Myofibrillar myopathies

If you have any questions about myofibrillar myopathies, do get in touch with our research team on 020 7803 4813 or research@musculardystrophyuk.org. If you’d like to speak to others with the same condition as yours, visit TalkMD, the active and friendly online forum for people living with muscle-wasting conditions. (You’ll find contact details at the end of the factsheet.)

What are myofibrillar myopathies?
Myofibrillar myopathies are a group of conditions called myopathies that affect muscle function and cause weakness. They primarily affect skeletal muscles. A weakening of the heart muscle (cardiomyopathy) is also common and may manifest as arrhythmia, conduction defects or congestive heart failure.

What causes myofibrillar myopathies?
Mutations in several genes can cause myofibrillar myopathies. These genes provide instructions for making proteins that play important roles in muscle fibres. Within muscle fibres, these proteins are involved in the assembly of structures called sarcomeres. Sarcomeres are necessary for muscles to contract. The proteins associated with myofibrillar myopathies are normally active on rod-like structures within the sarcomere called Z-discs. Z-discs link neighbouring sarcomeres together to form myofibrils, the basic unit of muscle fibres. The linking of sarcomeres and formation of myofibrils provide strength for muscle fibres during repeated muscle contraction and relaxation. See diagram below:

![Diagram of muscle fibre and sarcomere](image_url)
Gene mutations that cause myofibrillar myopathies disrupt the function of skeletal and cardiac muscle. Various muscle proteins form clumps (aggregates) in the muscle fibres of affected individuals. The aggregates prevent these proteins from functioning normally, which reduces linking between neighbouring sarcomeres. As a result, muscle fibre strength is diminished.

So far the following genes have been associated with myofibrillar myopathies. These are BCL2 associated athanogene 3 (BAG3), α-B crystallin (CRYAB), desmin (DES), filamin C (FLNC), LIM domain binding 3 (LDB3/ZASP), myotilin (MYOT), DnaJ (Hsp40) Homolog, Subfamily B, Member 6 (DNAJB6) and titin (TTN; common mutation associated to Hereditary myopathy with early respiratory failure (HMERF)). Mutations in these genes account for approximately half of all cases of this group of conditions. Mutations in the DES, MYOT, and ZASP genes are responsible for the majority of cases of myofibrillar myopathies when the genetic cause is known.

How are myofibrillar myopathies diagnosed?
Myofibrillar myopathies may be diagnosed in childhood but most often appear after 40 years of age. A diagnosis is made based on clinical findings, electromyography, nerve conduction studies and muscle biopsy. Molecular genetic testing for the DES, CRYAB, MYOT, ZASP, BAG3, DNAJB6, TTN and FLNC genes is available to confirm the diagnosis.

Condition onset and common symptoms
The signs and symptoms of myofibrillar myopathies vary widely among affected individuals, even within the same family, typically depending on the underlying genetic cause. Most people with this condition begin to develop muscle weakness (myopathy) in mid-adulthood. However, symptoms can appear anytime between infancy and late adulthood.

People with myofibrillar myopathies can experience weakness and wasting in the muscles of their hands, arms ankles and calves. Affected people may experience difficulties with small tasks using their hands owing to the weakness in their hands, or frequent falls owing to weakness in their feet.

With the progression of the condition, weakness in the muscles closer to the body can also develop, but occasionally this can be present from the onset. Other signs and symptoms of myofibrillar myopathies can include muscle pain (myalgia), joint stiffness (contractures) and abnormal side-to-side curvature of the spine (scoliosis).

Muscles responsible for speech and swallowing can also be affected leading to swallowing difficulties (choking episodes) and changes in the tone of voice.

Heart problems can be mild or severe and may manifest as arrhythmia, conduction defects or congestive heart failure.

Muscles used for breathing may also get weaker, causing breathing difficulties and leading to respiratory insufficiency.
Some people with myofibrillar myopathies may also experience loss of sensation (paresthesia, tingling and numbness) and weakness related to damage of the peripheral nerves (peripheral neuropathy).

In some cases people with myofibrillar myopathies can also develop blurred vision as a result of cataracts.

How are myofibrillar myopathies inherited?
These conditions are mostly inherited in an autosomal dominant pattern, which means that one copy of the altered gene is sufficient to cause the condition. Occasionally, the condition can be inherited in an autosomal recessive pattern, where a faulty copy of the gene will need to be inherited from each parent in order for the condition to develop. (For more information, see our factsheet: Inheritance and muscular dystrophies.)

In some cases, there is no previous family history and the condition is caused by a new mutation.

Is there a treatment or a cure?
Even though there is no cure for myofibrillar myopathies, individuals affected by arrhythmia and/or cardiac conduction defects or cardiomyopathy may consider implantation of a pacemaker and cardioverter-defibrillator (ICD). Heart transplantation may be considered if the cardiomyopathy is progressive or life-threatening.

Assisted ventilation and physiotherapy may be helpful for those with advanced muscle weakness.

Orthotics and other walking aids may be helpful, for example if foot drop develops.

What is the prognosis?
Myofibrillar myopathies are always progressive and muscle weakness worsens over time, however the rate of progression may vary from person to person and also depending on the specific condition. The course of the condition can be variable from mild weakness to severe, leading to loss of ambulation in some people. Life-expectancy is generally within the normal range, however this depends on identification and treatment of heart problems and breathing difficulties.

Other related publications and links
  ► Inheritance and muscular dystrophies
  ► Cmdir.org
  ► http://www.musculardystrophyuk.org/talkmd/

References
We’re here for you at the point of diagnosis and at every stage thereafter, and can:

- give you accurate and up-to-date information about your or your child’s muscle-wasting condition, and let you know of progress in research
- give you tips and advice about day-to-day life, written by people who know exactly what it’s like to live with a muscle-wasting condition
- put you in touch with other families living with the same muscle-wasting condition, who can tell you about their experiences
- tell you about – and help you get – the services, equipment and support you’re entitled to.

If you would like your GP or other health professional to have more information about myofibrillar myopathies, we have some relevant materials. We’ve developed an online training module for GPs, as well as one for physiotherapists working with adults with muscle-wasting conditions. Contact our helpline or email us to find out more.

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Here for you
The friendly staff in the care and support team at the Muscular Dystrophy UK’s London office are available on 0800 652 6352 or info@musculardystrophyuk.org from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

If they can’t help you, they are more than happy to signpost you to specialist services close to you, or to other people who can help.

www.musculardystrophyuk.org