Diaphragm PARAlysis : Surgery Or mechanicaL ventilation?

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51915

Source
ToetsingOnline

Brief title
Diaphragm PARAlysis : Surgery Or mechanicaL ventilation?
PARASOL

Condition

- Other condition

Synonym
Diaphragm paralysis

Health condition

Diaphragm paralysis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Diaphragm plication, Mechanical ventilation, Non-invasive ventilation

Outcome measures

Primary outcome

Main study parameter/endpoint

The primary question is whether a randomized trial comparing surgery versus non-invasive ventilation is feasible. The study is feasible if at least 50% of the patients fulfilling the inclusion criteria are randomized in this pilot study

Secondary outcome

Secondary endpoints are; the Medical Research Council (MRC) dyspnoea scale, the Diaphragmatic Paralysis Questionnaire, Borg dyspnoea score, Endurance Shuttle Walk Test (ESWT), spirometry in both sitting and supine position, a polysomnography and transcutaneous measurement of carbon dioxide an oxygen saturation at night.

Study description

Background summary

The diaphragm is a dome-shaped muscle which separates the thoracic cavity from the abdomen. It is the most important muscle of respiration innervated by the phrenic nerves. While many diseases might interfere with its function(1) , in the intended study we will focus on diaphragm paralysis due to phrenic nerve injury. Two types of diaphragm paralysis can be distinguished: unilateral and

bilateral. Patients with unilateral paralysis perceive exertional dyspnea, have an impaired exercise capacity and orthopnea(2). Patients with a bilateral paralysis usually have more symptoms and might even develop respiratory failure(3). In addition, all patients with a diaphragm paralysis may have poor sleep quality, as the diaphragm is the only active respiratory muscle during REM sleep(4). Currently, two treatment approaches for patients with diaphragm paralysis are used in clinical practice: surgical diaphragm plication and nocturnal non-invasive ventilation (NIV). Plication is a minimal invasive surgical procedure that aims to stiffen the diaphragm and such limits dysfunctional (paradoxical movement) excursions of the paralytic diaphragm. The procedure is performed in ±70 patients per year in the Netherlands. NIV is a non-invasive mode of positive pressure ventilatory assistance; through a facial mask the ventilator supports patient breathing effort. Patients with diaphragm paralysis use their ventilator mainly during night time, to improve quality of sleep and such to reduce day time symptoms. In the Netherlands, home mechanical ventilation is very well organized, as care is delivered by only 4 specialized centers. NIV for diaphragm paralysis is started in around 50 patients yearly.

Currently, both plication and nocturnal NIV appear beneficial, are standard care and are covered by health care insurance. However, it is unknown which intervention is most beneficial from a patient perspective. For instance, comparison on patient relevant outcome measures and complications between these treatment approaches is unknown. In addition, patients with diaphragm paralysis may develop severe symptoms, limiting daily activities including ability to perform their professional work. To assess the overall impact of this a detailed cost analysis is necessary to compare both treatments from a societal perspective. A solid cost effectiveness / cost utility study will reveal which therapy is the best option from a societal perspective.

This pilot study will be set up as a randomized pilot study to evaluate if patients are willing and able to participate in this trial. Question is, are participants willing to participate, are they willing to travel to the other institute and are they able to comply with the follow-up measurements. Participants referred to either one of the therapies might be biased towards that therapy and the questions is whether well informed about both therapies, they are willing to participate. To know what clinical effect of both therapies is relevant the EQ-5D-5L is used(5). It is unknown whether there is a significant difference on the outcome between both therapies. A search in trial registries did not reveal any study with similar research questions. Based on the outcomes of this pilot study we can develop an adequately powered randomized controlled study. Due to the acute origin of a diaphragm paralysis patients get suddenly severely impaired which is interfering enormously with their lives. As this is often happening in middle aged patients they often have to discontinue professional activities. This means that the potential impact of this disorder is huge from patient and societal perspective and needs to be assessed.
As both therapies are completely different for invasiveness, we need to compare

the side effects and possible complications. Possible complications of the surgery are infection, bleeding and abdominal pain while the well know side effects of ventilatory support are leakage of the mask, aerophagia and a-synchrony between breathing pattern of the patient and the ventilator. As this is also an important outcome of this pilot study participants will be closely monitored from the start of therapy and there will be a telephone call after 2 months

Study objective

The following questions will be addressed in the PARASOL study

• Is the proposed study design feasible?,
We will set up the study as a randomized pilot study to evaluate if patients are willing and able to participate in a randomized trial, i.e. are patients willing to participate, are they willing to travel to the other institute, are they able to comply with the follow-up measurements. Patients referred to either one of the therapies might be biased towards that therapy and the question is whether with good information about both therapies, they are willing to participate in a randomized controlled trial.
• What is the effect of plication or non-invasive mechanical ventilation on the EQ-5D-5L?
The pilot study is needed as we do not know the clinical relevant effect of both therapies on EQ-5D-5L. Moreover, it is unknown whether there is a significant difference on the outcomes between both therapies. A search in trial registries did not reveal any study with similar research questions as the current proposal. Based on the outcomes of pilot study a power analysis can be performed for the seminal study.
• What are the costs of both therapies from a societal perspective?
Due to the acute origin of a diaphragm paralysis patients get suddenly severely impaired which is interfering enormously with their lives. As this is often happening in middle aged patients they often have to discontinue professional activities. This means that the potential impact of this disorder is huge from patient and societal perspective needs to be assessed.
• What are the side effects - complications of both interventions?
As both therapies are completely different for invasiveness, we need to compare the side effects and possible complications. Possible complications of the surgery are infection, bleeding and abdominal pain while the well know side effects of ventilatory support are leakage of the mask, aerophagia and a-synchrony between breathing pattern of the patient and the ventilator. As this is also an important outcome of this pilot study patients will be closely monitored from the start of therapy and there will be a telephone call after 2 months

Study design

Open-label, multi center randomized controlled trial / pilot

Intervention

Surgical plication of the diaphragm
Mechanical Ventilation

Study burden and risks

The present study is the first to investigate either diaphragm plication or nocturnal NIV. Both options are standard care and covered by health care insurance. It is unknown which intervention is most beneficial from a patient perspective. For instance, comparison on patient relevant outcome measures and complications between these treatment approaches are unknown. In addition, patients with diaphragm paralysis may develop severe symptoms, limiting daily activities including ability to perform their professional work. To assess the overall impact of this a detailed cost analysis is necessary to compare both treatments from a societal perspective.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• >18 years
• diagnosed with a unilateral or bilateral diaphragm paralysis based on isolated phrenic nerve injury.
o Unilateral or bilateral diaphragm paralysis is defined as follows: complaints of dyspnea and / or orthopnea combined with a drop in VC of more than 15% when change from upright to supine position and a positive sniff test during fluoroscopy or ultrasonography. A positive sniff test means that the diaphragm stands still or even moves in cranial direction (paradoxical movement) during the sniff inspiratory maneuver.
• Ability to provide written consent
• Time between diagnosis and treatment should be at least 1 year

Exclusion criteria

• Patients diagnosed with a unilateral or bilateral diaphragm paralysis due to a more systemic neurological or neuromuscular disorder like for example Amyotrophic Lateral Sclerosis ,
• Hypercapnia during daytime ($PaCO_2$ > 6.0 kPa)
• Radiotherapy of the thorax
• Contra indication for diaphragm surgery.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-01-2023
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	mechanical ventilation
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	11-04-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Not approved

Date:	22-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL78661.042.22
Other	UMCG research 202100559