RESEARCH ARTICLE

Respiratory System Impairments in Children with Cerebral Palsy: Outpatient Surveillance, Diagnosis, and Treatment

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Declaration of conflicts of interest
The authors declare no conflicts of interest.

Abstract:

Introduction: Cerebral palsy is the most common physical disability of childhood. Respiratory problems are the main causes of morbidity and mortality in cerebral palsy.
Methods: The study is characterized by a scoping review. The search for articles was carried out in August 2021 in the PubMed, Medline, SciELO, LILACs and Google Scholar databases, with the keywords "cerebral palsy" and "respiratory".
Results: Overall, 1037 articles were found, 10 duplicates were removed and 167 were pre-selected after the analysis of titles and abstracts. Then, 90 were excluded due to lack of appropriateness after reading the full-texts, thus yielding a total of 77 studies.
Discussion: Risk of respiratory disease should be screened at least every 12 months based on the following criteria: a hospital admission for respiratory illness in the past 12 months; a Gross Motor Function Classification System level V; a Eating and Drinking Ability Classification System level III–V. The screening aims to lead to early diagnosis and treatment, and consists in actively evaluate the risk factors for emergency department visits and hospital admissions. A Gross Motor Function Classification System level V is the strongest predictor, but dysphagia and seizures are the strongest potentially modifiable factors. Aspiration pneumonia is the main cause of death. The main risk for aspiration are dysphagia; uncontrolled seizures; gastroesophageal reflux disease; and drooling. Other comorbidities should also be actively screened: undernutrition; tone disorders; skeletal malalignment; upper respiratory obstruction; airway clearence impairment; and restrictive lung disease. C**onclusion:** Respiratory impairments in cerebral palsy results from a complex multifactorial process influenced by several interrelated pathophysiological factors, directly and indirectly influenced by other common comorbidities in cerebral palsy. Active and early surveillance, diagnosis and treatment, involving multiple medical specialties and rehabilitation professionals is essential for success in improving the quality of life and reducing morbidity and mortality of these patients.

Keywords: cerebral palsy; respiratory

1. Introduction

Cerebral palsy (CP) is the most common physical disability of childhood with a general incidence of 2.11/1000 live births. CP is defined as a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain[1-5].

CP is a clinical diagnosis based on a combination of clinical and neurological signs, and degrees of involvement range from mild to severe. In addition to physical disability and the resulting limitations, CP can lead to clinical, neurological, orthopedic, sensory, mental health and neurodevelopmental disorders as comorbidities, with wide variability in frequency and severity[2,6-8].

Respiratory problems have a significant impact on morbidity and mortality in patients with CP[9], are multifactorial affected, and these factors often coexist and interact[10-14]. Respiratory disease accounts for a high proportion of hospital admissions in CP, affecting not only the child's overall health, but also neurodevelopment, quality of life (Qol) and family functionality[10]. One in four children with CP who go to hospital emergency departments (ED) and one in eight who are admitted to hospital need treatment for respiratory illness[10,15,16]. Most of them will go on to have another hospital admission for respiratory

problems within the same year[15], with hospital stays 2.5 times longer compared to other children[10,16].

Life expectancy is shorter in patients with CP than for the general population and decreases with increasing severity of motor and cognitive impairment[9,17,18]. Most deaths in CP are attributed to diseases of the respiratory system (14 times higher in relation to the general population), with aspiration pneumonia as the main cause in all age groups[17-19].

Therefor, it is very important to recognize potential contributors to lung disease development in children with CP[11]. The major risk factors for respiratory disease in young people with CP are known and most of them can be treated. Regular screening for these risk factors can prevent many respiratory illnesses, and reduce respiratory related morbidity and hospital admissions[15,20]. Regular screening, surveillance and treatment must be proactive and timely[20].

Given its relevance, this study aims to conduct a scoping review on outpatient surveillance, diagnosis, and treatment for respiratory system impairments in children with CP.

2. Materials and methods

The study is characterized by a scoping review, based on the criteria of the PRISMA Extension for Scoping Reviews (PRISMA-ScR) [21].

2.1. Search strategy

The search for articles was carried out in August 2021 in the PubMed, Medline, SciELO, LILACs and Google Scholar databases, using the last 20 years as a filter and the keywords "cerebral palsy" and "respiratory".

2.2. Recruitment and selection bias

The identification of articles for the study flowchart included four phases: (a) identification (study recruitment); (b) selection (duplicates); (c) eligibility (exclusion due to absence of eligibility according to the inclusion criteria) and (d) inclusion (inclusion of the remainders in the scoping review). Each phase was performed separately by two researchers who independently examined the title, the abstract and, when available, the main text of each study.

2.3. Inclusion criteria and study characteristics

The following inclusion criteria were used: to be directly related to the objectives of the review; to be published in English, Portuguese, Spanish and French; to be available in full text.

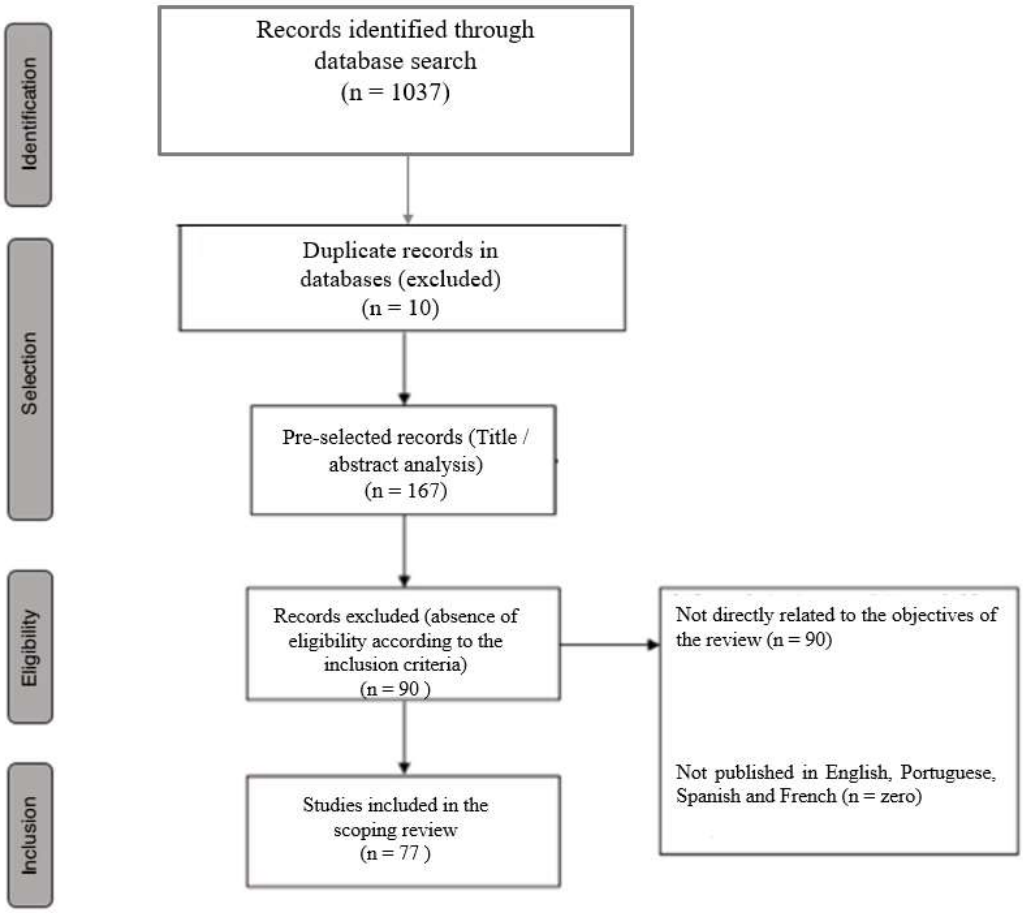
3. Results

Overall, 1037 articles were found in the initial search process. Of these 10 duplicates were removed, and 167 were pre-selected after the analysis of titles and abstracts. Then, 90 were excluded due to lack of appropriateness after reading the full-texts, thus yielding a total of 77 studies included, as shown in the flowchart (figure 1). Table 1 shows the number of articles retrieved, duplicated, pre-selected and included in each database.

Table 1. Number of articles retrieved, duplicated, pre-selected and included in each database

Database	Retrieved	Duplicated	Pre-selected	Included
Pubmed	320	zero	74	65
Medline	541	1	30	4
SciELO	23	2	2	zero
LILACs	37	2	37	zero
Google Scholar	116	5	23	8

Figure 1. Study eligibility flowchart according to PRISMA-ScR

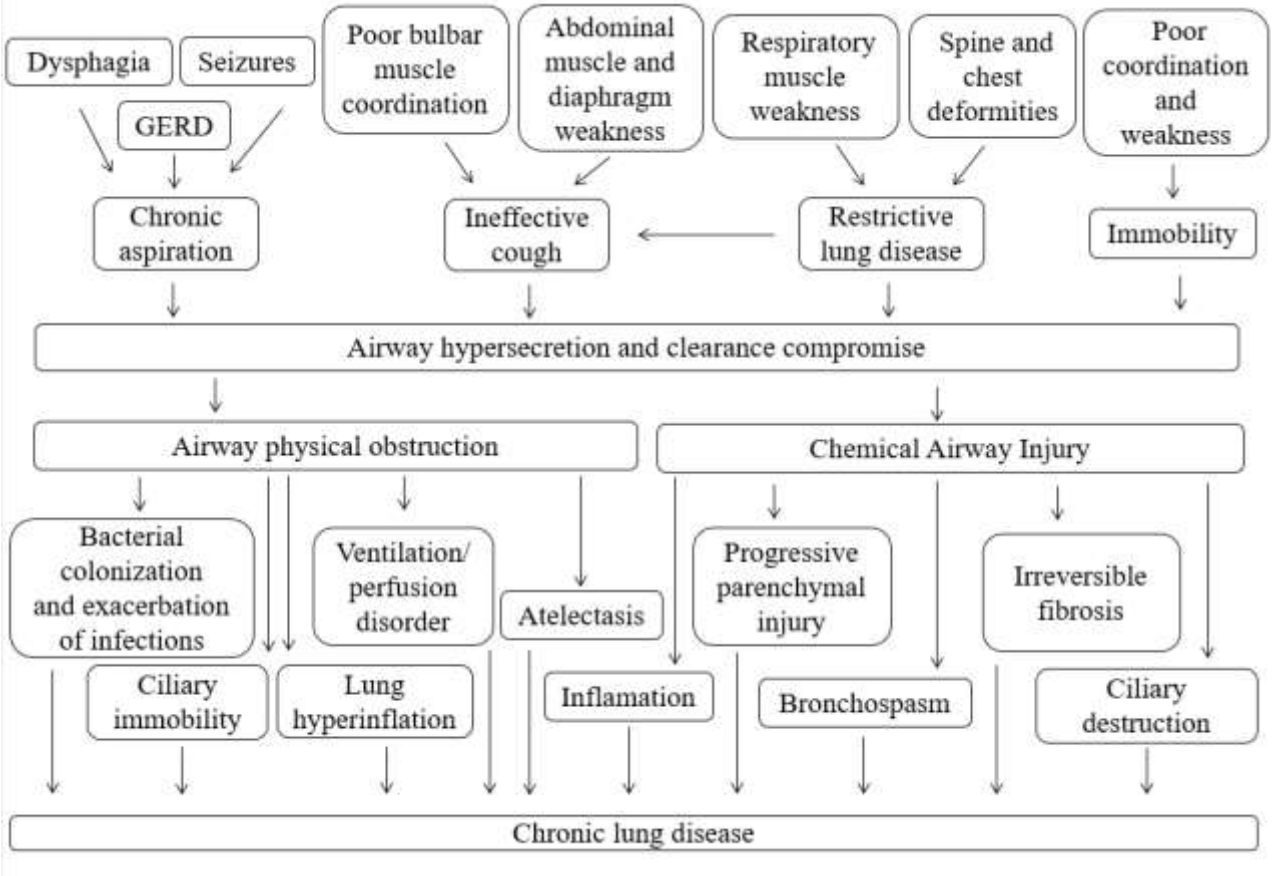


4. Discussion

4.1. Pathophysiology

Normal airway clearance requires effective cough reflex, functioning mucociliary apparatus, and unobstructed airway[9,22]. Respiratory illness in CP is a complex multifactorial process influenced by several interrelated pathophysiological factors (figure 2) that results in airway obstruction, chronic aspiration, ineffective cough, restrictive lung disease (RLD), immobility, respiratory hypersecretion, poor secretion clearance, and physical and chemical obstruction of the airways. These factors facilitates the occurrence of infectious exacerbations and bacterial colonization, immobilization of cilia, pulmonary overinflation, ventilation/perfusion mismatch, atelectasis, intensified inflammatory response, edema, bronchospasm, destruction of cilia, progressive parenchymal damage and irreversible fibrosis, resulting in chronic lung disease (CLD), and ultimately, in respiratory failure[9,11,22-27].

Figure 2. Schematic representation of the pathophysiology of respiratory system involvement in CP



4.2. Functional classification in CP

Gross motor function classification system (GMFCS), and eating and drinking ability classification system (EDACS) are organized into five (I, II, III, IV, V) increasing levels of severity (table 2) [28]. GMFCS and EDACS higher levels influence the risk of respiratory illness[20].

Table 2. GMFCS and EDACS[28]

Scale / Level	I	II	III	IV	V
GMFCS	Walks without limitations	Walks with limitations	Walks using a hand-held mobility device	Self-mobility with limitations; may use powered mobility	Transported in a manual wheelchair
EDACS	Eats and drinks safely and efficiently	Eats and drinks safely but with some limitations to efficiency	Eats and drinks with some limitations to safety; there may be limitations to efficiency	Eats and drinks with significant limitations to safety	Unable to eat and drink safely – tube feeding may be considered to provide nutrition

EDACS - Eating and drinking ability classification system; GMFCS - Gross motor function classification system

4.3. Early risk factors for respiratory disease in CP

The risk factors for ED visits is the same as those for hospital admissions (box 1), except for scoliosis and asthma that are statistically significant predictors of ED visits but not of hospital admissions. A GMFCS V classification is the strongest predictor, but dysphagia (directly linked to the EDACS level) and seizures are the strongest potentially modifiable factors[10].

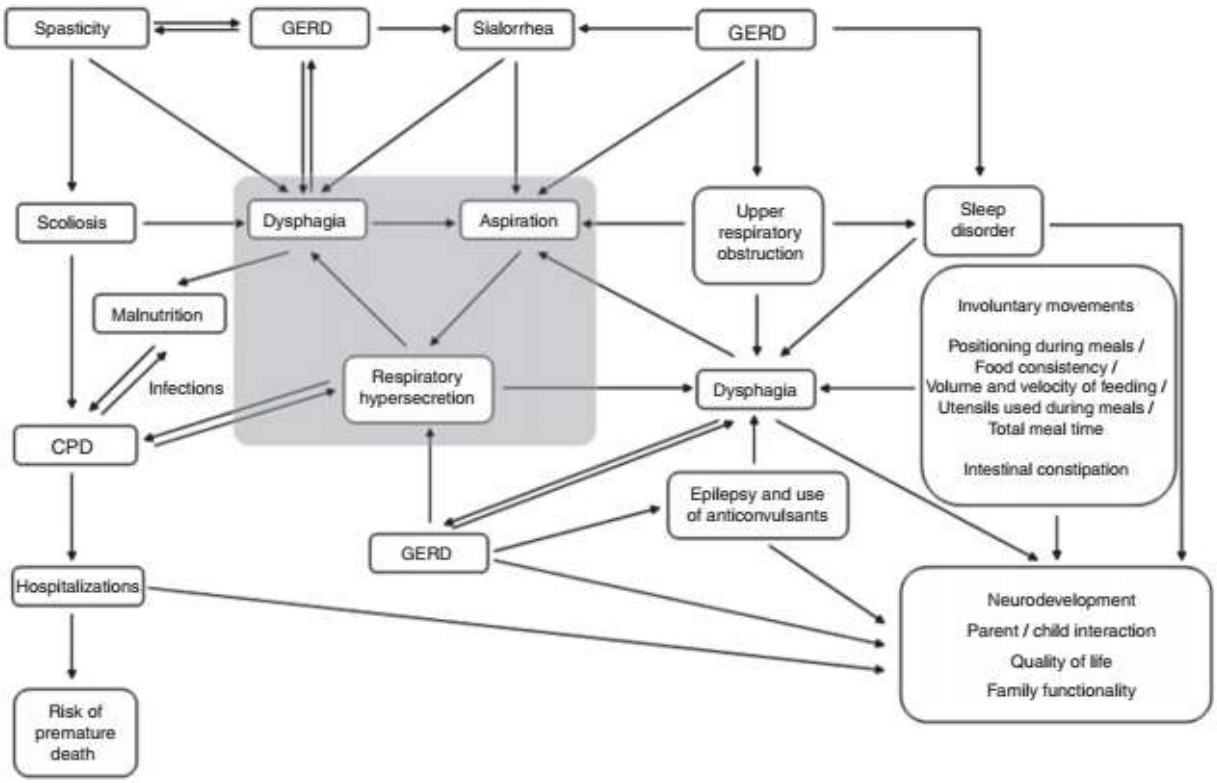
Box 1. Predictive factors for hospital admissions and for ED visits with a respiratory diagnosis[10]

- GMFCS level V
- At least one respiratory hospital admission in the year preceding the survey
- Oropharyngeal dysphagia
- Seizures
- Frequent respiratory symptoms
- Gastroesophageal reflux disease
- At least two courses of antibiotics in the year preceding the survey
- Mealtime respiratory symptoms
- Nightly snoring

4.4. The pathological vicious cycle of intervening comorbidities

The evaluation and treatment of any comorbidity in CP, must be accompanied by the evaluation and treatment of the other comorbidities. In CP the brain damage can generate, or make it more likely, failures not only in the central nervous system, but also in several other systems, in a cascade of dynamically intervening comorbidities, generating a pathological cycle of cumulative consequences called "the pathological vicious cycle of intervening comorbidities" (figure 3)[28,30].

Figure 3. The pathological vicious cycle of intervening comorbidities[28,30]



GERD - gastroesophageal reflux disease

Dysphagia, aspiration and respiratory hypersecretion are the core of the pathological vicious cycle of intervening comorbidities. Spasticity, scoliosis, CLD, GERD, sialorrhea, upper respiratory obstruction, sleep disorder, epilepsy, use of anticonvulsants, involuntary

movement, swallowing skills, positioning, food textures, utensils, volume and rhythm of feeding, and intestinal constipation negatively interfere (they are intervening) among themselves, exacerbate the dysphagia/aspiration respiratory hypersecretion core, lead to malnutrition, infections, CLD and hospitalizations, interfere with neurodevelopment, parent/child interaction, QoL and family functionality, and increase the risk of premature death[28,30].

4.5. General surveillance aspects

Young people with CP should be screened for risk of respiratory disease at least every 12 months ou more often according to the criteria showed in table 3[20].

In general, the screening consists in actively evaluate through anamnesis, physical examination and, when indicated, additional tests, the risk factors for ED visits and hospital admissions, and the intervening comorbidities cited above. For that, the general pediatrician must know what and how to look for, and act in a complementary way, or better yet, together with other medical specialties and with other professionals who are part of the rehabilitation team.

Table 3. Criteria for frequency of respiratory screening in CP[20]

Frequency of respiratory screening	Criteria
At least every 12 months	- A hospital admission for respiratory illness in the past 12 months; - GMFCS level V; - EDACS level III–V (for children over 3 years)
More often than every 12 months	- An increase in hospital admissions for respiratory illnesses; - A hospital admission for a respiratory illness since last review; - Poor control of seizures; - Significant change in nutritional status; - A change from oral intake to tube feeding; - Evidence of aspiration (from clinical swallow assessment, increased choking episodes, chest X-ray, and/or videofluoroscopy); - Deterioration in gross motor function, particularly decreased ability, or tolerance of sitting or standing; - Deterioration in oromotor function; - Difficulty managing secretions; - Presence of spine deformities; - Other changes in clinical status affecting ability to manage and clear secretions; - Any other respiratory-related concern identified by the family or clinician

4.6. General and initial treatment aspects

To optimize the reduction of respiratory exacerbations, ED visits, and hospital admissions, the general pediatrician should take general and initial measures for the various respiratory risk factors and intervening comorbidities (table 4)[9,11,24,28-31].

Table 4. General and initial measures for the various respiratory risk factors and intervening comorbidities[9,11,24,28,30,31]

Risk factors/intervening comorbidities	General and initial measures
Disphagia	Joint or complementary follow-up with a speech therapist; optimize positioning; feeding techniques; texture; equipment; and improve oral motor skills
GERD	Dietary guidance, correct positioning guidance after meals (bed, positioning chair and wheelchair), proton pump inhibitor
Drooling	Joint or complementary follow-up with a speech therapist; improve oral motor skills, GERD treatment; anticholinergics; botulinum toxin injection of salivary glands; correct positioning (bed, positioning chair and wheelchair)
Poor nutritional status	Joint or complementary follow-up with a nutritionist; optimize calorie intake; disphagia and GERD treatment
Impaired airway clearance	Joint or complementary follow-up with with a pediatric pulmonologist and a respiratory physiotherapist; airway clearance techniques; correct positioning (bed, positioning chair and wheelchair), stimulate cough
Respiratory infections	Keep a low threshold for treatment with antibiotics with prolonged course and based on sputum culture
Upper airway obstruction and hypoventilation	Joint or complementary follow-up with a otolaryngologist; polysomnography; lateral airways radiograph if polysomnography not possible; correct positioning (bed, positioning chair and wheelchair)
Deformity of the spine and chest wall	Joint or complementary follow-up with a pediatric orthopedist; active regular radiographic surveillance of spinal and chest wall deformities; correct positioning (bed, positioning chair and wheelchair)
Recurrent bronchospasm	Joint or complementary follow-up with with a pediatric pulmonologist; asthma is over-diagnosed and over-treated with wheeze usually due to other etiologies; assess the responses to asthma medications, if symptoms do not improve, consider stopping the medication
Immunization	Optimize influenza and pneumococcus vaccination
Dental care	Regular dental care, including education to carers about good dental hygiene including daily dental care and review with a pediatric dentist (twice a year)
Gross motor function	As GMFCS is still considered non-modifiable, joint or complementary follow-up with a physical therapist to maximize musculoskeletal function, and minimize any progressive musculoskeletal complications
Other issues	Tone management (joint or complementary follow-up with a pediatric neurologist for discussion of drug therapy and/or a pediatric neurosurgeon for discussion of invasive therapies such as baclofen pump and selective dorsal rhizotomy); epilepsy management (joint or complementary follow-up with a pediatric neurologist; regular control of serum levels of anticonvulsants and electroencephalogram in those with uncontrolled seizures); review of current medication (induction of respiratory or saliva hypersecretion)

GERD - Gastroesophageal reflux; GMFCS – Gross motor function classification system

4.7. Recurrent aspiration

Aspiration is the recurrent aspiration of saliva, food, and/or fluids below the level of the vocal folds. Overt aspiration (OA) is the laryngeal cough reflex, whereby the aspirated material stimulates mechanoreceptors or chemoreceptors of the hypopharynx and laryngeal aditus and generates a reflexive cough in an attempt to expel the aspirated material. Silent aspiration (SA) is the occurrence of aspiration in the absence of cough/other response. Most cases of aspiration involve SA[32].

There are four risk factors for aspiration: (1) dysphagia; (2) uncontrolled seizures; (3) GERD; and (4) drooling[20]. Clinical markers associated with radiographic evidence of OA are: wet voice (most sensitive and specific), wet breathing and cough[27].

4.8. Dysphagia

Swallowing is a complex process, requiring well-coordinated action of muscles in the mouth, pharynx, larynx, esophagus, and diaphragm. Dysphagia is characterized by impairments in one or more of the following stages of swallowing: oral, pharyngeal and esophageal. The prevalence of dysphagia in CP is 50.4%, with greater risk in those with more severely impaired functioning[28,33]. The cerebral lesions often compromise the cortical and subcortical regions responsible for the harmonic functioning of the digestive system, leading to problems in both the volitional oral movements and the more reflexive pharyngeal phase of swallowing. Moreover, impaired ability to plan and coordinate swallowing with ventilation are consistent with brainstem involvement leading to the risk of sequential direct aspiration[9,28,34,35]. Mishra A et al (2018) evaluated suprahyoid muscle activity and respiratory–swallow patterns with simultaneous surface electromyography and respiratory inductance plethysmography as children with spastic CP swallowed, and voluntary cough airflow measures. There were specific physiological deficits of both swallowing and voluntary cough assessments[36].

4.8.1. Anamnesis and physical examination essential and specific aspects

The red flags for dysphagia in CP are shown in box 2.

Box 2. Red flags for dysphagia in CP[28,37,38]

- Average meal duration ≥30 minutes on ≥2 days in a 3-day food record;
- Moderate meal stress (child/caregiver) in a scale where 1-2=None-mild, 3-5=Moderate-severe;
- Lack of weight gain over 2–3 months in young child, not just weight loss;
- Increased congestion at meal times, gurgly voice, respiratory illnesses;
- GMFCS III-V

Bell KL et al (2019) validated a screening tool for feeding/swallowing difficulties and undernutrition in children with CP that can be used independently by parents/caregivers (table 5). The tool successfully identified 100% of children with severe undernutrition and 100% of children in EDACS level IV or V. The 4-item tool total score of ≥3 refers for further assessment of feeding/swallowing and nutritional status[39].

Table 5. Screening tool for feeding / swallowing difficulties and undernutrition in children with CP[39]

Question	Possible response and scoring
Do you think your child is underweight?	Yes (1), No (0), Unsure (1)
Does your child have problems gaining weight?	Yes (1), No (0), Unsure (1)
Rate, on a scale from 0–10, whether you think your child has any problems eating compared to other children of his/her age	10cm long VAS with numbers at each centimetre ≥7 on the VAS=score 1
Rate, on a scale from 0–10, whether you think your child has any problems drinking compared to other children of his/her age	10cm long VAS with numbers at each centimetre ≥7 on the VAS=score 1

Table 6 describes the anamnesis and physical examination essential and specific signs and symptoms that must be actively addressed (several of them will be accessed by the speech therapist during the specific assessment of swallowing)[28,40,41].

Table 6. Anamnesis and physical examination essential and specific aspects of dysphagia in CP[28,40,41]

Impairment in swallowing phases	Signals and symptons	
Oral phase	Insufficient suck	Tongue action ineffective in forming bolus
	Incomplete lip closure	Pooling of bolus in lateral sulci
	Drooling	Prolonged bolus formation
	Inefficient capturing of food bolus	Insufficient chewing
	Food falls from the mouth	Inability to clear the oral cavity
Pharyngeal phase	Difficult swallowing	Coughing /choking at meal times
	Repetitive swallowing	Wet breathing
	Inadequate laryngeal elevation	Gagging
Esophageal phase	Hyperextension of head	Vomitus on pillow
	Food refusal	Vomiting
	Regurgitation	Acidic–smelling breath
	Nasal reflux	Unexplained irritability surrounding mealtimes
	Nighttime awakening	
Aspiration (OA and SA)	Increased congestion at meal times	
	Tachypnea/dyspnea at meal times	
	Tearing at meal times	
	Gurgly voice at meal times	
	Cianosis at meal times	
	Coughing at meal times	
	Recurrent pulmonary infection	
Systemic	Lack of weight gain over 2–3 months in young child, not just weight loss	
Others	Prolonged meal time with insufficient consumption	

OA – Overt aspiration; SA – Silent aspiration

4.8.2. Joint and/or complementary assessment with pediatric specialties and/or rehabilitation team

Dysphagia should be suspected and assessed in CP in all children with criteria based on the screening tool for feeding/swallowing difficulties and undernutrition[39], those with GMFCS III-V and/or those with red flags. The main objectives in the assessment are clearly to answer the following questions: (1) What are the indicated motor learning interventions?; (2) Are there indications for compensatory strategies to make oral feeding more functional, pleasurable and safe?; (3) Are the time and energy required of the caregiver and the child to finish a oral-feeding meal rewarding in terms of QoL?; (4) The current procedure by which the child is fed is sufficient to ensure satisfactory hydration and nutrition? (5) Are there intervening comorbidities acting to worsen the severity of dysphagia? (6) Is the oral-feeding safe and does not lead to aspiration risk?; (7) Is there an indication for enteral tube-feeding regimens?[28]

The full assessment, ideally, should be carried out jointly by the attending physician, the speech therapist, the nutritionist and the nurse. Each one will evaluate through anamnesis, physical examination, direct clinical evaluation of swallowing and complementary exams in order to answer all the questions mentioned above. Participation and opinions of the patient and family are essential in this process. Depending on the needs of each patient-family set (intervening comorbidities, child's physical characteristics and psychosocial needs of the family), case discussions and actions by other

medical specialties and by other rehabilitation professionals may be necessary[28].

4.8.3. Additional tests

A videofluoroscopic swallowing study (VFSS) is useful in the diagnosis of dysphagia and aspiration, but should, according to the UK National Institute for Health and Care Excellence (NICE) guideline, only be considered by a specialist multidisciplinar team in specific cases, including uncertainty about the safety of swallowing after specialist clinical assessment, recurrent chest infections without clinical signs of aspiration, deterioration in eating, drinking and swallowing with increasing age, uncertainty about the impact of modifying food textures, and in case parents or caregivers need better understanding of the swallowing to help with decision-making[9,42].

4.8.4. Joint and/or complementary interventions and follow-up with pediatric specialties and/or rehabilitation team

The general pediatrician must provide the general and initial measures described in table 4. The indirect interventions for dysphagia and aspiration envolve the treatment for the intervening comorbidities mentioned above (joint or complementary follow-up with other medical specialties and other rehabilitation professionals). The direct interventions can be grouped into two categories; those that align with motor learning principles, which aim to improve skills including suck-swallow-breath coordination, bolus formation or control, and swallowing[43,44], and those that primarily aim to immediately improve safety by compensating for impairments (compensatory strategies), including (positioning, food textures, utensils, volume and rhythm of feeding)[44]. In general gastrostomy is indicated in the following situations: the caloric intake is insufficient to maintain growth; and/or there is a high risk of aspiration; and/or the level of effort required by the child and his caregiver is excessive to maintain an adequate caloric intake by the oral route[45]. Gastrostomy leads to an improvement in QoL by reducing the frequency of aspiration pneumonia and hospitalizations[46,47]. However, gastrostomy does not decrease respiratory infections, because it does not prevent gastroesophageal reflux, nor does it prevent aspiration of saliva or upper airway secretions[14].

4.9. Drooling

The prevalence of drooling in CP is 44%[33]. In CP drooling do not occurs because patients produce too much saliva, but because they have trouble managing their saliva[20]. From a clinical point of view, drooling is classified into anterior and posterior; both can occur separately or simultaneously. Anterior drooling is the unintentional loss of saliva from the mouth, in itself it does not cause lung disease[24,30]. Posterior drooling is the flowing of saliva from the tongue to the pharynx[30]. Posterior drooling occurs in children with more severe pharyngeal phase dysphagia, and its prevalence is unknown. Normally the sensation of saliva in the hypopharynx initiates the swallowing reflex. However, when the trigger to swallow is impaired or missing, pooled saliva may lead to aspiration into the trachea, which can cause recurrent pneumonia, bronchiectasis, and may even go undiagnosed before significant lung injury develops[30,31,34,48,49].

4.9.1. Anamnesis and physical examination essential and specific aspects

The following signs and symptoms should be actively investigated: distressing congested breathing, coughing, gagging, vomiting outside meal times; recurrent pulmonary infection[31,48].

4.9.2. Joint and/or complementary assessment with pediatric specialties and/or rehabilitation team

There are quantification systems for anterior drooling, but not for posterior drooling. The Drooling Impact Scale is a simple, validated, and quick method for assessing response to treatment for anterior drooling [24,50]. Unfortunately, posterior drooling is harder to measure; investigations are similar to those for food aspiration[24]. Initially joint or

complementary follow-up with a speech therapist must be adopted.

4.9.3. Additional tests

Park et al (2012)[51] described saliva aspiration into the tracheobronchial tree successfully documented through a radionuclide assessment known as a salivagram. Saliva aspiration documented in fiberoptic endoscopic evaluation of swallowing (FEES) is significantly correlated in children with CP with findings of pneumonia, bronchial wall thickening and atelectasis in chest computed tomography (CT)[52].

4.9.4. Joint and/or complementary interventions and follow-up with pediatric specialties and/or rehabilitation team

The general pediatrician must provide the general and initial measures described in table 4. The literature describes several forms of therapeutic management. The advantages and disadvantages of the main treatment modalities are summarized in table 7[30]. Treatment options for posterior drooling are potentially diverse and ideally require a multidisciplinary approach because of the multifactorial etiology. Initial management consists of conservative measures such as consultation with a speech and language therapist and oral dietary modifications. Non-invasive strategies such as anticholinergic drugs may be attempted before more invasive treatments are considered. In persistent or severe posterior drooling, intraglandular injection with BoNT-A or surgical intervention on the submandibular glands is indicated[31,53-55]. These therapeutic options should be discussed in joint or complementary follow-up with an otorhinolaryngologist, a speech therapist and sometimes with a head and neck surgeon. Other measures involve treating intervening comorbidities such as reviewing medications (anticonvulsants and neuroleptics) that increase saliva production and treating GERD[9,20,30].

Table 7. Advantages and disadvantages of the main treatment modalities for sialorrhea[30]

Therapeutic modalities	Advantages	Disadvantages
Training of sensory awareness and oral motor skills	Treats the underlying cause; safe	Depends on the intellectual capacity; requires access to regular therapy and a trained speech therapist
Botulinum toxin	High efficacy; safe	Requires equipment and trained multidisciplinary staff; requires good clinical condition for sedation or anesthesia; do not treat the underlying cause
Surgical treatment	Definitive efficacy	Definitive side effects; requires general anesthesia; demands equipment and trained surgical team; do not treat the underlying cause
Pharmacological treatment with anticholinergics	Self-administered (by the patient or caregiver); does not require sedation or anesthesia; transient side effects	Frequently anticholinergic effects (vomiting, diarrhea, irritability, changes in mood and insomnia); does not treat the underlying cause.

4.10. Gastroesophageal reflux disease

Gastroesophageal reflux (GER) is defined as passage of gastric contents into the esophagus with or without regurgitation and vomiting. Gastroesophageal reflux disease (GERD) is defined as GER causing troublesome symptoms and/or complications[24]. The prevalence of GERD is quoted as 70–90% (by pH studies and upper gastrointestinal endoscopy) in children with CP[24,56]. Causes include slowed gastric emptying, constipation, seizures, esophageal dysmotility, chronic respiratory symptoms, medications, poor posture, scoliosis, increased intra-abdominal pressure due to abdominal wall spasticity, prolonged supine position, and certain foods[24,57]. The refluxed gastric content may be aspirated into the oropharynx or into the lungs because of oropharyngeal motor dysfunction. It results in throat irritation, chronic cough, chest congestion and lung inflammation leading to bronchospasm, pneumonia, and even interstitial

lung disease. A positive correlation was observed between recurrent pneumonia, abnormal esophageal body function as well as GERD[9,27].

4.10.1. Anamnesis and physical examination essential and specific aspects

Table 8 describes the main GERD signs and symptoms to be actively investigated[28,58].

Table 8. Main GERD signs and symptoms to be actively investigated[28,58]

Signs and symptoms	Infants	Older children
Common manifestations	Regurgitation (especially postprandially) Signs of esophagitis (irritability, arching, choking, gagging, feeding aversion) Failure to thrive Sandifer syndrome	Regurgitation during the preschool years Abdominal and chest pain in later childhood and adolescence Sandifer syndrome
Respiratory manifestations	Obstructive apnea or stridor or lower airway disease in which reflux complicates primary airway disease such as laryngomalacia or bronchopulmonary dysplasia, otitis media, sinusitis, lymphoid hyperplasia, hoarseness, vocal cord nodules, and laryngeal edema	More commonly related to bronchospasm or to otolaryngologic disease such as laryngitis or sinusitis

4.10.2. Joint and/or complementary assessment with pediatric specialties and/or rehabilitation team and additional tests

Investigations for GERD include an upper gastrointestinal series using barium, although reflux cannot be ruled out based on a normal study. Potentially more sensitive measures include gastroesophageal scintigraphy, multichannel intraluminal impedance pH monitoring, and esophageal pH monitoring, the latter of which is still considered the gold standard for the diagnosis of GERD[27]. The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPHAN) guidelines on gastrointestinal and nutritional complications in children with neurological impairment recommend the above cited objective measures for diagnosing GERD. However, given its high prevalence, a trial of a proton pump inhibitor (PPI) with careful follow-up is also acceptable[24,59].

4.10.3. Joint and/or complementary interventions and follow-up with pediatric specialties and/or rehabilitation team

The general pediatrician must provide the general and initial measures described in table 4. Management includes treatment of intervening comorbidities, lifestyle modifications, medications, and surgery. Lifestyle advice include thickened feeds, avoiding caffeine, acidic, fatty or spicy foods, sitting upright during and after eating, or having frequent, small meals, and weight loss if obese. There is limited evidence that medications for GERD improve lung disease, however medications that delay gastric emptying including antacids, histamine receptor blockers, PPI, ondansetron, anticholinergics can be tried[9,24,27,59,60]. Unresponsive cases must have joint or complementary follow-up with the pediatric gastroenteologist and the pediatric surgeon.

Surgical management includes gastrostomy, jejunostomy, fundoplication, and total esophagogastric disconnection. Furthermore, fundoplication has not been shown to affect the rate of hospitalization for aspiration pneumonia, apnea, or reflux related symptoms. With current evidence, gastrostomy insertion should occur first[9,24,27,59,60].

4.11. Epilepsy

The specific approach to epilepsy is beyond the scope of the review. The general and initial conduct to be taken by the generalist pediatrician is described in table 4.

4.12. Direct key factors for progression with chronic lung disease

Airway clearence impairment and RLD are direct key factors for progression with CLD. Early initiation of pulmonary rehabilitation in addition to conventional physical therapy may result in improvement and maintenance of chest mobility, airway clearence and respiratory function, with significant difference in improvement[26,61]. In general, a weekly frequency of training greater than or equal to 4 days per week results in significantly improved pulmonary functions[26].

4.12.1. Airway clearence impairment

4.12.1.1. Anamnesis and physical examination essential and specific aspects

The general pediatrician should assess how well the young person with CP is able to manage secretions, this should be done when the young person is well and again when the young person is unwell[20].

4.12.1.2. Joint and/or complementary assessment with pediatric specialties and/or rehabilitation team

The approach should involve a general pediatrician, a pediatric pulmonologist and a respiratory physiotherapist.

4.12.1.3. Joint and/or complementary interventions and follow-up with pediatric specialties and/or rehabilitation team

The general pediatrician should provide the general and initial measures described in table 4. Physiotherapists should prescribe changes to routine positioning to optimize lung function, and educate carers on how to do this, should assess the strength and effectiveness of the cough for clearing secretions; should show carers how to position them to improve effectiveness of coughing. This includes providing good support for the neck and spine; if they have an ineffective cough but adequate control of the upper airway, physiotherapists should show carers how to assist their cough manually; if non-invasive methods for clearing secretions are ineffective, and/or they cannot swallow safely, clinicians should show families how to suction; if they have a chronic wet/productive cough, should prescribe long-term daily airway clearance regimes; if they are on airway clearance regimens, physiotherapists should monitor and change these regimens according to changing individual respiratory needs, and should be alert to adverse events[20].

Airway clearance techniques (ACT) are used to facilitate removal of secretions from the lung and have been shown to improve sputum expectoration and lung function. Chest physiotherapy in the form of manual percussion is easily administered and can be used to mobilize secretions and remove secretions, often in conjunction with suctioning or postural drainage. Other forms of ACT include intrapulmonary percussive ventilation (IVP), which provides high frequency intermitent bursts of air during both the inspiratory and expiratory cycle causing intrapulmonary vibrations that mobilize secretions towards the mouth. In comparison to incentive spirometry (designed to encourage patients to take slow, deep breaths often to prevent microatelectasis in the post-operative period), IPV was shown to have a significant effect on reducing hospitalization days and antibiotic usage in adolescents with neuromuscular disorders. However, in some children, ACTs may be ineffective due to the inability to take deep breaths and lack of an effective cough. In such circumstances, cough augmentation devices are likely more effective in clearing secretions, particularly for those with significant neuromuscular weakness. Manual techniques for cough augmentation include glossopharyngeal breathing as well as lung volume recruitment[27].

The benefits of exercise for improving respiratory function and fitness are well known and widely accepted. Physical exercise causes deep breathing, and deep breathing helps shift secretions from the airways. Exercise particularly helps to clear smaller airways that cannot be cleared with coughing. Young people with CP should be as physically active and fit as possible[20].

4.12.2. Restrictive lung disease

RLD is a breathing disorder resulting from impairment of the elastic properties of the lungs and chest wall and characterized by static or reduced lung volumes and capacities[22].

4.12.2.1. Anamnesis and physical examination essential and specific aspects

The clinical assessment should include physical examination of the pattern of chest wall movement and chest wall shape[20], and abilities to take a big breath, to generate expiratory force, and to cough effectively[22].

4.12.2.2. Joint and/or complementary assessment with pediatric specialties and/or rehabilitation team

The approach should involve a general pediatrician, a pediatric pulmonologist, a respiratory physiotherapist, and sometimes the pediatric orthopedist.

4.12.2.3. Joint and/or complementary interventions and follow-up with pediatric specialties and/or rehabilitation team

The general pediatrician must provide the general and initial measures described in table 4, assist the person with CP and/or instruct their families on techniques to optimize chest wall mobility to prevent RLD, optimize management of movement disorders, assess individuals for spinal deformities and initiate a postural plan to prevent or manage these deformities. When surgery for scoliosis is under consideration, a multidisciplinar team must evaluate risks and benefits. Physiotherapists should prescribe and educate carers in techniques to maintain an individuals' chest mobility; maxime physical activity and minimize immobility, including regular position changes for non-ambulant individuals[20].

4.13. Motor disorder

Motor disorders that interfere with respiratory function can be organized into skeletal malalignment and tone disorders. Though GMFCS is still considered non-modifiable, therapy should maximize musculoskeletal function, and minimize any progressive musculoskeletal complications[24].

4.13.1. Skeletal malalignment

In terms of skeletal malalignment, the main issues are scoliosis, hip displacement and pelvic obliquity. Hip displacement with pelvic obliquity affects scoliosis development and diaphragmatic movement[24]. Thus, hip surveillance in CP is also important for respiratory health. Hip surveillance is beyond the scope of this review.

4.13.1.1. Scoliosis

4.13.1.1.1. Physical examination essential and specific aspects and additional tests

Curvature, rotation, and shortening of the spine result in thoracic cage deformity[9,62]. A deformed thoracic cage causes reduced lung volume, decreased lung compliance, increased stiffness of the chest wall, reduced force of the respiratory muscles, and increased mechanical dysfunction of the diaphragm. Lung disease in these patients is restrictive in nature[9]. The clinical assessment should include physical examination of the pattern of chest wall movement and chest wall shape[20]. The prevalence of scoliosis in CP is 20–25%[24,63]. The risk increases from a very low risk in patients in GMFCS levels I and II to 50% in those GMFCS levels IV and V which are more likely to evolve with more severe curves[9,20]. Scoliosis is progressive in nature and in these patients it may progress even after growth has ceased, which warrants early treatment[9,64,65]. Active regular radiographic surveillance of spinal and chest wall deformities must be performed.

4.13.1.1.2. Joint and/or complementary interventions and follow-up with pediatric specialties and/or rehabilitation team

Conservative measures like postural management have not shown benefits in small studies. Bracing is not tolerated and BoNTA is ineffective. Prevention of pelvic obliquity, hip dislocation, and fixed hip deformity may

minimize spinal deformity. Current evidence supports long instrumental fusion from T2 to pelvis. Surgery should be considered when a curve exceeds 50° or functional sitting deteriorates, and should be performed early, while lung function allows, to reduce the risks of the operation and to prolong survival. Surgery corrects deformity and improves the QoL of the child and their caregivers[9,24,66-68]. These therapeutic options should be discussed in a joint or complementary follow-up with a pediatric orthopedist.

4.13.2. Tone disorders

The specific approach to tone disorders is beyond the scope of the review. The general and initial conduct to be taken by the generalist pediatrician is described in table 4.

4.14. Obstructive sleep apnea syndrome/upper respiratory obstruction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent periods of increased upper airway resistance with partial or complete intermittent obstruction of the upper airway during sleep. This is usually accompanied by sleep fragmentation and abnormalities in gas exchange. Predisposing factors to the development of OSAS include structural and functional factors that increase upper airway collapsibility[27]. OSAS affects 0.7% to 3.0% of all children[69]. Children with CP are at increased risk of sleep disorders in general, and OSAS specifically, due to their pulmonary vulnerability. GMFCS III–V children often present abnormal muscle tone of the upper airway including laryngeal dystonia, severe laryngomalacia due to reduced tone in the supraglottic structures, concurrent pseudobulbar palsy, and adenotonsillar hypertrophy (ATH) which can result in several sleep related breathing disorders, including OSAS. The treatment of OSAS in children with CP improves QoL, prevents cardiovascular consequences such as pulmonary hypertension, decreases neurobehavioral consequences, and may improve seizure control[11,69-73].

ATH leads to mouth breathing, nasal congestion, chronic sinusitis, and recurrent otitis media. Some authors highlighted the role of inflammation in the development of ATH and OSAS, given the increased expression of various mediators of inflammatory responses in the tonsils[71]. The chronic inflammatory process of the upper airways contributes to greater respiratory morbidity in children with CP, with a consequent effect on the pathological vicious cycle of intervening comorbidities.

Clinicians should consider both waking and sleeping upper airway obstruction in children with CP, be mindful of changes in symptomatology related to the upper airway and consider the morbidity that may follow from an underappreciation of upper airway obstruction and its management[11]. The routine questionnaire-based assessment for OSAS should be a regular part of the care of all children with CP, especially in those with more severe CP and those with comorbid epilepsy[69].

4.14.1. Anamnesis essential and specific aspects

Most children with OSAS snore and have difficulty breathing during sleep. Snoring is often loud and is punctuated by pauses and gasping. The three most predictive symptoms of OSAS are snoring, difficulty breathing during sleep, and witnessed apnea[69].

The pediatric obstructive sleep apnea screening tool (PosaST) has high sensitivity and moderate specificity for the diagnosis of moderate to severe OSAS in preschoolers and school children. This tool can discriminate children at greater risk for OSAS and, consequently, indicates those with greater urgency to undergo polysomnography (PSG) and subsequent treatment of the underlying pathology[72,74,75].

4.14.2. Physical examination essential and specific aspects

Assessment of the presence of mouth breathing, inspection of the oropharynx looking for pharyngeal tonsil hipertrophy[20] and cervical

auscultation assessing the presence of inspiratory noise from the upper airways.

4.14.3. Additional tests

The first diagnostic tools are the overnight PSG in the laboratory (gold standard for the diagnosis of OSAS[27,76]) and the fiberoptic endonasal examination (FEE) to access adenoid and tonsillar tissues[77]. It would be reasonable to consider a lateral airways radiograph to assess the size of adenoidal tissue in relation to the airway[11]. In countries where access to PSG is precarious, the evaluations performed from questionnaires become of great clinical importance, with a low operational cost[72,76].

4.14.4. Joint and/or complementary assessment with pediatric specialties and/or rehabilitation team

Once OSAS and/or ATH are clinically suspected through anamnesis, physical examination and/or PosaST, the child should be referred for joint or complementary follow-up with a otolaryngologist.

4.14.5. Joint and/or complementary interventions and follow-up with pediatric specialties and/or rehabilitation team

Clinicians should start using positioning and tone management, and refer to ear, nose, and throat specialists so that. There is published evidence that surgery for upper airway obstruction in young people with CP improves blood oxygen levels, and improves sleep and the ability to function during the day time. However, none of these studies compared the children who had surgery with those without surgery[20]. In cases of ATH, adenotonsillectomy is generally considered first line treatment for moderate to severe OSA. Other surgical interventions may be indicated to relieve the location/cause of the upper airway obstruction. In mild OSA, non-surgical interventions include intranasal steroids and leukotriene receptor antagonists, both of which have been shown to reduce upper airway inflammation and improve sleep apnea. Alternative options to treat include noninvasive ventilation and tracheostomy with or without mechanical ventilation, with the goals of improving sleep quality, nocturnal gas exchange and reducing the mechanical load on the respiratory muscles[27].

Table 9. Anamnesis, physical examination, assessment, additional tests and interventions summarized aspects

Morbidity	Anamnesis and physical examination	Assessment and additional tests	Interventions
Dysphagia	Red flags; tables 5 and 6 data	Assess those with red flags, or criteria based on the screening tool, or GMFCS III-V; VFSS	Table 4 data; treatment for the intervening comorbidities; motor learning and compensatory strategies; gastrostomy when indicated
Drooling	Actively investigate signs and symptoms	Salivagram; FEES	Table 4 data; treatment for the intervening comorbidities; table 7 data
GERD	Table 8 data	Upper gastrointestinal series using barium, gastroesophageal scintigraphy, multichannel intraluminal impedance pH monitoring, and esophageal pH monitoring;trial of a PPI	Table 4 data; treatment for the intervening comorbidities; lifestyle modifications, histamine receptor blockers, PPI, ondansetron, anticholinergics, surgical treatment
Airway clearence impairment	Check ability to manage secretions	**Medical team** Table 4 data; treatment for the intervening comorbidities; positioning; show carers how to assist coughing manually	**Physical therapist** Show families how to suction; long-term daily airway clearance regimes; monitor and change these regimens according to changing individual respiratory needs; ACTs; exercise
Restrictive lung disease	Assess the pattern of chest wall movement and the chest wall shape, the ability to take a big breath, to generate expiratory force, and to cough	**Medical team** Table 4 data; treatment for the intervening comorbidities; Instruct families on techniques to optimize chest wall mobility, optimize management of movement disorders, assess spinal deformities; consider surgery for spinal deformities	**Physical therapist** Educate carers in techniques to maintain an individuals' chest mobility; maxime physical activity and minimize immobility, including regular position changes for non-ambulant individuals
Scoliosis	Physical examination of the pattern of chest wall movement and chest wall shape	Active regular radiographic surveil-lance of spinal and chest wall de-formities must be performed.	Table 4 data; prevention of pelvic obliquity, hip dislocation, and fixed hip deformity may minimize spinal deformity.; surgery should be considered when a curve exceeds 50° or functional sitting deteriorates
Upper respiratory obstruction	Investigate snoring, sleep dyspneia/apnea, mouth breathing, pharyngeal tonsil hipertrophy, inspiratory noise from the upper airways; PosaST scale	PSG, FEE, lateral airways radiograph	Positioning; adenotonsillectomy; intranasal steroids and leukotriene receptor antagonists, noninvasive ventilation; tracheostomy

ACTs - Airway clearance techniques; FEE – Fiberoptic endonasal examination; FEES - Fiberoptic endoscopic evaluation of swallowing; GMFCS – Gross motor function classification system; PosaST – Pediatric obstructive sleep apnea screening tool; PPI - Proton pump inhibitor; PSG - Polysomnography; VFSS - videofluoroscopic swallowing study

5. Conclusion

Respiratory impairments are an important cause of ED visits, hospital admissions, poor QoL and death in CP, that result from a complex multifactorial process influenced by several interrelated pathophysiological factors, which occurs more frequently and is more severe in those more severely affected (GMFCS V and EDACS V), and which is directly and indirectly influenced by other common comorbidities in CP. Active and early surveillance for respiratory impairments and intervening comorbidities involving multiple medical specialties and rehabilitation professionals, and taking into account the individual needs of each child and their family, is essential for success in improving the QoL and reducing morbidity and mortality of these patients.

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