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REVIEW ARTICLE

Defining outcomes following congenital diaphragmatic hernia using standardised clinical assessment and management plan (SCAMP) methodology within the CDH EURO consortium

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Treatment modalities for neonates born with congenital diaphragmatic hernia (CDH) have greatly improved in recent times with a concomitant increase in survival. In 2008, CDH EURO consortium, a collaboration of a large volume of CDH centers in Western Europe, was established with a goal to standardize management and facilitate multicenter research. However, limited knowledge on long-term outcomes restricts the identification of optimal care pathways for CDH survivors in adolescence and adulthood. This review aimed to evaluate the current practice of long-term follow-up within the CDH EURO consortium centers, and to review the literature on long-term outcomes published from 2000 onward. Apart from having disease-specific morbidities, children with CDH are at risk for impaired neurodevelopmental problems and failure of educational attainments which may affect participation in society and the quality of life in later years. Thus, there is every reason to offer them long-term multidisciplinary follow-up programs. We discuss a proposed collaborative project using standardized clinical assessment and management plan (SCAMP) methodology to obtain uniform and standardized follow-up of CDH patients at an international level.

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INTRODUCTION

In 2008, the Section on Surgery and the Committee on the Fetus and Newborn of the American Academy of Pediatrics (AAP) published an overview of the post-hospital discharge long-term sequelae of infants with congenital diaphragmatic hernia (CDH).[1] However, many of these studies were performed several decades ago, in an era before standardized postnatal management was introduced, and most studies focus on outcome in the first few years of life.

Meanwhile, the survival rates for neonates born with CDH have increased significantly as management strategies have evolved.[2,3] The "price of success", however, appears to be an increase in long-term morbidity. Chronic pulmonary obstruction and pulmonary vascular disease, neurodevelopmental and hearing impairment, and gastrointestinal dysfunction, in addition to late general surgical and orthopedic complications are increasingly described.[2,4]

In 2012, Chiu and IJsselstijn reviewed the long-term outcomes of survivors with CDH and reported the results of a web-based survey to evaluate how many of the 60 participating centers in the CDH study group had long-term follow-up in place. Of the 22 (37%) centers that responded, structured follow-up was performed in only 16 (73%).[5]

In 2008, a collaboration of large volume CDH centers in Western Europe led to the establishment of the CDH Euro consortium with the goals of standardizing care, and facilitating the conduct of multisite randomized controlled trials and structured prospective data collection. One of the first developments within the consortium was the consensus agreement of a standardized postnatal management protocol.[6] This permitted

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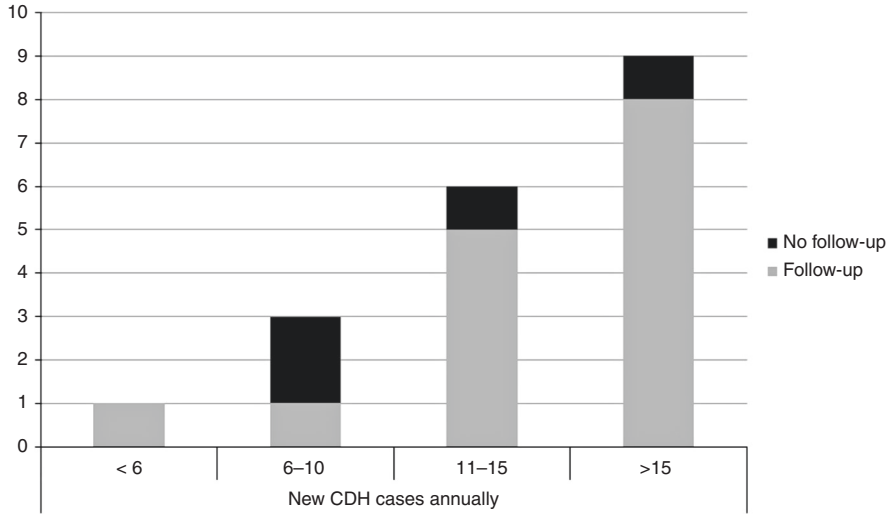

Fig. 1 Current practice of structured and standardized follow-up in 19 CDH centers stratified for the number of new CDH cases treated annually. The *x* axis represents the stratification for new CDH cases treated annually per center; the y axis represents the number of centers

the group to perform the first randomized controlled trial in CDH patients,[7] with subsequent revision of the consensus.[8]

Despite the successful efforts to provide standardized care to CDH patients, accurately assessing the impact of such interventions is extremely challenging without having standardized long-term follow-up.[9] Moreover, this lack of knowledge on long-term outcomes will impede optimal care for older CDH survivors.

In 2010, Rathod et al.[10] proposed a novel methodology to aid the rationalization of clinical management and permit evolution-of-care pathways. These "Standardised Clinical Assessment and Management Plans" (SCAMPs) are founded on the understanding that most clinical decisions are not necessarily evidence-based, and that there must be provision for flexibility in relation to changing practice. To inform such a change, however, assessment and management must be tightly structured and standardized, and data collected using clearly defined unambiguous treatment algorithms. This permits the exploration of hypotheses which are embedded a priori. As CDH is a rare disease, multicenter collaboration is mandatory to apply the SCAMP methodology successfully. We hypothesized that initiation of SCAMPs would be possible within the framework of the CDH EURO consortium.

The aims of this study were (1) to evaluate the current practice of long-term follow-up within the CDH EURO consortium centers, (2) to review literature by the system on outcomes in CDH published from 2000 onward, and (3) to discuss SCAMP methodology as a potential approach to obtain uniform and standardized follow-up of CDH patients.

METHODS

Survey

We developed a two-part web-based questionnaire. Part 1 aimed at gathering background information and broadly understanding the follow-up practices in participating centers. Part 2 aimed specifically at understanding the current follow-up practice in those centers with a structured CDH follow-up program. One representative from each of the 20 participating centers was contacted by e-mail and invited to coordinate completion of the survey on behalf of their institution. The survey was deliberately concise with both multiple-choice and open-ended questions. It was unanimously approved at a meeting of the follow-up working group within the CDH EURO consortium in April 2016.

Literature review

We defined, by consensus, seven areas of interest with respect to long-term morbidities: pulmonary function, pulmonary hypertension (PH), neurodevelopment, sensorineural hearing loss (SNHL), growth and gastrointestinal morbidities, general surgical outcomes, and musculoskeletal outcomes. We conducted an extensive literature search from 2000 onward (Supplementary File S1). Since the main goal of the literature review was to explore unanswered questions, we decided not to use the systematic literature review methodology. Based on title and abstract, articles were categorized and included for evaluation. Members of the working group, focusing on their area of expertise, summarized the current knowledge base in predefined tables delineating the most important issues.

RESULTS

Survey

Nineteen centers answered the first part of the survey in its entirety (95%). Among the respondents were nine neonatologists (47%), seven pediatric surgeons (37%), one pediatrician (5%), one pediatric intensivist (5%), and one obstetrician (5%). The annual case volume of responding centers is shown in Fig. 1.

All centers reported that CDH patients were followed up at their institution, however, 4/19 (21%) respondents reported that follow-up was not structured and standardized. Two centers discontinued structured follow-up at 1 year of age. The reasons provided were lack of resources or personnel, or a large catchment area.

Three centers (16%) endorsed following up all CDH patients routinely, whereas 16 centers (84%) supported the review of only those at the highest risk of morbidity. The presence of chronic lung disease was selected as the most important risk factor (94%; Table 1). All respondents unanimously agreed and endorsed standardization of follow-up and were willing to adopt such a collectively agreed pathway within the EURO consortium.

Fifteen participating centers answered the second part of the survey (79%); 13 provided follow-up standardized both for time points and data collection (87%), the remainder (13%) for time points alone. A summary of the follow-up services currently provided is shown in Table 2. None of the centers performed annual follow-up until 16 years of age; only one center offered

Table 1. Factors suggested for risk stratification of long-term follow-up in CDH patients

Risk factors	
Chronic lung disease	16 (94%)
Feeding difficulties or growth problems	14 (82%)
Neurologic morbidity	13 (74%)
Need for ECMO	11 (65%)
Mode of closure/use of patch	10 (59%)
Gastrointestinal issues	9 (53%)
Observed/expected lung-to-head ratio	4 (24%)
Pulmonary hypertension/ICU issues	1 (6%)

Multiple options were applicable; this question was answered by 17 participants, two centers that provide a uniform follow-up program for all CDH patients replied that risk stratification was not applicable. Data are shown as *n* (%)
ECMO extra corporeal membrane oxygenation

annual review until 10 years of age. Only half of the centers performed follow-up after the age of 12 years (Table 2). For the five centers that provided follow-up until 16–20 years, the time intervals between reviews were usually 3–6 months within the first 2 years of life, with wider intervals of up to 2–6 years once school aged.

Pulmonary assessments. In 11 centers (73%), chest radiographs were performed routinely in every CDH patient; in five of those (33%) within the first year of life only. In three centers (20%), follow-up chest radiographs were taken routinely but restricted to CDH patients repaired with a patch. One center that applied pH-metry routinely at 0.5 and 8 years carried out chest radiographs for assessing tube position and diaphragmatic integrity. One center which offered fetal tracheal occlusion, performed a chest CT routinely at 1 year of age. One center performed chest MRIs routinely at 2 and 10 years of age. Two centers performed routine pulmonary function testing within the first year of life; in five other centers, pulmonary function testing was done in childhood. One center discontinued pulmonary function testing after the age of 6 years, whereas the four other centers performed repeated measurements at 4–5-year intervals at older ages.

Cardiac assessments. Four centers performed routine echocardiograms within the first year of life, irrespective of the presence of pulmonary hypertension prior to discharge. In one of those centers, evaluations at 5 and 12 years were scheduled for those with pulmonary hypertension identified at 1 year. One other center restricted routine echocardiograms to those with chronic pulmonary hypertension. Two centers evaluated pulmonary hypertension at 14 or 16 years; one of these centers provided routine echocardiograms every 2–4 years after the age of 2 years.

Neuroimaging and neurodevelopmental assessments. Only one center provided routine cranial MRI (at 2 and 10 years). Hearing assessments were offered routinely after discharge in 6/19 centers (32%); two centers performed hearing assessments after the age of 5 years. One center offered hearing assessments every 6 months until 6 years of age. Routine neurodevelopmental assessments were performed until 2 years in half of the participating centers; in 5/19 centers (26%) it was carried out until 5 years of age. Two centers offered routine neuropsychological assessments after 5–6 years of age.

Anthropometry and gastrointestinal studies. All participating centers evaluated height and weight at each assessment. Upper gastrointestinal studies to evaluate reflux were routinely performed after discharge in 6/19 (32%) centers; one center did this at school age (8 years). Esophagoscopy was offered in one center prior to discharge. A single center reported screening for oral aversion (OA) at each hospital visit.

Table 2. Follow-up programs provided within the CDH EURO consortium centers

Age of follow-up	Infancy	15 (100%)
	Toddler	13 (87%)
	(Pre)school	13 (87%)
	Adolescence (>12 yrs)	8 (53%)
	Up till 20 yrs	1 (7%)
Disciplines involved	Pediatric surgeon	14 (93%)
	Pediatrician	11 (73%)
	Pulmonologist	11 (73%)
	Pediatric physical therapist	6 (40%)
	Dietician	5 (33%)
	Pediatric cardiologist	5 (33%)
	Speech-language pathologist	4 (27%)
	Psychologist	3 (20%)
	Neonatologist	2 (13%)
	Orthopedic surgeon	1 (7%)
	Clinical geneticist	1 (7%)
Assessments performed	Anthropometry (height, weight)	15 (100%)
	Chest radiograph	11 (73%)
	Gastroesophageal reflux	11 (73%)
	Pulmonary function	10 (67%)
	Mental development	8 (53%)
	Motor-function development	8 (53%)
	Audiometry	8 (53%)
	Echocardiography	6 (40%)
	Maximal exercise test	5 (33%)
	Social–emotional well-being	4 (27%)
	Extensive neuropsychological testing	3 (20%)
	Electrocardiogram	3 (20%)
	Quality-of-life assessment	3 (20%)
	Intracranial imaging ultrasound	3 (20%)
	Orthopedic assessment	2 (13%)
	CT chest	1 (7%)
	Ventilation/perfusion scan	1 (7%)
	Intracranial imaging MRI	1 (7%)
	Thoracic MRI	1 (7%)
	Genetic assessment	1 (7%)
	Cardiac catheterization	0

Other investigations. Specific orthopedic assessment for chest-wall deformities was reported by two centers.

We now present the literature review on these long-term morbidities in CDH survivors.

Literature review

Pulmonary function. A literature overview is provided in Supplementary Table S1. Follow-up studies assessing pulmonary symptoms in CDH have yielded conflicting results. Wheezing and recurrent cough are reported in ~10–50% of preschool children.[11–14] Asthma appears to be more prevalent in survivors

and is reflective of malformation severity.[15,16] Symptoms of obstructive airways appear to abate with age despite persistence of airflow obstruction on objective measurement.[17] Indeed, those assessed at mid (4.5 ± 1.8 years) and long term (21 ± 5.7 years) by Arena et al.,[17] reported no respiratory symptoms.

CDH survivors have been reported to suffer from recurrent respiratory tract infections,[15,18] but whether this is greater than in other term-born, ventilated infants is unclear. Respiratory syncytial virus (RSV) infection may be severe in CDH patients necessitating hospitalization and sometimes further surgery.[18] Pneumonia has been reported in 7% of CDH patients during infancy both due to infection and aspiration.[1]

Regarding functional residual capacity (FRC) in infancy, reduced, normal, and even increased FRC are reported. The latter reflects compensatory overinflation of the contralateral lung.[19–21] Additionally, lower tidal volume, higher resistance, and lower compliance of the respiratory system are reported in infancy.[21–23] Conversely, persistent obstructive and restrictive abnormalities are described in older children.[24–28] At 8 years of age, CDH survivors had comparatively lower forced vital capacity (FVC), forced expiratory volume at one second (FEV_1), and mean forced expiratory flow between 25 and 75% of the FVC ($FEF_{25–75}$).[28] In another study, at 8 years of age, the majority had normal lung function,[27] whereas at 11.9 years, lower FEV_1, FVC, and FEV_1/FVC results were reported.[26] Twenty-six CDH adolescents and 30 controls born between 1985 and 1991 (mean age of 13 years at follow-up) demonstrated significant differences in FEV_1, $FEF_{25–75}$, FRC, residual volume/total lung capacity (RV/TLC), maximal voluntary ventilation (MVV), and reduced muscle strength. A correlation between lung function results and body mass index has been reported.[16,29] At a mean age of 24.3 years, 12 young people had a lower FEV_1, although their quality of life was comparable to the general population.[30] Hyperpolarized 3He magnetic resonance (3HeMR) and anatomical 1H magnetic resonance imaging (1HMRI) studies in those who are 28 years of age have shown that functional changes persist into adulthood.[31]

Optoelectronic plethysmography in 14 children demonstrated significant thoracoabdominal and trans-thoracic asynchrony and a marked asymmetry in the expansion of the pulmonary rib cage. In those who had a patch repair, the overall diaphragmatic contribution to breathing was significantly reduced.[32]

Ninety-eight patients aged between 11 days and 44 months had pulmonary function testing between one and five occasions using the raised volume rapid compression technique. Forced expiratory flows were below normal and residual volumes and FRCs were elevated.[19] In another series, there was catchup of lung volume, but airflow remained significantly reduced. In 27 CDH and 30 controls (mean age 26.8 years at the last follow-up), a longitudinal study demonstrated mild deterioration in airflow obstruction and diffusion capacity since 11.8 years.[33]

Reduced exercise performance is reported in CDH survivors, but may improve with increasing age. At 5 years of age, CDH patients had reduced FEV_1 and maximal exercise performance.[34] Exercise testing at 7 years revealed lower anaerobic exercise capacity in CDH children than controls. Self-reports on daily activities may identify CDH survivors with low maximum peak oxygen consumption and thus identify those who may benefit from physical training.[35] In one study, 10–16- year-old survivors born in 1985–1991 had mildly reduced exercise capacity, although cardiorespiratory response to exertion was similar to controls.[36] Among 27 CDH and 30 controls treated for neonatal respiratory failure, all born at term, similar levels of exercise capacity, daily activity, and fatigue were seen at a mean age of 26.8 years.[37] Whether reduced exercise capacity impacts unfavorably remains controversial. At 6.6 years, those CDH children who had a higher level of exercise performance had less perception of dyspnea and effort.[38]

Ventilation perfusion of the ipsilateral lung has been reported in those with pulmonary morbidity and lower body weight at 1 and 2 years of age.[39] Sixty-one percent of 46 patients who had at least two scans at a mean age of 1.3 years and 6.3 years had abnormal scans.[15,40] An association between patch repair and V/Q mismatch has been reported.[25,40]

Pulmonary hypertension. The incidence and course of PH in children after CDH repair has been studied in a limited number of observational studies (Supplementary Table S2). The underlying pathophysiology and natural history of PH in CDH are not well understood. Although a number of mediators of smooth muscle tone and vascular development have been identified (nitric oxide-VEGF pathway, endothelin, and prostacyclin pathways), subclassification based on these, or other criteria, is not currently possible. There are no agreed standards to stratify PH in CDH per se. A variety of stratifications have been employed, based on echocardiographic assessment of pulmonary arterial pressures (PAP).[27,41–45]

Whether the functional and structural abnormalities of the pulmonary vasculature at birth improve or deteriorate through childhood and beyond is unknown. Observational studies with small numbers of patients have assessed PAP and cardiac function in childhood survivors. At 3 weeks of age, 51% of cases had a PAP of at least half systemic blood pressure.[46] In another study, the median age of "resolution" of PH in infants with CDH was 14[7–21] days with moderate or severe PH in 11% at discharge.[41] Behrsin and coworkers reported that 17% of infants with repaired CDH were discharged on sildenafil.[47] Approximately 40% of CDH survivors are reported to have echocardiographic evidence of PH in the first 3 years of life.[42] Echocardiographic studies in older survivors (6–11 years) have not observed increased PAP.[25,27] However, evidence of RV dysfunction has been observed at 7 years of age.[43] Cardiac catheterization studies have demonstrated elevated pulmonary vascular resistance and PAP in CDH survivors up to 12 years of age.[42,48] Although these studies suggest that chronic PH can occur after CDH repair, they are limited by study size, variation in treatment eras, and illness severity. They also highlight the current lack of standardized definitions of PH, diagnostic techniques, and prospective multicenter data collection.

Neurodevelopment. Despite arguably creating the greatest patient burden, neurodevelopmental morbidity from CDH has, until recently been underreported due to limited follow-up. Additionally, standardized assessments cannot be performed in children with severe disabilities. A literature overview is provided in Supplementary Table S3.

From infancy until school age, normal scores for cognition have been reported in CDH survivors. Overall, the cognitive and language-development scores at preschool age are normal to mildly delayed[9,49–54] with ECMO exposure, an independent predictor of impaired mental development.[50,52,55]

The findings across published studies are difficult to compare because of variability in age at assessment and study design. In CDH survivors, Danzer[56] reported that 44% of infants had mild, and 13% severe neurodevelopmental delays in at least one domain at 1 year of age. Benjamin reported that 44% were at risk for neurocognitive delay at median age of 4.9 years.[57]

At school age, intelligence appears in the average range[58–63] with only a single Japanese study reporting overall low intelligence in a cross-sectional cohort of 6–17-year olds.[64] Despite overall average cognition, many children (up to 50%) struggle in standard educational programs.[63] By school age survivors also experience concentration/attention problems.[59,63] ECMO-treated CDH patients have significantly lower scores on visual motor integration compared with neonatal ECMO controls.[62] Other studies report normal[59] to slightly impaired scores[55,58] on visual motor integration. The children report that their perception of

general health is reduced when compared to the reference norm,[65,66] positively they report a well-developed feeling of self-confidence.[63,66] Such neurocognitive delays recorded in earlier life may improve.[55]

Data on motor function in children with CDH are scarce, but problems occur in ~40% of children at preschool age and 20–30% at school age. Preschool motor development scores in CDH patients are usually reported to be normal or subnormal[9,49,51–53,55,61,67] seeming to improve between 1 and 3 years of age.[51,53] In a population of 47 CDH patients of whom 26% received ECMO, mild to severe motor-function delay was reported in 45 and 19% at 1 and 3 years, respectively.[51] At 5 years, 47% of ECMO-treated CDH patients had normal motor function; the remaining 53% had gross delays.[60] In another study, 58% of 5-year olds, both with and without the need for ECMO, had normal motor function.[68] In a cross-sectional cohort of 15 non-ECMO-treated CDH patients aged 6–15 years old, Tureczek et al.[61] observed gross motor-function problems in 80%, whereas motor performance was normal in all eight participants aged 3–5 years in the same study. Although motor function seems to improve at the age of 8 years,[63,69] it deteriorates when the children get older.[69] This suggests that CDH patients grow into their deficits when tasks become more complex.

Sensorineural hearing loss. SNHL is the most common sensory deficit in humans with a prevalence ranging from 1.5 to 6 per 1000 live births[70] with a tenfold higher prevalence (1–3%) in those who require neonatal intensive care.[71] A literature overview is provided in Supplementary Table S4.

In patients with CDH, SNHL has been reported with a variable prevalence, ranging from 0[72] to 100%.[73] Although earlier studies tend to present a higher prevalence of SNHL, Amoils and coworkers report a prevalence of SNHL over 50% in 2015.[74] Controversies exist on the impact of the diagnosis of CDH on the risk of SNHL development. In a study on 111 ECMO graduates, Fligor and coworkers reported a 26% overall prevalence of SNHL in neonates with severe respiratory distress and described CDH as an independent risk factor.[75] Conversely, a more recent study of 136 ECMO survivors observed a prevalence of 9% of SNHL, irrespective of the underlying diagnosis.[76] As far as the natural history is concerned, in CDH patients, SNHL tends to present as late-onset and progressive. Most studies with data from neonatal hearing screening, report normal findings.[73,74,77–81] Therefore, the extreme variability in length of follow-up in available reports, precludes firm conclusions on the actual prevalence.

The most frequently reported factors associated with SNHL are ECMO treatment,[74,75,82,83] length of mechanical ventilation and/or stay in the NICU or in hospital,[74,78,79,83–85] need for inhaled nitric oxide,[84] patch repair,[74] and dose and duration of specified drugs: loop diuretics,[74,78,82–84] aminoglycosides,[75,83,84] and pancuronium bromide.[78, 84] Overall, these factors suggest that the most critically ill CDH patients are at greatest risk. Identifying definite factors that place CDH patients at high risk for SNHL will permit their modification and may aid prognostication.

Gastrointestinal morbidity and growth. CDH-related gastrointestinal morbidity is common.[86] The main morbidities are OA, need for tube feeding (NFT), failure to thrive (FTT), and gastroesophageal reflux disease (GERD) (Supplementary Table S5).

Slower growth velocity in infants with CDH during the early postnatal period is described.[22] Approximately 20–30% experience FTT within the first few years of life which may persist into adolescence.[87,88] However, Gien et al.[89] revealed the highest risk for comorbidities at both extremes of growth velocity. Leeuwen et al.[88] observed stunting and wasting up to 12 years of age, although growth failure became less prevalent after correcting for individual target height. Several risk factors expressing the severity of CDH have been identified: the intensity of respiratory support, ECMO use, and oxygen supplementation at discharge.[90–92] Data about the underlying mechanism for FTT in CDH are scarce. Increased work of breathing, OA, GERD, and acute metabolic stress have been identified as contributing factors.[93–95]

A recent study demonstrated that 58% of infants with CDH were in a hypermetabolic state measured by indirect calorimetry supporting the need for increased caloric intake for appropriate growth.[90] The best nutritional strategy for these infants is uncertain and an individually tailored approach is generally used. The optimal growth targets for this population remain unidentified, and whether a strategy of hyperalimentation risks later cardiovascular disease.[96]

GER is present in up to 86% of infants with CDH in the first year of life.[97] Ascertaining whether GER is pathologic or not is a key issue. Identified risk factors include antenatal diagnosis, intrathoracic liver position, patch closure, stomach position, esophageal dysmotility, and tube feeding at discharge.[98–100] Gastrointestinal symptoms (GERD, FTT, and OA) are associated with a longer hospital course, prolonged mechanical ventilation, and a longer need for parenteral nutrition.[101] The diagnostic approach for suspected GERD in infants with CDH should be based on standard guidelines.[102] Therapeutic approaches include proton pump inhibitors and surgical fundoplication. In one study, the need for antireflux surgery related to gestational age and defect size.[101] Not all infants demonstrate improvement in anthropometric scores following treatment.[87] GERD can lead to worsening of chronic lung disease, aspiration pneumonia, malnutrition, and FTT. Its presence has an effect on quality of life.[16] There are a few studies on primary antireflux surgery and its effect on growth and GERD with conflicting results.[101,103] Patients without prophylactic antireflux surgery typically undergo this treatment before 6 months of age.[104] The long-term outcome of GERD in CDH patients is unclear. However, Barrett's esophagus and esophageal adenocarcinoma have been described in CDH patients.[105]

The reported incidence of OA is as high as 25%; the underlying etiology is largely unknown.[16,72] It has been suggested that the endotracheal tube might interfere with the development of a normal swallow.[94] The incidence of OA in patients with CDH is associated with a more severe postnatal clinical course. Early aggressive intervention failed to reduce its incidence.

NTF is described in association with FTT in CDH patients. Data on its use are scarce with a reported incidence between 18 and 70%, and an association with markers of disease severity.[13,90,93]

General surgical morbidity. Long-term general surgical morbidities include recurrence of the diaphragmatic defect, chronic patch infections, and volvulus in those with rotational anomalies (Supplementary Table S6).

All literature reports identified were retrospective, mostly single center and with variable follow-up time points. Hence, comparison across studies is not feasible. Small defects (A and most of B) according to the CDH study group staging system[106] are closed primarily by direct non-absorbable sutures. In large defects (large B, C, or D) a patch is typically employed. The risk for recurrence relates to closure technique—which is not standardized,[107–112] liver position,[113] and patch material.[112] Minimally invasive surgery (MIS) has become more common, with a corresponding increase in recurrence rates.[108,114,115] Up to 2/3 of recurrences are found incidentally. Plain x-ray does not have a high sensitivity for detecting recurrences, but remains the most commonly used diagnostic tool.

The incidence of small bowel obstruction may be higher with patch closure[113] but reports are contradictory.[110] A MIS approach may be protective.[116]

Infectious complications are seldom encountered and conservative therapy with antibiotics seems to be appropriate.[110]

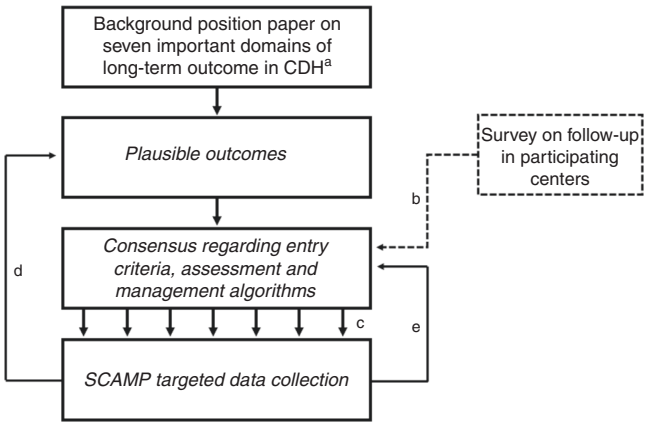

Fig. 2 Standardized clinical assessment and management plan (SCAMP) proposal for long-term follow-up in congenital diaphragmatic hernia (CDH). The figure is based on the schematic representation of SCAMPs (solid boxes) proposed by Rathod et al.[10] Steps that still need to be taken are indicated in italics. **a** By consensus, seven domains of interest were selected: pulmonary morbidity, pulmonary hypertension, neurodevelopmental morbidity, sensorineural hearing loss, gastrointestinal morbidity and growth, surgical morbidity, and musculoskeletal morbidity; **b** to explore the feasibility of development of SCAMP and performing assessments within the CDH EURO consortium, we performed a survey on current practices of follow-up of CDH patients (dashed box); **c** multiple plausible outcomes based on literature review of seven domains and involvement of patient support groups will be explored simultaneously; **d** capture and explore deviations;[10] **e** iterative data analysis and SCAMP modification[10]

Data on malrotation management and need for follow-up in children with CDH are lacking. Only two studies report on volvulus[109,117] with a prevalence of 0.3% when no Ladd's procedure was performed.[117]

Musculoskeletal morbidity. Until recently, there have been few reports on musculoskeletal morbidity in CDH patients (Supplementary Table S7). While the prevalence of idiopathic scoliosis at school age is ~0.5%,[118] it was reported in 2–26% of children with CDH. However, application of the more restrictive current definition of scoliosis results in a lower prevalence. While Kuklova and coworkers showed no impact of closure technique,[119] Russell reported the prevalence of sciolosis following muscle flap or patch repair to be twice that of those following primary closure (13%, 15%, and 7%, respectively).[120] Jancelewicz et al.[109] noted scoliosis in 10% of children who underwent non-primary repair.

Chest-wall deformity (i.e., pectus excavatum) occurs in 4–50% of patients (Supplementary Table S7) and may relate to defect size and closure technique.[119,120] Jancelewicz et al.[108] reported that mild chest deformity was extremely common at all ages, but major deformity requiring referral and eventually further treatment occurred in only 8% of patients and at a median age of 5 (range 1.1–6.8) years.

DISCUSSION

We aimed to evaluate the current practice of long-term follow-up within the CDH EURO consortium centers and to review the literature informing such activity. All respondents agreed that standardization of follow-up was needed and were willing to adopt a collectively agreed standardized follow-up pathway within the consortium. Although follow-up was structured and standardized in 15 of 19 participating centers, only three centers supported following up all CDH patients without any risk stratification. The majority of centers supported the review of only those at the highest risk of morbidity. Lack of resources or personnel were identified as the most important barriers to implementing a structured follow-up program.

Literature review showed that children with CDH suffer from substantial long-term morbidity across several domains. However, most data arise from retrospective chart reviews, usually from single centers of a small series of patients and the proportion of eligible patients is frequently low or unknown. In short, the current literature is insufficient to provide clear guidance on what constitutes ideal follow-up of children with CDH.

To optimize long-term care with standardized follow-up for children with CDH, a task force of members of the CDH EURO consortium agreed to use the standardized clinical assessment and management plan (SCAMP) methodology to establish care pathways. SCAMPs outline a data-backed, consensus-based, care pathway for a diverse patient population with a particular diagnosis or condition.[121] The methodology aims at improving patient outcomes, reduces practice variation, and reduces unnecessary resource utilization. Assessment of the effectiveness of diagnostic testing and management interventions is included in the process.[10,121] This approach, which has been used extensively in health care since its introduction in 2009,[122] may—in the long run—reduce the burden of lack of resources or personnel to perform standardized follow-up. Moreover, it may contribute to standardization of assessments facilitating international multicenter collaboration.[9] The first step in the process—which includes formulation of a background position paper based on literature review and evaluation of current practice[121,122]—has been undertaken by the CDH EURO consortium members (Fig. 2). This step will be followed by definition of plausible outcomes (closely specified statements potentially refutable by accumulating and reviewing unbiased follow-up data), identification of entry criteria, and assessment and recommended management algorithms. Thereafter, targeted data collection, recorded on SCAMP data forms will be followed by iterative data analysis enabling modification of the follow-up algorithms.[10,122] This process will be labor intensive and requires careful thought. We expect that this initiative will stimulate multicenter collaboration within the consortium and lead to the evidence-based provision of long-term multidisciplinary care for CDH patients, and ultimately improved clinical outcomes. With increased survival rates after the introduction of standardized treatment protocols for CDH patients,[3] more children will reach adulthood and participate in society. Recommendations for optimal multidisciplinary follow-up are expected to disseminate into adult care.

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ADDITIONAL INFORMATION

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