Facioscapulohumeral muscular dystrophy (FSHD) Guideline

Introduction to the English translation of the Dutch 2018 Guidelines for FSHD

The following text offers a direct translation of the Dutch guidelines for care for FSHD patients and their families. The topics for these guidelines and the questions they raised were identified by a panel of patients, patient representatives and medical experts on the management of this disease. These topics relate to areas of perceived or suspected absence of consensual answers in the published literature.
The internationally accepted grade methodology for analysing the published literature was used, which led to the demonstration of a poor evidence for most questions asked. The panel then formulated recommendations which are the reflection of its extensive experience in managing the disease. These are to some extent specifically written for and applicable to the Dutch health care system and might not be seen in a similar way in other countries. The recommendations are an ongoing project in The Netherlands and could be presented as a to do list for future clinical studies which are dearly needed.

We hope these recommendations trigger a discussion and are curious to hear your feedback.

On behalf of the Dutch guidelines panel.

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Summary
FSHD (facioscapulohumeral muscular dystrophy) is an inherited muscle disorder that most often manifests with weakness of the muscles of the face (facies), the shoulder blade (scapula) and the upper arms (humeri). Weakness of the facial muscles varies in severity, and can present in different ways such as an inability to (fully) close the eyes, to (forcefully) close or pucker the lips, or to whistle. The foot dorsiflexors, the abdominal and pelvic muscles, and the hip and upper leg muscles may follow. Initial symptoms can occur at any age, so children can also get FSHD. In the end, about 20% of patients older than 50 become wheelchair-bound, and a very small number develop weakness of the respiratory muscles.

People with this disease adapt (often unconsciously) to the slowly increasing limitations. Sometimes they find out from care providers or from family members that there is no treatment for it. This is partly why some patients do not see the need to go to the physician – at least not in time. And yet good, multidisciplinary care can be beneficial early on as well as later in the course of the disease. This guideline is intended for physicians and paramedics who are involved in the care of individuals with FSHD; topics covered include pain alleviation, treatment of fatigue, and improvement of mobility and communication.

Chapter 1 General introduction

Facioscapulohumeral muscular dystrophy (FSHD)

FSHD (facioscapulohumeral muscular dystrophy) is an inherited muscle disorder that most often manifests with weakness of the muscles of the face (facies), the shoulder blade (scapula) and the upper arms (humeri). There is some variation in the sequence of muscle involvement and its severity, within and between families. As a result, FSHD can manifest itself in many ways, and is not always easy to recognise in its early beginnings.

Muscle weakness in the shoulder girdle as well as often-minimal and asymmetric weakness in facial muscles can go unnoticed for a long time. Pain is common and could be indicative of other diseases. Walking is something everyone does on a daily basis. FSHD demands a lot from muscles of the lower extremities, which makes weakness of these muscles more noticeable and can lead to a patient's first symptoms. The initial presentation of symptoms can vary considerably, whereas the general pattern of recognisable weakness during clinical examination and the progression of the muscle weakness over the years are both fairly uniform. The rate of this progression can be quite variable, both within and across family lines. At present, this progression can only be partially explained by the known genetic changes that FSHD patients undergo.

There are two types of FSHD – FSHD1 and FSHD2 – which cannot be distinguished from each other in terms of severity or course. In the vast majority of patients (>95%), FSHD is caused by a defective chromosome 4; this type is called FSHD1. FSHD2 is much rarer and is the result of a mutation in chromosome 18.

Muscle weakness is the main characteristic of FSHD. Other, less frequent characteristics include fatigue and pain as well as respiratory and auditory problems. Because of the genetic component of FSHD, genetic advice should be sought early on. Some patients may not need to involve a physician. This may be because the disease progresses slowly and goes unnoticed, or because the patient knows about the clinical picture from the family and believes that it cannot be treated. There are also patients who do not want this disease on record for insurance or work-related reasons.

Motivation behind creating this guideline
In the Netherlands there is great variation in the way patients with FSHD are treated and assisted. This is partly because there is no clear guideline for treating these patients. As FSHD is so rare, many care providers have limited knowledge of the course of this disease. Lack of knowledge about the prognosis and limited experience with complications can get in the way of a proactive and optimally supportive policy as there was no nationwide policy.

Dedicated care can significantly improve the quality of life of patients with FSHD. This stresses the importance of multidisciplinary treatment and care management of these patients.

These considerations motivated Spierziekten Nederland[1] and the FSHD Expertise Centre to develop a multidisciplinary, evidence-based guideline for the treatment of FSHD. This guideline was created thanks to a subsidy of the Innovatiefonds Zorgverzekeraars,[2] in the context of the *Zorg voor Zeldzaam* project, an initiative to help people with rare diseases. The guideline focuses on the most common problems that present with FSHD.

Goal of the guideline
The goal of this guideline is to help improve the quality of the care management and treatment of adult patients with FSHD by following a uniform policy. The guideline can help primary, secondary and tertiary care providers (including neurologists, rehabilitation physicians, physical therapists, occupational therapists, social workers, speech therapists and general practitioners) in their choices for the treatment or care management of patients with FSHD.

Important focal points of this guideline are:
- timely detection of complications, symptom alleviation, psychosocial support, and reduction of pain and fatigue;
- maintenance and/or improvement of functions, activities and participation;
- maintenance of independence at work and at home, in order to optimise functioning and preserve the quality of life of patients and their families.

Delineation of the guideline
This guideline is intended for adult patients (18 years or older) with FSHD1 and FSHD2.

[1] Dutch advocacy group for people with muscular diseases.
[2] Dutch health insurer's innovation fund.

Chapter 2 How the guideline was developed

Validity

The VRA[3] together with the FSHD Expertise Centre and Spierziekten Nederland will determine by 2021 at the latest whether this guideline is still current. A new working party will be deployed to revise the guideline as needed. The validity of the guideline will expire sooner when new developments give cause for a revision course.

The other scientific associations participating in this guideline or users of the guideline have a shared responsibility and inform the VRA about relevant developments in their specialised fields.

General information

The Professional institute of medical specialists[4] (www.kennisinstituut.nl) had an advisory function during the development of the guideline. The guideline was financed by the Innovatiefonds Zorgverzekeraars.

Objective and target group

Objective

The objective of the guideline is to arrive at a uniform policy in the diagnosis, treatment and support of adults with FSHD.

Target group

This guideline is written for all members of the scientific associations that are involved in the care of patients with FSHD and for other physicians who are involved in the care of these patients.

Participants of the working party

To develop the guideline, a multidisciplinary working party was formed in 2015 consisting of representatives of all relevant specialties and the patient associations involved in the care of patients with FSHD (see the composition of the working party). The working party members were delegated to participate by their scientific associations. The working party worked for three years to create the present guideline, and is responsible for its entire contents.

[3] Dutch association of rehabilitation physicians (*Nederlandse Vereniging van Revalidatieartsen*).
[4] Kennisinstituut van Medisch Specialisten

Disclosures

Working party	*Function*	*Secondary functions*	*Personal financial interests*	*Personal relationships*	*Reputation management*	*Externally financed research*	*Knowledge valorisation*	*Other interests*
Esch	Project manager	Workshop staff, European Neuromuscular Centre (ENMC), paid	none	none	Member, core group Spierziekten Nederland for physical therapists and occupational therapists	Involved in the following projects: Zorg voor Zeldzaam: VSOP; Innovatiefonds Zorgverzekeraars - development of care standards and physiotherapy brochures	none	none
Geurts	Rehabilitation physician and advisor	Board member, Dutch association of rehabilitation physicians (VRA), unpaid; vice-president, Dutch Society for Neurorehabilitation (DSNR), unpaid; former medical advisor for the FSHD working party of Spierziekten Nederland, unpaid.	No direct financial interests. Ad hoc consultancy for Ipsen Pharma and Merz Pharma	none	Executive board member, European Federation of Neurorehabilitation Societies (EFNR), unpaid; member, Council for science and innovation of the Dutch federation of medical specialists (FMS), unpaid; member, scientific advisory Council for the Dutch brain foundation (*Hersenstichting*), unpaid.	Regular PI or project leader at ZonMw or third cashflow fund financed research. Relevant to the guideline: FACT-2 FSHD (PBS/ZonMw), Energetic (ZonMw, rehabilitation fund)	none	none
Groothuis	Rehabilitation physician	Medical advisor, diagnosis working party for FSHD, Spierziekten Nederland, unpaid; chair, Special Interest Group Plexopathies with the World Federation for Neurorehabilitation (WFNR), unpaid	none	none	Member, International Wheelchair Rugby Federation anti-doping committee judicial panel and therapeutic use exemptions panel, unpaid	Project leader for PBS-financed research for neuralgic amiotrophy	none	none
Horemans	Project manager		none	none	Member of several committees: secretary, VRA working party for neuromuscular disorders; board member, ISNO (inter-university support centre for neuromuscular disorders). Unpaid activities	Involved in the following projects: - Zorg voor Zeldzaam: development of care standards and general practitioner brochures; initiator: Innovation fund for health insurers - KIDZ	none	none

Lanser-Weber	Patient representative	Senior executive, Spierziekten Nederland	none	none	none	none	none	none
Mul	Neurologist-in-training and researcher-physician	none	none	none	none	Research projects financed by the PBS, Spieren voor Spieren (muscles for muscles), and the FSHD Foundation.	none	none
Maas	Physical therapist, teacher	none	none	none	Member, core group Spierziekten Nederland for physical therapists and occupational therapists	none	none	none
Padberg	Prof. emeritus, neurologist	Medical advisor, FSHD diagnosis working party for Spierziekten Nederland, Research Director ENMC, stipend; board member, FSHD foundation; member, Scientific Advisory Board of the FSH Society; Science Committee of the FSH Society and vice-chair of the Supervisory Board of Alzheimer Nederland; all unpaid. Advisor and consultant, Facio Therapies and aTyr Pharma USA, cost statements, confidential advisor for work conflicts of the research staff of Radboud University, reimbursement of expenses.	none	none	none	none	none	none
Voet	Rehabilitation physician	none	none	none	none	FACTS-2 FSHD research subsidised by the PBS, ZonMw, rehabilitation fund, VRA, FSH Global, Revalidatie Nederland	none	none
Vliet	Rehabilitation physician	Member, Supervisory Board, Liberein (paid)	none	none	none	none	none	none
Voermans	Neurologist	Medical advisor of diagnosis working party for congenital and metabolic myopathies (Spierziekten Nederland)	none	none	none	Research financed by PBS, not related to this guideline	none	none

Input of patient perspectives
Input of patients was used during all the development phases of this guideline. One patient representative was part of the working party and three patient representatives participated in the patient advisory board. This input was deemed to develop high-quality guidelines – after all, quality care needs to meet the wishes and requirements of both care providers and patients. Together with the patient representatives a bottleneck analysis was set up from patients' perspectives prior to starting with the development of this guideline. At important moments throughout the guideline's development advice was requested from various patient representatives of Spierziekten Nederland and all drafts were also submitted for comments to patient representatives

Procedure
AGREE
The report is based on the AGREE II-instrument (Appraisal of Guidelines for Research & Evaluation II, www.agreetrust.org), which is an instrument with wide international acceptance.

Bottleneck analysis
At an invitational conference the working party identified the bottlenecks. Representatives of scientific and other involved associations and Dutch health insurers were invited for a meeting and asked whether they experienced additional bottlenecks based on the framework of the guideline. Representatives of the following associations were present:
- Dutch association of rehabilitation physicians (VRA);
- Dutch association for neurology (NVN);
- Royal Dutch Society for Physical Therapy (KNGF);
- Patient association Spierziekten Nederland.

Primary questions and outcome measures
Based on the outcomes of the bottleneck analysis, the chair and the project managers drafted some primary questions. These questions were discussed with the working party, after which it formulated the definitive research questions. The research questions were defined using the PICO method. Next, the working party discussed per research question which outcome measures were relevant for the patient, looking at desired as well as undesired effects. The working party assessed these measures according to their relative importance as critical, relevant and irrelevant.

Strategy for searching and selecting literature
For each research question, searches were conducted in various electronic databases.

Quality assessment of individual studies
Individual studies were systematically assessed based on previously defined methodological quality criteria in order to estimate the risk of biased results. The evidence tables, the search criteria, the quality assessment and the exclusion table can be requested at Spierziekten Nederland.

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Evaluating the strength of the scientific evidence
The strength of the scientific evidence was evaluated by using the GRADE method. GRADE stands for 'Grading Recommendations Assessment, Development and Evaluation' (see www.gradeworkinggroup.org) (Atkins, 2004).

GRADE distinguishes four gradations for the quality of scientific evidence: high, moderate, low and very low. These gradations refer to the degree of confidence in the conclusion from the literature (see www.guidelinedevelopment.org/handbook).

GRADE	Definition
High	− There is high confidence that the actual effect of treatment is close to the estimated effect of treatment as indicated in the conclusion from the literature; − It is improbable that the conclusion from the literature would change if further research was conducted.
Moderate	− There is moderate confidence that the actual effect of treatment is close to the estimated effect of treatment as indicated in the conclusion from the literature; − It is possible that the conclusion could change if further research was conducted.
Low	− There is limited confidence that the actual effect of treatment is close to the estimated effect of treatment as indicated in the conclusion from the literature; − It is probable that the conclusion would change if further research was conducted.
Very low	− There is little confidence that the actual effect of treatment is close to the estimated effect of treatment as indicated in the conclusion from the literature; − The conclusion is very uncertain.

Formulating conclusions
The conclusion does not refer to one or several articles, but is drawn based on all studies together ('body of evidence'). The working party assessed the balance of each intervention. The favourable and unfavourable effects for the patient were weighed in the balancing process.

Considerations
Besides the scientific evidence, other aspects are important for a recommendation, such as expertise of the working party, patient preferences, costs, availability of facilities and organisational matters. Those aspects that are not part of the literature summary are listed under the heading 'Considerations'.

Formulation of recommendations
The recommendations answer research questions and are based on the best available scientific evidence and the most important considerations. The strength of the scientific evidence, together with the weight that the working party ascribes to the considerations, determines the strength of the recommendation. According to the GRADE method, a low power of evidence of conclusions in the systematic literature analysis does not rule out a strong recommendation, just like a high power of evidence can result in a weak recommendation. The strength of the recommendation is always determined by weighing all relevant arguments together.

Preconditions (organisation of the care)
In the bottleneck analysis and during the development of the guideline, organisation of care was explicitly taken into account – all aspects that constitute a prerequisite to provide care (such as coordination, communication, financial and other tools, manpower and infrastructure). Prerequisites relevant to answering a specific research question are part of the considerations for that question.

Comment and authorisation phase
The draft guideline was presented to the involved scientific associations for comments. The comments were compiled and discussed with the working party. Based on the comments, the draft guideline was modified and a definitive version was prepared by the working party. The definitive guideline was presented to the involved scientific associations for authorisation, and authorisation was given.

Chapter 3 Pain

Primary question: What is the best strategy to diagnose, treat and assist FSHD patients regarding questions of pain?

3.1 What is the best method to determine pain, pain type, pain intensity and pain localisation of patients with FSHD?
3.2 What is the best pain treatment and care management for patients with FSHD?

Introduction

Pain is a very common health problem in patients with FSHD (de Groot 2013; Jensen 2008); about 80% of patients suffer from chronic pain (Jensen, 2008; Guy-Coichard 2008; Padua, 2009). In FSHD pain (muscular/joint) is often localised in the lower back, legs, shoulders, hips and neck (Jensen, 2008; Tawil, 2015). Based on the experience of the working party, lower back pain is the type most mentioned by patients. Pain is also commonly reported under the ribs and around the shoulder. Pain strongly influences daily functioning, mood, social interaction, work absenteeism and work disability. Many patients with chronic pain seek a balance between possibilities, obligations and expectations (Jensen 2008, de Groot 2013).

The definition of pain used by the International Association for the Study of Pain (IASP, 1994), reads:

> *[Pain is an] unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.*

This notwithstanding, in current practice pain is not always part of the treatment for FSHD. The common opinion is that treating pain requires an integral and therefore multidisciplinary approach. In this module the working party gives a recommendation about the diagnosis and treatment of pain for patients with FSHD.

Search and selection

To answer the primary question about pain, a systematic literature analysis was conducted by formulating two research questions:

Primary question: What is the best strategy to diagnose, treat and assist FSHD patients regarding questions of pain?

3.1 What is the best method to determine pain, pain type, pain intensity and pain localisation of patients with FSHD?
3.2 What is the best pain treatment and care management for patients with FSHD?

A literature search was conducted into the following databases:

- PubMed 1966-present
- Embase (OvidSP) 1947-present
- MEDLINE (OvidSP) 1946-present
- Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, 2015)

Because of the expected limited results, the literature search for questions 3.1 and 3.2 was merged.

Studies were selected by the working party on the basis of the following criteria: systematic reviews or meta-analyses, RCTs, or other comparable research that describes and/or investigates treatment of pain for FSHD. This selection yielded 191 results.

Based on title and abstract, 55 studies were preselected. After consulting the full text, 51 studies were excluded and a total of four studies with different research designs were selected definitively. Literature was found for one of the two research questions.

The evidence tables, the search criteria, the quality assessment and the exclusion table can be requested at Spierziekten Nederland.

Search and selection

3.1 What is the best method to determine pain, pain type, pain intensity and pain localisation of patients with FSHD?

Relevant outcome measures
For question 3.1 the working party assessed pain, pain type and pain intensity as relevant outcome measures. After consulting the full text, no known studies were definitively selected according to the GRADE method for question 3.1.

Literature summary
Not applicable.

Considerations
The diagnosis of pain in patients with FSHD is not specifically aimed at FSHD but is a standard diagnostic process for pain. The American guideline for FSHD (Tawil et al. (2015) advises assessing pain routinely when treating FSHD. The physician first examines whether a cause for the pain can be established. To diagnose pain, medical history and physical examination are needed. The diagnostic process begins with a systematic anamnesis based on the biopsychosocial model in addition focused physical examination of the locomotor apparatus and the neurological status are needed. To rule out specific causes of pain such as cervical hernia or infectious lesions, referral to a neurologist (specialised in neuromuscular disorders) is recommended.

To get a view of the severity of the pain problem and the possible consequences, a physician can ask about biopsychological factors. These factors are within the ICF, in order to set up a treatment plan.

Type of pain: There are different types of pain that can occur simultaneously: nociceptive, neuropathic and central sensitisation pain. The type of pain determines the choice of intervention and any medication and/or interventional pain treatment. The working party advises informing patients about the various types of pain. Central sensitisation can be assessed by using the Central Sensitisation Inventory (CSI) (Mayer, 2012; Kregel, 2016).

Pain intensity: The experienced severity of the pain depends on different factors (biopsychosocial). Numerical and/or visual pain scales can be used to quantify pain severity. Commonly used measurement instruments to assess pain are the Visual Analogue Scale (VAS) (Padua, 2009) and the Numerical Rating Scale (NRS), ranging from 0 [no pain] to 10 [extreme pain]) (Jensen, 2008; Guy-Coichard, 2008; de Groot, 2013). The working party prefers the NRS (scale 1-10) to measure severity of pain in FSHD. This advice fits with the international recommendations for measuring pain (de Groot, 2013). It is also advised to measure pain at each medical specialist consultation and collect information on treatments that have been deployed already.

Pain location: Investigate where the pain is localised. The biopsychosocial approach takes physical, mental and social factors into account and forms the starting point for multidisciplinary care for pain.

Recommendations

Measure pain at each consultation with a medical specialist and take note of all treatments that have already been deployed.

Distinguish between different types of pain: nociceptive, neuropathic and central sensitisation pain.

Assess the severity of the pain, preferably measured with the Numerical Rating Scale (range 0 to 10) for patients with FSHD.

Determine the type of treatment based on the type and severity of the pain.

Discuss these recommendations with the patient.

Search and selection

3.2 What is the best pain treatment and care management for patients with FSHD?

Relevant outcome measures
For question 3.2 the working party assessed pain as relevant outcome measure. After consulting the full text, four articles ended up being definitively selected for question 3.2 – three systematic reviews and one RCT.

Strength of evidence from the literature
The methodological quality of the individual studies was assessed using evidence tables and the GRADE method.

The strength of evidence for the outcome measure of pain was lowered by two levels because of the low number of patients included in the studies (imprecision) and because there was only one study (two publications, in 2005 and 2007). Because RCTs begin with a high evidence of quality, the strength of evidence of the two studies was assessed as low-quality.

The strength of evidence for the outcome measure of shoulder pain was lowered by three levels because of the low number of patients included in the studies (imprecision), study design limitations (risk of bias), and inconsistency of study results.

Literature summary
Three systematic reviews and one RCT were found that answer question 3.2. For this question, specific attention was given to shoulder pain within the theme of pain.

<u>Pain</u>
The study of training and the effects of salbutamol, the primary outcome was strength, pain was a secondary outcome. Van der Kooi (2007) randomised 65 participants into a training (N=34) and a non-training group (N=31). Participants did maximum voluntary isometric strength training (MVIC) of the elbow flexors and ankle dorsiflexors. After 26 weeks the two groups were split up again and randomised into a salbutamol (albuterol) and a placebo group. Neither salbutamol nor maximal isometric strength training had an effect on pain. For the outcome measure of pain there were no significant differences between the training/non-training group and the salbutamol/no-salbutamol group.

The Cochrane systematic review of van der Kooi (2005) examined the effect of MVIC and aerobic training for various neuromuscular disorders. One single study was found that met the criteria for FSHD (Van der Kooi 2004). The intervention consisted of maximum isometric strength training of the

elbow flexors and ankle dorsiflexors. Pain was measured using the McGill Pain Questionnaire. Both the training and the non-training group had reduced pain in the neck, shoulder and elbow, but no significant differences were found between baseline and post intervention measurement.

Shoulder pain

The Cochrane review of Mummery (2003) investigated the evidence for effectiveness of scapular fixation techniques to improve upper body functions (especially for FSHD). Scapular winging is caused by weak thoracoscapular muscles. The review lists various past interventions to fixate the scapula. Two surgical techniques are known, scapulodesis and scapulopexy. No RCTs were found that studied the effectiveness of scapular fixation. For this reason, no statistical analyses were conducted in the Cochrane review that could provide a clear answer to the association between scapular fixation techniques and pain in FSHD.

The Cochrane review of Orrel (2010) is an update of the Mummery (2003) review. That review did not find any RCTs that measured the effects of shoulder fixation and of pain either.[5] The authors concluded that few surgeons are trained to perform shoulder fixation surgery.

Conclusions

Low GRADE	Pain Maximal isometric strength training (MVIC) and salbutamol appear to have no effect on the pain of patients with FSHD. Van der Kooi, 2007; Van der Kooi 2005

Very low GRADE	Shoulder pain The effect of treating pain through surgical fixation of the scapula has not been sufficiently studied. Mummery, 2003; Orrel, 2010

Considerations

The amount of research conducted so far into pain in FSHD is limited. It has to do partly with the elusive, subjective nature of pain. This is why treatment of pain for patients with FSHD is not specifically aimed at FSHD, but involves standard recommendations given for pain. The common opinion is that pain in FSHD patients should be treated in a multidisciplinary setting as is the common advice for treatment in pain.

The working party advises alertness for physical overload, which can worsen the pain. The balance between exertion and rest is very important for patients with FSHD. In some cases a soft or semi-rigid lumbar corset brace can provide additional stability to the trunk without getting in the way of daily activities (Rijken, 2014). Experience tells it is known that not every patient benefits from wearing such as corset to reduce pain.

When there is a treatable biomechanical explanation for the pain, or when psychosocial factors play a role, a variety of interventions can be considered. It is advised to always discuss the intended treatment with the patient. Depending on what the patient wants, the following interventions could be deployed in a multidisciplinary setting:

[5] One retrospective study was found (Krishnan et al. 2005) describing 22 patients (five with FSHD) with previous shoulder operations. That study found no significant difference in pain before or after the operation (P>0.05), and details for FSHD are not specified.

- *Exercise therapy:* The American guideline stated that physical therapists can often educate patients about the mechanism of pain (Tawil 2015).
- *Medication:* The American guideline (Tawil 2015) recommends prescribing medication as needed, depending on type of pain. This advice fits with the Dutch situation. For medicated treatment physicians follow a stepped approach, based on the pain ladder of the WHO (1986).
- *TENS (transcutaneous electrical nerve stimulation):* The effect of TENS on pain in FSHD has not been studied, and its use for chronic pain is not sufficiently proven. *Occupational therapy:* An occupational therapist thinks along with the patient when it comes to performing daily activities, for example when pain is involved. Proper analysis of the loading activity, subsequent advice on performing actions differently, and the use of aids can contribute to facilitate daily life. Reducing strenuous activities in the total activity pattern can also contribute to improve functioning. The recommendation in the Netherlands is that the treatment should preferably be given by an occupational therapist from a specialised musculoskeletal rehabilitation team
- *Pain treatment centre/pain team:* in suspicion of other causes of pain, patients would be referred to a pain clinic. Some known interventions are drug induced nerve root blocks and treatment of small peripheral nerves with radio frequencies.
- *Psychological intervention:* The most researched and applied interventions are graded activity and graded exposure. The working party does not recommend graded exposure for patients with FSHD, and graded activity has not been studied for these patients. The working party indicates that graded activity can be used in FSHD patients by physicians or paramedics specialised in neuromuscular disorders. Cognitive behavioural therapy, mindfulness and/or ACT (acceptance and commitment therapy) can also be used, although their effects on pain and FSHD have not been studied properly.
- *Alternative therapies:* The effects of alternative healing modalities on pain and FSHD have not been sufficiently studied.

Recommendations

FSHD patients should ideally be treated by an expert multidisciplinary team.

Define any treatment options for pain in consultation with the patient.

Literature chapter 3

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Chapter 4 Fatigue

Primary question: What is the best diagnosis and treatment strategy for fatigue (physical condition, movement, continuous load) in patients with FSHD?

4.1 What is the best method to assess fatigue in patients with FSHD?
4.2 What is the best treatment and care management for fatigue in patients with FSHD?

Introduction

Severe fatigue is experienced by more than 60% of patients with FSHD. Fatigue causes limitations in physical functioning and social participation in patients with FSHD, and leads to problems with concentration and planning (Kalkman 2005).

A distinction is made between experienced fatigue and physiological fatigue (Kalkman 2008). Experienced fatigue is defined as an overwhelming sensation of fatigue, lack of energy and feeling of exhaustion (Kalkman 2008). Physiological fatigue is defined as the inability to produce the original maximal strength during exertion.

FSHD patients also experience fatigue as a main symptom. In practice, FSHD patients do not always admit or recognise symptoms of fatigue. Not all physicians are aware of the treatment options, so adequate treatment for fatigue – if any – is not always offered.

In this chapter the working party offers a recommendation for treatment of fatigue in patients with FSHD.

Search and selection

To answer the primary question, a systematic literature analysis was conducted by formulating two research questions:

4.1What is the best method to assess fatigue in patients with FSHD?
4.2 What is the best treatment and care management for fatigue in patients with FSHD?

A literature search was conducted into the following databases:

- PubMed 1966-present
- Embase (OvidSP) 1887-present
- Embase (OvidSP) 1947-present
- MEDLINE (OvidSP) 1946-present
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO) 1985-present
- Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, 2015)

Because of the expected limited results, the literature search for questions 4.1 and 4.2 was merged.

These studies were selected based on the following selection criteria: systematic reviews of meta-analyses, RCTs, or other comparable research that describes and/or investigates the prevention and/or treatment of fatigue in FSHD. The literature search action yielded 590 results.

Based on title and abstract, 102 studies were preselected. After consulting the full text, 101 studies with different study designs were excluded, and a total of one study was definitively selected. Literature was found for one of the two research questions. No literature was found to determine the best method to measure fatigue, and one study was selected for the question about optimal treatment for or care management with fatigue.

To formulate the considerations, studies with different designs and/or a lower degree of scientific evidence were also included.

The evidence tables, the search criteria, the quality assessment and the exclusion table can be requested at Spierziekten Nederland.

Search and selection

4.1 What is the best method to assess fatigue in patients with FSHD?

Relevant outcome measures

For question 4.1 the working party assessed fatigue as a critical outcome measure.

After consulting the full text, no paper studies ended up being definitively selected based on the GRADE method for question 4.1.

Literature summary

Not applicable

Considerations

To optimally treat fatigue it is important to adequately identify the symptoms of experienced fatigue. To supplement the medical history, fatigue should be assessed using standardised measurement instruments. In 2010 the European NeuroMuscular Centre (ENMC) organised an international workshop about pain and fatigue in neuromuscular conditions (de Groot 2013). International agreements were made about specific instruments to measure pain and fatigue. The Numerical Rating Scale (NRS) for pain and the Checklist Individual Strength (CIS) as recommended to measure fatigue. It was also recommended to look at biological/biomechanical causes and measure forced vital capacity (de Groot 2013).

The NRS and CIS questionnaires are recommended in several studies. The NRS is preferred over the Visual Analogue Scale (VAS). A review by Hjermstad (2011) shows the NRS to be a universal scale that measures pain intensity. The NRS can also be used to measure fatigue. The fatigue subscale of the CIS has also been used in multiple Dutch studies to measure fatigue (Kalkman 2005, Kalkman 2007, Voet 2010, and Voet 2014).

The working party advises care coordinators to measure symptoms of fatigue at every patient visit. To measure the fatigue symptoms in patients with FSHD, the working party recommends using the NRS (for a short screening) and/or the regular CIS-fatigue).

Recommendations

At every visit, ask patients with FSHD about their fatigue symptoms.

Measuring fatigue is important for patients with FSHD. The Numerical Rating Scale or the fatigue subscale of the Checklist Individual Strength can be used to this end.

Search and selection

4.2 What is the best treatment and counselling strategy for fatigue in patients with FSHD?

Relevant outcome measures

For this question too, the working party assessed fatigue as a critical outcome measure. After consulting the full text, one paper study ended up being definitively selected for question 4.2 – an RCT (Voet 2014).

Strength of evidence from the literature

The methodological quality of this individual study was assessed using evidence tables and the GRADE method. The strength of evidence for the outcome measure of fatigue was lowered by two

levels because of the low number of patients included in the studies (imprecision) and because there was only one study. The evidence tables can be requested at Spierziekten Nederland.

Literature summary

The study of Voet (2014) investigated the effects of aerobic training and cognitive behavioural therapy in FSHD patients with severe experienced fatigue. The participants were randomly divided into three groups: 1) aerobic training, 2) cognitive behavioural therapy, and 3) a usual care control group. Aerobic training consisted of cycling for 30 minutes three times a week (+ warming-up and cool-down). Cognitive behavioural therapy was given by a cognitive behavioural therapist (at least three 50-minute sessions). Both treatments lasted 16 weeks. Outcome measurements were collected after 16 weeks and 28 weeks (period 1). After 28 weeks the control group received one of the interventions (period 2). After both 16 weeks and 28 weeks, aerobic training and cognitive behavioural therapy resulted in a significant improvement in experienced fatigue.

Conclusions

Aerobic training

Low GRADE	Fatigue Aerobic training has a positive effect on experienced fatigue in patients with FSHD, measured over a period of 16 weeks. Voet, 2014

Cognitive behavioural therapy

Low GRADE	Fatigue Cognitive behavioural therapy has a positive effect on experienced fatigue in patients with FSHD, measured over a period of 16 weeks. Voet, 2014

Considerations

Previous studies have investigated possible perpetuating factors for fatigue in FSHD. Physical inactivity appears to be an important factor (Kalkman 2007). Because of muscle weakness it is difficult for patients with FSHD to remain physically active. Pain and sleeping disorders are other factors that can perpetuate fatigue. This can lead to a vicious circle.

Fatigue can be a manifestation of nightly hypoventilation. Moderate to severe respiratory insufficiency is also found in one-third of wheelchair-bound patients with FSHD (Wohlgemuth 2017). The severity of the muscle weakness, kyphoscoliosis and wheelchair dependency are known risk factors for the development of respiratory insufficiency (Wohlgemuth 2004). Complaints of nightly hypoventilation and respiratory insufficiency should therefore be proactively asked about and assessed in patients with FSHD.

To reduce fatigue, ***cognitive behavioural therapy*** appears to have an added value for patients with FSHD. Cognitive behavioural therapy is a psychological treatment aimed at stimulating a physically active lifestyle and is based on the model of perpetuating factors of fatigue (Kalkman 2007). Cognitive behavioural therapy consists of six modules aimed consecutively at:

1. dysfunctional coping;
2. non-helpful cognitions about fatigue, activity, pain or other complaints;

3. catastrophising thoughts about fatigue;
4. sleep disorders;
5. inactivity or a fluctuating activity pattern;
6. discrepancy between expected and actual social support and interaction.

Cognitive behavioural therapy appears to be effective in stimulating an active lifestyle (Voet 2014).

Aerobic training also appears to have an added value towards reducing experienced fatigue in patients with FSHD (Voet 2014). Another study found no difference in fatigue (Andersen 2015). Andersen (2015) conducted research on the effect of aerobic training and a protein supplement. Fatigue was a secondary outcome measure (n=41). Training consisted of cycling three times a week (70% of the VO2max) for 12 weeks. The test subjects were divided into three groups: 1) aerobic training with protein supplement (n =18), 2) aerobic training with placebo supplement (n =13), and 3) a control group (n=10). Neither 12 weeks of aerobic training nor protein supplementation had a significant effect on experienced fatigue. The differences in effect between the studies of Voet (2014) and Andersen (2015) could be explained by an increase in the degree of physical activity measured in the Voet study, in contrast to Andersen's. The working party hypothesised that an increase in daily physical activity in case of disuse is essential towards limiting experienced fatigue. In addition, severe experienced fatigue was an inclusion criterion in the Voet study, but not in Andersen's. This increases the chances of seeing a decrease in experienced fatigue.

The American guideline for FSHD (Tawil 2015) describes aerobic training as safe and effective, the same as for other neuromuscular disorders. Aerobic training is important for general health. It is nevertheless recommended to adapt the training to the possibilities of the patient by using low/moderate resistance. The American working party recommends training under the supervision of a physical therapist (Tawil 2015). This is not necessary on a constant basis, but guidance from a physical therapist before starting the training and with a low frequency (twice a year) during the programme is advised. Adapt the training to the possibilities of the patient. For advice and for any questions about training, care providers can contact the FSHD Expert Centre of Radboudumc or another neuromuscular rehabilitation team; to this end, visit www.spierziekten.nl/zorgwijzer.

The Energiek rehabilitation programme combines aerobic training with education about training as well as coaching and energy management, integrated with sustainable implementation in daily life (Veenhuizen et al., BMC Neurol 2015). This outpatient rehabilitation treatment consists of a combination of physical therapy and occupational therapy. Energy management is aimed at optimal use of the energy available in daily life (Mathiowetz 2007). This energy-management coaching is given by occupational therapists and targets everyday situations that all individuals encounter (Packer et al, 1995). This coaching – i.e. supporting the application of energy-saving strategies – has not been specifically studied for FSHD but has been researched for other neurological conditions (Mathiowetz et al., 2007). The Energiek programme has been researched for clinical and cost effectiveness in a multicentre RCT (Veenhuizen, et al, 2015), and definitive results are expected in 2018.

Submaximal strength training and salbutamol, as described in the study of van der Kooi 2007, do not lead to an improvement in fatigue Van der Kooi 2007, Van der Kooi 2004) This was a secondary outcome measure. The study of Voet, fatigue was a primary outcome. Cognitive behavioural therapy as well as aerobic training have been proven effective in reducing experienced fatigue. No research has yet been conducted to find out which therapy is most effective for which type of patient. When choosing between the two treatments it is recommended to take into account the wishes and preferences of the patient. It is also recommended to consider cognitive behavioural therapy if there are additional perpetuating factors of fatigue other than just physical inactivity. The principle of stepped care can be applied, by already using motivational interviewing techniques during consultations to motivate patients to become more active.

Lifestyle also seems to be an important factor affecting fatigue, but no studies are available. Based on patient experiences, weight seems to play a special role. The association between overweight or underweight and fatigue in FSHD has not yet been studied. Based on the experience of the working party, it is recommended to implement energy-saving strategies with optimal use of the available energy and an adequate input of aids, under the guidance of an occupational therapist and possibly a psychologist.

Recommendations

Consider cognitive behavioural therapy to reduce severe fatigue symptoms in patients with FSHD, targeting perpetuating factors that apply to the patient. Deploy the principle of stepped care with minimal involvement of a psychologist in treatment programmes and diagnoses.

Consider referral to a multidisciplinary individual or group rehabilitation programme (e.g. Energiek) aimed at aerobic training, education about training and energy-management coaching, integrated with sustainable implementation in daily life.

Consider using occupational therapy to coach energy-saving strategies and adequate use of aids.

Consider aerobic training by a specialised physical therapist to optimise severe fatigue symptoms in patients with FSHD:

- adapt the training to the possibilities of the patient;
- consider coordinating the training programme in consultation with the FSHD Expertise Centre or one of the neuromuscular rehabilitation teams;
- pay attention to physical inactivity. Reducing physical inactivity seems essential towards optimising experienced fatigue in patients with FSHD.

Literature chapter 4

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Chapter 5 Mobility

Primary question: What is the best treatment and care management for mobility problems of patients with FSHD defined as balance and gait problems?

5.1 What is the best method to measure the balance and gait of patients with FSHD?
5.2 What is the value of physical training to improve the mobility of patients with FSHD?
5.3 What is the value of fall prevention training to maintain or improve the mobility of patients with FSHD?
5.4 Which aids and adjustments play a role in maintaining or improving the mobility of patients with FSHD?

Introduction

Patients with FSHD develop reduced muscle strength in the trunk, the pelvis and the lower extremities, which results in postural, balance and gait limitations (Rijken 2014; Horlings 2009). This can lead to reduced functional mobility and increased inactivity, further reducing muscle function and quality (due to inactivity), physical endurance, and energy levels. This can limit options to engage in activities and, consequently, to participate in social interactions and maintain social contacts (Rijken 2014; Horlings 2009).

Patients with FSHD have a reduced gait speed, and foot dorsiflexor paresis is often present (Iosa 2007). Because of the reduced mobility and balance, patients with FSHD are six times as likely to fall than healthy controls (Horlings 2009). Falls constitute a major risk of injuries, and can also lead to fear of falling and, thus, to further inactivity (Pieterse 2006). Patients with FSHD tend to fall forward. This happens most frequently at home, for example when climbing stairs or when getting up from a chair (Horlings 2009). The fatigue and pain – sometimes severe – of a large proportion of FSHD patients (Kalkman 2005) can further worsen mobility and balance (see also Chapters 3: Pain and 4: Fatigue).

Search and selection

To answer the primary question, a systematic literature analysis was conducted by formulating four research questions:

5.1 What is the best method to measure the balance and gait of patients with FSHD?
5.2 What is the value of physical training to improve the mobility of patients with FSHD?
5.3 What is the value of fall prevention training to maintain or improve the mobility of patients with FSHD?
5.4 Which aids and adjustments play a role in maintaining or improving the mobility of patients with FSHD?

A literature search was conducted into the following databases:

- PubMed 1966-present
- Embase (OvidSP) 1947-present
- MEDLINE (OvidSP) 1946-present
- Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, 2015)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO) 1985-present

Because of the expected limited results, the literature search for questions 5.1 to 5.4 was merged.

Studies were selected based on the following selection criteria: systematic reviews of meta-analyses, RCTs, or other comparable research; assessment of treatment for mobility in FSHD and the outcome measures used were included. The literature search action yielded 501 results.

Based on title and abstract, 42 studies were preselected by the working party. After consulting the full text, 38 studies were excluded and a total of four studies with different research designs were definitively selected. Literature was found for one research question (5.2).

The evidence tables, the search criteria, the quality assessment and the exclusion table can be requested at Spierziekten Nederland.

To formulate the considerations, studies with different designs and/or a lower degree of scientific evidence were also included.

Search and selection

5.1 What is the best method to measure the balance and gait of patients with FSHD?

Relevant outcome measures
For question 5.1 the working party assessed balance, mobility and gait as critical outcome measures. After consulting the full text, no paper studies were definitively selected for question 5.1.

Literature summary
Not applicable.

Considerations
Two studies (Iosa 2007 and Rijken APMR 2015) measured balance, gait and mobility in patients with FSHD. Both are exploratory studies and were therefore not graded according to the GRADE method.

Balance and gait: The study of Rijken (APMR 2015) assessed four anti-gravity tests on a small group of subjects with and without FSHD. The anti-gravity tests consisted of sit-to-stand, stand-to-sit, step-up and step-down. These were compared with conventional tests to measure mobility (six-minute walking test (6MWT), 10-meter walking test, Berg Balance Scale, and Timed Up and Go). Conventional tests allow for compensatory strategies because the strength of the trunk, the pelvis and the legs is not challenged enough. As a result, those tests give overestimated results. Results show that anti-gravity tests have a clinically stronger correlation with disease severity than conventional tests (Rijken, APMR 2015). Because a small number of patients (n=19) included, additional research would have to be conducted.

Mobility: The study of Iosa (2007) examined an instrumented movement analysis making use of a 9-camera stereo photogrammetric system to measure the mobility of a small group of subjects with and without FSHD (both n=12). The subjects had to perform four tasks: arm movement, walking, getting up and squatting. The manual muscle strength test, the clinical severity scale (CSS) and magnetic resonance imaging were also used to clinically assess the subjects.

The analyses yielded that gait speed and the shifting of balance when squatting were reduced in patients with FSHD. Additionally, reduced mobility was seen in the shoulder joint, excessive ankle plantar flexion when walking and getting up, and reduced knee flexion-extension motion when squatting. An instrumented movement analysis could help measure the mobility of patients with FSHD. No clear answer can be given yet in this respect due to the small number of patients in this study. Further research with a larger cohort is warranted.

Functional mobility is an important topic to inquire about, examine and monitor in patients with FSHD. Specific questions about frequency, mechanism and circumstances of stumbling and falling, and the influence of fatigue (prolonged load) should be included. An inventory of the ability to go up and down stairs, get up from a chair and sit back down, get up from the ground and walk upwards/downwards can give a good indication of an individual's functional balance and gait (Horlings, JNNP 2009). To supplement the medical history, gait and balance should be assessed by observing these capacities under different conditions and by administering manual strength tests and conventional functional tests (such as the six-minute walking test (6MWT), 10-meter walking test, Berg Balance scale and Timed Up and Go). Supplementary, simple anti-gravity tests (sit-to-stand, stand-to-sit, step-up, step-down) (Rijken APMR 2015) can be useful because such tests allow for fewer compensatory mechanisms than conventional functional tests. Besides an assessment in a test environment, an analysis in and of the home situation by an occupational therapist can yield relevant information.

To monitor mobility and balance in time and thus timely anticipate any training indication, use of aids and/or essential environmental adjustments, regular assessments are necessary – at least once a year. An ample selection out of the listed strength and functional tests should be used. A specialised primary-and secondary-care physical therapist can play an important, supportive role in this process.

Recommendations

When conducting a medical history and physical examination in patients with FSHD, pay attention to functional ability and balance skills using clinimetric tools such as the six-minute walk test (6MWT), 10-meter walking test, Berg Balance Scale, and Timed Up and Go.

Ask specific questions about frequency, mechanism and circumstances of stumbling and falling, keeping the influence of fatigue (prolonged load) in mind. Have the patient keep a fall diary if necessary.

Consider using simple anti-gravity tests (sit-to-stand, stand-to-sit, and step-up, step-down). These tests constitute a useful supplement to standard physical examinations and conventional functional tests.

Regular assessments, at least once a year, are recommended to monitor mobility and balance in FSHD over time so that deterioration can be detected.

NOTE: THESE RECOMMENDATIONS ARE BASED ON EXPERT OPINION AND EXPERIENCE WITH SIMILAR CONDITIONS. THEY SHOULD BE FURTHER EXAMINED AND ASSESSED FOR FSHD.

Search and selection

5.2 What is the value of physical training to improve the mobility of patients with FSHD?

Relevant outcome measures

For question 5.2 the working party assessed balance, gait and mobility as critical outcome measures, and muscle strength, physical activity and aerobic capacity as relevant outcome measures.

After consulting the full text, four articles were definitively selected for question 5.2 (Andersen 2015, Voet 2013, Voet 2014, and Van der Kooi 2004).

Strength of evidence from the literature
In the systematic review by Voet (2013), the methodological quality of the individual studies was assessed for FSHD using evidence tables and the GRADE method. The evidence tables can be requested at Spierziekten Nederland.

The strength of evidence for the outcome measure 'mobility' was lowered by two levels because of the low number of patients included in the Andersen study and because only one study was found for this outcome measure (imprecision).

The strength of evidence for the outcome measure 'muscle strength' for the two studies was lowered by two levels because of the low number of patients included in the studies (imprecision) and the limited extrapolation potential of the two different studies (treatments differed between the studies in terms of content and duration) (inconsistency).

The strength of evidence for the outcome measure 'aerobic capacity' was lowered by two levels because of the low number of patients included in the studies, and again because it concerned only one study (imprecision).

Literature summary
Three RCTs and one systematic review were found that address question 5.2.

Description of the studies
Muscle strength (strength training): The systematic review by Voet (2013) includes a total of five studies that measured the effect of training (strength and aerobic) in neuromuscular disorders. Only one study investigated the effect of submaximal strength training in FSHD (Van der Kooi 2004). The other studies examined different neuromuscular disorders.

Muscle strength and aerobic capacity and mobility (aerobic training): The literature search yielded two studies (Voet 2014, Andersen 2015) that investigated the effect of aerobic training on the outcome measures muscle strength and aerobic capacity. Andersen (2015) studied 41 test subjects with FSHD. The test subjects were randomised into three groups: 1) aerobic training with protein supplement (n =18), 2) aerobic training with placebo supplement (n =13), and 3) a control group (n=10). The training consisted of cycling three times a week (70% of the VO2max) for 12 weeks.

Voet (2014) investigated the effects of aerobic training and cognitive behavioural therapy in fatigued FSHD patients. The subjects were randomised into three groups: 1) aerobic training, 2) cognitive behavioural therapy, or 3) a control group. The aerobic training consisted of cycling three times a week (starting from 60% to 75% of the heart rate reserve (HHR)) for 30 minutes plus warm-up and cool-down). HHR is the difference between maximum and resting maximal oxygen uptake (VO2max). The cognitive behavioural therapy was given by a psychologist (at least three 50-minute sessions) and was based on known fatigue-perpetuating factors. Participants trained for 16 weeks with a 12-week follow-up (period 1). After 28 weeks the control group received one of the interventions based on a second randomisation (period 2).
Results of studies per outcome measure
1) Muscle strength (aerobic training): The study of Andersen (2015) showed no significant differences in maximal strength (of the elbow flexors/extensors and knee flexors/extensors) in either the aerobic training group or the protein supplement group. The study by Voet (2014) showed significant differences in maximal strength of the m. quadriceps in the aerobic training group (versus the control group) after 16 weeks. This was not the case for the behavioural therapy group: after 12 weeks follow-up no significant differences were found in quadriceps strength between the aerobic training group and the control group.
Muscle strength (strength training): The studies by Van der Kooi (2004) and Voet (2013) showed no significant differences between the training and control groups. Strength training was not harmful either. Van der Kooi (2004) showed that only submaximal strength training resulted in a

significant increase in dynamic strength of the elbow flexors, which was 1.17 times higher in the training group than in the control group.

2) Aerobic capacity: To assess aerobic capacity, Andersen (2015) used a maximum cycling exertion test to measure VO2max. Voet (2014) used a submaximal Åstrand cycling test to calculate VO2max.

- Andersen (2015) showed that aerobic training improved VO2max by 9.5% (CI 4–15%) (p=0.002). The control group and the protein supplement group showed no significant differences. The difference between the training group and the control group was 6.4% (CI 3-10%) (p = 0.001). The level of clinical relevance of the improved VO2max was not clear.
- Voet (2014) found that VO2max did not improve after 16 weeks of aerobic training or cognitive behavioural therapy.

3) Mobility: This search yielded one study that examined the association between aerobic training (with and without protein supplementation) and mobility (Andersen, 2015). Mobility was defined in operational terms and assessed with the 1) 5x sit-to-stand test; 2) 14-step-stair test; 3) standing balance test; and 4) physical symptoms questionnaire. Aerobic training and protein supplementation had no effect on the functional ability of patients with FSHD.

Conclusions

Low GRADE	Mobility Aerobic training does not improve the functional mobility of patients with FSHD. Andersen 2015

Low GRADE	Muscle strength There are few indications that submaximal strength training can improve the muscle strength of patients with FSHD (measured over a period of one year). Van der Kooi 2004; Voet 2013

Low GRADE	Muscle strength There are few indications that aerobic cycling training can improve the strength of the m. quadriceps in patients with FSHD measured over a period of 16 weeks. Voet 2014

Low GRADE	Aerobic capacity There are few indications that aerobic training can improve the VO2max in patients with FSHD measured over a period of 12 weeks. Andersen 2015

Considerations

Aerobic training (cycling and general) in patients with FSHD seems to have an added value for improving aerobic capacity, muscle strength in the upper legs, physical activity and fatigue, yet these favourable effects were not proven for functional mobility or balance (Van der Kooi 2004; Andersen 2015; Voet 2014). This latter conclusion should be drawn with caution, because only the study by Andersen (2015) included functional mobility as an outcome (in the form of simple functional tests

and a questionnaire). Aerobic training may improve mobility and balance problems that develop or increase with fatigue and prolonged load, but this has never been studied. The 16 weeks of aerobic training and cognitive behavioural therapy in the study by Voet (2014) also showed improvement in physical activity immediately after the intervention as well as after 12 weeks follow-up. Submaximal strength training did not lead to an improvement in strength of the trained muscles, neither did it lead to muscle damage or reduced muscle strength (Van der Kooi 2004). There may nevertheless be a carryover effect with an increase in strength in non-trained muscles (Van der Kooi 2004). Hence, there does not seem to be a contraindication for muscle strength training in FSHD (Van der Kooi 2004), but one should be prevent overtraining. Strength training of specific muscle groups (such as the iliopsoas and the gluteus maximus, both relatively unaffected by FSHD) or trunk stability training can result in useful compensation to optimise gait and balance capacities, especially if disuse is suspected (Rijken 2014). Disuse is defined here as loss of muscle strength and volume due to a lack of physical activity.

Recommendations

Consider aerobic training (cycling or general) for patients with FSHD. It appears to have an added value for improving aerobic capacity, physical activity and fatigue (see Chapter 4). Aerobic training may improve functional mobility and balance problems that develop or increase with fatigue and prolonged load, but this has not been studied.

Consider strength training, especially when disuse is suspected. Strength training of preserved muscles such as the iliopsoas and gluteus maximus or trunk stability training can be considered for compensation to optimise gait and balance capacities under the guidance of a physical therapist specialised in neuromuscular disorders.

NOTE: THESE RECOMMENDATIONS ARE BASED ON EXPERT OPINION AND EXPERIENCE WITH SIMILAR CONDITIONS. THEY SHOULD BE FURTHER EXAMINED AND ASSESSED FOR FSHD.

Search and selection

5.3 What is the value of fall prevention training to maintain or improve the mobility of patients with FSHD?

For question 5.3 the working party assessed balance and gait, mobility and incidence of falls as critical outcome measures. After consulting the full text no paper studies were definitively selected for question 5.3.

Literature summary

Not applicable.

Considerations

Many patients with FSHD are more prone to falling (>1 fall per year and/or having difficulty with walking); 65% fall once a year and 30% fall more than once a month (Horlings, 2009), and a minority stumble regularly. Risk factors for falling in FSHD patients are reduced strength of the lower and upper leg muscles and of the pelvic and trunk muscles (Horlings 2008; Orr 2010). Reduced strength of the lower leg muscles involves the tibialis anterior (mostly early) and the calf muscle (usually later). This lowers the effectiveness of ankle strategies (primary strategies to maintain balance in the sagittal plane) and increases the chance of stumbling. Reduced strength of the upper leg muscles involves the quadriceps and the hamstrings, therefore hip strategies (secondary strategies to maintain balance in the sagittal plane) and stepping strategies (including reactive stepping upon external perturbations) are less effective. When pelvic and trunk muscles are affected (especially m. rectus abdominis and m. erector spinae), the consequences are detrimental to the trunk stability that is needed for all balance strategies. This will also necessitate compensatory adaptation of posture (including lumbar hyperlordosis) (Rijken 2014). Studies on the frequencies of fractures, trauma's wrist and hip fractures are not available.

An increased risk of falling also entails an increased risk of injuries due to falls as well as fear of falling. These negatively affect the activity level and, thus, functional mobility, balance, energy level and well-being. Once patients develop fear of falling, they often find themselves in a vicious circle of inactivity and further loss of motor skills. Specific fall training that teaches patients how to best break a fall can have a positive effect on fear of falling, thereby reducing potential functional deterioration and progressive risk of falling. Fall training has no direct effect on the risk of falling, yet there is a chance that an increased risk of falling is partly determined by disuse related to inactivity and fear of falling. This disuse can be at the level of the muscles (atrophy, weakness) or at the level of the central nervous system (loss of coordination and skills). To the degree that disuse is plausible, functional training of simple and more complex balance and gait skills can be considered to regain at least part of the preventable capacity loss. Such training should preferably be combined with specific fall prevention training. Fall prevention training is important to lower the risk of falling and fear of falling. This involves a detailed analysis of any fall incidences and mechanisms of increased fall risk and a subsequent evaluation of alternatives for safe displacement (see 5.4).

Recommendations

To target increased risk of falling (>1 fall per year and/or having difficulty with walking) in patients with FSHD, consider fall training. Patients are taught how a fall can be broken/caught, and chances of injury can be reduced.

When disuse is suspected, consider supplementary functional training of (complex) balance and gait skills. This can be useful towards regaining preventable loss of motor capacities and lowering the risk of falling.

NOTE: THESE RECOMMENDATIONS ARE BASED ON EXPERT OPINION AND EXPERIENCE WITH SIMILAR CONDITIONS. THEY SHOULD BE FURTHER EXAMINED AND ASSESSED FOR FSHD.

Search and selection

5.4 Which aids and adjustments play a role in maintaining or improving the mobility of patients with FSHD?

For question 5.4 the working party assessed balance and gait, mobility and incidence of falling as critical outcome measures.

After consulting the full text no paper studies were definitively selected for question 5.4.

Literature summary

Not applicable.

Considerations

Ankle dorsiflexor paresis occurs early in the course of the disease process in patients with FSHD. At first it tends to manifest when walking long distances, and later on it is present in every walking motion. In a mild paresis reduced dorsiflexion leads to an accelerated first rocker, because after heel strike the foot can no longer be controlled when loaded. In a more severe paresis the foot may ‘drag’ because the toes will touch (or almost touch) the ground during the swing phase of gait. A dragging foot will lead to an enhanced risk of stumbling, possibly resulting in a fall incident. The latter will occur even more easily if the calf muscles are also weakened because, when stumbling, calf strength of the stance leg (based on push-off power) is extremely important so be able to catch up with the forward acceleration of the body (Pijnappels 2005 & 2008). Loss of push-off power Weakness of push-off power will also lead to reduced walking speed, particularly if there is additional weakness of the trunk muscles (Rijken 2015).

Especially the consequences of ankle dorsiflexor weakness can be managed with an ankle-foot orthosis (AFO). When providing an AFO, it is important to maintain as much ankle mobility and residual push-off power as possible by using lightweight, dynamic posterior AFOs. If the calf muscle is weakened to such an extent that there is hardly any active push-off and the risk of increased knee flexion is imminent during the stance phase, a stiffer AFO providing anterior support to the leg (using the energy conservation principle) would be the preferred option to preserve as much energy as possible during gait. In the case of severe weakness of the thigh muscles (especially the quadriceps), a knee-ankle orthosis (KAFO) can be indicated. The orthosis should be as lightweight as possible and preferably be equipped with a movable knee hinge with stance-phase stabilisation. To indicate the best orthosis and evaluate it functionally, it can be helpful to use instrumented (3D) gait analysis (see above). The final choice is always made in consultation with the patient, based on the patient's experiences and needs. Activities other than walking should be taken into account, such as climbing stairs, squatting, kneeling, cycling, and driving a car, sports and work.

For patients with FSHD who are severely limited due to decreased strength of the trunk muscles, a dynamic thoracolumbar brace could improve posture and balance (Rijken 2014; King and Kissel 2013). Trunk stability can especially benefit from such a brace during simple daily activities. A brace does present limitations though, because of the reduced freedom of movement, especially during more complex activities such as turning, bending and reaching. Hence the pros and cons have to be weighed against each other. This should be assessed together with the patient, in terms of the activities a brace is useful for and/or the degree to which production of such a relatively expensive customised aid is purposeful. When providing a leg orthosis or for a thoracolumbar brace it makes sense, whenever possible, to have a testing period with a temporary (try-out) orthosis before actually indicating and manufacturing a custom-made aid.

Walking aids such as a cane, Nordic walking sticks, or a walker can considerably support the individual balance and gait capacities of patients with FSHD. A cane is generally used *unilaterally* for balance problems to compensate for instability in one leg (e.g. hip weakness). If there is leg instability, the cane is used on the contralateral side of the body. With *bilateral* leg instability or severe balance problems, a walker is often more suitable than the use of two canes, because with a walker one can carry things, or even take a rest if the walker has a seat and solid brakes. The disadvantage of a walker is that one tends to walk with the trunk slightly bent forward, which can be uncomfortable and tiring because the back and trunk muscles are loaded differently. In such cases a posterior walker can be considered. Nordic walking sticks are almost always used *bilaterally* and are primarily useful for balance support, not for carrying weight in the case of weakness of the leg muscles. They allow for a more active gait and are also suitable for walking on irregular terrain (e.g. in wooded areas). The most suitable length for Nordic walking sticks has to be assessed individually. This length is often shorter than for healthy persons, because with FSHD they are mainly used for balance purposes and less for propulsion support.

Biomechanical limitations can negatively influence the gait pattern of FSHD patients, which requires attention for the lower extremities as well as for the thoracolumbar spine and shoulders. Examples are shoulder muscle weakness/pain that affect gait (less arm sway, postural changes) and a lower ability to properly use walking aids.

Walking aids and/or orthoses should always be used on prescription and should be trained – the latter especially in the case of anteriorly supported AFOs. From a safety perspective, it is absolutely necessary that some FSHD patients use these aids at all times. For other patients the need is relative, depending for example on the level of fatigue or type of activity planned. It is therefore important for patients to regularly discuss proper use of walking aids and orthoses with the treating rehabilitation physician and/or physical therapist. Together with the patient one should examine his/her individual situation and wishes, modifying clinical advice accordingly in terms of walking aids and/or orthoses.

Depending on the situation, in addition to walking aids and/or orthoses, alternative aids can be considered for safe movement at home and outside, such as a triple chair, wheelchair, walking bike or scooter. It is very important to make such choices together with the patient with the aim to prevent unnecessary risks and/or undesirable energy loss while walking.

Recommendations

Indicate an ankle-foot orthosis (AFO) to compensate for ankle dorsiflexor weakness in FSHD. Aim to use lightweight, dynamic posterior AFOs to preserve as much push-off power as possible.

If there is severe calf muscle weakness, consider a stiffer AFO with anterior support that uses the energy-conservation principle.

If there is disabling trunk muscle weakness, assess the usefulness of a dynamic thoracolumbar brace, preferably at (or in consultation with) an FSHD Expertise Centre.

When considering an orthosis, always discuss its use with the patient, weighing its pros and cons for all daily activities as well as its efficiency (cost versus effectiveness).

Indicate a walking aid (such as a cane, Nordic walking sticks, walker) for balance problems to increase safety and walking distance.

Walking aids can also be used to compensate for weakness of the leg muscles, but Nordic walking sticks are not suitable for this purpose.

NOTE: THESE RECOMMENDATIONS ARE BASED ON EXPERT OPINION AND EXPERIENCE WITH SIMILAR CONDITIONS. THEY SHOULD BE FURTHER EXAMINED AND ASSESSED FOR FSHD.

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Chapter 6 Communication (facial expression, speech)

Primary question: How can patients with FSHD be best supported in terms of communication (privately, at work, in care settings)?

6.1 What is the best way to support FSHD patients with reduced facial expression and speech problems to improve communication (in the private and work domains)?

6.2 What recommendations are given for the communication between physician and patient that lead to focused questions about specific FSHD-related problems?

Introduction

Patients with FSHD regularly deal with communication problems, among other reasons because of their facial weakness and subsequent reduced facial expression. Their facial expressions can be misunderstood. Research by Swearingen (1998) shows that patients with facial weakness can be physically and socially affected when dealing with other people and their reactions. As a result of the facial weakness they can experience a diminished sense of well-being, lower self-esteem, fear, depression and social isolation, as well as personal and work-related problems.

The psychosocial influence of the disease also plays a role in communication. The study of Bakker (2016) and the bottleneck analysis among patients both show that a diagnosis of FSHD can have a great impact. The course of the disease is unpredictable. Bakker (2016) showed that learning to deal with loss of function, wheelchair dependency and walking with aids all have a major influence on daily life. This insecurity can sometimes unlock intense emotions. It is important for physicians to show understanding towards the reactions of patients with FSHD. Feelings of powerlessness, shame, panic, fear and gloom are very common reactions to the situation.

Offering support with communication and making problems open to discussion are therefore essential. In this chapter the working party gives a recommendation on how to deal with communication problems due to FSHD.

Search and selection

A systematic literature analysis was conducted for the chapter on communication. This search did not yield concrete results to write conclusions according to the GRADE method. The working party developed this chapter of the guideline according to the consensus-based guideline development method.

Literature summary

No literature was found that yielded concrete results to write conclusions according to the GRADE method.

6.1 What is the best way to support FSHD patients with reduced facial expression and speech problems to improve communication (in the private and work domains)?

Considerations

FSHD (facioscapulohumeral muscular dystrophy) is an inherited muscle disorder that most often manifests with weakness of the muscles of the face (facies), the shoulder blade (scapula) and the upper arms (humeri). Weakness of the facial muscles varies in severity, and can present in different ways such as an inability to (fully) close the eyes, to (forcefully) close or pucker the lips, or to whistle. Another important, yet less frequently reported, is the reduced facial expression caused by this muscle weakness (Mul, 2016).

A bottleneck analysis among patients showed that the facial weakness, often resulting in a reduced facial expression, can lead to problems in verbal as well as nonverbal communication:

1. ***Nonverbal communication*** *can be disturbed as a result of facial weakness.*
    - **Facial expressions will often show an emotion other than intended.** The general message that the body is sending (posture and facial expression) lead to misinterpretation of the message sent. Hanging shoulders, an inability to smile, and limited use of emotional motor functions (such as looking surprised, angry or happy) can give an impression of the patient being disinterested. Patients with asymmetric facial weakness are sometimes mistaken for stroke patients.

2. *In terms of* ***verbal communication****, intelligibility is often diminished.*
    - The muscle weakness may affect **articulation**. This is most pronounced for sounds in which lips play an important role.
    - **Speech** is sometimes less melodic and has fewer accents.
    - Loudness and quality of voice and speech can also be diminished due to a slumped posture (kyphosacral sitting) and/or fatigue.

The bottleneck analysis shows that paying attention to the communication problems (verbal and nonverbal) as a result of reduced muscle strength in patients with FSHD is essential when counselling and/or guiding them. Physicians are advised to be aware that FSHD patients are less intelligible and suffer from facial weakness, with potential consequences as described above. The working party also recommends actively asking during consultations about the problems that FSHD patients may experience as a result of speech limitations and facial weakness, at work as well as at home. This gives patients the possibility to discuss the problems openly and/or become aware of them. Patients can be referred to a specialised social worker or a psychologist as needed. If there are speech problems, it is recommended to promptly involve a speech therapist with specific expertise in neuromuscular diseases. Muscle weakness in FSHD can also lead to mild swallowing problems. A speech therapist specialised in neuromuscular disorders can counsel and offer help in this respect.

Suggestions for the physician:
- Verify the message and check the interpretation of the patient (am I right that you are angry?).
- Patients can be less intelligible when fatigued, for example on the telephone (at the end of the day). Preferably, do not schedule telephonic consults with FSHD patients at the end of the day.

Recommendations

Be aware of potential communication problems resulting from reduced intelligibility and facial expressions.

Verifying the message and check the interpretation of the patient regularly during consults.

If speech or swallowing problems occur, refer to a speech therapist with specific expertise in neuromuscular diseases.

During consults, make facial weakness and any limitations caused by it openly discussable, and refer to a professional such as a specialised social worker or a psychologist as needed.

6.2 What recommendations are given for the communication between physician and patient that lead to focused questions about specific FSHD-related problems?

Considerations

Communication with FSHD patients and their relatives remains an important focus even after the diagnosis has been established (at check-up appointments after an initial consultation). Because of

the progressive nature of the disease it is important for patients to keep being able to express themselves as well as possible. How patients are approached, and how well a physician listens and continues to ask questions (also about those things that are not going well) are essential. Continuing to proactively ask for potential issues is imperative. The working party advises to point out and discuss communication problems (resulting from the facial weakness and speech limitations) during the consultation. Below are some suggestions that lead to focused questioning.

Suggestions for communication between physician and patient

- **Patients get used to a body that functions less well.** The disease often progresses slowly. Ask the patient to answer a question in which they sketch themselves next to a healthy person of the same age. For example, instead of asking: *Can you walk up the stairs?* Preferably ask *Can you walk up the stairs like an average person of your age does?* Other questions, for example about walking distance, household chores, etc., can be asked in the same way. Be aware that FSHD patients often push their boundaries.
- **People often do not understand.** In addition to muscle deterioration, less visible complaints such as fatigue and pain also contribute to the disease burden. Fatigue, pain and beginning/ongoing muscle weakness are not always visible. As a result, other people may not understand these issues.
- **Pay attention to how families with FSHD communicate information.** Even if several family members have already been diagnosed with FSHD, presumed knowledge or information about the disease may be lacking. It is good to be aware that, for all kinds of reasons, in some families the disease is hardly talked about, if at all.
- **Work situation.** Ask about the patient's employment status and work situation. Work-related problems are common among patients with FSHD. Some patients are deemed partially or totally unfit for work as a result of the disease. Also discuss whether the patient has noticed his employer about the and whether it has already been discussed with company physician.
  For young adults, timely career planning, like study and work choices, is advised. Recommendations for progressive neuromuscular disorders often entail attaining the highest possible educational level and choosing a job that is not physically taxing.

Recommendations

During consults, ask proactively about any verbal or nonverbal communication problems.

Recommendations for focused questioning:

- Patients get used to a body that functions less well. Be aware that patients often push their boundaries. Ask about their self-image too.
- Take into account a possible lack of understanding from the patient's surroundings.
- Observe how families with FSHD communicate information.
- Ask about the patient's work situation.
- With younger patients, timely discuss career plans like study and work choices.

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Chapter 7 Organisation of the care

Primary question: What is the best way to organise the care for patients with FSHD?

7.1	**Who coordinates the care process, and what other care providers are involved in the optimal care of patients with FSHD in its various phases?**
7.2	**What is the role of the FSHD Expertise Centre?**
7.3	**What is the role of Spierziekten Nederland in the education of patients with FSHD?**

Introduction

Some patients will not need to involve a physician. This is probably because the disease progresses slowly and is not noticed, or because the patient knows about the clinical picture from the family and thinks that there is no treatment for it. There are also patients who do not want the diagnosis on record for insurance or work-related reasons. This can cause the diagnosis to be established or confirmed relatively late. The care for patients with FSHD is currently not aimed at curing but at: 1) timely detection of complications, symptom alleviation, psychosocial support, and reduction of pain and fatigue; 2) maintenance/improvement of functioning, activities and participation; 3) counselling of patients and their relatives; 4) maintaining independence at work and at home, and preserving the quality of life of patients and their families.

Search and selection

A systematic literature analysis was conducted for the chapter on organisation of care. This research did not yield concrete results to write conclusions according to the GRADE method. The working party developed this chapter of the guideline according to the consensus-based guideline development method.

Literature summary

No literature was found that yielded concrete results to write conclusions according to the GRADE method.

7.1 Who coordinates the care process, and what other care providers are involved in the optimal care of patients with FSHD in its various phases?

Considerations

FSHD is a progressive condition with a complex demand for care and with major differences between patients in terms of symptoms and course of the disease. The working party considers that patients with FSHD benefit from a care coordinator (main care provider). The working party has defined three phases in the care for FSHD: a diagnostic phase, a treatment phase and an end-of-life phase.

Care coordinator

It is important for the coordinator to have specific expertise in FSHD. The coordinator is familiar with FSHD, coordinates the care, and monitors the quality of the care as well as the care process. The coordinator directs the process so that the proper care is given at the right moment. The care coordinator is the regular point of contact for the patient and the care providers, identifies any developments, and makes referrals to other care providers. The coordinator should also be familiar with the functioning, participation and psychosocial situation of the FSHD patient (see also the chapter on communication). As needed, the coordinator will deploy medical/paramedical and/or psychosocial care, and will synchronise the various medicated recommendations of the involved physicians/paramedics. The coordinator will do this in tandem with the patient. Because the care coordinator can timely detect risks and inventory them, it is highly recommended that every patient with FSHD has a care coordinator.

The role of coordinator is recognised and accepted by care providers. The coordinator is available and reachable to care providers as well as patients. General practitioners and specialists have consultations with the coordinator. The tasks of the coordinator are to give information about the clinical picture of FSHD and the consequences and risks of interventions to both the general practitioner and the patient, and depending on the phase also about diagnosis, treatment or care management. The tasks of the coordinator are defined in consultation with the patient. The working party recommends explicitly coordinating with the patient and the involved physicians as to who the care coordinator will be.

The working party recommends that a neurologist should be the coordinator in the diagnostic phase. In the treatment phase it makes sense for a rehabilitation physician from a neuromuscular team to be the care coordinator. If the patient so wishes on dependent on local differences in care, a neurologist specialized in neuromuscular disorders can assume this role too. For future medicated therapies, the neurologist will coordinate together with the rehabilitation physician. Obviously the coordinating role can be modified in the course of time. In the end-of-life phase the general practitioner will most probably be the coordinator.

Expertise Centre and other musculoskeletal rehabilitation teams
In 2009 the European Council recommended that member states set up a strategy for rare diseases, including an orientation towards Expertise Centres. The steering group for orphan drugs (*Stuurgroep Weesgeneesmiddelen*) took this task upon itself, resulting in a comprehensive consultation document (2010–2011) that describes how rare conditions are often complex, chronic and severely disabling. FSHD is one of these rare conditions. Striving towards concentration of care by setting up an Expertise Centre is recommended for such conditions. In addition to the general daily care available to anyone with a chronic disease, Expertise Centres have an added value. An Expertise Centre offers multidisciplinary treatment, care management and periodic control while delivering highly specialised complex patient care. An Expertise Centre also coordinates the total care management and is responsible for giving treatment advice and spreading disease-specific knowledge to peers throughout the country. Lastly, an Expertise Centre ensures data registration of patients with FSHD, in order to design and conduct scientific research as well as for publications and communications about such research. Whether the chronic care is given by an Expertise Centre or a different institution depends on multiple factors like complexity of the care, transferability of the care-specific knowledge, and distance the patient has to travel to the Expertise Centre. The underlying premise for safeguarding the quality of care of an Expertise Centre is to provide care from close-by when you can and from far away if you must. See also the EUCERD criteria for Expertise Centres (http://www.eucerd.eu/?page_id=13).

The working party recommends that all patients with FSHD will be offered a consultation at an Expertise Centre within a year of being diagnosed, and in case that does not happen to bring it up again with the patient later on. At this first visit the frequency of follow-up visits are discussed (once a year or twice a year); the follow-up visits would take place at the FSHD Expertise Centre. The Expertise Centre can refer back to the referring neurologist or rehabilitation physician for follow-up treatment as long as the physician has enough expertise in neuromuscular disorders. The underlying premise for safeguarding the quality of care of an Expertise Centre is to provide care from close-by when you can and from far away if you must. Reasons to visit an Expertise Centre can vary: to get answers to questions about the disease from a neurologist with ample experience in this area; patient registrations and the ability to inform patients about ongoing or expected clinical studies; and the ability to offer specialised rehabilitation and related advice through an appointment combined with the rehabilitation. Since 2015 patients can participate in the patient registration initiated from the Expertise Centre, which aims to present a picture of the course and consequences of the disease.

Various rehabilitation venues have a multidisciplinary musculoskeletal rehabilitation team with expertise in the treatment and care management of patients with neuromuscular disorders. For advice and questions about FSHD regarding problems in daily life resulting from FSHD you can contact a musculoskeletal rehabilitation team.

The patient is a partner
Decisions that influence a patient's treatment, health and quality of life are taken through shared decision-making between care provider and patient. Hence also the treatment itself for FSHD is given in consultation with the patient. Together with the patient an analysis is made of the complaints, then joint treatment goals are defined in combination with the patient's request for help and wishes, resulting in a treatment agreement.

Various phases in the care of FSHD patients
As previously noted, the working party lists three different phases for the care of FSHD patients.

Diagnostic phase: To diagnose the FSHD phase, first a medical history (individual and family) and physical examination are performed by a neurologist or a clinical geneticist, who later has DNA tests conducted at the FSHD Expertise Centre (Leiden UMC). In the Netherlands, presymptomatic genetic diagnosis is generally done only after counselling by a clinical geneticist. If the clinical geneticist establishes the diagnosis, the patient can then be referred to a neurologist.

The neurologist[6] in the Netherlands assesses any other additional medical problems, and as needed further refers to other specialists such as an ENT physician, pulmonologist, psychologist, ophthalmologist, or home respiratory care physician. For questions about testing asymptomatic family members or prenatal tests, a referral can be made to a clinical geneticist. Alternatively, the corresponding relative asks their general practitioner first for a referral to a neurologist at a neuromuscular centre to check for signs of FSHD.

After the diagnosis is established, the working party recommends that adult patients be referred to a rehabilitation physician from a musculoskeletal rehabilitation team and to agree on who the care coordinator will be[7]. Make sure to always consult with the patient about decisions taken in the diagnostic phase. The working party recommends that all patients with FSHD have a consultation at the Expertise Centre of Radboudumc (neurology and rehabilitation department) within a year of diagnosis.

Recommendations for the diagnostic phase

A neurologist[8] specialised in neuromuscular disorders is the care coordinator in the diagnostic phase.

Symptomatic genetic testing for FSHD ordered by a neurologist who is knowledgeable about neuromuscular disorders and heredity.

Presymptomatic genetic diagnosis in the Netherlands takes place only after counselling by a clinical geneticist.

Within the first year of establishing the diagnosis, refer the patient to a rehabilitation physician from a musculoskeletal rehabilitation team with specific knowledge of FSHD, even when an inventory

[6] For children, a pediatric neurologist.
[7] In the Netherlands there are around 40 rehabilitation centres that are specialised in neuromuscular diseases. There are also rehabilitation centres in the academic centres, for example the rehabilitation department of the FSHD Expertise Centre.
[8] For children, a pediatric neurologist.

shows no clear limitations (for purposes of familiarisation, information about options and advice aimed at maintaining function).

After the first consultation at the FSHD Expertise Centre, it is advised to plan follow-up visits once every year or every two years. The patient can be referred back to the referring neurologist for follow-up treatment as long as the physician has enough expertise in neuromuscular disorders. Define the follow-up policy in consultation with the patient.

Treatment phase: After establishing the diagnosis, in the treatment phase a rehabilitation physician with expertise in FSHD usually has the coordinating role. A neurologist knowledgeable about FSHD can also be the coordinator. The neurologist or clinical geneticist discuss the hereditary aspects of FSHD with patients and their families. The rehabilitation physician can offer support with diminished functioning and deconditioning resulting from the disease, and guides the musculoskeletal rehabilitation team. Depending on the severity of the care needs, in this team various paramedics can be involved as described in the NMA Treatment framework for neuromuscular conditions (*Behandelkader NMA*). Physical therapists, occupational therapists, speech therapists, dietitians and social workers with expertise in/knowledge about neuromuscular disorders are generally involved in FSHD. If indicated, other disciplines with knowledge about FSHD are deployed. In case of early-onset FSHD, attention should also be paid to the transition phase from adolescence to young adulthood and the start of participation in the labour market.

For any additional medical problems, in the treatment phase it is the coordinator's task to refer the patient to the right physician, such as a neurologist or a rehabilitation physician at the FSHD Expertise Centre, a rehabilitation physician from a musculoskeletal rehabilitation team, a home respiratory care physician, or any other medical professionals such as a company physician, ENT physician, pulmonologist, internist or ophthalmologist knowledgeable about neuromuscular conditions. See also the Care guide at www.spierziekten.nl/zorgwijzer. The patient can also opt to remain under minimal supervision of a neurologist (e.g. once every two years) while a rehabilitation physician coordinates the care. Always discuss the treatment goals with the patient.

There is also a checklist for FSHD available to medical professionals. This checklist can be found via www.spierziekten.nl/checklistfshd.

Recommendations for the treatment phase

A rehabilitation physician (with specific knowledge about FSHD) has the coordinating role in the treatment phase[10]; if preferred, it can also be a neurologist specialised in neuromuscular disorders. Consult with the patient about this.

As a rehabilitation team, proceed in conformity with the treatment framework for rehabilitation for neuromuscular conditions (2013), depending on the care level (1 to 4).

ADDENDUM: Treatment framework for neuromuscular conditions 2013

Determine the composition required for a musculoskeletal rehabilitation team in conformity with the valid treatment framework for rehabilitation for neuromuscular conditions (2013), depending on the care level (1 to 4). A musculoskeletal rehabilitation team includes various disciplines. Physical therapists, occupational therapists, speech therapists, dietitians and social workers are generally involved in FSHD. Per indication, other disciplines with expertise in/knowledge about neuromuscular disorders are involved.

ADDENDUM: Treatment framework for neuromuscular conditions 2013

If there are other medical problems, as coordinator you should refer the patient to the right physician, such as a neurologist or a rehabilitation physician at the FSHD Expertise Centre, a home respiratory care physician or other medical professionals knowledgeable about

neuromuscular disorders such as a company physician, ENT physician, pulmonologist, internist or ophthalmologist, and inform all the physicians.

If the patient is experiencing psychosocial problems, make a referral for minimal monitoring by a psychologist or social worker with expertise in/knowledge about neuromuscular disorders.

In case of early-onset FSHD, attention should also be paid to the transition phase from adolescence to young adulthood.

Always discuss the treatment goals with the patient.

End-of-life phase: Patients with FSHD generally have a normal life expectancy. The working party does note that patients with FSHD are more vulnerable than patients who do not have this neuromuscular disorder. In most cases the general practitioner is the coordinator for the end-of-life phase, availing himself of the expertise of the rehabilitation physician, the neurologist and the home respiratory physician. The general practitioner offers patients with FSHD general medical care in the end-of-life phase, in conformity with the official standpoints for palliative care of the Dutch College of General Practitioners (*NHG-Standpunt Huisarts*): 'To offer adequate care to patients in the palliative phase it is crucial for the general practitioner to practice an anticipating policy. This can be accomplished as soon as the patient reaches the palliative phase, in coordination with other professionals, the patient and the informal caregivers, by systematically charting the care needs of the patient and diligently entering them into a file. This covers somatic, mental, social and spiritual aspects, and anticipates potential problems. The general practitioner ensures that the out-of-hours medical post is aware of the patient's current situation.' The general practitioner also has an advisory function towards the patient.

Points of attention for the general practitioner with respect to end-of-life:

- Being aware of additional FSHD-based risks in this phase, and informing the patient and others involved about this.
- Contact with the home respiratory physician in the context of discontinuing any non-invasive artificial respiration being given.
- Ensuring that acting physicians (including the medical post) are familiar with the patient and with the special characteristics and circumstances that FSHD entails in this phase.
- Agree on policy for medical emergency situations, including patient-preferred limitations of medical treatments (ICU admission, intubation and artificial respiration, antibiotic treatment). Make agreements with the patient about the resuscitation policy.
- Involve home care services as needed.
- Anticipate admissions to the hospital, nursing home or hospice, if the circumstances make it necessary.
- Provide palliative care/end-of-life support.
- Provide aftercare to relatives.
- Inform the coordinator about the death, and the Expertise Centre too if they were involved (when, where).

Recommendations for end-of-life phase:

In the end-of-life phase the general practitioner is generally the coordinator, supported by a rehabilitation physician and/or a neurologist specialised in neuromuscular disorders from a musculoskeletal rehabilitation team or Expertise Centre.

7.2 What is the role of the FSHD Expertise Centre?

The clinical task of the FSHD Expertise Centre (neurology and rehabilitation departments of Radboudumc) is to coach and advice:

- second opinion (for complex care questions about diagnosis and treatment);
- provide information (consultation and advice) about the disease (symptoms, calls, prognosis) to both physicians and patients;
- provide information about current and future research;
- gather information about the natural course of the disease and specific symptoms, also outside the context of trials; to this end, patients are examined following a fixed protocol – this is being developed at the FSHD Expertise Centre in the LUMC Leiden;
- management and maintenance of patient registration; conducting scientific research using data from this database;
- education and training of medical students in neurology and rehabilitation as well as paramedics: partial internships; postgraduate training;
- medical consultancy for Spierziekten Nederland, contact person for FSHD foundation and participation in yearly congresses for neuromuscular disorders;
- coordinator for clinical research:
  - point of contact for companies that want to start a trial;
  - point of contact for other venues that want to conduct research into FSHD or with FSHD patients;
- foster national and international collaboration;
- discuss the possibility of presymptomatic clinical genetic testing on relatives.

The role of the human genetics department of Leiden UMC at the FSHD Expertise Centre consists of supporting clinical activity and scientific research:

- provide information about current and future research;
- gather information about the natural course of the disease and specific symptoms, also outside the context of trials; to this end, patients are examined according to a fixed protocol – this is being developed at the FSHD Expertise Centre;
- conduct DNA diagnoses into different types of FSHD;
- unravel the pathophysiological mechanism of the disease, aiming to develop medicated treatments or genetic therapies.

Recommendations

When in doubt about diagnosis, treatment or complex problems, consult the FSHD Expertise Centre.

When in doubt about the genetic diagnosis, first consult the FSHD Expertise Centre and reassess the patient.

7.3 What is the role of Spierziekten Nederland in the education of patients with FSHD?

Considerations

After being diagnosed, patients can also approach Spierziekten Nederland. Spierziekten Nederland is the patient association for patients with FSHD. Spierziekten Nederland advocates for patients with neuromuscular disorders. Spierziekten Nederland:

- offers information, support and advice to individuals with FSHD;
- provides information for physicians and other care providers ;
- fosters a better quality of care;
- promotes patient participation in research;
- advocates for the interests of patients with neuromuscular disorders;

- brings people into contact with each other;
- stimulates national and international research and patient participation in research.

Recommendations

After diagnosis and during treatment, alert FSHD patients of the existence of patient organisations for purposes of information, contact with fellow patients, patient participation in research, and patient advocacy.