Evidence-Based Guidelines and Beyond

Rabi Tawil, MD

FSHD Connect Meeting

Las Vegas, June 9, 2018
Facioscapulohumeral muscular dystrophy

Author: Baill T Darras, MD
Section Editor: Douglas R Nordli, Jr, MD, Jeremy M Steiner, MD, PhD
Deputy Editor: John F Dache, MD, PhD

Facioscapulohumeral muscular dystrophy (FSHD) is the third most common type of muscular dystrophy. It is a complex genetic disorder characterized in most cases by slowly progressive muscle weakness involving the facial, scapular, upper arm, lower leg, and hip girdle muscles, usually with asymmetric involvement.

The clinical aspects of facioscapulohumeral muscular dystrophies are discussed here. Other muscular dystrophies are presented separately. (See "Duchenne and Becker muscular dystrophy: Clinical features and diagnosis" and "Emery-Dreifuss muscular dystrophy" and "Limb-girdle muscular dystrophy" and "Myotonic dystrophy: Etiology, clinical features, and diagnosis" and "Oculopharyngeal, distal, and congenital muscular dystrophies")

Etiology and Genetics — Although the precise details are not entirely resolved, the most probable causal factor of FSHD is inappropriate expression of the double homeobox protein 4 gene (DUX4). The DUX4 gene lies within...
FSHD Care Guidelines 2015

Best available evidence-based guideline for the management of FSHD

FSHD is a muscle disease with two genetic causes. People with either genetic cause show similar signs and symptoms. In the majority of cases, genetic testing can confirm an FSHD diagnosis. Doctors should know about and help manage related health problems.

What is FSHD?
FSHD is one of the most common forms of muscular dystrophy (MD). MD is a group of several different genetic diseases. These cause muscle wasting (damage) and weakness. Depending on the MD type, different muscles of the body can be affected. These may include the muscles that control breathing.
Evidence-based guideline summary:

- FSHD Genetic testing
  - Is it accurate and reliable?

- Risk factors for disease severity
  - Are there measurable factors that predict severity?

- Complications
  - What non-muscular complications occur in FSHD and who is most susceptible?
  - Approach to surveillance and prevention/mitigation

- Treatment
Genetic testing

**Diagnosis**

| Clinicians caring for people who may have FSHD type 1 | Order genetic testing to confirm FSHD type 1 diagnosis in people with unusual patterns of signs and symptoms and no first-degree relatives with the disease | Moderate |

**4q**

- Normal: >10
- FSHD1: 1-10
- Normal: >38 kb
- FSHD1: 10-38 kb

**Suspect FSHD**

- Genetically confirmed 1st Degree Relative?
  - Yes
  - FSHD1
  - Test for presence of D4Z4 Contraction
    - Yes
    - Clinically typical FSHD?
      - Yes
      - Other myopathies:*
        - LGMD2A
        - Acid maltase def.
        - Mitochondrial myopathy
      - No
      - FSHD1 confirmed
    - No
      - Other myopathies*
Factors that Effect Disease Severity

<table>
<thead>
<tr>
<th>Factors That Can Predict Disease Severity</th>
<th>Clinicians caring for people with FSHD</th>
<th>Look for certain information from genetic test results (large D4Z4 deletion sizes) that may point to more significant disability at an earlier age</th>
</tr>
</thead>
</table>

- **1-3 Repeats: 10-18 kb**
  - Most severe, earlier onset, infantile onset

- **4-7 Repeats: 20-31 kb**
  - Most common, very variable in overall severity

- **8-10 Repeats: 33-38 kb**
  - Later onset and more likely to have no symptoms
## Non-muscular Complications

### Monitoring for Complications: Breathing (Pulmonary)

| Clinicians caring for people with FSHD | Order baseline pulmonary (breathing) function testing for all patients with FSHD. Monitor regularly if patient has abnormal test results or any combination of severe weakness near the lungs or chest, kyphoscoliosis, wheelchair dependence, or related conditions that affect breathing. |
| Clinicians caring for people with FSHD and 1) poor results from pulmonary function tests or 2) symptoms of extreme daytime tiredness or poor sleep | Refer patients for pulmonary or sleep medicine consultation for possible nighttime sleep monitoring or nighttime breathing machine in order to improve quality of life. |
| Clinicians caring for patients with FSHD who do not get regular pulmonary function testing | Order testing before any surgery requiring general anesthesia (such testing may uncover hidden breathing problems). |

### Monitoring for Complications: Cardiac (Heart) Abnormalities

| Clinicians caring for patients with FSHD | Refer for cardiac (heart) evaluation if the patient has clear signs or symptoms of heart disease (shortness of breath, chest pain, palpitations). Routine screening is not needed in patients with no clear signs or symptoms. |
# Non-muscular Complications

## Monitoring for Complications: Retinal Vascular Disease (Eye Disease)

| Clinicians caring for patients with FSHD and certain genetic signs (large deletions) | Refer the patient to an experienced ophthalmologist (eye doctor) for dilated indirect ophthalmoscopy (an eye test to examine the retina). Eye doctor should use presence of disease on first screening in order to determine how often to follow up with the patient |

## Monitoring for Complications: Hearing Loss

| Clinicians caring for young children with FSHD | Screen at diagnosis and yearly afterward until the children start school (hearing loss not always present at diagnosis and can be progressive) |

## Monitoring for Complications: Pain

| Clinicians caring for patients with FSHD | Ask regularly about pain. May refer for physical therapy as a helpful first step. If pain continues, may prescribe nonsteroidal anti-inflammatory drugs for acute (short-term) pain and antidepressants and epilepsy drugs for chronic (long-term) pain |
## Treatment

<table>
<thead>
<tr>
<th>Treatment: Pharmaceutical Drugs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians caring for patients with FSHD</td>
<td>Should not prescribe albuterol, corticosteroid, or diltiazem for improving strength</td>
</tr>
</tbody>
</table>

**Treatment: Scapular Surgical Fixation (Surgery to Lock Shoulder Blade)**

| Clinicians caring for patients with FSHD | Might offer surgical scapular fixation (surgery to lock the shoulder blade) to certain patients after careful consideration of arm muscle problems, potential gain in range of motion, rate of disease progression, and potential for poor outcomes from surgery and long periods of bracing |

<table>
<thead>
<tr>
<th>Treatment: Aerobic Exercise</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians caring for patients with FSHD</td>
<td>Might encourage patients to do low-intensity aerobic exercise program (program might be developed with help of physical therapist). Might use guidelines for physical activities for people with disabilities from US Department of Health and Human Services¹</td>
</tr>
<tr>
<td>Clinicians caring for patients with FSHD who are interested in strength training</td>
<td>May refer patients to physical therapists to develop safe exercise program using appropriate weights and resistance and is tailored to the patient’s abilities</td>
</tr>
</tbody>
</table>
Scapular Fixation: Choosing the Right Patient
Scapular Fixation

- Choosing the right surgeon
- Choosing the right procedure
  - Sling
  - Wiring
  - Scapulothoracic fusion

Courtesy of John Kissel
# Treatment

## Treatment: Pharmaceutical Drugs

| Clinicians caring for patients with FSHD | Should not prescribe albuterol, corticosteroid, or diltiazem for improving strength |

## Treatment: Scapular Surgical Fixation (Surgery to Lock Shoulder Blade)

| Clinicians caring for patients with FSHD | Might offer surgical scapular fixation (surgery to lock the shoulder blade) to certain patients after careful consideration of arm muscle problems, potential gain in range of motion, rate of disease progression, and potential for poor outcomes from surgery and long periods of bracing |

## Treatment: Aerobic Exercise

| Clinicians caring for patients with FSHD | Might encourage patients to do low-intensity aerobic exercise program (program might be developed with help of physical therapist). Might use guidelines for physical activities for people with disabilities from US Department of Health and Human Services¹ |
| Clinicians caring for patients with FSHD who are interested in strength training | May refer patients to physical therapists to develop safe exercise program using appropriate weights and resistance and is tailored to the patient’s abilities |
Limitations of Evidence-based Guidelines in FSHD

- FSHD has a wide spectrum of disease severity and rate of progression
  - Cannot have a one-size fits all guidelines
- Most studies are retrospective, do not involve large numbers of patients and often involve a non-representative group of patients
BEYOND EVIDENCE-BASED GUIDELINES
Weakness of Eyelid Muscles

- Weakness can lead to conjunctival dryness, irritation and exposure keratitis.
- Consider implantation of gold weight in the upper eyelid. Routinely used for facial palsy.
Weakness of the Lower Facial Muscles

- Weakness with eversion of the lower lip results in poor pronunciation, drooling and spillage of food when eating.

- Various minimally-invasive surgical techniques have been utilized in individual patients leading to cosmetic as well as functional improvement.
How do we Improve Care Guidelines

- Need for more longitudinal information in larger numbers of individuals with FSHD
- This can only be practically done in a registry
- The National FSHD Registry has about 1000 patients
- Given the estimated prevalence of FSHD, there is potentially 20,000 individuals with FSHD in the US
National Registry for Myotonic Dystrophy (DM) & Facioscapulohumeral Dystrophy (FSHD)

Help Us Advance Research
The National Registry advances research in myotonic dystrophy (DM) and FSHD by helping patients to participate in clinical studies. These studies help doctors, investigators, and care providers better understand the biology, progression, and other important issues in DM and FSHD.

Help Us Learn What's Important to You and Your Family
Registry members complete questionnaires every year about their symptoms. We collect and track your clinical information which can lead to a better understanding of DM and FSHD, how symptoms change over time, and how to better care for patients.
Medicine of the Highest Order