Pediatric Surgery Congenital Anomalies Prospective Follow-up Clinic: Gastrochisis, Omphalocele, Esophageal Atresia and Tracheoesophageal Fistula

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A Capstone Project Submitted to the Master of Physician Assistant Studies Program

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May 2017
Abstract

Infants born with gastroschisis, omphalocele, tracheoesophageal fistula or esophageal atresia are increasingly likely to survive beyond the Neonatal Intensive Care Unit due to improved supportive care. After the acute management and surgical interventions have been completed, these patients are variably followed by their pediatric surgeons. Therefore, a review of the existing literature to create disease-specific guidelines for the long-term follow-up of patients was deemed necessary to improve and standardize care. The guidelines will be tailored to the resources and expertise available at Winnipeg Children’s Hospital at Health Sciences Centre. This report will also outline the role of a PA in a Pediatric Surgery follow-up clinic and describe how PA involvement can enhance the accessibility and quality of care provided. **Methods:** The PRISMA reporting guideline for systematic reviews was used to select papers that met the criteria for this literature review. Publications within the last 15 years were chosen and deemed eligible by searching for each congenital anomaly with the terms “follow-up” and/or “outcomes” and/or “long-term” and/or “quality of life”. **Results:** The literature review identified long-term sequelae for survivors of each congenital anomaly. Neurodevelopmental delay, gastrointestinal symptoms and disease, poor growth, malnutrition and cosmetic concerns were common sequelae noted to potentially impact the quality of life of survivors. **Conclusion:** These individuals are likely to face a variety of health and developmental challenges in life. Establishing a clinic that applies these proposed guidelines will help ensure that each child has the best chance to access needed investigations and treatments in a timely manner, while maintaining a quality of life comparable to that of the general population. Physician Assistants should be viewed as essential to the success of this
clinic. Their competency and skill set can meet the broad demands of the clinic while freeing physicians to focus on less-routine, more complex tasks related to the clinic or elsewhere.

**Introduction**

As the supportive care of neonatal patients improves, more fragile infants are surviving beyond the Neonatal Intensive Care Unit. This includes infants born with congenital surgical anomalies such as gastroschisis, omphalocele, tracheoesophageal fistula and esophageal atresia. After the acute management and surgical interventions have been completed, these patients are variably followed by their pediatric surgeons. Presently, the surgical follow-up is based on the experience and preference of the individual pediatric general surgeon. This has resulted in different follow-up for patients with the same congenital anomaly. In addition, delayed identification of complications and lack of patient and/or family support may result from the present pattern of care.

Given these gaps in care, it is necessary to review the existing literature and to create disease-specific guidelines for the long-term follow-up of patients with gastroschisis, omphalocele, tracheoesophageal fistula and esophageal atresia. The guideline will be tailored to the resources and expertise available at Children’s Hospital Health Sciences Centre Winnipeg.

**Gastroschisis**

Gastroschisis (GS) describes a congenital defect in the anterior abdominal wall through which abdominal viscera herniate.\(^1\) The defect is believed to be the result of a disruption of the vascular infrastructure of the developing abdominal wall. It occurs in 1
in 2000 live births.\textsuperscript{1} Fetuses with GS are usually identified with prenatal ultrasound. When delivered, babies present with evisceration of the intestine, liver, spleen and/or gonads. Treatment involves returning the viscera to the peritoneal cavity and closing the abdominal wall.\textsuperscript{1}

While the short-term survival for infants with GS is very good, the long-term outcome is poorly defined. In 2008, the Canadian Pediatric Surgical Network (CAPSNet) reported an overall survival to discharge of 96\% for infants with GS.\textsuperscript{2}

\textbf{Omphalocele}

An omphalocele (OC) is a midline abdominal wall defect of variable size, covered by a membrane and containing abdominal viscera. The defect occurs at the base of the umbilical cord, with the umbilical vessels inserting at the apex of the OC sac. It occurs in approximately 1 of every 6000 live births.\textsuperscript{3} OC may be described as small, giant, ruptured, or liver-containing versus non-liver-containing. Almost all cases are diagnosed by ultrasound at the end of the first trimester. After delivery, surgical management involves returning the herniated viscera to the abdominal cavity and closing the abdominal wall.\textsuperscript{3}

A North American study of 348 neonatal intensive care units involving 1500 cases found that 92\% of live-born OC patients survived to discharge.\textsuperscript{4} Despite this high short-term survival rate, the long-term outcomes are inadequately defined. Children with OC often have additional congenital anomalies. And, although survival is heavily influenced by the severity of the associated anomalies, survivors frequently have sequelae that are attributable to the abdominal wall defect.
Esophageal atresia and tracheoesophageal fistula

Esophageal atresia (EA) is a congenital defect characterized by a lack of continuity of the upper gastrointestinal tract. EA is often associated with a persistent fistula between the trachea and esophagus, referred to as tracheoesophageal fistula (TEF). The incidence of EA with or without TEF is approximately 1 in every 3500 live births. EA and TEF are caused by a defect in the separation of the primitive foregut into esophagus and trachea. EA/TEF are classified anatomically (Figure 1). Type C, which consists of a proximal esophageal pouch and a distal TEF, accounts for 84% of EA/TEF presentations.

Figure 1. Types of tracheoesophageal fistulas (Data from: Clark, DC. Esophageal atresia and tracheoesophageal fistula. Am Fam Physician 1999;59:910. TEF types classified according to the scheme developed by EC Vogt in 1929, as modified by Gross.)
EA/TEF should be suspected shortly after birth when an infant drools, chokes, experiences respiratory distress or has problems feeding. The diagnosis of EA can be made by failure to pass a catheter from the oropharynx into the stomach. A water-soluble contrast study is required to demonstrate TEF in the absence of EA. Treatment of EA with TEF involves surgical ligation of the fistula and anastomosis of the esophageal ends.

The outcomes of EA with or without TEF depend heavily on the presence of associated congenital anomalies. CHARGE syndrome and VACTERL association are two disorders that may include EA/TEF in the presence of associated anomalies. Patients with CHARGE syndrome may have coloboma, heart defects, atresia of choanae, retardation of growth or development, genital hypoplasia and ear anomalies. VACTERL describes the association of vertebral, anorectal, cardiac, tracheoesophageal, renal and limb anomalies. A single-center study in Missouri reported an 87% survival rate for children with EA and TEF, with the majority of early deaths being associated with cardiac or chromosomal abnormalities.6

**Purpose**

The purpose of this project is to review the literature and create disease-specific guidelines for the long-term follow-up of patients with gastroschisis, omphalocele, tracheoesophageal fistula and esophageal atresia. The literature will be searched using combinations of the terms: follow-up, outcome, long-term and quality of life, with the disease names. The guidelines will be tailored to the resources and expertise available at Winnipeg Children’s Hospital at Health Sciences Centre (HSC). Physician Assistants (PA) are one of HSC’s resources. This report will outline the role of a PA in a Pediatric
Surgery follow-up clinic and describe how PA involvement can enhance the accessibility and quality of care provided.

Methods

The PRISMA reporting guideline for systematic reviews was used to select papers that met the criteria for this literature review. Publications were chosen and deemed eligible by searching for each congenital anomaly with the terms “follow-up” and/or “outcomes” and/or “long-term” and/or “quality of life”. Additional criteria restricted eligible publications to those published within the last 15 years and written or translated in English. Google Scholar and PubMed were the two databases used to identify relevant studies. A completed PRISMA guideline for the electronic search of PubMed for papers relevant to follow-up of EA/TEF can be found in Figure 2. A similar process was performed for the GS and OC reviews.

Publications that met the eligibility criteria were read in their entirety with attention directed to the material/methods and results sections. The materials/methods sections usually detailed the evaluations, questionnaires, investigations or procedures performed on the survivors of each respective congenital anomaly. The results sections detailed the age range or mean age of the study participants and the findings and outcomes of the evaluations, questionnaires, investigations or procedures.

Guidelines for the long-term follow-up of patients with each disorder were summarized from the selected papers. Investigations or procedures not currently available at Children’s Hospital Winnipeg were not considered for inclusion in the guidelines.
Results

Many of the papers that met inclusion criteria included assessments of neurodevelopment and/or ‘quality of life’ in patients with congenital anomalies. Because neurodevelopment and quality of life were not considered to be disease-specific sequelae, and to simplify follow-up, a single guideline for the follow-up of neurodevelopmental outcomes and quality of life in survivors of GS, OC and EA/TEF was proposed.
**Gastroschisis**

Eight papers were identified that described disease-specific outcomes for children with GS.

Koivusalo did a small survey of 11 GS patients at a median of 26.5 years of age in Finland. The survey consisted of three parts: a questionnaire focusing on health and disease, a questionnaire measuring psychosocial functioning and a validated measure of quality of life. The results of this study suggest that although functional gastrointestinal disorders are common among patients with GS, these intestinal disorders do not cause serious problems. Furthermore, the quality of life for these patients is no different from the general population.

Henrich used 3 standardized data collection forms and structured follow-up examinations to assess abdominal muscle function, development, cosmetic results and quality of life in 22 children with GS. The median age of follow-up was 6.3 years. Henrich found that 7.1% of children had ‘frequent’ gastrointestinal problems, while 77.4% had them ‘rarely’ or ‘never’. The weight of 9% of children and the height of 14% of children was below the 3rd percentile. Cosmetic results regarding scarring were described as ‘good’ or ‘excellent’ in 82% of patients. However, 23% of patients had had umbilical reconstruction and 77% had no umbilicus. The degree of concern about the cosmetic appearance of the abdominal wall scar was variable. Thirty-two percent of children had delayed sitting or walking, and 77% started kindergarten at the appropriate age.

South reported on the growth and neurodevelopment of 17 children born with GS. Weight, length, bowel function and Bayley Scales of Infant Development were reported
between 16 and 24 months of age. Nearly one-third of the children were less than the 10th percentile for weight. The Rome criteria were used to identify functional bowel problems; 35% and 59% of patients had symptoms of diarrhea and constipation, respectively.

A study from Australia in 2012 reported on the growth and developmental outcomes of 117 children born with GS.\textsuperscript{10} The outcomes of interest were long-term neurodevelopment, failure to thrive and prolonged duration of hospital stay. Failure to thrive at 1 year of age was defined as z-scores for weight less than -1.28 (\textless 10th percentile). There were no significant differences between z-scores for weight or length at birth and at 1 year of age. However, almost 30% of children had a weight z-score below the -1.28 (\textless 10th percentile) at 1 year of age.

Recently, a group from Edmonton, Canada, described the outcomes for 61 children with GS.\textsuperscript{11} They reported on gastrointestinal complications, visual and hearing impairment, developmental delay and cerebral palsy. Data collection was completed at a median age of 20 months. Ninety percent of children were receiving treatment with gastric motility or acid reducing medications for presumed gastroesophageal reflux disease (GERD). At a median of 20 months of age, 15% of children still required tube feeds. Ten percent of 39 children had sensorineural hearing loss requiring aids. Two of 39 children evaluated at a median of 20 months had visual impairment; both children were syndromic.

In 2014, Harris described the long-term physical outcomes for 50 children with GS at a median of 9 years of age.\textsuperscript{12} A health questionnaire, physical assessment, bone density and nutritional blood parameters were assessed. Weight, length and head
circumference improved over time, with 24% of patients eventually becoming overweight and 9.5% becoming obese. Systolic and diastolic blood pressures were above the 90\textsuperscript{th} percentile for 3 and 2 children, respectively, out of 34 children from whom measurements were available. Forty-one percent of children reported abdominal pain occurring at least once per week and 13\% reported that the pain had recently kept them from school or work. Fifteen percent and 9\% described their stools as constipated or watery, respectively, which would be expected in a control population. According to Harris, 18\% of children had evidence of iron deficiency anemia, 13\% had vitamin D deficiency and 6\% had vitamin B12 deficiency. Deficiencies of vitamin A and zinc were less frequently identified. Twenty-four percent of patients had elevated fasting cholesterol levels. Thirty percent of children that their abdominal scar was a ‘small’ problem and 13\% reported it to be a ‘major’ problem.

An Argentinean study of 62 children born with GS reported assessments at a standardized follow-up clinic at 1, 3 and 6 years of age.\textsuperscript{13} Children were examined for deficits in growth, vision, hearing, neuro-psychomotor development, language, re-hospitalization rates and surgical re-intervention rates. This study found that patients were at risk for growth delay, late onset hearing loss, neuro-psychomotor delay, surgical re-intervention and re-hospitalization but for causes unrelated to the history of GS; respiratory causes were usually suspected. Twenty percent of children were below the 10\textsuperscript{th} percentile for growth at ages 1 and 6 years. Twenty-four percent of children had abnormal hearing at 3 and 6 years. Rehabilitation improved the hearing in most children. At 1 year of age, 98\% of children had normal vision, but by 6 years of age only 53\% had normal vision. Neuro-psychomotor development declined between 1 and 6 years of age;
64% of patients achieved normal scores at 1 year of age, while only 35% achieved normal scores at 6 years of age. Language skills remained stable but suboptimal from 1 to 6 years of age with less than 65% of patients achieving normal scores over the 5 years of follow-up.

**Omphalocoele**

Five papers were identified that described outcomes of children with OC. In addition, Gamba provided a good summary of studies done by other researchers. They found up to 60% of survivors facing long-term medical problems such as GERD, pulmonary insufficiency, recurrent lung infections or asthma and feeding difficulties. They also reported that intermittent abdominal pain was an issue into young adulthood in one-third of patients. Overall it was cosmetic concerns such as abdominal scars or lack of umbilicus that was most prevalent in Gamba’s review of literature on giant OC survivors. They concluded that early intervention and intensive surgical correction of minor or giant OC in the absence of concurrent anomalies results in patient’s health and quality of life being comparable to that of the general population.

Zacarra evaluated OC patients greater than 7 years of age using clinical examination, exercise stress testing and spirometry to evaluate cardio and pulmonary performances. They used the Bruce protocol, which involves stepwise increases in inclination and speed of a treadmill while measuring heart rate, oxygen consumption and systolic blood pressure. Compared to the normal pediatric population, OC survivors did not differ significantly in any parameter measured.
Biard from Philadelphia performed a small study of 5 children with giant OC at a mean age of 33.2 months. The parents and physicians completed a questionnaire regarding the children’s health issues including: height, weight, dietary habits, surgical procedures and a systematic review of major body systems. The general health questionnaire revealed pulmonary, gastrointestinal and abdominal wall issues. Two children were below 5th percentile for height and weight at 33 months of age. Four children were below the 25th percentile for weight and height. Wound herniation occurred in 2 patients. The 2 male patients had bilateral inguinal hernias requiring repair. Developmental delay, including hearing deficiency, was reported in 2 children. Feeding problems were reported in 3 children, and 2 had failure to thrive. The health questionnaire showed 3 patients had reactive airway disease requiring medication, 2 had recurrent pulmonary infections, and 2 patients had severe bronchomalacia. Four patients suffered from reflux. Reflux was treated medically in 3 patients and surgically in 1.

Predicting that giant OC survivors would have a high incidence of pulmonary insufficiency and respiratory failure, Danzer subjected 14 giant OC survivors to pulmonary function testing (PFT). The evaluation included measures of forced expiratory flows and bronchodilator responsiveness, and body plethysmography to calculate lung volumes and the passive mechanics of the respiratory system. The mean age at assessment was 19.3 months. The mean forced vital capacity (FVC), mean forced expiratory volume in the first 0.5 second and total lung capacity (TLC) were reduced compared to normal controls, but functional residual capacity, residual volume and residual volume to total lung capacity ratio were within the normal range. Danzer reported a significant response to bronchodilators in 6 of 13 patients (46%) tested.
In Finland, Koivusalo did a survey of 46 OC patients at a median age of 26.5 years. The survey consisted of three parts: a questionnaire focusing on health and disease, a questionnaire measuring psychosocial functioning and a validated measure of quality of life. The results of this study suggest that although functional gastrointestinal disorders are common among patients with OC, these disorders do not cause serious problems. Half of the patients reported gastrointestinal disorders, with 5% being ‘severe’, 14% ‘moderate’ and 31% ‘mild’. These disorders varied from regurgitation to bloating and heartburn. Koivusalo noted that 37% of patients found their umbilical scar troublesome.

Henrich used three standardized data collection forms and structured follow-up examinations to assess abdominal muscle function, development, cosmetic results and quality of life. Fifteen children with OC participated in the study at a median age of 6.3 years. The median age was an approximation because it included GS patients in the cohort. Thirteen percent and 20% of patients assessed by Henrich were below the 3rd percentile for height and weight, respectively. Seventy-three percent of patients in reported ‘good’ or ‘excellent’ feelings towards their abdominal wall scar, yet 20% reported a hernia. Thirty-two percent of children had delayed sitting or walking and 77% started kindergarten at the appropriate age. Thirteen percent of patients had limitations in sports and 7% had limitations in everyday activities. Henrich found that 7.1% of children had ‘frequent’ gastrointestinal problems, while 77.4% had them ‘rarely’ or ‘never’.

**Esophageal atresia and tracheoesophageal fistula**

Fourteen papers were identified that described the long-term outcomes of patients with EA/TEF. In addition, a group from Rotterdam described an EA/TEF follow-up
protocol currently in use (personal communication). Also, Mirra performed a literature review to develop a clinical algorithm to systematically follow-up lung disease in EA/TEF patients (Appendix C).^{19}

In Finland, Koivusalo studied the incidence of GERD in EA/TEF patients.^{20} They followed children using endoscopy and pH-probe testing at 1, 3, 5 and 10-years post-correction of their anomalies. Endoscopic biopsies were taken to correlate symptoms with histological findings. The group was also clinically assessed for the presence of GERD symptoms every 2 months in the first year of life. Sixteen percent of patients were diagnosed with significant GERD by 6 months of age, 39.3% by 12 months, 44.2% by 3 years, 51.2% by 5 years and 44.4% by 10 years.

Malmstrom performed bronchoscopy and endoscopy at less than 3 years of age, between 3 and 7 years of age, and then over 7 years of age as follow-up for EA/TEF repair.^{21} Furthermore, a questionnaire regarding respiratory and esophageal symptoms was completed at a mean of 13.7 years. The questionnaire focused on asthma and allergy symptoms using the validated International Study of Asthma and Allergies in Childhood (ISAAC). Questions regarding pneumonia, dysphagia and GERD were also asked. At 13.7 years patients also underwent physical examination and PFTs. The ISAAC questionnaire revealed 14% of patients endorsed respiratory symptoms and 22% had doctor-diagnosed asthma. PFTs revealed 35% of patients with a restrictive pattern, 30% with an obstructive pattern, and 78% showed an increased bronchial response to histamine.

Gischler followed the respiratory morbidity and physical condition of 23 EA/TEF patients from birth until 5 years of age.^{22} Patients were assessed for the incidence and
severity of bronchopulmonary dysplasia (BPD) using the National Institute of Child Health and Human Development guideline (NICHD) (see Appendix A). Follow-up at 6, 12, 24 and 60-months involved a full physical exam. At 5 years of age the children were subjected to PFTs and maximal exercise testing. The exercise performance was assessed by increasing the inclination and speed on a treadmill according to the Bruce protocol. A barium swallow x-ray and a non-validated gastrointestinal questionnaire were also performed at 5 years. Gischler diagnosed 3 patients with BPD. The study noted 73.9% of patients had more than 5 respiratory tract infections in 5 years of follow-up. Therapeutic antibiotic courses decreased with age while prophylactic courses increased. Twenty-six percent used bronchodilators, while 8.7% used inhaled steroids. PFTs at approximately 5 years of age found flow-volume curves were not reproducible and 25% had abnormally low forced expiratory volume in the first second (FEV$_1$). Furthermore, weight, height and BMI were all significantly reduced.

Peetsold’s study compared the pulmonary function of TEF patients with GERD to those without GERD.$^{23}$ Children with GERD but born without TEF were included as controls. The children had to be 8 years of age or older to undergo PFT and cardiopulmonary exercise testing. The mean age of the groups was 13.8 years with GERD and 13.2 years without. PFTs revealed low FVC and TLC in patients with TEF, with and without GERD when compared to controls with GERD but without TEF. The study also revealed that patients with TEF and GERD had reduced FEV$_1$ when compared to TEF survivors without GERD, demonstrating that GERD may play a role in impeding pulmonary function.
In 2010, Gatzinsky examined the respiratory status of adult survivors of EA/TEF with a mean age of 31.7 years. A questionnaire was applied, asking about obstructive respiratory disease, respiratory symptoms, rhinitis, smoking and family history of asthma or allergy. Many adult survivors of EA/TEF had asthma or asthma-like symptoms as well as a high prevalence of allergy. Thirty percent of survivors had physician-diagnosed asthma, 24% were on asthma medications, 44.4% experienced wheezing in the last 12 months, 28.8% had recurrent wheeze, 30% had long-standing cough, 34% produced sputum with coughing and 13.7% had chronic bronchitis.

Gastzinsky subsequently investigated the peripheral airway function in adults with repaired EA/TEF. The study made use of the same questionnaire as in 2010, along with spirometry and allergy testing of the 28 adults with a median age of 35 years. The study showed that not only do adult EA/TEF survivors complain of respiratory symptoms, but also their respiratory function is abnormal. At 35 years of age, 61% had abnormal ventilation distribution and peripheral airway function on PFTs, and 50% had reduced FEV₁.

Sistonen studied 101 EA patients in 2011, with the majority having an associated TEF at birth. The study focused on survivors later in life ranging from 22-56 years of age with a mean of 36 years. All patients responded to symptom questionnaires regarding esophageal, respiratory, musculoskeletal symptoms and quality of life. Sistonen used the 36-item short form health survey (SF-36), the Gastrointestinal Quality of Life Index (GIQLI), and the Respiratory Symptom-related Quality of Life Index (RSRQLI). The patients also underwent endoscopy with biopsy, esophageal manometry and PFTs. Orthopedic evaluation with radiographs were also performed, as previous studies had
shown the EA/TEF population being afflicted by skeletal and vertebral anomalies. Sistonen found 34% of patients had GERD and 85% experienced dysphagia. When scoped, 58% had abnormal scopes (hiatal hernia, macroscopic Barrett’s, esophagitis or anastomotic stricture). X-rays found 45% of survivors had vertebral anomalies and 56% had scoliosis.

Beucher, from France, performed a series of same-day examinations on 31 EA/TEF survivors with a median of 8 years of age. The main purpose was to study long-term respiratory status after repair of EA/TEF including PFTs and airway hyper-responsiveness. The examinations also involved chest x-rays, cardiopulmonary stress tests on a bicycle ergometer and an assessment of nutritional status. No significant differences were found in electrocardiogram or blood pressure recordings at rest or with exercise compared to healthy controls. However, 68% of EA/TEF patients had abnormal PFTs, 19% had an obstructive pattern and 23% had a restrictive pattern. Parenchymal abnormalities were seen on 10% of chest x-rays, including pleural and rib abnormalities. The body-mass index z-scores were -0.67 compared to healthy population.

Legrand assessed the nutritional status of EA/TEF patients with a proximal pouch and distal tracheoesophageal fistula at a mean of 13.3 years. Height and weight were recorded; BMI was calculated. Digestive and respiratory symptoms were assessed by questionnaire. Dysphagia, how long it took to eat a meal, if early sensation of satiety was experienced or if abdominal pain occurred were evaluated. The presence of chronic cough, barky cough (suggestive of bronchomalacia), number of episodes of bronchitis and the presence of dyspnea on exertion were recorded. PFTs and endoscopy were performed. Sixteen percent of children were overweight and 9% were undernourished.
Chronic cough (> 2months/year) occurred in 19%, barky cough in 24.5%, one or more episodes of bronchiolitis per year in 42%, and 37% experienced dyspnea on exertion. Fifty percent of patients had an obstructive pattern and 11% had a restrictive pattern on spirometry.

In 2013, Pedersen evaluated gastroesophageal problems in 59 patients with EA/TEF at a mean of 10.2 years. Information was gathered regarding medical history, heartburn and regurgitation, use of medications, eating habits and swallowing difficulties. The questionnaire was not validated. Upper endoscopy with biopsy, endoscopic ultrasonography, manometry and pH impedance measurements were also performed. Almost 56% of patients reported GERD symptoms; 69.5% endorsed dysphagia monthly and 15.3% experienced it daily. Endoscopy demonstrated 33.9% had esophagitis; biopsy abnormalities such as esophagitis, hyperplasia and granulocytes were found in 44.1% of patients. Pedersen’s suggested that routine follow-up with endoscopy and pH-metry is warranted in EA/TEF patients, but no specific timeline was provided.

Koziarkiewicz from Poland evaluated EA/TEF survivors at 13.7 years of age by physical examination, 24-hour esophageal pH monitoring, endoscopy and x-ray of the chest and spine. Forty-four percent reported esophageal symptoms. Anastomotic stricture was found on endoscopy in 66.7% patients. The orthopedic evaluation found that 66.7% had scoliosis, 20% had vertebral abnormalities and 13.3% had rib anomalies.

In 2016, Krishnan recognized the lack of a systematic approach to care for survivors of EA/TEF. Krishnan developed clinical questions pertaining to gastrointestinal and nutritional complications in EA/TEF survivors. The questions were answered using results of a systematic literature review and the expert opinions of a GI
working group. The group developed three algorithms; one for EA survivors without symptoms, another for EA survivors with symptoms, and another for EA survivors with symptoms and anastomotic stricture. Regardless of symptoms, the group recommended the use of PPI-therapy in the neonatal period (low level evidence), and continuation of therapy dependent on the presence of GERD symptoms thereafter (low level evidence). The group recommended that all EA patients undergo endoscopy and biopsy at time of discontinuation of antacid therapy (high level evidence), again before the age of 10, and again at transition to adult care (low level evidence). In cases of unremitting symptoms of GER, the group suggested performing barium contrast studies, endoscopy and biopsy, and pH-metry before considering fundoplication (high level evidence). The group also recommended survivors be evaluated by pulmonology and otolaryngology teams, regardless of symptoms (low level evidence). The group recommended that anatomic abnormalities should be ruled out in those survivors with respiratory symptoms (high level evidence). When it comes to patients with dysphagia, the group recommended work-up by upper GI contrast study or upper endoscopy with biopsy (low level evidence). In cases of dysphagia, the group recommended ruling out vascular malformations via CT or MR chest angiography. The group supported aggressive enteral and oral nutrition intervention to avoid long-term malnutrition complications (low level evidence). Krishnan found high level of evidence that showed EA survivors have a high incidence of dysphagia, symptoms of GER, esophagitis and Barrett’s esophagus in adulthood. Because of this, they recommended routine endoscopy every 5 to 10 years after transition to adulthood (no evidence).
Quality of Life

A total of five papers included investigations into the quality of life of children born with TEF/EA, or GS, and/or OC. The tools employed in these papers had to have been validated to meet criteria for inclusion in this guideline.

Koivusalo evaluated the quality of life in GS and OC survivors using the SF-36 questionnaire, a generic and easy to use measure of quality of life that relies on patient self-reporting. The questionnaire is most commonly used for routine monitoring and assessment of care outcomes. The median age of patients was 27 years, but ages ranged from 17 to 48 years. After scoring the questionnaires, it was found that low self-esteem existed in 12% of patients but overall quality of life as within the normal range of the general population.

Legrand made use of the adapted versions of the PedsQL 4.0 questionnaire when evaluating EA/TEF patients at the average age of 13.3 years. The PedsQL 4.0 questionnaire is a modular approach to measuring health-related quality of life in healthy children and adolescents and those with acute and chronic health conditions. The PedsQL integrates both generic core scales and disease-specific modules into one measurement system. The questionnaire revealed significantly lower scores in EA/TEF patients compared to healthy controls.

In 2016, Rankin did a pilot assessment of the validity of the KIDSCREEN-52 questionnaire as a measure of quality of life in children with GS. KIDSCREEN-52 is used to assess the physical and psychological well-being, moods and emotions, self-perception, autonomy, parent relations and home life, social support and peers, school environment, social acceptance (bullying) and financial resources. The conclusion was
that the questionnaire has adequate validity and is acceptable to parents and children. Employing the questionnaire, Rankin demonstrated that children with GS have similar quality of life scores to age-matched controls.

Quality of life as it related to health in children and adolescents born with EA/TEF and TEF was studied by Dellenmark-Blom.\textsuperscript{32} The aim of the study was to develop the framework for a condition-specific health-related quality of life (HRQoL) questionnaire for EA/TEF-afflicted children and their parents. Eighteen children ages 8-17 years and 32 parents of children 2-17 years of age took part in focus group discussions. These discussions resulted in the first condition-specific HRQoL questionnaire for children with EA/TEF. The questionnaire revealed impairment in eating and drinking in 26.8\% of patients, concerns regarding social relationships in 20.6\% and perceived health problems in 14.7\%.

A comparison of patients with minor and giant OC from the Netherlands in 2009 compared the mortality, morbidity and quality of life to a control group using questionnaires.\textsuperscript{32} One questionnaire included questions about health, gastrointestinal and urogenital disorders, cosmetic results and social function. A second questionnaire, the Dartmouth COOP Functional Health Assessment Charts/WONCA was used as a validated measure of adult functional status and quality of life. The COOP/WONCA measures physical fitness, feelings, daily activities, social activities, change in health and overall health on a 5-point ordinal scale. Sixty-four patients completed the first questionnaire and 21 patients completed the second. The median age at the time of the first survey was 11.3 years for giant OC and 16.6 years for minor OC. The median age at the time of the second survey was 26 years for females and 20 years for males. Forty-four
percent of giant OC and 19% of small OC survivors had cosmetic complaints regarding their umbilical scar. The functional status and quality of life was ‘generally good’ in giant OC patients and ‘very good’ in minor OC patients. Physical and emotional health did not limit social activities. Minor OC patients had no problems with feelings or daily activities, while giant OC patients were only slightly bothered by feelings or daily activities. The most frequent medications used by OC patients were for pulmonary dysfunction, 19% of giant OC patients and 17% of minor OC patients. Gastrointestinal complaints were common in both giant and minor OC patients; 25% of giant and 15% of minor OC patients had gastrointestinal disorders more than 4 times per month. Abdominal pain was the most common complaint, occurring in 19% of giant OC and 33% of minor OC patients. Special diets were used by 13% of giant OC and 4% of minor OC patients.

Krishnan reported a moderate level of evidence to support their claim that HRQoL in child or adult EA survivors is impaired compared to the general population, and that medical and psychosocial supports are recommended.

**Neurodevelopment**

There is conflicting evidence on the prevalence and significance of neurodevelopmental delay in congenital anomaly survivors. Some argue that the rate of delay attributable to the anomalies is low when confounding variables, such as gestational age and birth weight, are controlled. Others have emphasized the need for intervention and claim that the low rate of neurodevelopmental delay in anomaly survivors is due to early intervention.
Garra studied the neurodevelopmental outcomes of GS survivors at 2 years of age using the Developmental Tracking Infant Progress Statewide program. Garra reported “no statistically significant difference in performance on screening assessments of in the rate of enrollment in early intervention between GS survivors and birth weight and gestational age-matched controls.”

Henrich commented on the motor development of OC and GS patients. Of 26 children with giant OC having a mean age of 6.3 years, delay in sitting or walking was reported in 27%. In 22 GS survivors, a delay was reported in 23%.

Danzer studied short-term neurodevelopmental outcomes in infants with giant OC. Fifteen children between ages 6 and 26 months with a median age of 12 months were evaluated using the Bayley Scales of Infant Development II (BSID-II), which is a series of developmental “play-tasks” used to measure the development of infants and toddlers from 1 to 48 months of age. Motor scores were mildly delayed in 40% of participants and severely delayed in 47%. A total of 26% were severely delayed in motor, language and cognitive outcomes.

Gischler’s 2008 publication reported the neurodevelopmental evaluation of 17 EA/TEF patients. The patients were assessed by the BSID-II every 6 months from birth until 24 months. Overall neurologic and mental development was normal but psychomotor scores were significantly decreased.

In 2015, Walker investigated the developmental outcomes of EA/TEF patients at 3 years of age using the BSID-II. Twenty-four children were assessed at 1 and 3 years of age. Walker reported that at 1 year there was no significant difference in EA/TEF
patients versus healthy controls, and by 3 years the survivors were within the normal range.

**Discussion**

GS, OC, and EA/TEF are congenital anomalies with significant multi-system sequelae, even after surgical correction, that may be consequential in the adult lives of survivors. Therefore, it is important to establish guidelines to consistently follow and evaluate the health and development of survivors with the goal of maximizing health and quality of life.

After reviewing the literature, the following recommendations will be presented to the pediatric surgeons at Health Sciences Centre Winnipeg. With their feedback, these recommendations will form the basis of a long–term follow-up clinic. The goals of the clinic will be to provide evidence-based standardized care to all children with GS, OC or EA/TEF. Consideration will be given to the expertise and resources available in Winnipeg when making the recommendations.

Children will be invited to clinic every 3 months in the first year of life, every 6 months in the second, and then annually until 16 years of age. Adults will be followed intermittently but less frequently. Appendix B outlines the proposed timing of follow-up assessments and the evaluations recommended at each assessment.

Eventually the clinic will address the specific follow-up needs of patients with 6 other surgical congenital anomalies. These anomalies are: congenital diaphragmatic hernia, congenital lung lesions, intestinal atresia, Hirschsprung’s disease, imperforate anus and biliary atresia.
Gastroschisis

Follow-up of GS patients have focused on growth and nutrition, gastrointestinal function, hearing and vision and abdominal wall scars. The HSC follow-up clinic will address these issues based on the evidence reported in the literature.

Appropriate growth is a common concern for GS children; both poor growth\(^8,10,12,13,14\) and obesity\(^12\) have been described. Children with a history of GS may be considered ‘fragile’ and discouraged from an active lifestyle. This may contribute to obesity. Therefore, height, weight, head circumference and body mass index will be recorded on World Health Organization (WHO) growth charts at every assessment. Children deviating significantly from the norms will be assessed further.

Although, inappropriate growth may suggest nutritional excesses or deficiencies, patients will be questioned directly about nutritional habits. The nutritional deficits are obvious for children requiring enteral or parenteral nutritional support, however, patients with subtle deficits may be overlooked. A screening nutrition questionnaire will be administered at every follow-up visit.

Like growth parameters, vital signs will be part of each clinical assessment. These measures cost little and are of no discomfort to patients. Furthermore, hypertension has been reported in a small number of GS children\(^12\)

Gastrointestinal dysfunction affects many GS survivors\(^8,9,11,12\). Thus, it is appropriate to screen for gastrointestinal problems. Age appropriate Rome IV questionnaires for identifying functional bowel problems will be used at regular intervals. The questionnaire translates the Rome IV diagnostic criteria into questions that can be answered by patients or parent-proxies to help clinicians make provisional diagnoses. The
parent-proxy questionnaire for neonates and toddlers will be used at discharge, 3, 6, 18, 24 and 36 months of age. The parent-proxy questionnaire for children will be used annually from 4 years until 9 years. Then the questionnaire for children will be administered to patients annually from 10 years until 16 years. The questionnaire for adults will be used subsequently. If functional gastrointestinal problems, such as abdominal pain, constipation or diarrhea are identified appropriate investigations and treatments will be considered.

Because GERD is common in GS patients, screening will be routine. Validated screening tools, will be used. The GERD Symptom Questionnaire for Infants (GSQ-I) will be administered at discharge, 3, 6, 9 and 12 months. The GERD Symptom Questionnaire for young children will be used annually on survivors at 24 months to four years of age. Clinicians will use the Pediatric Gastroesophageal Reflux Disease Symptom and Quality of Life questionnaire, parent-caregiver or self-reported, for 5 to 8 year olds and 9 to 16 year olds, respectively. Finally, the GERD-Q screen will be used for follow-up of adult GS survivors.

Manitoba recently initiated a Universal Newborn Hearing Screening Program to evaluate all newborns prior to discharge. This program will be important to GS patients for whom hearing loss is a concern. If, however, a GS infant fails to undergo the prescribed assessment, they will be identified at the follow-up clinic and referred to audiology.

Impaired vision is not as common in GS patients as is hearing loss. However, visual impairment will be assessed. Babies born at 31 weeks’ gestational age or earlier, or have a birth weight less than 1500 grams, are routinely tested prior to discharge.
however, an infant with GS does not meet these criteria, they will be referred to ophthalmology at 2 years of age if they have a syndrome or 5 years of age if they do not.\textsuperscript{13}

Finally, GS survivors frequently reported concerns about the cosmetic result of their abdominal wall surgery.\textsuperscript{8,12} Therefore, an abdominal wall scar assessment will be performed at 6 months, 1 and 2 years, and then every 2 years until 16 years of age. In addition to asking about the patients’ perception of their scar, patients will have a physical examination. Abdominal wall and inguinal hernias\textsuperscript{17} will be ruled-out.

**Omphalocele**

Patients with a history of OC share many long-term issues with GS patients. Therefore, follow-up for these groups will be similar. Growth and nutrition\textsuperscript{8,17}, functional abdominal complaints,\textsuperscript{7,8,17,38} hearing\textsuperscript{17} and scar\textsuperscript{7,8,17,38} issues will be assessed in OC patients as recommended for GS patients.

Respiratory dysfunction was more commonly reported in OC patients than GC patients, but cardiorespiratory function in OC survivors is not clearly defined. Although some OC survivors describe decreased activity and exercise tolerance, and limitations of respiratory function have been documented\textsuperscript{18}, objective measures of cardiorespiratory function have also been reported as normal\textsuperscript{16}. Given the lack of consistent evidence, physical activity will be encouraged at each follow-up visit. Routine exercise testing and pulmonary function tests is not justified by the present literature. However, referral and testing will be recommended should cardiorespiratory complaints become apparent when discussing physical activity with the patient or parent-proxy.
Esophageal atresia and tracheoesophageal fistula

Like the other congenital anomalies, EA/TEF will have growth parameters assessed at every follow-up appointment. Height, weight, BMI and head circumference will be recorded on WHO growth charts.22,27

Gastrointestinal dysfunction will be followed by the Rome IV questionnaires and GERD questionnaires in the same manner as GS and OC.20,25,27,28 Given the prevalence of esophagitis, mucosal hyperplasia, strictures and Barrett’s esophagus in EA/TEF survivors, endoscopy and biopsy will be performed as recommended by the European and North American Societies for Pediatric Gastroenterology, Hepatology and Nutrition in their joint guideline published in 2016.31 All EA/TEF patients, including those that are asymptomatic, will undergo esophagoscopy when proton pump inhibitors are discontinued, before 10 years of age and at transition to adult care.31 In the presence of abnormal anatomic or histological findings, follow-up endoscopy will be performed at the discretion of an endoscopist.20,21,25,27,28,30,31

Respiratory compromise can be significant in survivors of EA/TEF. Therefore, oxygen requirements prior to discharge will be evaluated to identify and grade the severity of bronchopulmonary dysplasia according to criteria defined by the NICHD. Follow-up with respirology will be ensured in the presence of BPD.22 Given the prevalence of doctor-diagnosed asthma and asthma like symptoms recorded in adolescent studies of TEF/EA survivors, the ISAAC Phase 3 questionnaires for 6 to 7, and 13 to 14 year olds will be used.21 Respiratory questionnaires were vital in the studies of survivors to gauge the severity of pulmonary dysfunction.22,24,25,27 Incidences of respiratory tract infections, hospitalizations, therapeutic and prophylactic antibiotic use, bronchodilator
and inhaled steroid use, the presence of chronic or barky cough, bronchiolitic episodes, and the presence of dyspnea on exertion will be documented at each assessment. Gischler’s poor PFT results in 5 year olds support Beucher’s claims that quality PFT results cannot be obtained until children reach 8 years of age.\textsuperscript{22,26} Screening spirometry pre- and post-bronchodilator treatment, $\text{FE}_{\text{NO}}$ and methacholine challenge testing will be performed in EA/TEF survivors at 8 years.\textsuperscript{21-23,25-27,29} Mirra’s algorithm (see Appendix C) will be used to further investigate respiratory dysfunction identified at screening.\textsuperscript{19}

As in OC, there was no objective data supporting cardiopulmonary stress testing in follow-up of EA/TEF survivors.\textsuperscript{22,26} However, these patients should still be encouraged at every assessment to exercise regularly to maintain their cardiopulmonary health.

Rib or vertebral abnormalities and scoliosis can be detected, diagnosed and treated earlier than the ages indicated in Koziarkiewicz and Sistoen’s publications.\textsuperscript{25,30} Orthopedic evaluation including vertebral and chest X-rays will be performed when clinically indicated. Physical examination will be performed at all follow-up visits.

**Quality of Life**

The results of quality of life assessments in the congenital anomaly survivor populations varied in degree of impedance and there was no consistency in the questionnaires used. Despite this, quality of life would be a good benchmark to follow via parent reporting at early assessment by pediatricians, then early childhood and adolescents, all the way until teenage and adult follow-up care for CA repair. Tracking quality of life changes can direct practitioners to seek additional resources and supports for their patients.
Neurodevelopment

Although the reported incidence of neurodevelopmental delay in survivors varies, studies that describe delays should not be ignored. Given consideration to this issue, we recommend that all children with GS, EA/TEF or OC be referred for neurodevelopmental screening in order that interventions and supports can be accessed as early in the child’s life as possible.

Physician Assistants in Long-term CA Follow-up Clinics

The goal of the pediatric surgery long-term follow-up clinic is to improve the health and quality of life for surgical patients. This clinic will require a significant commitment for resources and manpower. Clinical responsibilities will include taking detailed histories, performing physical exams, scoring questionnaires, ordering and reviewing investigations, making referrals to consultants and counseling patients.

The Conference Board of Canada (CBOC) stated, “Governments are looking for new ways to innovate and improve performance. One way to meet heightened demand is through interprofessional and collaborative care teams.”39 This is an important idea given Canada’s health system budget of $228 billion in 2016, or 11 percent of GDP.40 The CBOC’s two-part report outlined the utility of physician assistants (PAs), and subsequently modeled how “physician assistants can be an efficient substitute for designated medical tasks.”39

The CBOC reported on the value of PAs, asserting “the work of a PA can include conducting patient interviews, histories, and physical examinations; performing selected diagnostic and therapeutic interventions; providing medical orders and prescriptions; and
counseling on preventive health care.\textsuperscript{41} The value is proven with the report’s conclusion that PAs can perform these tasks with the same, or better outcomes, freeing the physician to perform less-routine tasks.\textsuperscript{41} PAs have been shown in case studies of other medical and surgical disciplines to increase productivity of extra or “add-on” clinics, as well as reduce wait times.\textsuperscript{39}

Since there is a lack of literature on PAs impact on the fiscal efficiency of the Canadian health care system, the CBOC modeled the cost savings that could result from delegating routine tasks to PAs in various clinical settings over the next sixteen years.\textsuperscript{41} The savings were especially apparent in specialized practice areas where wages and other factors, such as office and clinic overhead expenditures are elevated. The modeling detailed a range of 25-45% PA productivity, provided the numerous variables to be considered. Averaging the modeled results of all practice areas, 5.7 to 10.2 million additional hours can be made available to physicians between now and 2030 if PA growth and acceptance continues. This could mean efficiency gains between $89.2 million and $1.14 billion within that time frame.\textsuperscript{39}

Literature does not yet exist examining the true productivity of PAs to support the CBOC’s modeled predictions, but government and pediatric surgeons should recognize that incorporating PAs into a follow-up clinic will not jeopardize patient outcomes. Once incorporated, PAs can begin to prove their worth.

**Conclusion**

Reviewing the literature concerning the long-term outcomes of survivors of GS, OC and EA/TEF has revealed that these individuals are likely to face a variety of health
and developmental challenges in life. The challenges differ, depending on the congenital anomaly. However, one common theme across the disorders is that early intervention has the potential to improve quality of life. Establishing a clinic that applies the standardized guidelines developed here from discharge until adulthood will help ensure that each child has the best chance of accessing needed investigations and treatments in a timely manner.

Physician Assistants should be viewed as essential to the success of this clinic. Their competency and skill set can meet the broad demands of the clinic while freeing physicians to focus on less-routine, more complex tasks related to the clinic or elsewhere.
References:


40. Canadian institute for Health information, *National Health Expenditure Database*. 
## Appendix

### Appendix A. National Institute of Child Health and Human Development Criteria for Diagnosis of Bronchopulmonary Dysplasia*

<table>
<thead>
<tr>
<th>Stage of Development</th>
<th>&lt; 32 Wk Gestational Age†</th>
<th>≥ 32 Wk Gestational Age‡</th>
<th>Diagnosis</th>
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<tr>
<td>Breathing room air at 36 wk PMA or discharge, whichever comes first</td>
<td>Breathing room air by 56 days postnatal age or discharge, whichever comes first</td>
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<td>Mid BPD</td>
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<tr>
<td>Need for &lt; 30% O₂ at 36 wk PMA or discharge, whichever comes first</td>
<td>Need for &lt; 30% O₂ at 56 days postnatal age or discharge, whichever comes first</td>
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<td>Moderate BPD</td>
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<tr>
<td>Need for a 30% O₂, positive pressure, or both at 35 wk PMA or discharge, whichever comes first</td>
<td>Need for a 30% O₂, positive pressure, or both at 56 days postnatal age or discharge, whichever comes first</td>
<td></td>
<td>Severe BPD</td>
</tr>
</tbody>
</table>

*These criteria are in addition to the baseline requirement of > 21% O₂ for at least 28 days.
†Assessed at 36 wk PMA.
‡Assessed at age 27 to 35 days.
BPD = bronchopulmonary dysplasia; PMA = postmenstrual age.

### Appendix B. Long-term Follow-up Guidelines for Gastrochisis; Omphalocele; and Esophageal atresia and Tracheo-esophageal fistula

<table>
<thead>
<tr>
<th>Months/years Post-operation</th>
<th>GS</th>
<th>OC</th>
<th>EA/TEF</th>
</tr>
</thead>
</table>
| Pre-discharge               | 1. **ROME IV QUESTIONNAIRE** FOR NEONATES/TODDLERS  
2. **NEWBORN HEARING SCREENING TEST**  
3. **VISION TEST** (MEETING GESTATIONAL AGE/BIRTH WEIGHT CRITERIA)  
4. **REFERRAL FOR NEURODEVELOPMENTAL SCREEN** | 1. **ROME IV QUESTIONNAIRE** FOR NEONATES/TODDLERS  
2. **NEWBORN HEARING SCREENING TEST**  
3. **VISION TEST** (MEETING GESTATIONAL AGE/BIRTH WEIGHT CRITERIA)  
4. **REFERRAL FOR NEURODEVELOPMENTAL SCREEN** | 1. **ROME IV QUESTIONNAIRE** FOR NEONATES/TODDLERS  
2. **REFERRAL TO RESPIROLOGY FOR DIAGNOSIS OF BRONCHOPULMONARY DYSPLASIA**  
3. **REFERRAL FOR NEURODEVELOPMENTAL SCREEN** |
| 3 months                    | 1. **AUXIOLOGICAL DATA** RECORDED ON WHO GROWTH CHARTS/VITAL SIGNS  
2. **SCREENING NUTRITION QUESTIONNAIRE**  
3. **ROME IV QUESTIONNAIRE** FOR NEONATES/TODDLERS  
4. **GERD SCREEN—GSQ-I**  
5. **REFERRAL TO AUDIOLOGY IF PRE-DISCHARGE SCREEN MISSED** | 1. **AUXIOLOGICAL DATA** RECORDED ON WHO GROWTH CHARTS/VITAL SIGNS  
2. **SCREENING NUTRITION QUESTIONNAIRE**  
3. **ROME IV QUESTIONNAIRE** FOR NEONATES/TODDLERS  
4. **GERD SCREEN—GSQ-I**  
5. **REFERRAL TO AUDIOLOGY IF PRE-DISCHARGE SCREEN MISSED**  
6. **ENCOURAGE REGULAR ACTIVITY** | 1. **AUXIOLOGICAL DATA** RECORDED ON WHO GROWTH CHARTS/VITAL SIGNS  
2. **ROME IV QUESTIONNAIRE** FOR NEONATES/TODDLERS  
3. **RESPIRATORY QUESTIONNAIRE**  
4. **ENCOURAGE REGULAR ACTIVITY** |
| 6 months                    | 1. **AUXIOLOGICAL DATA** RECORDED ON WHO GROWTH CHARTS/VITAL SIGNS  
2. **SCREENING NUTRITION QUESTIONNAIRE**  
3. **ROME IV QUESTIONNAIRE** | 1. **AUXIOLOGICAL DATA** RECORDED ON WHO GROWTH CHARTS/VITAL SIGNS  
2. **SCREENING NUTRITION QUESTIONNAIRE**  
3. **ROME IV QUESTIONNAIRE** | 1. **AUXIOLOGICAL DATA** RECORDED ON WHO GROWTH CHARTS/VITAL SIGNS  
2. **ROME IV QUESTIONNAIRE** FOR NEONATES/TODDLERS  
3. **RESPIRATORY QUESTIONNAIRE** |
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<th>Processes</th>
<th>Child Health Questions</th>
<th>Other Questions</th>
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<td>2. Screening nutrition questionnaire</td>
<td>2. Screening nutrition questionnaire</td>
<td>2. Rome IV questionnaire for neonates/toddlers</td>
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<td>5. Encourage regular activity</td>
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- **4 years**: Rome IV questionnaire for children, Endoscopy and biopsy if previously diagnosed with mild esophagitis or worse, Respiratory questionnaire, Encourage regular activity.
- **5 years**: Rome IV questionnaire for children, Endoscopy and biopsy if previously diagnosed with mild esophagitis or worse, Respiratory questionnaire, Encourage regular activity.
- **6 years**: Rome IV questionnaire for children, Endoscopy and biopsy if previously diagnosed with mild esophagitis or worse, ISAAC Phase 3 questionnaire for 6-7 year olds, Respiratory questionnaire, Encourage regular activity.
- **7 years**: Rome IV questionnaire for children, Endoscopy and biopsy if previously diagnosed with mild esophagitis or worse, Respiratory questionnaire, Encourage regular activity.
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<td>5. Encourage regular activity</td>
<td>5. PFTs and apply findings to Mirra algorithm</td>
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| 12 years | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
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3. Rome IV questionnaire for children  
4. GERD screen—PGSQ-A  
5. Abdominal wall scar assessment | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
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4. Respiratory questionnaire  
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| 13 years | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
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5. Encourage regular activity | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
2. Rome IV questionnaire for children  
3. Endoscopy and biopsy if indicated  
4. ISAAC phase 3 questionnaire for 13-14 year olds  
5. Respiratory questionnaire  
6. Encourage regular activity |
| 14 years | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
2. Screening nutrition questionnaire  
3. Rome IV questionnaire for children  
4. GERD screen—PGSQ-A  
5. Abdominal wall scar assessment | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
2. Screening nutrition questionnaire  
3. Rome IV questionnaire for children  
4. GERD screen—PGSQ-A  
5. Abdominal wall scar assessment  
6. Encourage regular activity | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
2. Rome IV questionnaire for children  
3. Endoscopy and biopsy if indicated  
4. ISAAC phase 3 questionnaire for 13-14 year olds  
5. Respiratory questionnaire  
6. Encourage regular activity |
| 15 years | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
2. Screening nutrition | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
2. Screening nutrition | 1. Auxiologial data recorded on WHO growth charts/Vital signs  
2. Rome IV questionnaire |

**Notes:**
- Auxiologial data includes height, weight, and body mass index (BMI).
- A Rome IV questionnaire is used to assess symptoms and severity of GERD.
- GERD screen—PGSQ-A is a specific questionnaire for GERD screening.
- Encourage regular activity includes physical activity and dietary recommendations.
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<th>Age</th>
<th>Procedures and Measures</th>
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<td>As Indicated</td>
<td>1. <strong>Referral to adult specialists as clinically indicated</strong>&lt;br&gt;2. <strong>Quality of Life assessment by General Practitioner</strong></td>
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</table>
Appendix C. Mirra’s algorithm for the evaluation and surveillance of chronic pulmonary manifestations in esophageal atresia survivors with or without tracheoesophageal fistula. * = to be obtained by all patients. FEV₁ = forced expiratory volume in 1 second. FVC = forced vital capacity. SpO₂ = arterial oxygen saturation measured by pulse oximetry.

**History and physical exam**

**Severity-driven selection of diagnostic procedures**

- SpO₂*
- Chest radiography*
- Spirometry (in cooperating patients)*

Also consider: body plethysmography for lung volumes measurement and maximal exercise test for exercise-induced symptoms

- SpO₂ at rest from 90% to 93% and/or normal-to-slightly abnormal chest radiography and/or FEV₁ ≥ 70% predicted and/or FVC ≥ 70% predicted

**Mild airway disease**

- Adequate primary care follow up
- Prompt aggressive treatment of airway infections
- Functional assessment, at least once per year
- Consider tertiary care referral in case of clinical deterioration

- SpO₂ at rest < 90% and/or relevant abnormalities at chest radiography and/or FEV₁ < 70% predicted and/or FVC < 70% predicted

**Moderate-to-severe airway disease**

- Regular tertiary care follow up including functional assessment, at least every 6 months
- Advanced lung imaging (high resolution computed tomography, magnetic resonance), at least at baseline
- Consider airway endoscopy