Congenital Myopathy

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Myopathy

- Myopathy is a general term that refers to diseases that affect the muscles that connect to your bones (skeletal muscles).
- Myopathies may be passed on in families (inherited) or they may develop later in life (acquired).
- People living with myopathy may have difficulty performing activities of daily living like bathing, combing their hair or standing up from a chair.

What is myopathy?

- Myopathy refers to diseases that affect skeletal muscles (muscles that connect to your bones).

- These diseases attack muscle fibers, making your muscles weak.

Are there different types of myopathies?

- Myopathy can be categorized by its cause.

- Basically, myopathies are separated into two categories: inherited and acquired.

Inherited myopathies

- **Inherited myopathies** are those that you're born with, often from inheriting an abnormal gene mutation from a parent that causes the disease.

- Conditions that are inherited myopathies include:

Congenital myopathies

- Symptoms of congenital myopathies usually start at birth or in early childhood, but may not appear until the teen years or even later in adulthood.

- Congenital myopathies are somewhat unique compared with other inherited myopathies, as weakness typically affects all muscles (not just proximal [closest to the center of your body] ones) and is often not progressive.

Mitochondrial myopathies

- Mitochondrial myopathy is caused by a defect in the mitochondria, which are the energy-producing part of cells.
- These conditions have muscle weakness, but also a variety of other symptoms, as mitochondrial disorders typically affect other organ systems like your heart, brain and gastrointestinal tract.
- Diseases in this group can be caused by gene mutations with or without a family history.

Metabolic myopathies

- Defects in genes that code for enzymes that are needed for normal muscle function and movement cause metabolic myopathies.
- They often show as exercise intolerance, exertional muscle pains in your shoulders and thighs, or non-traumatic rhabdomyolysis (muscle fiber condition).
- These can also happen with episodes of weakness that come and go with other times of normal strength.

Muscular dystrophies

- Muscular dystrophies are characterized by progressive degeneration of muscle tissue due to abnormal or insufficient structural support proteins being present.

- They all involve your arms and/or legs to varying degrees, and some involve the muscles of your eyes or face.

Myotonias and periodic paralysis

- Patients with myotonias suffer from myotonic reactions in which there is delayed relaxation after contraction

Acquired myopathies

- **Acquired myopathies** develop later in life and can be due to other medical disorders, infections, exposure to certain medications or electrolyte imbalances, among other possibilities.

- Conditions that are acquired myopathies include:

Acquired myopathies

- Autoimmune/inflammatory myopathy
- Toxic myopathy
- Endocrine myopathies
- Infectious myopathies
- Electrolyte imbalance
- Critical illness myopathy

Who gets myopathy and how common is it?

- Anyone can get a myopathy.
- Factors that might increase your risk include:
- **Having a family history of myopathy.** This increases the likelihood you might inherit an abnormal gene that causes muscle disease.

Who gets myopathy and how common is it?

- **Being designated male at birth (DMAB).** Some myopathies are carried on the X chromosome, and actually affect more men than women.
- Other inherited forms of myopathy carried on other chromosomes affect all sexes equally.
- **Having an autoimmune, metabolic or endocrine disorder.**
- **Being exposed to certain medications or toxins** (see toxic myopathy below for a list of some of these medications).

Characteristic features of congenital myopathies:

- Onset in early life with hypotonia, hyporeflexia, generalized
- Muscle weakness(atrophy due to weakness)
- Poor muscle bulk
- Dysmorphic features
- Relatively non-progressive
- Hereditary
- Some cases have been reported as adult onset or as a progressive

Classification of congenital myopathies

1. Myopathies with protein accumulation

a. Nemaline myopathy
b. Myosin storage myopathy
c. Cap disease
d. Reducing body myopathy

2. Myopathies with cores

a. Central core disease
b. Core-rod myopathy
c. Multiminicore disease

3. Myopathies with central nuclei

a. Myotubular myopathy
b. Centronuclear myopathy

4. Myopathies with fiber size va nation

Congenital fiber type disproportion

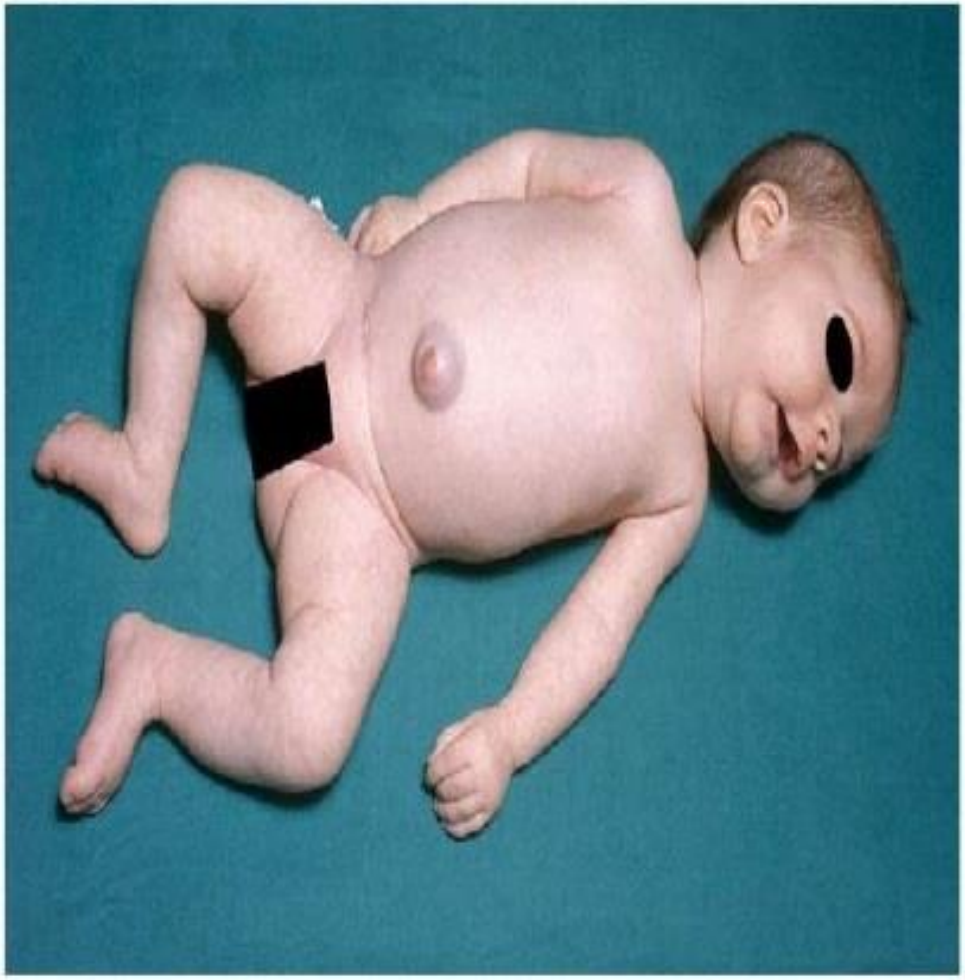
Floppy infant

Clinical signs in a floppy infant

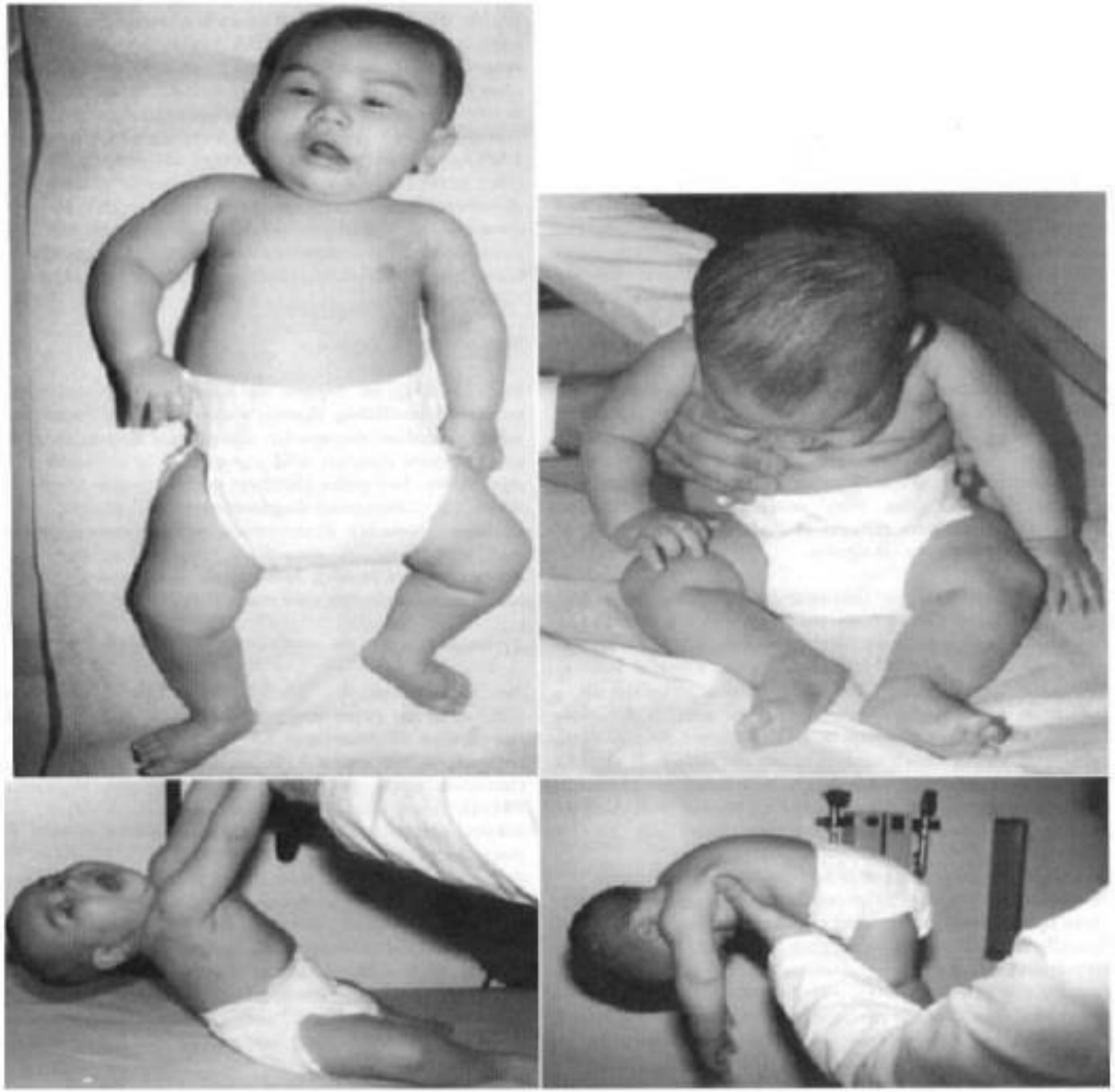
- Observation of a ‘frog-leg’ posture.
- Reduced spontaneous movement, with the legs fully abducted and arms lying beside the body either extended or flexed
- Significant head lag on traction or pull-to-sit manoeuvre and excessively rounded back when sitting (>33 weeks)
- Rag-doll posture on ventral suspension
- Vertical suspension test – feeling of ‘slipping through the hands’ when the infant is held under the arms
- Various associated examination findings such as flat occiput or congenital dislocation of the hips, arthrogryposis

Hypotonia

pith frog position



Hypotonia



Differential diagnosis

anatomical localisation	pathological processes
central nervous system	*deep tendon reflexes typically preserved*
brain/systemic disease	hypoxic-ischaemic encephalopathy sepsis congestive cardiac failure
brainstem	Down's syndrome Prader-Willi syndrome
craniocervical junction	congenital malformations perinatal cord injury
motor unit	
anterior horn cell	spinal muscular atrophy
peripheral nerve	hereditary motor-sensory neuropathy
neuromuscular junction	myasthenia myasthenic syndromes
muscle	congenital myopathies metabolic myopathies muscular dystrophies

Indicators of hypotonia of central origin

- Social and cognitive impairment
- Dysmorphic features
- Fisting of hands
- Normal or brisk tendon reflexes
- Features of pseudobulbar palsy
- brisk jaw jerk
- crossed adductor response or scissoring on vertical suspension
- Features that may suggest an underlying spinal dysraphism
- History suggestive of HIE, birth trauma or symptomatic hypoglycaemia
- Seizures

Indicators of peripheral hypotonia

- Delay in motor milestones with relative normality of social and cognitive development
- Family history of neuromuscular disorders/maternal myotonia
- Reduced or absent deep tendon jerks and increased range of joint mobility
- Frog-leg posture or 'jug-handle'
- Myopathic facies (open mouth with tented upper lip, poor lip seal when sucking, lack of facial expression, ptosis and restricted ocular movements)
- Muscle fasciculation

Investigations

Laboratory Studies

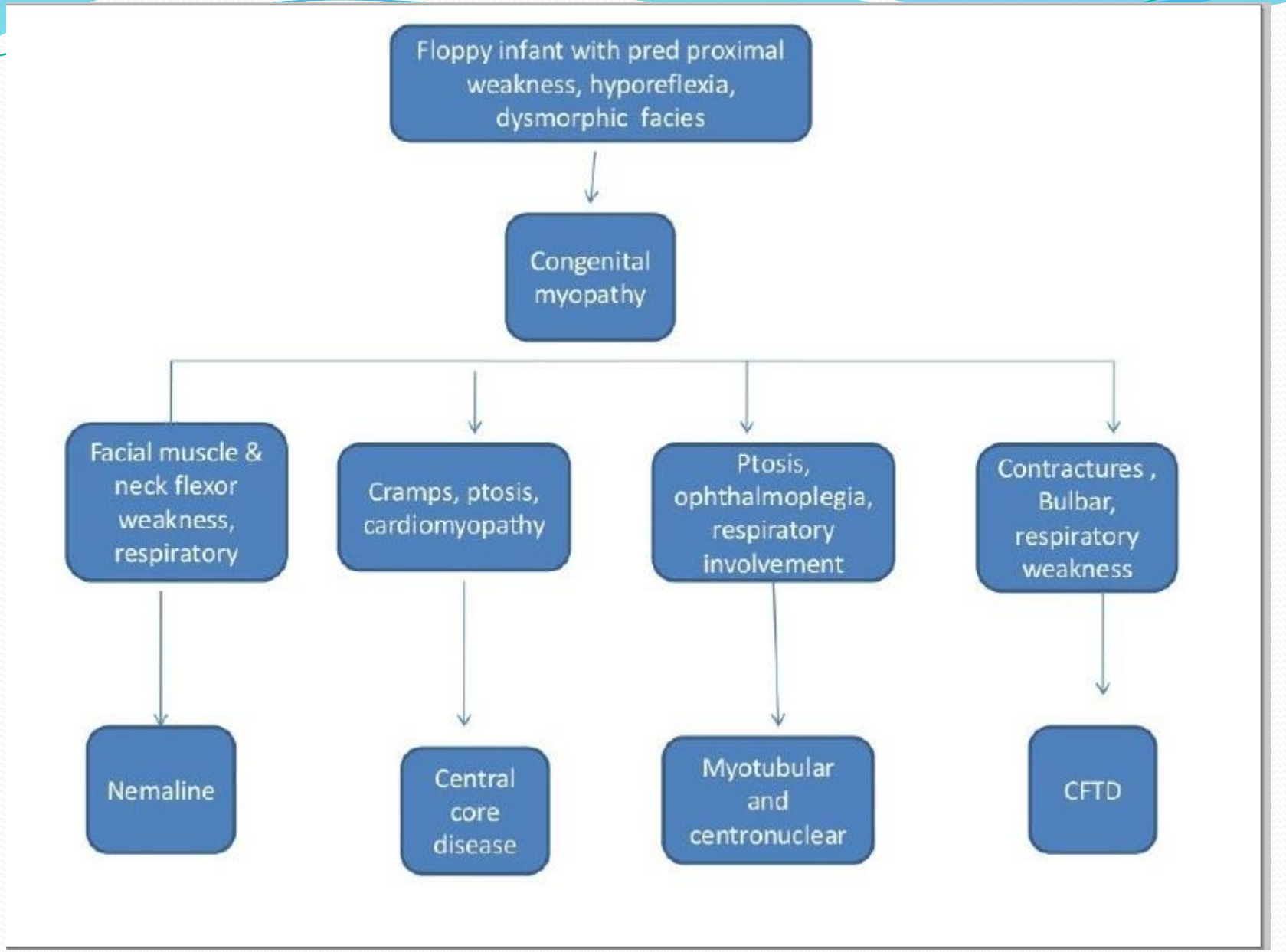
- Creatine kinase level
  - Normal or mildly elevated.
  - Moderately in central core disease (CCD) and also in asymptomatic carriers of the ryanodine receptor mutation in CCD.

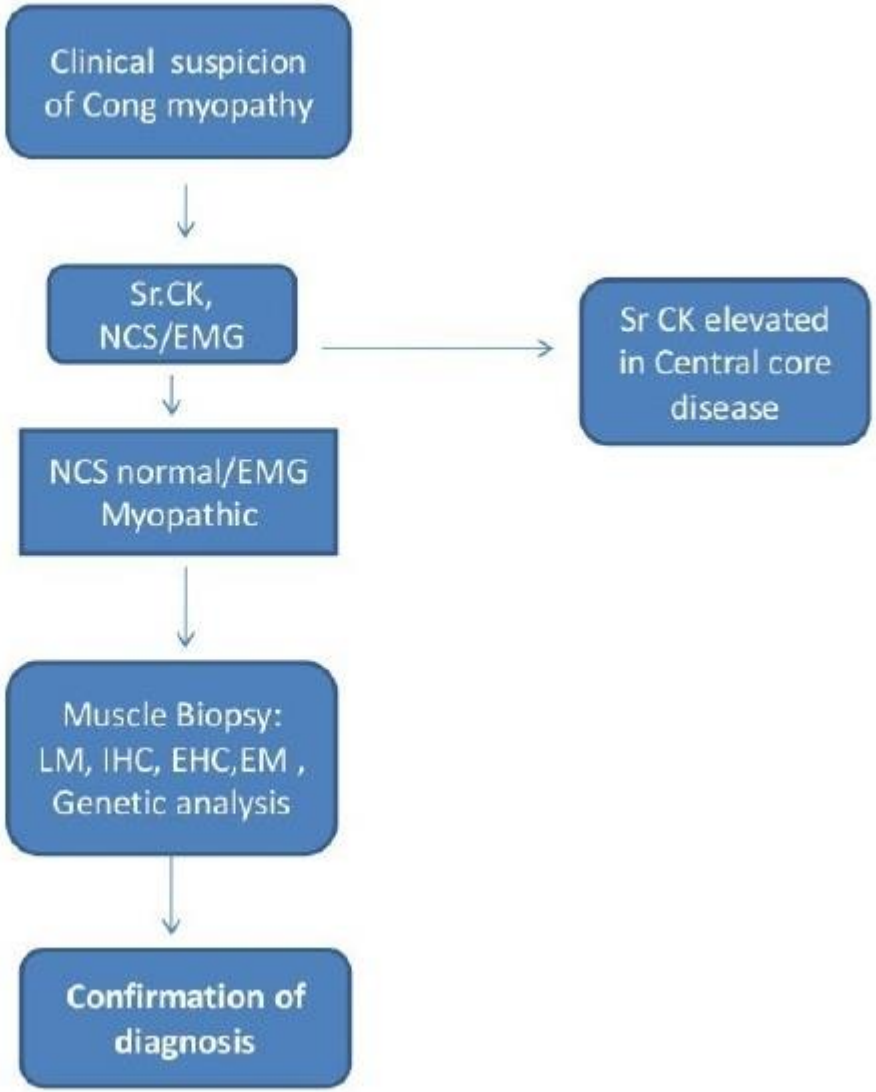
Other Tests

- Electromyography and nerve conduction studies
  - Nerve conduction study is normal.
  - EMG is normal or shows myopathic pattern.
  - Rule out other diseases such as spinal muscular atrophy, congenital myasthenia, and hereditary neuropathy.
- Electrocardiography (ECG)

- **Imaging:** Ultasound, MRI of the muscle may be helpful.
- **Procedures**
- **Muscle biopsy: Gold standard**
  - Light microscopy(H/E stain), Gomori trichrome stain, enzyme histochemistry, immunocytochemistry.
  - Ultrastructural examination of muscle is often necessary, since several of the pathologic features are based on the EM appearance of muscle.

  - **Genetic analysis:**
  - Not required for diagnosis
  - Very sensitive and specific in CCD
  - Only a research level tool


Floppy infant with pred proximal weakness, hyporeflexia, dysmorphic facies
Congenital myopathy
Facial muscle & neck flexor weakness, respiratory
Cramps, ptosis, cardiomyopathy
Ptosis, ophthalmoplegia, respiratory involvement
Contractures , Bulbar, respiratory weakness
Nemaline
Central core disease
Myotubular and centronuclear
CFTD


Clinical suspicion of Cong myopathy
Sr.CK, NCS/EMG
Sr CK elevated in Central core disease
NCS normal/EMG Myopathic
Muscle Biopsy: LM, IHC, EHC,EM , Genetic analysis
Confirmation of diagnosis

Treatment:

- No definitive treatment.
- Physiotherapy, occupational therapy
- Use of splints, braces and orthosis
- Contracture release, corrective surgeries.
- Chest physiotherapy, prevention and management of aspiration pneumonitis, non invasive ventilation.
- Nutrition and gastrostomy feeding.
- Management of heart failure.

Thanks....