Clinical Management Guidelines for Friedreich Ataxia

Chapter 5. Surgical and anesthetic considerations in Friedreich ataxia

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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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These Guidelines are made available as general information only and <u>do not constitute medical</u> <u>advice</u>. These Guidelines are intended to assist qualified healthcare professionals make informed treatment decisions about the care of individuals with Friedreich ataxia. They are not intended as a sole source of guidance in managing issues related to Friedreich ataxia. Rather, they are designed to assist clinicians by providing an evidence-based framework for decision-making.

These Guidelines are not intended to replace clinical judgment and other approaches to diagnosing and managing problems associated with Friedreich ataxia which may be appropriate in specific circumstances. Ultimately, healthcare professionals must make their own treatment decisions on a case-by-case basis, after consultation with their patients, using their clinical judgment, knowledge and expertise.

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5. Surgical and anesthetic considerations in Friedreich ataxia

Individuals with Friedreich ataxia are considered at high risk of complications related to surgery and anesthesia due to comorbidities such as cardiomyopathy, scoliosis, diabetes and compromised lung function (1, 2). Cardiomyopathy is present in most individuals with Friedreich ataxia and left ventricular outflow obstructions should be avoided (1). The presence of scoliosis presents challenges for the use of central neuraxial blockade (1). In addition, concerns have been reported about the use of general anesthesia (3); however, the successful implementation of techniques such as combined spinal epidural anesthesia and total intravenous anesthesia have been reported (2, 4).

This chapter describes the particular surgical and anesthetic considerations relevant to individuals with Friedreich ataxia, focusing on monitoring cardiac function peri-operatively and managing the needs of individuals, both during and after surgery. In writing best practice statements and recommendations, the authors were tasked with answering the following questions:

For individuals with Friedreich ataxia, what management strategies could be implemented to monitor cardiac function peri-operatively? (see 5.1)

For individuals with Friedreich ataxia, what management strategies could be implemented regarding fluid and operative management? (see 5.2 to 5.4)

5.1 Management strategies for monitoring cardiac function peri-operatively

Roger Peverill, David Lynch and Ronald Mark Payne are acknowledged for the content of this section from the previous version of the guidelines (2014).

The increased thickness of the left ventricle in Friedreich ataxia (FRDA) results in a reduction in coronary flow reserve and less tolerance to tachycardia. The reduced size of the left ventricular (LV) cavity in FRDA means a greater reliance on heart rate to maintain cardiac output and a reduction in stroke volume reserve. Hearts of individuals with FRDA will therefore have less tolerance for changes in hemodynamics, such as bradycardia, tachycardia, low blood pressure, and increases or decreases in LV filling.

Individuals with FRDA undergoing major surgery, such as scoliosis repair, should undergo EKG, echocardiography and have a cardiology consultation within a reasonable time frame prior to the surgery (e.g., 2 to 4 months prior) to evaluate LV structure and left ventricular ejection fraction. Because of the increased risk of cardiovascular instability and complications during major surgery in FRDA, a multi-disciplinary approach to evaluate and manage these patients during and after surgery is recommended. This may include consultation and collaboration between the cardiologist, anesthesiologist, intensivist and surgeon. Access to an intensive care unit capable of supporting a patient with severe heart failure is also recommended.

Best practice statements

Patients with Friedreich ataxia being considered for scoliosis surgery, or other major surgery, are at risk of poor outcomes and require a multi-disciplinary approach to the management of heart function during surgery and in the postoperative period.

As per the 2014 guidelines, it is the view of the expert authors that evaluation by a cardiologist should take place prior to major surgery; cardiac monitoring should take place during major

surgery; and major surgery should ideally be conducted in a center with cardiac intensive care facilities.

5.2 Strategies for fluid and operative management – fluids

Roger Peverill, David Lynch and Ronald Mark Payne are acknowledged for the content of this section from the previous version of the guidelines (2014).

Individuals with FRDA are at increased risk of cardiovascular instability and complications during major surgery particularly if major fluid shifts are part of the surgical procedure.

Best practice statement

Careful monitoring of fluid balance is essential in individuals with Friedreich ataxia undergoing stressful events such as scoliosis surgery or hydration therapy in the emergency room setting.

5.3 Strategies for fluid and operative management – early mobilization

Phoebe Sansom

Low mobility levels are prevalent in the hospitalized adult population (5). The negative consequence of prolonged bed rest affecting the cardiovascular, respiratory, gastrointestinal, musculoskeletal, renal, endocrine and nervous systems are well documented (6). Prolonged immobility is associated with adverse outcomes such as functional decline, prolonged length of hospital stay, falls and an increased risk of mortality (5). 'Standard post-operative management' in regards to mobilization can vary considerably across settings and institutions. Early mobilization would involve a patient participating in out-of-bed activity as early as possible once deemed medically appropriate.

The complex presentation of individuals with FRDA may affect the confidence of therapists and staff in assessing and mobilizing this cohort, thus placing them at greater risk of low mobility levels in hospital. However, the complex clinical features of FRDA and the decreased strength reserve predispose this population to deconditioning and deterioration in physical functioning with prolonged immobility. Should this occur, the consequences for this already physically compromised population can be devastating.

Early mobilization is recommended to promote maintenance of physical functioning and independence during and after hospitalization. The potential positive effects of early mobilization include maintenance of mobility and physical ability to optimize a return to pre-surgical functional and independence status. Ensuring appropriate physical support and assistance, environmental setup and equipment requirements both within the hospital setting and after discharge may mitigate the effects of post-surgical immobilization. However, the resources, hospital staff assistance and care-giver support required to facilitate early mobilization need to be considered.

Recommendation

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 | $\uparrow\uparrow$ | High | $\oplus \oplus \oplus \oplus$ |
| Conditional for intervention | \uparrow | Moderate | $\oplus \oplus \oplus \bigcirc$ |
| Neither intervention nor comparison | _ | Low | $\Theta \Theta \odot \odot$ |
| Conditional against intervention | \downarrow | Very low | 000 |
| Strong against intervention | $\downarrow \downarrow$ | | |

Early mobilization

| Should early/aggressive (out of bed) physical therapy versus standard post-operative management be used for patients undergoing surgery with Friedreich ataxia? | Strength | Level of evidence | | | |
|--|----------|----------------------|--|--|--|
| We suggest early mobilization following surgery over standard post- operative management for individuals with Friedreich ataxia undergoing surgery. | 1 | ⊕○○○ | | | |
| We cannot recommend a particular approach to the timing of getting someone out of bed post-surgery. It is probably best to mobilize as soon as possible with consideration for the following: cardiac/medical status, mobility needs, and decreased reserve of strength. | | | | | |
| Justification: The complex clinical features of Friedreich ataxia and the decreased strength reserve predispose this population to deconditioning and deterioration in physical functioning with prolonged immobility. There is no clinical reason to limit early mobilization in the Friedreich ataxia population, other than individual circumstances. Early mobilization is recommended to promote maintenance of physical functioning and independence during and after hospitalization. However, this does not mean there should be early discharge from hospital. | | | | | |
| The resources, hospital staff assistance and care-giver support that may be required to allow early mobilization to take place need to be considered. | | | | | |

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia undergoing surgery. For non-ambulant (hoist transfer dependent) individuals with Friedreich ataxia, a hoist transfer to sit out of bed is a form of mobilization.

5.4 Strategies for fluid and operative management – anesthesia

Ludger Schöls, Kimberley Y. Lin, Ronald Mark Payne, Lisa Montenegro and David Lynch

Kelly Sullivan and Theresa Zesiewicz are acknowledged for some content taken from the previous version of the guidelines (2014).

Peri-operative pain management is a concern in managing people with FRDA. Surgeries and associated anesthesia may be required to treat cardiac, orthopedic and obstetric issues. However,

diabetes mellitus, cardiomyopathy and compromised pulmonary function make anesthetic management challenging.

While practice guidelines have not been established, there are case reports of successful anesthesia using remifentanil and propofol (7), alfentanil and propofol (8), and isoflurane (3) in individuals with FRDA. Use of muscle relaxants has been reported with mixed results in individuals with FRDA and there has been one report of hypersensitivity to tubocurarine (9). A more recent report by Schmitt et al (10) described the response of two adolescent girls with FRDA to rocuronium. In particular, the clinical duration of rocuronium for both girls was comparable to children without neuromuscular disease, indicating successful anesthetic management (10). Other reports describe a normal or near normal response to various nondepolarizing neuromuscular blocking agents, such as tubocurarine, atracurium and vecuronium (11, 12). Schmitt and colleagues (10) recommend accurate assessment of neuromuscular block throughout anesthesia for individuals with FRDA. In the case of obstetrics, successful use of fentanyl and bupivacaine has been reported in a case of a vaginal delivery (13) and a caesarean section (14). More recently, Ozgul and colleagues reported the successful anesthetic management of a person who underwent posterior spinal fusion (15).

A related review of the effects of anesthesia in individuals with a variety of muscular dystrophies (which did not include people with FRDA) reports cardiac complications associated with inhaled anesthetics and post-operative rhabdomyolysis (16). The authors recommend avoiding use of succinylcholine which has been associated with life-threatening hyperkalemia (16). This recommendation may also be applicable to individuals with FRDA.

Finally, changes to cardiac function in people with FRDA indicate the capacity to tolerate lower blood pressure and large fluid shift as may be associated with surgery and anesthesia may be compromised. It is important to carefully monitor fluid loss and cardiovascular function during extensive surgery in FRDA (17).

Best practice statements

Consideration should be given to appropriate management of peri-operative pain in people with Friedreich ataxia; consideration should be given to the use of nondepolarizing muscle relaxants, in particular accurate assessment of neuromuscular block throughout anesthesia; consideration should be given to avoiding risks associated with hyperkalemia; there should be careful monitoring of fluid balance and cardiovascular function in people with Friedreich ataxia undergoing anesthesia.

Propofol has been used in a large number of individuals with Friedreich ataxia and there is no published evidence that documents adverse events related to the use of propofol in this population. This suggests that theoretical concerns of possible mitochondrial toxicity with propofol are not likely to be clinically meaningful.

Lay summary

Lay summary of clinical recommendations/best practice statements for surgical and anesthetic considerations in Friedreich ataxia

Why these recommendations/best practice statements?

Friedreich ataxia is often associated with heart problems, scoliosis, diabetes and reduced lung function. This means individuals with Friedreich ataxia may be at greater risk of complications while undergoing surgery than other people.

Particular types of anesthetics and careful monitoring of heart function and fluids may be needed when an individual with Friedreich ataxia has surgery. In addition, surgery and the reduction in activity after surgery may mean a person with Friedreich ataxia will quickly lose physical condition while they recover from the surgery.

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

If you are considering surgery it might be important for you to speak with your healthcare professional about Friedreich ataxia and surgery and what it means for you.

We suggest that individuals with Friedreich ataxia considering surgery should be seen by a cardiologist before surgery. In addition, monitoring of heart function should occur during surgery, particularly if there is significant loss of blood or extra fluid is required. Ideally surgery should be done in a center with cardiac intensive care facilities. It is best if mobilization (getting out of bed) commences as soon as possible after surgery.

Health providers may consider a range of anesthetic options for you, including spinal nerve blocks or anesthetics given intravenously.

Who are these recommendations/best practice statements specifically for?

These recommendations and best practice statements are for all individuals with Friedreich ataxia who may be considering or are undergoing surgery.

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