Clinical Management Guidelines for Friedreich Ataxia

Chapter 3.1. Upper limb dysfunction 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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3.1 Upper limb dysfunction in Friedreich ataxia

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

For individuals with Friedreich ataxia, what management strategies could be implemented for upper limb dysfunction?

3.1.1 Upper limb function in Friedreich ataxia

Despite the potential negative impact on function, independence and quality of life, there have been few studies examining motor function of the upper limbs in people with Friedreich ataxia (FRDA). Moreover, there has been little systematic evaluation of the motor components of upper limb function in FRDA that contribute to decline in functional capacity. Evaluation of upper limb dysfunction can be more difficult than that of the lower limbs as the upper limbs are used to perform complex and multidimensional tasks, including reaching, grasping and stabilizing, as well as fine manipulation. Ataxia, apparent in the upper limb as dysmetria and dysdiadochokinesia, is the most common presenting symptom of FRDA (1) and has a profound impact on fine motor dexterity, manipulation and hand function. In addition, the complex multi-system involvement of the disease impacts upper limb function across multiple domains.

Corben and colleagues (2) have systematically evaluated the motor components of the distal upper limb in 19 individuals with FRDA by examining spasticity, strength and range of motion. Individuals with FRDA present with an unusual pattern of upper limb hypertonicity that appears to predominantly affect long finger flexors. Associated weakness of lumbrical and interrosei muscles, sensory changes, incoordination and potential bony changes such as subluxation of the metocarpopharangeal joints, further compound useful hand and arm function (2). The study showed that spasticity and weakness in the dominant hand are significant predictors of reduced functional independence (2). Amyotrophy is commonly observed in the lumbricals, interossei and extensor musculature of the wrist and fingers (3). Such underlying weakness is an important component of loss of hand function and should be factored into any potential interventions. In addition, loss of light touch, pain, and temperature sensation contribute to afferent ataxia (4), while loss of joint and vibratory senses (5) further compound upper limb difficulty.

In summary, the combination of ataxia, weakness, sensory changes and potential spasticity can have a devastating impact on upper limb function in individuals with FRDA warranting regular and proactive assessment and management.

3.1.2 Functional consequences of disturbance of upper limb function

Optimum upper limb function for people with FRDA is an essential component of daily function. For example, the capacity to use a keyboard is crucial for those in whom profound dysarthria precludes comprehensible speech. Moreover, those individuals who have lost the capacity to walk depend on robust upper limb function to propel their wheelchair and participate in daily tasks including feeding and dressing. As the disease progresses, individuals with FRDA often lose functional use of their arms

rendering them dependent on others for the most basic of self-care activity. Unpublished data from 119 individuals with FRDA who completed the Friedreich Ataxia Impact Scale (FAIS) (6) indicated that completing intricate upper limb tasks are often problematic, such as taking a spoon to the mouth (rated as problematic for 88% of participants), writing (87%) and picking things up (84%). Likewise, in a recent study examining the efficacy of electrical stimulation to improve upper limb function, individuals with FRDA reported limitations with fastening (zippers, buttons); manipulating (taps, keys, packets, pages); grasping (toothbrush, cutlery, cup, pen); and accessing technology (typing, phone) (7).

In the electrical stimulation study, results from the Functional Independence Measure (FIM) (8) indicate that individuals with FRDA experience some degree of difficulty with eating, grooming, bathing, dressing, toileting, transfers and mobility, all of which are impacted by reduced upper limb function (7). Specifically, using the Goal Attainment Scale (GAS) (9), individuals identified functional activities that were difficult to complete, including the following tasks affected by reduced upper limb function:

- typing using a tablet or keyboard
- reaching for a drinking vessel
- self-propelling a wheelchair
- using cutlery
- picking up and holding a mobile phone (7).

In the 2017 “The Voice of the Patient” meeting (10), nearly 90% of individuals with FRDA reported issues with manual dexterity, apparent as difficulty in performing tasks such as dressing and eating, reinforcing the profound impact upper limb impairment has on the functional capacity of a person living with FRDA.

3.1.3 Management of upper limb dysfunction

Despite the significance of the problem, there is little evidence to support specific upper limb management techniques. Expert authors reviewed the following general upper limb interventions for similar neurological conditions.

3.1.3.1 Intensive upper limb rehabilitation

Intensive upper limb rehabilitation broadly describes techniques that aim to improve upper limb movement. Different training regimes have been employed for upper limb neurorehabilitation, ranging from more traditional strategies of repetitive task training to newer techniques emphasizing the learning and practice of functional motor skills within a “task-specific” context (11-13). There is no definitive agreement on which exercise therapy program can be considered most successful in improving activities and participation; however, it is well established that task-specific practice is required for motor learning to occur (14). Several techniques (or combination of techniques) were examined during the guideline development. To assist interpretation of the Recommendations, short descriptions of the techniques follow.

Combined upper limb and breathing exercise program

Grubic and colleagues (15, 16) implemented a combined upper limb and breathing exercise program under physiotherapist guidance with exercises targeting upper limb range of motion, coordination and strengthening exercises with minimal resistance. Breathing exercises included diaphragmatic

and thoracic breathing. Additionally, a home exercise program was performed independently (15, 16).

Home based upper limb training program

Oritz Rubio and colleagues (17) employed a home-based upper limb training program that was individually developed and supervised by an occupational therapist or physiotherapist. Each session involved three parts: fine motor exercises (performed with resistance therapeutic putty); dexterity and coordination exercises (based on handling activities); and strengthening exercises (performed with elastic bands). Each session ended with upper limb stretching exercises (17).

Task specific upper limb rehabilitation

Task orientated training involves integrating tasks that are relevant to daily life into rehabilitation programs (18) and consists of motor tasks that are focused on improvement of performance and function through goal-directed practice and repetition (19).

Bonzano and colleagues (13, 20) designed a rehabilitation protocol with exercises to improve proprioceptive sensibility, muscle strength, stability and coordination of the upper limbs with the goal to improve activities of daily living. Boffa and colleagues (21) also engaged participants in task orientated exercises to improve motor control.

Passive upper limb rehabilitation

Passive intervention, as employed by Boffa and colleagues (21) and Bonzano and colleagues (13, 20), utilized a physiotherapist to help the patient perform tasks without detectable muscle activity. This was achieved by passive mobilization of the shoulder, elbow, wrist and fingers (13, 20, 21).

Combined task specific, repetitive task training and general exercise program

The rehabilitation program employed by Nociti's study group (22) involved specific exercises for the upper limb and a standard exercise program. The upper limb training component included exercises for improving functional use and coordination, repetitive activity based training and somatosensory stimulation. The standard exercise program included techniques for improving posture, stretches, weight bearing, positioning and splinting for hypertonicity, proximal stability and coordination.

Combined arm cycling and task specific upper limb training

Gervasconi and colleagues (23) trialed arm cycling (using an arm ergometer) and task orientated training. The task orientated protocol included unimanual/bimanual exercises to improve proprioception, muscle strength, stability and coordination of the upper limbs. The activities selected where based on participant goals and aligned with a task orientated approach (23).

Arm and hand intensive therapy could be helpful for anyone with Friedreich Ataxia whose arms and hands are affected, but particularly in the early stage of the disease.

3.1.3.2 Sensory specific training

Given the potential impact of sensory loss on upper limb function, sensory specific training was considered. Sensory specific rehabilitation can be divided into either active sensory training (manual exploration of objects with the hand) or passive sensory training (24-26). The studies reviewed here are categorized as passive sensory training techniques, as briefly described below.

Wearable proprioceptive stabilizer: a device that emits focal mechanical vibrations to the person wearing the device with the aim of improving limb ataxia (27).

Controlled whole-body vibration training: involves trainees standing on a vibration platform where mechanical vibrations are transmitted to the person with the aim of leading to physiological and neuromuscular changes (28).

Augmented transcutaneous electrical nerve stimulation (aTENS): involves continuous asymmetrical biphasic pulses of current delivered through pairs of electrodes. The level of electrical stimulation engages a broad range of sensory nerve fibers that produce a tingling sensation with minimal levels of discomfort (29).

At this point in time, based on very little research evidence, sensory therapy has no clear advantages or disadvantages for improving upper limb function in individuals with FRDA.

3.1.3.3 Splinting

Splinting involves the application of an external force to the upper limb with the expectation that muscle length will be maintained and therefore contracture prevented (30). It is typically employed as an adjunct hypertonicity intervention. There are three main theoretical approaches to splinting: biomechanical (promoting musculoskeletal integrity); neurophysiological (regulating sensory input); and restorative (30). Individual assessment within the domains of impairment, activity and participation, with consideration of personal and situational factors should guide decisions about splint design, positioning and wearing regimes (30).

3.1.3.4 Pharmacological agents

Baclofen

Baclofen is used to treat the symptoms of spasticity, in particular the relief of spasms and concomitant pain, clonus and muscular rigidity. Baclofen belongs to a class of drugs called skeletal muscle relaxants. The precise mechanism of action of baclofen is not fully known. Baclofen is capable of inhibiting both monosynaptic and polysynaptic reflexes at the spinal level (https://www.rxlist.com/baclofen-drug.htm#description).

Botulinum toxin type A

Botulinum toxin type A is a prescription medication used to treat the symptoms of spasticity and belongs to a class of drugs called neuromuscular blockers. Botulinum toxin type A for injection is a sterile, vacuum-dried purified botulinum toxin type A and is intended for intramuscular use (https://www.rxlist.com/botox-drug.htm#dosage).

Botulinum toxin type A has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by fixed contracture. The clinical experience of the expert authors suggests caution against the use of botulinum toxin for management of upper limb spasticity in FRDA as the unmasking of underlying weakness may diminish what little hand function remains.

3.1.3.5 Neuromodulation

Neuromodulation is an emerging treatment modality that is divided into invasive and non-invasive stimulation techniques (31). These applications either stimulate or block the flow of action potentials through the nervous system (32) and complement conventional neurorehabilitation therapies. The techniques reviewed here are categorized as non-invasive and are summarized below.

Electrical stimulation and functional electrical stimulation

Electrical stimulation (ES) and functional electrical stimulation (FES) are non-invasive neuromodulation techniques whereby electrical current stimulates muscle contraction via surface electrodes. The aim of ES is to strengthen targeted muscles, increase or maintain muscle range, decrease spasticity, and improve contractile properties. FES involves ES delivered during the performance of a functional activity, with the aim to improve performance of that specific activity (7). Standard contraindications and precautions for the use of ES, including absent or diminished sensation, poor skin integrity, pregnancy and the ability to self-monitor, should be comprehensively assessed before application.

Cerebellar transcranial direct current stimulation

Cerebellar transcranial direct current stimulation (tDCS) is a non-invasive application of a low intensity (1-2 mA) steady current through a surface electrode over the cerebellum which has been demonstrated to elicit changes in cerebellar excitability in a polar-specific manner (33, 34).

Cerebellar transcranial magnetic stimulation

Cerebellar transcranial magnetic stimulation (cTMS) is a non-invasive technique applied over the cerebellum contralateral to the most clinically affected side. It uses a double cone coil oriented at a tangent to the scalp capable of reaching the deeper brain structures such as the dentate nucleus. It aims to correct disrupted cerebellar networks to enable symptomatic control (35). In this study, where cTMS was administered to 24 patients with ataxia, no severe side effects were reported. However, nine patients presented with mild side effects (five after active cTMS and four after sham) (35).

Cerebello-spinal transcranial direct current stimulation

Cerebello-spinal tDCS is a combined treatment of cerebellar anodal tDCS and spinal cathodal tDCS. tDCS is delivered by a battery-driven constant current stimulator through a pair of surface sponge electrodes. The anode is placed on the scalp over the cerebellum area and the cathode is positioned over the spinal lumbar enlargement. The aim of the treatment is to modulate cerebello-motor connectivity (36).

Note: these techniques are also discussed in Chapter 3.11: Cognitive function in Friedreich ataxia.

Presently there is little evidence to guide the use of tDCS and TMS for upper limb dysfunction in FRDA and further research is warranted. However, based on benefits seen under trial conditions (unpublished), electrical stimulation may be considered for the management of upper limb function in individuals with FRDA in a clinical setting, with appropriate evaluation prior to treatment, careful monitoring during treatment and identification of realistic goals of treatment.

Best practice statement

At a minimum, annual comprehensive assessment of upper limb function should be conducted by a multidisciplinary team to optimize independence and minimize the effects of primary and secondary symptoms of Friedreich ataxia (5).

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	↓↓		

Upper limb rehabilitation

Should intensive (upper limb) rehabilitation versus no rehabilitation be used for all individuals with Friedreich ataxia?	**Strength**	**Level of evidence**
We conditionally recommend intensive upper limb rehabilitation for individuals with Friedreich ataxia in a clinical setting.	↑	⊕◯◯◯
Justification: We have conditionally endorsed intensive upper limb rehabilitation for individuals with Friedreich ataxia based on strong evidence in like populations, the clinical reasoning of experienced clinicians and the potential harm of not providing the intervention.		
Subgroup considerations: We consider that intensive upper limb rehabilitation may be particularly beneficial in the early stage of the disease and for individuals with a point mutation.		

Sensory specific training

Should sensory specific training versus no training be used for all individuals with Friedreich ataxia?	**Strength**	**Level of evidence**
We cannot recommend either the use or non-use of sensory specific training of the upper limbs for individuals with Friedreich ataxia in a clinical setting.	—	⊕◯◯◯
Justification: We acknowledge the role of sensory input, particularly proprioception, on upper limb functional task performance and that sensory specific training attempts to mitigate the loss of sensation. However, the pathology of sensory impairment in Friedreich ataxia is different to like populations and therefore we are unable to say that sensory impairment secondary to Friedreich ataxia is amenable to intervention.		

Subgroup considerations: None

Upper limb splinting/orthoses

Should upper limb splinting/orthoses versus no splinting/orthoses be used for Individuals with spasticity, spasm, contracture with Friedreich ataxia?	**Strength**	**Level of evidence**
We conditionally recommend considering upper limb splinting/orthoses for individuals with Friedreich ataxia who experience spasticity, spasm or contracture.	↑	⊕◯◯◯
Justification: Clinical experience indicates judicious use of customized orthoses may assist in the management of spasticity and prevention of contracture. Upper limb splinting /orthoses should be an adjunct to other therapies such as a hand exercise program incorporating stretch and strengthening (as indicated). Consideration should also be given to ensuring the device does not interfere with active movement opportunities. An assessment of sensation, skin integrity and the ability to monitor the correct device positioning (either self-monitoring or a carer) should also inform decision making.		
Subgroup considerations: This recommendation is for individuals with Friedreich ataxia with upper limb spasticity, spasm or contracture.		

Pharmacological agents

Should pharmacological (baclofen, botulinum toxin) to manage upper limb function versus no pharmacological be used for Individuals with spasticity, spasm with Friedreich ataxia?	**Strength**	**Level of evidence**
We recommend *against* the use of pharmacological agents (baclofen and botulinum toxin) for specific management of upper limb function in individuals with Friedreich ataxia experiencing spasticity and spasm.	↓↓	⊕◯◯◯
Justification: This recommendation was made in the absence of any evidence for the intervention (pharmacological therapy) and clinical experience of undesirable effects associated with the use of botulinum toxin for upper limb spasticity and spasm in individuals with Friedreich ataxia. Anecdotally, baclofen can have multisystem effects which have potential to compromise postural control, alertness and swallowing safety. Non-pharmacological management strategies should be used for upper limb spasticity or spasm.		
Subgroup considerations: This recommendation is for individuals with Friedreich ataxia with spasticity or spasm, for management of upper limb function.		

Neuromodulation

Should neuromodulation (i.e. stimulation, tDCS, TMS) versus none be used for all individuals as indicated with Friedreich ataxia?	**Strength**	**Level of evidence**
We conditionally recommend considering electrical stimulation (but not tDCS or TMS) for management of upper limb function in individuals with Friedreich ataxia in a clinical setting, with appropriate evaluation prior to treatment.	↑	⊕◯◯◯
Justification: Anecdotal observations whilst administering electrical stimulation (ES)/functional electrical stimulation (FES) under trial conditions reinforce the importance of using clinical reasoning to guide the treatment and that the intervention needs to be driven by a suitably		

qualified clinician. Setting and adjusting the stimulation parameters requires careful consideration and monitoring for fatigue effects. Identification of realistic upper limb functional goals is particularly important.
Subgroup considerations: Pilot data (unpublished) indicates ES/FES may improve upper limb function in individuals with later stage Friedreich ataxia. There are well documented contraindications for ES/FES and screening for these indications is part of routine clinical care. Sensation should be comprehensively evaluated prior to commencing ES and skin integrity should be carefully monitored. Access to carer support for the application of ES/FES is essential.

Lay summary

Lay summary of clinical recommendations for upper limb dysfunction in Friedreich ataxia

Why these recommendations?

These recommendations are for the best ways to manage the arms and hands for people with Friedreich ataxia.

Intensive therapy

Regular exercises for the arms and hands are helpful for people with Friedreich ataxia, particularly in the early stages of the disease. The benefits of arm and hand exercise may be greater than not having any arm and hand exercise therapy.

Sensory therapy

Exercises that improve the way the hands are able to feel everyday objects can sometimes be helpful in other conditions. However, it is not clear whether these types of exercises could help individuals with Friedreich ataxia.

Splinting/orthoses (braces that hold the arm in a position)

Customised splints or orthoses should be considered for arm and hand positioning when the hands and wrists are becoming more flexed because the overall benefits outweigh possible harms of not wearing a splint.

Pharmacological (medication such as baclofen and botulinum toxin)

Medications such as baclofen or botulinum toxin for tightness *only* in the arms and hands is not recommended because the harm they can cause may be greater than not having medication. Using baclofen or botulinum toxin for the legs and feet is not considered to have much effect on the arms and hands.

Neuromodulation (including electrical stimulation of the arms and brain)

Electrical stimulation therapy for the arms and hands is helpful for some people with Friedreich ataxia, but is not suitable for everyone. You should speak to your occupational therapist or physiotherapist to see if this intervention is appropriate for you. Other kinds of neuromodulation such as electrical stimulation of the brain through the scalp are not available as a therapy and are still being researched.

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

Arm and hand management is complex so it is important to speak with your healthcare professional, such as your occupational therapist or physiotherapist, about what it means for you.

How your arms and hands are managed depends on how they are affected and the impacts on how you use your hands and arms in daily life.

Seeing a healthcare professional with skills in this area is important to make sure you are getting the right treatment for your specific needs.

Who are these recommendations specifically for?

These recommendations are for all people with Friedreich ataxia who experience problems with their arms and hands.

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