Clinical Management Guidelines for Friedreich Ataxia

Chapter 3.7. Vision in Friedreich ataxia

Contents

This chapter of the Clinical Management Guidelines for Friedreich Ataxia and the recommendations and best practice statements contained herein were endorsed by the authors and the Friedreich Ataxia Guidelines Panel in 2022.

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3.7 Vision in Friedreich ataxia

David Lynch

This chapter describes the effects of Friedreich ataxia on vision, the functional consequences of disturbance of vision, and strategies for managing disturbance of vision. In making recommendations for management, the authors were tasked with answering the question:

For individuals with Friedreich ataxia, what management strategies could be implemented for disturbance of vision?

3.7.1 The effects of Friedreich ataxia on vision

Friedreich ataxia (FRDA) leads to decreased ability to see based on loss of cells that give rise to the optic nerve. This leads to loss of peripheral vision, color vision and varying degrees of loss of central vision, from slight vision loss in some to complete blindness in the most affected individuals. FRDA-related vision loss is not related to diabetes; diabetic visual dysfunction is important to rule out and has its own separate issues.

In particular, both afferent and efferent visual abnormalities may be found in individuals with FRDA. Oculomotor findings associated with FRDA include optic atrophy, square wave jerks, and difficulty with fixation (1, 2). Most people with FRDA have normal high-contrast visual acuities, but a subpopulation has mildly decreased high contrast visual acuity, usually not worse than 20/30. On the other hand, people with FRDA have significantly worse low-contrast visual acuity, a hallmark of optic atrophy, as compared to controls (3). Clinical or subclinical optic neuropathy is found in approximately two-thirds of people with FRDA, although severe visual loss is uncommon (4). While most individuals with FRDA have a degree of visual field dysfunction, visual field defects range from severe visual field impairment to only isolated regions of reduced sensitivity, as measured by optical coherence tomography (OCT). Therefore, optic nerve involvement and axonal loss most likely begins early in the condition and slowly progresses to the point of clinical involvement. However, a few individuals have rapid system dysfunction, similar to that observed in other mitochondrial diseases such as Leber hereditary optic neuropathy (LHON) (5, 6). This may be more commonly identified in people who are heterozygous for a point mutation on one allele and a GAA repeat expansion on the other, rather than being homozygous for expanded *FXN* alleles, although there is little systematic evidence for this conclusion and rapidly progressive optic neuropathy has been noted in people carrying two expanded GAA repeats.

Visual abilities have been measured both functionally using techniques such as low contrast letter acuity (3) and anatomically using optical coherence tomography (OCT) (4, 7). OCT is a non-invasive, high resolution technique that quantifies the thickness of ocular structures, particularly the retinal nerve fiber layer, and can generate a complete picture of anatomic structure of the retina. OCT has demonstrated that a significant number of people with FRDA have thinning of the retinal nerve fiber layer (7). However, this thinning is not always clearly reflected in overt visual dysfunction (as measured by visual acuity testing), suggesting that not all retinal abnormalities manifest clinically.

Individuals with FRDA classified as having “classical” or late-onset forms of the disease can all experience loss in visual function. When tested using low-contrast visual acuity, loss of visual function correlates with poorer scores on neurologic exams such as the FARS (3). This demonstrates that more severely affected individuals are also more likely to develop decreased visual acuity. The

loss of visual function is not as strongly associated with age of onset; thus, individuals with symptom onset at any age can develop vision loss at later stages of disease progression.

Efferent visual abnormalities are less commonly discussed in FRDA, perhaps because they contribute less to dysfunction. They include primarily fixation abnormalities (ocular flutter, square wave jerks), and to a lesser extent nystagmus or saccadic abnormalities. Efferent visual abnormalities are traditional diagnostic features of FRDA but have less need for therapy in the overall context of the disorder. Despite 20:20 vision, people with FRDA may report reduced visual quality of life as reported by Fahey and colleagues (1).

3.7.2 Functional consequences of disturbance of vision

Visual impairment may lead to difficulty performing all visually guided tasks such as driving, eating, using limbs for precise movements and reading.

3.7.3 Management of visual disturbance

There are no approved treatments or proposed treatments for vision loss in FRDA. The only strategy is to optimize vision in other ways: proper refraction, using magnification on tasks requiring visual control and consultation with low vision specialists.

Best practice statement

Individuals with Friedreich ataxia with vision worse than 20/200 in each eye should be evaluated by a low vision specialist.

Recommendations

Grading for strength of recommendation and level of evidence

For the rating of the **strength** of the recommendation, in addition to evidence from studies in FRDA, evidence from like conditions, clinical experience and expert consensus are taken into account when published evidence is not available.

The **level of evidence** is based on published evidence from studies in FRDA. If there is no published evidence in FRDA, evidence from other like conditions or clinical expertise may have been used to make the recommendation – this is graded as 'very low' or in some cases 'low' level evidence. See the table below for an explanation of the symbols used to grade recommendations.

Strength of recommendation	Symbol	Level of evidence	Symbol
Strong for intervention	↑↑	High	⊕⊕⊕⊕
Conditional for intervention	↑	Moderate	⊕⊕⊕◯
Neither intervention nor comparison	—	Low	⊕⊕◯◯
Conditional against intervention	↓	Very low	⊕◯◯◯
Strong against intervention	↓↓		

Visual impairment unrelated to Friedreich ataxia

Should medications versus conservative therapy be used for visual loss and efferent visual problems that are unrelated to Friedreich ataxia in individuals with Friedreich ataxia?	**Strength**	**Level of evidence**
We suggest standard treatments for visual impairment that is unrelated to Friedreich ataxia be used as appropriate in individuals with Friedreich ataxia. There is insufficient evidence to recommend the use of medications over conservative therapy for visual impairment unrelated to Friedreich ataxia in individuals with Friedreich ataxia.	—	⊕◯◯◯
Justification: There are no published studies supporting the use of medications in the management of visual impairment that is unrelated to Friedreich ataxia in individuals with Friedreich ataxia.		
Subgroup considerations: This recommendation is for individuals with Friedreich ataxia with visual loss and efferent visual problems that are unrelated to Friedreich ataxia.		

Optic neuropathy

Should medications versus conservative therapy be used for optic neuropathy in Friedreich ataxia?	**Strength**	**Level of evidence**
We suggest standard treatments for optic neuropathy be used as appropriate in individuals with Friedreich ataxia. There is insufficient evidence to recommend the use of medications over conservative therapy for optic neuropathy in individuals with Friedreich ataxia.	—	⊕◯◯◯
Justification: There are no published studies supporting the use of medications in the management of optic neuropathy in Friedreich ataxia.		
Subgroup considerations: This recommendation is for individuals with Friedreich ataxia with optic neuropathy.		

Optic radiation lesions

Should medications versus conservative therapy be used for optic radiation lesions in Friedreich ataxia?	**Strength**	**Level of evidence**
We suggest standard treatments for optic radiation lesions be used as appropriate in individuals with Friedreich ataxia. There is insufficient evidence to recommend the use of medications over conservative therapy for optic radiation lesions in individuals with Friedreich ataxia.	—	⊕◯◯◯
Justification: There are no published studies supporting the use of medications in the management of optic radiation lesions in Friedreich ataxia.		
Subgroup considerations: This recommendation is for individuals with Friedreich ataxia with optic radiation lesions.		

Diabetic retinopathy

Should medications versus laser treatment be used for people with diabetic retinopathy in Friedreich ataxia?	**Strength**	**Level of evidence**
We suggest standard treatments for diabetic retinopathy be used as appropriate in individuals with Friedreich ataxia. There is insufficient evidence to recommend the use of medications over laser treatment for diabetic retinopathy in Friedreich ataxia.	—	⊕◯◯◯
Justification: There are no published studies supporting the use of medications or laser therapy in the management of diabetic retinopathy in Friedreich ataxia.		
Subgroup considerations: This recommendation is for individuals with Friedreich ataxia with diabetic retinopathy.		

Lay summary

Lay summary of clinical recommendations for disturbance of vision in Friedreich ataxia

Vision loss in Friedreich ataxia is part of the overall disease. Vision loss begin years after initial presentation, varies in severity, and can develop rapidly or slowly. Some individuals with Friedreich ataxia develop severe loss of vision, while others have minimal to no vision loss. Individuals with Friedreich ataxia may also develop conditions affecting their vision (i.e., cataracts, glaucoma) that are unrelated to Friedreich ataxia.

Why these recommendations?

There are no specific treatments for the vision loss related to Friedreich ataxia. It is useful to see an ophthalmologist who specializes in low vision and can advise on aids to manage vision loss.

Visual problems unrelated to Friedreich ataxia (such as glaucoma, cataracts or diabetes-related visual problems) should be managed according to usual care for these conditions.

There are currently no specific interventions for vision loss in Friedreich ataxia and thus no recommendations other than standard ophthalmologic care.

What does this mean for you as a person living with Friedreich ataxia or caring for someone living with Friedreich ataxia?

It is important to recognise that vision loss in Friedreich ataxia is a possibility so that management strategies can be put in place when vision loss happens.

Who are these recommendations specifically for?

These recommendations are directed to all individuals with Friedreich ataxia, but particularly those who have more severe neurological symptoms as they are more likely to have significant vision loss.

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