What are reference values of the thickness and the thickening fraction of the diaphragm in children aged 0-8 years?

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Primary objective: To determine diaphragm thickness and thickening fraction in healthy children below or equal to 8 years of age.Secondary objective: To determine the interrater reliability of operators performing the ultra-sound

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Muscle disorders
Study type	Observational non invasive

Summary

ID

NL-OMON49711

Source
ToetsingOnline

Brief title
Norm data of diaphragm thickness in children

Condition

- Muscle disorders
- Respiratory disorders NEC

Synonym
normal diaphragm

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Children, Reference values, Thickness and thickening fraction of diaphragm, Ultrasound

Outcome measures

Primary outcome

To determine diaphragm thickness and thickening fraction in healthy children

below or equal to 8 years of age.

Secondary outcome

To determine the interrater reliability of operators performing the

ultra-sound

Study description

Background summary

Critically ill children treated with invasive mechanical ventilation (iMV) in a paediatric intensive care unit (PICU) may suffer from complications leading to prolonged duration of ventilation and PICU stay. (6-8) These complications may prolong the durations of iMV and PICU stay, which in turn could lead to a cascade of extensive complications, such as ventilator associated pneumonia and delirium, especially if deeper sedation is needed.(8-11)
Nevertheless, premature extubation should be prevented, as it may necessitate re-intubation, with increased risk of morbidity and mortality. (12) The consequences of a longer duration of iMV should be weighed agains those of too early intubation.(13) Failure to wean of iMV is associated with haemodynamic dysfunction, neuromuscular insufficiency, malnutrition, metabolic disorders and diaphragmatic muscle weakness.(9, 13)
Studies in adult ICU patients support the existence of ventilator-induced diaphragmatic dysfunction (VIDD), defined as iMV-induced loss of diaphragmatic force-generating capacity, characterised by muscle fibre atrophy, myofibril necrosis and disorganization.(14, 15) A study by Levine et al. (16) showed

atrophy of slow and fast fibers in ventilated adults. Diaphragm atrophy occurs within as few as 18 hours of iMV, progresses at a rate between 4% and 7% per day of iMV and is associated with extubation failure and increased mortality.(17, 18) The progression of diaphragm atrophy was exacerbated by the length of iMV, low spontaneous breathing fraction, use of neuromuscular blockade, and exposure to corticosteroids

Diaphragm function or contractility can be assessed by measuring the diaphragm thickening during inspiration and expressed as a thickening fraction (TF) with ultrasound. Diaphragm TF correlates strongly with diaphragm strength.(19) Absence of diaphragm thickening has been seen in patients with diaphragm paralysis.(20, 21)

Goligher et al. showed in adult ventilated ICU patients that a low diaphragm contractile activity was associated with rapid decreases in diaphragm thickness, whereas high contractile activity was associated with increases in diaphragm thickness (P=0.002). Contractile activity decreased with increasing ventilator driving pressure (P=0.01) and controlled ventilator mode (P=0.002). Maximal thickening fraction (a measure of diaphragm function) was lower in patients with decreased or increased diaphragm thickness than in patients with unchanged thickness (p=0.05).Titrating ventilatory support to maintain normal levels of inspiratory effort may prevent changes in diaphragm configuration associated with iMV.(4)

Dres et al. have showed a large difference in the diaphragm TF between patients with or without diaphragm dysfunction (mean TF of 19 ± 9 % vs. 35 ± 12 %) under the same pressure support values. This suggested a much lower contribution of the diaphragm reflected by a lower tidal volume at VIDD. (22) Several adult studies have provided evidence of more frequent reintubation if the diaphragm cannot sufficiently thicken.(1, 3, 4, 17, 22-28)

Literature about diaphragm atrophy and VIDD in children is scarce. A recent study showed that diaphragm atrophy is also present in critically ill children receiving iMV for acute respiratory failure, like in adults. In that study, the diaphragm contractility, measured as thickening fraction, was strongly correlated with a spontaneous breathing fraction (beta coefficient 9.4 [95% CI, 4.2-14.7]; p=0.001).(24) Because diaphragm atrophy and less TF in adults have been associated with a longer duration of iMV (caused by a longer weaning period) it seems logical that diaphragm atrophy and VIDD also will negatively affect the outcome of children with acute respiratory failure.(27)

There is no gold standard for the weaning off ventilation, and validated extubation criteria are lacking.(29-31) A spontaneous breathing trial does not provide sufficient information about the work of breathing that has to be performed after extubation. This also depends on the sedation depth. A TF index could be a predictor for successful extubation. So far, this has been confirmed by one study in 31 ventilated children.(25) That study found that in the first 24 hours of iMV, the diaphragm thickness and TF substantially decreased and thereafter gradually decreased. TF after attempted extubation was significantly different between the children who were successful extubated and the children in whom this failed (P<0.001). A TF value of < 17% was associated with extubation failure. Ultrasound studies to measure the diaphragm thickness and

TF had been performed daily until the child*s discharge from the PICU. (25)
Glau et al. found in 56 ventilated children that diaphragm contractility measured as TF is linearly correlated to a spontaneous respiratory fraction. They did the first ultrasound within 36 hours and a final one just before extubation. The study was underpowered, however, to measure daily atrophy for different levels of respiratory support for extubation, and only two children needed to be re-intubated. The clinical impact of diaphragm atrophy on extubation success has therefore not yet been sufficiently demonstrated.
Failure of extubation occurs in approximately 6-8% of children and half of these have upper airway obstruction due to airway damage through the tube.(29, 32, 33)
Diaphragmatic dysfunction is difficult to measure without knowing norm data for normal diaphragmatic thickness and thickening fraction in infants and children. Norm data is only available for healthy neonates (n=15) and from the age group 8-20 years (n=48).(34, 35)
The purpose of this study is to determine values of normal diaphragm thickness and TF in children aged 0-8 years old by ultrasound. This age group represents the largest patient group treated in the PICU. Once these values are known, the clinical relevance of the measuring of the diaphragm thickness of ventilated children by ultrasound can be further studied.

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Study objective

Primary objective: To determine diaphragm thickness and thickening fraction in healthy children below or equal to 8 years of age.
Secondary objective: To determine the interrater reliability of operators performing the ultra-sound

Study design

prospective, cohort study.

Study burden and risks

A non-invasive ultrasound study does not carry any risks. A possible burden is that the child is expected to lie still for ten minutes, but they may be supported by the parents.
The necessity to lie still cannot be explained to children aged 0-2 years; therefore we will we attempt to distract them.
It is important to know the normal thickness of the diaphragm in children and there is no other way to get this. An ultrasound study is the least stressful method and does not give radiation exposure, unlike a CT scan.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

In order to be able to include 120 children, two groups are included:

Inclusion:
Group 1
- Children aged 0-8 years old undergoing one of the following daycare procedures:
- Surgery: inguinal hernia and umbilical hernia surgery
- Urology: hypospadias surgery
- Throat/nose/ear surgery: tympanostomy tubes, removal of throat and nasal tonsils
- Orthopedics: congenital club feet surgery, hip luxation surgery, removing pins
- Plastic surgery: protruding ears surgery, removing of accessory auricle, removing additional toes and fingers
- Ophthalmology: cataract and strabismus surgery
- Immunology: infusion therapy: e.g. prophylaxis of immunoglobulins

Group 2
-Children aged 0-8 years old recruited by colleagues, or relatives of colleagues, friends and neighbours of members of the research group

Exclusion criteria

Neuromuscular diseases
- respiratory tract disorders
- Recent abdominal or thoracic surgery (less than 3 month ago)
- Deviations of the diaphragm

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-01-2020
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	09-03-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL70476.078.19