Monitoring Fabry disease in adult patients

An overview of treatment and monitoring guidelines based on Ortiz A, Germain DP, Desnick RJ, Politei J, Mauer M, Burlina A, Eng C, Hopkin RJ, Laney D, Linhart A, Waldek S, Wallace E, Weidemann F, Wilcox WR. Fabry disease revisited: Management and treatment recommendations for adult patients. *Mol Genet Metab*. 2018;123(4):416-427.

Highlights from the guidelines:

- Development initiated in July 2014 in the US when a meeting of experts spanning several subspecialties convened to discuss Fabry guidelines
- Additional discussions took place during a panel meeting in February 2015, also in the US
- Guideline recommendations were amended and revised until all panelists were in agreement

Monitoring organ involvement in adult patients with Fabry disease

Clinical vigilance and regular monitoring are vital

Even if no apparent symptoms are present at baseline or at follow-up appointments, complications involving the organs can still occur. For this reason, routine assessments and monitoring are key in the management of Fabry disease. In addition, baseline values should always be obtained.

Please refer to the chart below for recommended assessments and schedules for monitoring specific organs affected by Fabry.

Recommendations for assessing and monitoring specific organs affected by Fabry

Organ/ system	Assessment	Monitoring schedule					Notes
		3 months	6 months	Annually	As clinically indicated	Other	
 Cellular	*GLA* mutation analysis					●	If not previously determined.
	alpha-Gal A enzyme activity					●	If not previously determined.
 Renal	Measured GFR	●	●	●			If moderate risk, monitor every 6 months. If high risk, monitor every 3 months.
	Albuminuria and/or proteinuria	●	●	●			If moderate risk, monitor every 6 months. If high risk, monitor every 3 months.
	25 OH vitamin D				●		Monitor in late fall/early winter.
	Kidney biopsy				●		Podocyte foot process effacement may precede pathological albuminuria.

Recommendations for assessing and monitoring specific organs affected by Fabry (cont'd)

Organ/ system	Assessment	Monitoring schedule					Notes
		3 months	6 months	Annually	As clinically indicated	Other	
 Cardiac	Blood pressure and cardiac rhythm					●	Monitor at every clinic visit.
	ECG and echocardiography			●	●		
	48-h Holter monitoring			●	●	●	More frequent monitoring may be necessary based on age and risk factors. An implanted loop recorder is advised for patients with significant hypertrophic cardiomyopathy. If arrhythmia is found, monitoring efforts should increase.
	Cardiac MRI with gadolinium					●	Monitor regularly every 2 years or when disease progression is evident.
	Brain natriuretic peptide			●			Monitor annually for patients with cardiomyopathy or bradycardia.
 Cerebrovascular	Brain MRI				●	●	Monitor every 3 years. TOF MRA at first assessment in males over age 21 and females over 30, then according to the clinical picture.
	CT imaging					●	Monitor in case of acute stroke. Use CT imaging if MRI is contraindicated due to cardiac pacing.
 Peripheral nervous system	Pain evaluation and history Cold and heat intolerance, vibratory thresholds Autonomic symptom evaluation by orthostatic blood pressure			●			Less frequent monitoring is needed for older patients. Neuropathic Pain Symptom Inventory or Brief Pain Inventory can be used as pain measurement scales.
	Skin biopsy					●	Consider. For IENFD assessment, if available.

alpha-Gal A, alpha-galactosidase A; CT, computed tomography; ECG, electrocardiography; GFR, glomerular filtration rate; *GLA*, galactosidase alpha gene; IENFD, intra-epidermal nerve fiber density; MRI, magnetic resonance imaging; TOF MRA, time-of-flight magnetic resonance angiography (head and neck).

Recommendations for assessing and monitoring specific organs affected by Fabry (cont'd)

Organ/ system	Assessment	Monitoring schedule					Notes
		3 months	6 months	Annually	As clinically indicated	Other	
Auditory	Audiometry				●		
Pulmonary	Spirometry				●	●	Monitor every 2 years. Monitoring to include response to bronchodilators, treadmill exercise testing, oximetry, and chest X-ray. Chest X-ray when clinically indicated.
GI	Endoscopic or radiographic evaluation				●		
Overall glycolipid burden	Plasma and urinary sediment lyso-GL-3, GL-3			●			Currently, this is for research purposes only. Biobanking of samples is recommended, if possible.
Skeletal	Bone dual-energy X-ray absorptiometry					●	Consider.
Ophthalmological	Ophthalmological screening				●		

Genetic counseling is a vital component to the management of Fabry disease

Fabry disease places a physical and emotional burden on both patients and their families. Genetic counseling by either a medical geneticist or counselor is critical after diagnosis and plays an important role in the multidisciplinary management of Fabry.

In addition, during routine clinic visits, a complete history and physical exam should take place. This may include documenting family history, evaluating quality of life, noting any GI symptoms, and recording feelings of depression and/or anxiety. And if not previously determined, alpha-Gal A enzyme activity and a *GLA* mutation analysis should be assessed.

GI, gastrointestinal; GL-3, globotriaosylceramide.

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NP-GA-US-00010519 June 2019