Cardiovascular disease is the most common cause of death for both men and women with Fabry disease[1]*

- Fabry disease is a rare lysosomal disorder affecting both male and female patients. It is caused by variants (mutations) in the galactosidase alpha gene (*GLA*), leading to functional deficiency of alpha-galactosidase A (alpha-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[2]

- Cardiac symptoms often begin in the 4th and 5th decades of life and are usually asymptomatic until well into adulthood[3]
- 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[2,4]
- The late-onset phenotype of Fabry disease is more closely associated with cardiac variants than the classic phenotype, which may explain the many cases of midlife cardiac disease seen in these patients[5]

When to consider testing for Fabry disease? Prominent cardiac symptoms include[2]:

- Left ventricular hypertrophy
- Cardiomyopathy
- Arrhythmia and impaired heart rate variability
- Cardiac ischemia leading to angina and myocardial infarction

Additional signs and symptoms that may be present in Fabry disease include:

- **Renal:** Proteinuria of unknown origin; microalbuminuria/albuminuria; decreased glomerular filtration rate and progressive renal failure; chronic kidney disease[2,6]
- **Dermatologic:** Angiokeratoma; dyshidrosis leading to temperature and exercise intolerance[2]
- **Gastrointestinal:** Abdominal pain (often after eating); diarrhea; nausea and vomiting, which may lead to anorexia[2]
- **Nervous:** Acroparesthesia (burning pain in hands and feet); headache; neuropathic pain; pain crises; stroke; transient ischemia attack[2,7]
- **Otolaryngologic:** Cornea verticillata; dizziness/vertigo; hearing loss; tinnitus[2]

*In the study, 53% (35 out of 66) of patient deaths were classified as being due to cardiovascular disease.[1]

Diagnosis of Fabry disease can be challenging and often delayed[2]

Fabry disease is "often seen, rarely diagnosed"[8]

- While Fabry disease is considered "rare," many of its signs and symptoms are seen with more common disorders[2,9]
- It is estimated that patients visit an average of 10 different specialists before a Fabry disease diagnosis is confirmed, leading to a delay of ~15 years from symptom onset to diagnosis[9,10]

GLA gene sequencing confirms a diagnosis of Fabry disease[9]

- In addition, gene sequencing helps:
  - Establish the disease phenotype[3]
  - Provide additional information regarding disease prognosis and treatment[11]
  - Permit the testing of at-risk family members[3]

- It is important to note that in males with the suspected classic phenotype, an absence or low levels of alpha-Gal A activity in blood cells or dried blood spots is sufficient to make the diagnosis. However, *GLA* gene sequencing is required for women[9]

- On average, each Fabry disease diagnosis leads to the diagnosis of 5 additional family members[12]

Prompt diagnosis is important because treatment options are available.[2]

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