and affect multiple organ systems)
2. Those with the non-classic/later-onset phenotype (symptoms occur later and are sometimes limited to the kidneys and/or heart, presenting in the 4th to 6th decades of life)

Cardiac involvement often presents early in life during adolescence in both genders, with cardiac symptoms appearing ~10 years earlier in males than in females.[1,5,6] Both sexes are affected by cardiac symptoms, with ~90% of patients being affected by cardiomyopathy.[6]



MRI of 65-year-old female patient with Fabry disease[9]

- MRI with typical late gadolinium enhancement in the basal segment of the posterolateral wall (white myocardial area) and basal short-axis T1 mapping of the myocardium at 1.5 Tesla with homogenous low T1 values (in blue, corresponding to a T1 at 800 ms)



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As Fabry disease progresses, major organ system dysfunction may worsen. This may lead to a shortened lifespan and death[7,10], especially if left unmanaged.

Fabry disease symptoms are diverse and multisystemic

- When should you suspect Fabry disease? Along with cardiac impairment, patients exhibiting these signs and symptoms should be considered[9]:

HCM (unexplained LVH ≥ 15 mm)

Systematically consider Fabry disease in males ≥ 30 years and females ≥ 40 years particularly if:

Unexplained LVH 13 to 15 mm

Systematically consider Fabry disease in males ≥ 30 years and females ≥ 40 years particularly if:

Alert signs and symptoms:

- **Extracardiac abnormalities:** kidney dysfunction, stroke/TIA, angiokeratoma, cornea verticillata
- **ECG/48-hour Holter:** short PR interval, AV block, decreased HRV, pacemaker, arrhythmias
- **Echocardiography:** concentric LVH (13 to 22 mm), non-obstructive HCM, abnormal infero-lateral longitudinal strain, right ventricular hypertrophy, thinning of the basal infero-lateral LV wall
- **Cardiac MRI:** Postero-lateral LGE, reduction in non-contrast T1 signal, elevated T2
- **Biological testing:** decreased GFR, proteinuria, high-sensitivity troponin (hs-TNN)
- **Family history** (no father-to-son transmission, cryptogenic stroke, severe kidney failure)

Refer patients for genetic testing at Fabry disease/HCM reference centres

Males: α-Gal A and gene testing
Females: gene testing

Adapted with permission from Hagege A, et al. *Arch Cardiovasc Dis.* 2019;112(4):278-287.

- As Fabry disease progresses, cardiac symptoms and cardiomyopathy develop, as indicated by myocardial fibrosis, which, in end-stage patients, can result in congestive heart failure and death[1,11]

Identifying symptoms beyond cardiac impairment is critical to establishing a diagnosis

- Non-cardiac manifestations may include:

RENAL	proteinuria and progressive renal failure[1,12]
DERMATOLOGIC	angiokeratoma and dyshidrosis[1]
GASTROINTESTINAL	abdominal pain (often after eating), nausea, vomiting[1]
NERVOUS	acroparaesthesia (burning pain in extremities), pain crises, neuropathic pain[1,13]; pain is a common early symptom of Fabry disease, often beginning in adolescence[1]
OPHTHALMOLOGIC	cornea verticillata and retinal tortuosity[1]
OTOLARYNGOLOGIC	dizziness/vertigo and tinnitus[1]

AV, atrioventricular; GFR, glomerular filtration rate; HCM, hypertrophic cardiomyopathy; HRV, heart rate variability; LV, left ventricle; LGE, late gadolinium enhancement; MRI, magnetic resonance imaging; TIA, transient ischemic attack.

Fabry disease is a family affair

- Family history of Fabry-related symptoms may be suggestive of Fabry disease[1]
- Earlier genetic testing in patients with a family history of Fabry disease could help to reduce delayed diagnosis and potentially identify patients with Fabry disease before symptoms begin, so that disease management can be optimised and personalised over time[1]
- On average, each Fabry disease diagnosis leads to the diagnosis of 5 additional family members[14]
- Does your patient's medical or family history exhibit any of the following?
  - Any of the symptoms listed on pages 2 and 3
  - Any signs of kidney failure such as uraemia or hypocalcaemia
  - Any unexplained incidents of death

Establishing when and how to look for Fabry disease

THINK	Think Fabry disease in cases of unexplained LVH or HCM[9]
SCREEN	Male patients aged >30 years and females aged >40 years with unexplained LVH or HCM should be screened for Fabry disease, especially when other tell-tale signs for Fabry disease are present[9]
REFER	If a diagnosis of Fabry disease is suspected, refer patients for genetic testing to your local State Fabry Disease centre.

For more information about Fabry disease and disease-related cardiac manifestations, visit www.amicusxchange.com.au

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