

# News or innovations in neonatal surgery

Giorgia Totonelli, Francesco Morini, Pietro Bagolan

Bambino Gesù Children's Hospital-Research Institute, Department of Medical and Surgical Neonatology, Newborn Surgery Unit, Rome, Italy

## Proceedings

Proceedings of the 11<sup>th</sup> International Workshop on Neonatology and Satellite Meetings  
Cagliari (Italy) · October 26<sup>th</sup>-31<sup>st</sup>, 2015

*From the womb to the adult*

Guest Editors: Vassilios Fanos (Cagliari, Italy), Michele Mussap (Genoa, Italy), Antonio Del Vecchio (Bari, Italy), Bo Sun (Shanghai, China), Dorret I. Boomsma (Amsterdam, the Netherlands), Gavino Faa (Cagliari, Italy), Antonio Giordano (Philadelphia, USA)

## Abstract

Over the last decades, because of the development of several clinical and technological advances, there has been a revolution in the management of neonatal and pediatric patients. These progresses reported an improvement in the survival rate of extremely ill neonates, who now have the chance to survive into adulthood. The intent of this review is to highlight not only the advances obtained in the neonatal surgery, but also the results of a multidisciplinary work focused on the fetus, preterm and newborn baby with a surgical anomaly or disease.

Attention is also paid to the recent tendency to share knowledge, protocols and database out of the single Institution or country and to follow these delicate and fragile neonatal patients to the adulthood, developing the transitional care.

## Keywords

Neonatal surgery, foetal therapy, innovation, minimal invasive surgery, transitional care, regional anaesthesia, surgical refinements, long gap esophageal atresia.

## Corresponding author

Pietro Bagolan, Department of Medical and Surgical Neonatology, Newborn Surgery Unit, Bambino Gesù Children's Hospital, Research Institute, P.zza S. Onofrio 4, 00165, Rome, Italy; e-mail: pietro.bagolan@opbg.net.

## How to cite

Totonelli G, Morini F, Bagolan P. News or innovations in neonatal surgery. *J Pediatr Neonat Individual Med.* 2015;4(2):e040256. doi: 10.7363/040256.

## Introduction

About 35 years ago, children were exclusively handled by pediatric surgeons and even general surgeons interested in pediatrics. Significant progresses have been made since. In the last few decades a remarkable improvement in the survival rate of neonates and children with life-threatening pathologies was achieved. Fifty years ago most of the major neonatal anatomical anomalies were considered incurable and premature low birth weight neonates died at birth. Thanks to clinical, neonatal intensive care, obstetrical, surgical and radiological progresses and to the development of specialized multidisciplinary teams, neonates with severe congenital diseases have now the chance to survive into adulthood. Gastroschisis and esophageal atresia are two examples, whose survival improved from 15-20% to 90% and 65-70% to 95%, respectively [1]. The advent of the neonatal intensive care units (NICU), with the presence of full-time neonatologists, innovative monitoring devices and improved ventilators enabled to improve the survival of these tiny patients. The development of total parenteral nutrition is another example of technical progress allowing long-term survival of patients without bowel function for different diseases that would not have lived. The development of multidisciplinary teams, made of different specialists, each with its knowledge, was of paramount importance to obtain good results in the treatment of such complex babies. More recently, several further progresses, both technical and organizational, were introduced in different fields of the neonatal surgery. Remarkable advances have been reported not only in the surgical techniques (i.e. minimal access surgery), but also in the management of these vulnerable patients, from the prenatal period to the adulthood. Infact, as neonatal and pediatric surgeons, providing optimal care for infants with several pathological conditions, we can improve the survival rates of our patients. However, today this is not sufficient anymore. We need to ensure to our patients the best quality of life possible, ideally into adulthood, using evidence based treatments. Our intent in the following paragraphs

is to highlight some of the major recent novelties introduced in neonatal surgery, ranging from technical innovations to transition care, and the foundation of international registries aimed to foster evidence-based management and sharing of experience, all with the objective to improve survival and long term quality of life of our baby patients.

A few examples of these pivotal improvements of neonatal surgical care are here shortly reported to highlight the advances of a multidisciplinary activity in this fascinating field of pediatrics.

## FETO and EXIT

Recent advances in imaging techniques, such as 3D and 4D ultrasound and fetal magnetic resonance imaging (MRI) have significantly improved the knowledge and the management of structural anomalies of the fetus in the prenatal period. This is mainly observed for those anomalies, which cause a mechanical extrinsic or intrinsic airway obstruction, including giant neck masses (vascular/lymphatic malformations), congenital high airway obstruction (CHAOS), thoracic masses and large congenital cystic adenomatoid malformations (CCAM).

*Ex utero intrapartum treatment (EXIT)*: it was firstly described by Norris et al. in the late 1980s to manage a fetus with a large neck mass. Later, the EXIT procedure was considered whenever concern exists about the establishing of the airway of the fetus at birth. Infact, the morbidity and mortality of fetuses with airway obstruction are mainly due to the difficulty of quickly establishing the upper airway. With the EXIT procedure, the fetal-maternal circulation is maintained until the airway is secured. This is generally performed under general anaesthesia, electively, at around 37-38 weeks of gestation. It is of paramount importance the presence of a multidisciplinary team consisting of an obstetrician, gynaecologist, neonatologist, pediatric surgeon, ENT (ear, nose and throat) surgeon, anaesthetist and a dedicated theatre team. Once a caesarean section is performed, head and neck of the fetus are delivered. If the endotracheal intubation of the neonate is unsuccessful, a rigid bronchoscopy is attempted. If this also fails, there is time for tracheostomy. The fetal-maternal circulation can be comfortably maintained for 60 minutes. Once the neonate airway is secured, the umbilical cord is clamped and cut. During

the EXIT procedure the fetus is continuously monitored by electrocardiography, pulse-oximetry and transesophageal echocardiography. The indications for the EXIT have increased over the years. Small case series or single case report have been published, describing their experience with the EXIT for several airway malformations. Hirose et al. reported their series of 52 EXIT procedures performed in a 10-years period on neonates affected by congenital diaphragmatic hernia (CDH) (45), neck mass (5) and CHAOS (2). Of the 52 babies, 51 were born alive and 27 (52%) were alive at 1-year follow-up. There was no maternal death [2]. In the series by Bouchard et al., the main indication to EXIT was the airway obstruction by neck mass (13) and the reversal of tracheal occlusion in fetuses with CDH (13) [3]. Only 1 fetus with a giant neck lymphangioma died because of the inability to secure the airway at birth. As also shown in the above series, one of the main indications to the EXIT procedure is the reversal of tracheal occlusion (FETO) in fetuses with CDH (see below).

*Fetal endoluminal tracheal occlusion (FETO):* FETO is reserved to the more severe cases of CDH (low lung-to-head ratio [LHR] with liver herniation), whose mortality and morbidity at birth is increased. Tracheal occlusion induces pulmonary hyperplasia. This reduces the herniation of abdominal viscera, accelerates fetal lung growth and improves post-natal oxygenation and ventilation of the lungs [4]. The FETO is ideally performed between the 26 and 29 weeks of gestation. FETO has now developed in a percutaneous procedure in which an endotracheal balloon is inserted through a fetoscope and removed ideally at 34 weeks of gestation either by fetoscopy, or US-guided puncture, or electively at birth on EXIT. In 2009, Deprest et al. reported their experience with 210 consecutive FETO in severe cases of CDH. The procedure was successful at the first attempt in 97% of cases. Reversal of tracheal occlusion was performed prenatally either by fetoscopy or ultrasound-guided puncture, intrapartum by EXIT procedure, or postnatally either by tracheoscopy or percutaneous puncture. The most relevant complication was the early delivery, mainly as a consequence of preterm premature rupture of the membranes (PPROM) [5]. In severe cases of CDH the FETO increases the survival rate. However, its side effects (PPROM and preterm delivery) cannot be ignored as well as the technical difficulties of the

procedure. Hence, authors advice the investigation of new and non-surgical methods to induce lung growth. Studies on stem cells or pulmonary vascular remodelling are some examples of these possible clinical applications.

### Minimal access surgery

Over the last few decades, the advance of minimal invasive surgery (MIS) for adults is considered one of the most important developments of surgical practice. The introduction of MIS in the pediatric population has been much slower, especially in neonates. Among the several obstacles to this delay, one of the main concerns relates to the small space for the surgical equipment in neonates. With the progressive development of skills, instrumentation and its miniaturization currently, also the more complicated neonatal surgical procedures can be performed laparoscopically and thoracoscopically. Potential advantages of this operative technique include less postoperative pain, less disruption of the anatomy, less adhesions and scar tissue and better cosmesis. However, concern has been raised recently over the impact of CO<sub>2</sub> insufflation on the neonate and its potential negative effects [6]. The relatively few experimental data available have shown a higher CO<sub>2</sub> sensitivity of the neonatal cardiovascular system and its possible compromising effects on the immature respiratory system of the newborn [7]. Moreover some adverse complications such as paradoxical embolus, through the foramen ovale have been reported. Hence, the concept of “minimal invasive” should refer not only to the benefits of an incisionless surgery but to the newborn safety at 360 degrees.

The idea of “minimal invasive” should not be limited to as laparoscopic and thoracoscopic approaches but includes several techniques which have been recently introduced in the current surgical practice for neonates. For instance, the use of the awake surgery for minor surgical procedures represents a safe, not invasive and effective alternative to the general anaesthesia in the newborn. In fact, as described in the following paragraph, regional anesthesia reduces the risk of intra and post-operative cardiological and respiratory complications, and the potential long-term effects of general anesthesia on neurodevelopmental outcomes. A further example of minimal invasive technique is the minimal access open surgery, described for several surgical procedures on neonates. In 2008, Gauderer

reported his experience with the transumbilical intracavitary pyloromyotomy. This represents a safe procedure, combining the advantages of the traditional “open” approach to the less invasiveness of the laparoscopy [8]. The pylorus is not delivered, the trauma is minimised and the scar is invisible. The attention to the scar cosmesis also led Adrian Bianchi to undertake neonatal lateral thoracotomy through a high axillary skin crease approach. In 1998, he described his experience with 27 neonates who underwent surgery for esophageal atresia and 2 neonates for PDA ligation [9]. This minimal access approach is preferred to the conventional lateral thoracotomy, allows an excellent access to the posterior mediastinum, carries minimal morbidity (risk of musculoskeletal deformity), and provides perfect long-term scar aesthetics. These examples show that minimal surgical (open or endoscopic) invasion is possible also in neonates (**Fig. 1** and **Fig. 2**). The pediatric surgeon should be committed to find further possible applications of this concept to reduce the surgical stress to the delicate neonate requiring surgery.

### **Awake surgery**

Complications related to general anaesthesia are mainly reported in preterm and low birth weight neonates because of their immature organ development. In fact, they often require post-operative respiratory support and intensive care assistance. Awake surgery with regional anaesthesia has been proposed by different authors as a valid alternative for ex-preterm neonates and term neonates, who underwent elective and relatively minor surgical procedures, such as inguinal herniotomy and pyloromyotomy for pyloric stenosis [10]. Also, in preterm babies a higher incidence of inguinal hernia with incarceration and bowel obstruction has been reported and surgery cannot be delayed. Hence, regional anaesthesia without general anaesthesia has been recommended in neonates to reduce the risk of post-operative respiratory complications. Briefly, spinal anaesthesia for inguinal herniotomy is performed after the baby performs the regular pre-operative check (blood test, ECG). Feeding is stopped 4-6 hours before surgery. No premedication is given and lidocaine 2.5%/prilocaine 2.5% cream is applied 60 minutes before surgery over the sacrococcygeal region. Intraoperative monitoring consists of ECG, pulse oximeter, temperature and blood pressure. After

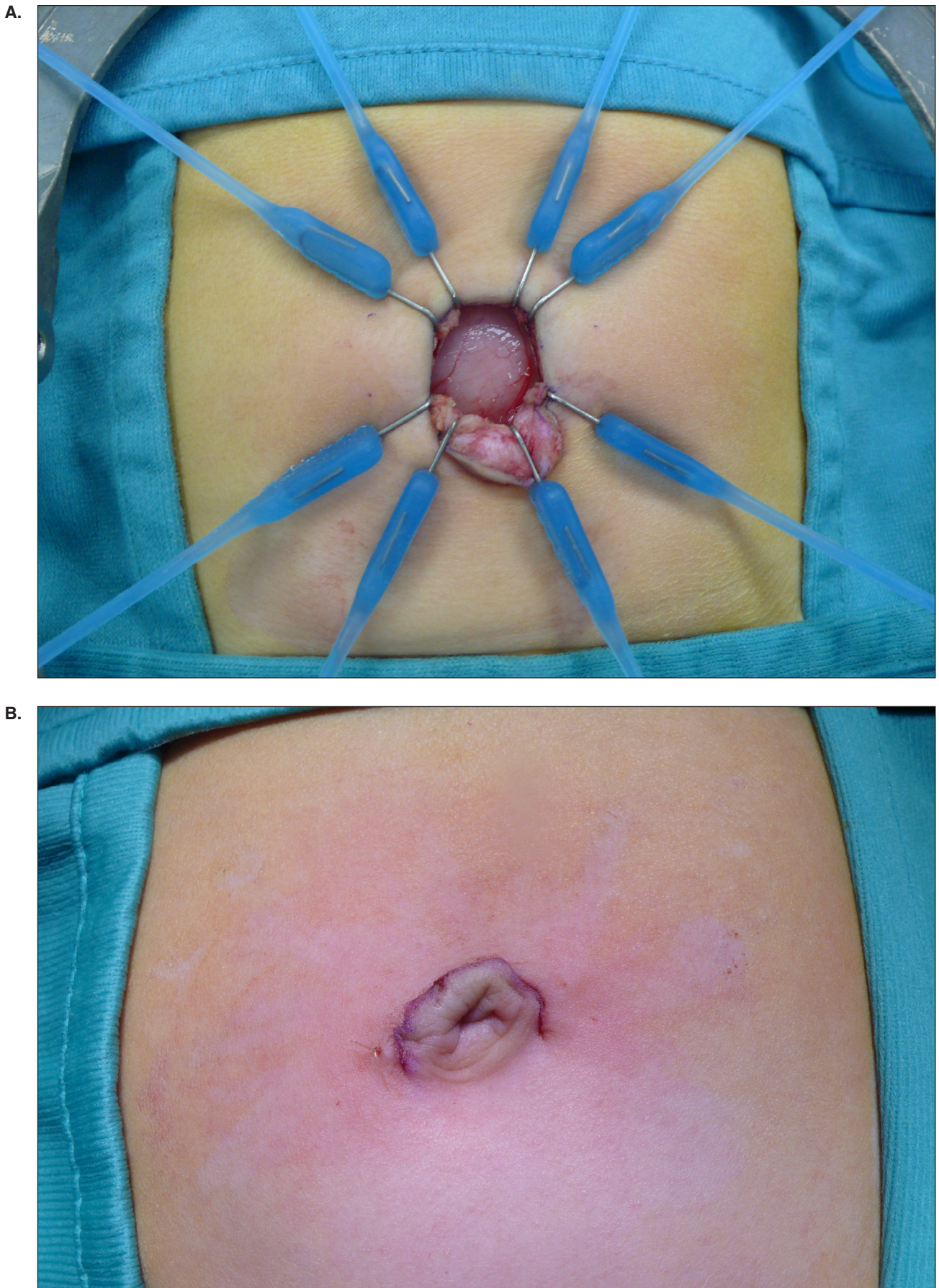
giving the baby sublingual dextrose, a theatre nurse holds the baby in the left lateral position with the hips flexed. The back is exposed and cleaned with chlorhexidine 0.5% solution. Spinal puncture is performed by an experienced anaesthetist, with a midline approach through either the fourth or fifth lumbar space using a 26G disposable styletted needle. Once a free flow of cerebral fluid is obtained, spinal isobaric bupivacaine 0.5%, 0.8mg/kg is injected. The needle is then removed and the baby is positioned for surgery. The main advantage of the awake surgery for neonates is to avoid the cardiorespiratory complications that can occur in the post-operative period, such as apnea, urinary retention or bradycardia, which can require intensive care assistance. Intraoperatively, this anaesthetic technique is generally well tolerated by the baby who can also start feeding immediately after surgery. Regional anaesthesia is safe in skilled hands and guarantees a comfortable intra- and post-operative period for the baby. Recently, Geze et al. reported the successful use of a single shot caudal anaesthesia in 15 conscious low birth weight infants for inguinal hernia repair [11]. No serious cardiological or neurological complication has been recorded in this series. Surgery was performed with neonates in spontaneous breathing and no post-operative complications were encountered. Babies recovered immediately after surgery. Somri et al. recently performed spinal anaesthesia as a sole technique in a series of 23 infants (both premature and full term) undergoing pyloromyotomy [12]. No intra- or postoperative apnoea or other respiratory complications were reported and all infants recovered well after surgery. As also described in this series, a further advantage of the use of spinal anaesthesia for pyloromyotomy is to avoid the risk of gastric content aspiration in these patients.

### **Esophageal atresia**

Nowadays survival of babies affected by isolated esophageal atresia (EA) is near 100%. The most difficult cases are those affected by “long” gap EA and/or those with severe associated anomalies. Many technical refinements, as reported in this paragraph, have been pointed out to preoperatively assess the patients, to plan the best treatment choices, to avoid intraoperative complications, to reduce the number of babies that need esophageal substitution as the sole possible procedure due to their difficult esophageal anomaly.



**Figure 1.** Minimal invasive axillary “open” approach“. The line of the incision in the axillary pyramid (**A**); the axillary scar at the end of the procedure (**B**).



**Figure 2.** Minimal access peri-umbilical “open” in a case with hypertrophic pyloric stenosis. The visible pylorus through the incision (A); the minimal scar at the end of the procedure (B).

### *Routine tracheobronchoscopy*

In the last few years, preoperative tracheobronchoscopy (TBS) gained attention to evaluate the presence of proximal tracheo-esophageal fistula (TEF). However, in a recent European survey it was demonstrated that only 43% of respondent consultants routinely perform preoperative TBS [13]. Nonetheless, beyond confirming the presence and number of TEF, TBS offers the possibility to evaluate vocal cord motility, to assess the presence of other foregut specific associated anomalies (tracheomalacia, tracheal clefts, etc.) [14], and to preoperatively define the esophageal gap. Finally, endoscopic assessment is essential to define the surgical management.

### *Preoperative gap evaluation*

Preoperative evaluation of esophageal gap length is a critical part of assessment in patients affected by EA, even though no consensus has been gained yet.

Preoperative gap measurements promote comparability between centres, and limit intraoperative findings of unsuspected difficult cases. Very few authors have tried to find a reproducible way to assess preoperatively the esophageal gap length, and in most of the cases, this evaluation is limited to those cases of EA without distal fistula [15]. The common opinion persists that only EA without distal TEF may present with a gap “long.” However, the evidence demonstrates that type C is the most frequent variant of long-gap EA (LGEA) [16].

Firstly proposed to measure esophageal gap was the infusion of water-soluble contrast via the gastrostomy tube to evaluate the lower esophageal pouch. This is a simple method since neither special equipment nor anesthesia is needed. In this case the gastroesophageal junction must be incompetent to allow the reflux.

The insertion of a Hegar dilator through a gastrostomy into the lower pouch was also proposed as another simple and safe approach. However, some authors consider a difficult procedure to blindly pass a rigid dilator through the gastroesophageal junction into the distal pouch.

Therefore, others authors suggested to measure esophageal gap using a flexible endoscope to intubate the lower pouch but, with this technique, it is not possible to quantify and standardize the

boost pressure applied, losing information on elasticity of the lower pouch. Common limit of above-mentioned techniques is that they are not suitable for cases without a previously fashioned gastrostomy.

Preoperative CT evaluation of EA patients was also proposed, but it involves significant exposure to ionizing radiation and possible risk of radiation-induced cancer. Additionally, in 1 out of 5 of cases, the fistula could not be located [17], limiting the indication to evaluate complex associated malformations (cardiac, tracheal, etc.).

Since 2004, we developed a preoperative standardized approach to measure the gap, reducing intraoperative “surprises” such as laryngotracheal anomalies and vocal cord dysfunction in all spectrum of EA [15]. TBS is performed in all patients to define the presence of proximal TEF (defining/excluding Gross type B/D), vocal cord motility, and foregut anomalies. Subsequently to anatomical definition, TBS is used to immediately measure the gap in types C/D: a 10 Ch radiopaque Nelaton probe is inserted under pressure into the upper pouch. At the same time, the tracheoscope’s tip is placed at the level of the tracheal opening of the distal fistula. A chest fluoroscopy shows the distance, thus the gap, between them [15]. When a carenal fistula is present, the option of its occlusion (by a 3.5-Fr Fogarty catheter; the balloon inflated with 0.2 mL of saline solution) is discussed with the anesthesiologist to allow an easier mechanical ventilation, by avoiding both gastric overdistension and gastroesophageal reflux [18].

Instead, gap measurement is delayed 15 days after gastrostomy fashioning in types A/B EA. A number 4 or 5 Hegar dilator is inserted into the lower esophagus through the gastrostomy and pushed upward to evaluate esophageal elasticity. The thrust applied is measured with an electronic device (dynamometer) connected to the Hegar. The force applied to the dynamometer ranges between 250 and 300 g. The gap is then measured, under fluoroscopy, both without and under pressure. A similar method is used for patients with cervical esophagostomy, marking the stoma with a radiopaque device or with a small quantity of contrast medium [15, 18].

### *Esophageal lengthening: traction and growth*

When the esophageal gap cannot be bridged, the technique exploited by most authors is the traction and growth procedure [19]. Lengthening

of the neck by traction is an ancient practice for cosmetic reasons; just think of the giraffe women of the Kenyan tribes who wear rings to lengthen it. Other examples of stretching and growth procedures are surgical techniques of limb traction, such as the Ilizarov procedure, or the use of skin expanders, causing the skin and soft tissue growth, as well as autologous bowel-lengthening procedures. Therefore, traction has been considered a good system to induce esophageal growth and elongation. In a rat animal model of EA, continuous traction on the esophagus has been shown to increase esophageal mass preserving histopathological morphology of the esophagus without major tissue damage. Many esophageal-lengthening procedures, such as hydrostatic pressure, serial bougienage, and magnets, among others, have been reported even though they have never gained widespread popularity [20, 21].

#### *External traction (ET, Foker's technique)*

In 1994, Boyle et al. reported preliminary results on the systematic primary repair of ultra-long-gap EA (3.5 cm or greater) without lengthening procedures in 8 consecutive patients, concluding that although tension may contribute to strictures and gastro-esophageal reflux, primary repair results in a clinically functional native esophagus [22]. A few years later, the same group reported their personal experience on 70 consecutive EA (not only "long gap") concluding that the esophageal anastomosis can withstand considerable tension, and allows a reliable true primary repair for the full EA spectrum [23]. In 2003, the group from Montreal published 3 consecutive LGEA treated with definitive esophageal anastomosis 10-14 days after birth, adopting the same technique of ET [24] and Skarsgard reported 2 cases of LGEA successfully treated with ET technique as well [25]. Currently, the Foker procedure, or its modifications, has been successfully used in more than 100 infants with LGEA worldwide [26].

Recently we reported a large case series based on traction and growth approach, without external traction, arrived at the same conclusions [15]. This report includes 57 cases with LGEA (3 vertebral bodies), 27 of which were referred cases after a failed attempt. Only 1 referred patient, with cervical esophagostomy (CE)/no lower esophagus and cardia stretch, ultimately required esophageal substitution. Referred LGEA patients, showed a higher rate of CE (44% vs. 3%) [15]. In 2013, Sroka

et al. [19] reported their comparable experience on 15 LGEA cases (5-14 cm), 9 of which with a previous CE fashioned. Only 2 referred patients with CE required esophageal substitution due to postoperative complications.

Early complications (after traction procedure and anastomosis) are anastomotic leaks (mostly minor leaks and subsided spontaneously) in up to 50% of patient. Major disruption and failure of conservative management (with need for drainage or reoperation was reported) in up to 15% of dated series and in up to 13% of the last reports [15, 19, 27]. Lastly, esophageal replacement for unsatisfactory results after delayed anastomosis was required in 14%.

To compare the ET Foker technique to the more conventional delayed primary anastomosis, Nasr and Langer performed a cumulative meta-analysis to critically evaluate the existing literature on this topic [28]. Overall, 71 infants undergoing the ET procedure were compared with 451 children utilizing delayed primary anastomosis. The initial gap length was 5.4 cm (range: 3-12.5 cm). No study reported data about the preoperative gap length. The Foker procedure, despite the risk of bias due to the retrospective cohort, was associated with a significantly shorter time to definitive anastomosis and with a significantly lower risk of complications (primary outcome of the study) [28].

Since delayed primary anastomosis, with either "wait-and-see" or with "traction to induce growth" to bridge the more difficult gap, provides good immediate and long-term functional outcomes, a concerted and rigorous effort to achieve an end-to-end esophageal anastomosis should be made before considering esophageal substitution.

#### *Extrathoracic esophageal elongation (ETEE, Kimura's technique)*

Ken Kimura firstly reported ETEE in a child with LGEA whose parents requested the reconstruction the esophagus using the native conduit [29]. Since then, ETEE has been widely used in different ways: 1) as a "traction" procedure, as a technique of choice in patients who had been electively treated with CE for a variety of reasons (primary esophagostomy); 2) as an esophagus "rescue" procedure for those babies in which an esophagostomy had been performed because of a previous failed attempt (secondary esophagostomy) [15, 19]. Advantages of the ETEE are to maintain the native esophagus, to allow early



oral alimentation, and to shorten hospital stay while waiting for the final esophago-esophagostomy. Preferably, the esophagostomy is created on the right side of the neck. The upper pouch is dissected as proximal as possible and brought to the skin. To make the possible subsequent dissections of the esophageal stump easier, the proximal esophagus can also be wrapped with Gore-Tex® (W.L. Gore and Associates, Inc., Flagstaff, AZ, USA) [30]. At each elongation step, the neck is flexed and the esophagus gently stretched caudally and possibly anchored to the pectoralis major fascia with 2 or 3 absorbable sutures. Neither thoracotomy nor prolonged sedation and muscle paralysis is needed. Only few studies report comparison of esophageal-lengthening techniques. Long-term outcomes are limited, and patient selection is frequently different. Recently, Sroka et al. mixed the experiences of 2 European centers to compare ET and ETEE techniques. They conclude that ET of both pouches results in a high rate of primary repairs in children with LGEA and no previous esophageal operations. However, the combination of ETEE and ET applied to patients with a CE already fashioned at a previous failed attempt of esophageal anastomosis, results in an equivalent rate of primary repair, but the number of complications increase significantly. Therefore, the ETEE has been considered the first choice for those selected patients with a previous cervical esophagostomy [19].

#### *Upper esophageal flap (UEF, Gough and Bianchi)*

MH Gough initially reported the anterior full-thickness flap of the upper pouch to bridge a long gap, in 5 consecutive patients with a difficult anastomosis. None required reoperation, but 2 or more dilatations were necessary in all infants [31]. After 15 years, the same group reported the outcome (mean 1/4 2 years) of 15 consecutive LGEA in which an UEF had been performed to preserve the native esophagus. Complications included leaks (27%); strictures (87%), 2 of which requiring a segmental resection; gastro-esophageal reflux requiring fundoplication (20%); recurrent TEF (13%); and esophageal motility incoordination (60%). Overall, 7 out of 10 of patients achieved normal growth, leading the authors to conclude that, despite the considerable morbidity, flap procedure reduces the need for esophageal substitution with a satisfactory outcome [32]. In 2006, Castanon et al. reported UEF in 3 cases with LGEA, concluding

that it represents their first choice for treatment of LGEA since it allowed esophageal preservation, despite re-intervention in 2 patients for persistent stenosis [33]. Morabito et al. reached the same conclusion, reporting a population study of 67 cases (6 type A LGEA) treated with UEF and lower pouch augmentation. Minor leaks (spontaneous resolution) were observed in 11 (16%) patients; anastomotic stricture in 2 (3%), which eventually required redo-anastomosis; and recurrent TEF in 5 (7.5%), all requiring a second operation [34]. Finally, our group has recently reported the use of esophageal flap in selected patients with LGEA. Comparison between patients with LGEA requiring (6 patients) or not (13 patients) UEF to bridge a type C LGEA showed that only stricture length was significantly higher in neonates with an esophageal flap (2.2 vs. 1.0 cm) [35]. At subsequent long-term follow-up, only 1 patient out of 9 treated with UEF, required segmental resection of a persistent stenosis, unresponsive to dilatation, 13 months after surgery [15].

#### **Registries**

Modern medical treatment should be founded on evidence. According to the Scottish Intercollegiate Guidelines Network, available evidence ranges from the lower grade of “expert opinion” to the higher one of high quality meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with a very low risk of bias [36]. The corollary is that studies on treatment modalities require an adequate number of patients to reach a high level of evidence. This may represent a significant problem in most complex diseases that pediatric surgeons face, since their incidence is usually small and most fall in the rare diseases category. CDH represents a good representative condition. Its incidence ranges between 1 in 2,000 to 5,000 live births, leading to approximately 100 to 250 newborns with the disease every year in Italy. According to the Italian Society of Pediatric Surgery database, in the same country there are 51 hospitals with pediatric surgical facilities [37], leading to a theoretical number of 2 to 5 patients with CDH each year. It is clear that these numbers will not allow studies with adequate cohorts of patients to achieve an acceptable level of evidence in favor or against any treatment modality. Two major actions have been put into effect, centralization of cases and development

of multicenter, international registries. The CDH study group (CDHSG) was the first registry dealing with CDH, founded in 1995 by Prof. Kevin Lally and Dr. Pamela Lally. The CDHSG consists of tertiary referral centers, distributed over four continents that voluntarily provide data to a central registry. Data on all infants with CDH who are born at or transferred to a participating center are inserted into the database. Data were prospectively collected on all live born patients with CDH from 1995 in participating hospitals and included information on delivery and subsequent hospital care (including surgery when applicable) until death or hospital discharge. Patient demographics, birth information, treatment received and outcome were recorded. So far, over 8,000 patients have been registered allowing several important contributions to the understanding of CDH. It made possible to study infrequent problems in CDH, the conclusions of these studies are based on a very large cohort of patients, making them more reliable, different centres may compare their results with those of the whole group, and it can allow to describe changes over time of management and their effects on the outcomes. The reverse of the medal is that the data are, only observational, voluntary with no central control, and complex data are difficult to collect, reducing the level of evidence achieved by the analysis performed. Recently, a European collaborative network of expert centers was formed. The CDH EURO-Consortium is a more agile form of collaboration that allowed to develop a shared standardized treatment protocol and to finalize a randomized controlled trial on type of initial ventilation in CDH [38, 39].

Between 2009 and 2013, the span of the trial, over 600 patients were treated from the participating centres. This allows some optimism that studies with adequate patients populations and high level of evidence recommendations can be designed in the future. The development of multicenter, international registries is not limited to CDH. Other neonatal surgical conditions for which registries have been developed include esophageal atresia (European Pediatric Surgeon's Association's Esophageal Atresia Registry), biliary atresia (European Biliary Atresia Registry), gastroschisis (Canadian Pediatric Surgical Network), and anorectal malformations (ARM-NET Consortium), and it is recommendable that the same route will be followed by other complex rare diseases in the future.

## Transition care

Over the last few decades, the prognosis of most congenital anomalies significantly improved, leading to a higher survival rate of neonates affected by abnormalities previously considered lethal. The increase in survival rates of patients with congenital anomalies unveiled the previously unseen problem of long-term morbidity, and eventually shifted the focus of doctors treating neonates in this direction. As a consequence, particular attention is now developing to find the best way to follow these patients long term, ideally into adulthood. Actually, concern has risen about the implications of chronic pediatric disease later in life. Children with a chronic disease tend to suffer more than average from behaviour problems (especially depression, anxiety, and social withdrawal), often have an increased dependency on caretakers and reduced participation in peer- and school-based activities, and puberty may be delayed, depending on the initial illness. However, adult with long term morbidities from congenital anomalies treated in the neonatal period often lay in a "no man's land" where neither neonatal/pediatric nor adult doctors have experience and there is the need to establish organized transition from child-centered to adult oriented care for them. Moreover, transitioning care into adulthood has proved to be a challenge. Blinks et al. [40] identified barriers and key elements necessary for a successful transition. The barriers to this process include the inability of pediatric health care providers to let go the patients, the reluctance of the patients (or the parents) to leave the familiarity of the pediatric center and the lack of interest by adult health care providers. The key elements include adequate preparation of the patient and caregivers, flexible timing of transition early introduction to the adult clinic, knowledgeable adult care providers, and coordinated care. Pediatric oncology well represents a fields of pediatric medicine that has already faced this issue, and showed that this process is possible. For childhood cancer survivors, the Institute of Medicine has recognized the serious health risks faced and has recommended lifelong health care to mitigate the impact of late effects. Such care includes a systematic plan for periodic surveillance and prevention adapted to the specific risks that arise from the individual patient's previous cancer, therapy, genetic predisposition, health behaviours and comorbid conditions [41].

Several neonatal surgical anomalies can develop long-term sequelae, and we will report three of

them, just to illustrate the problem. CDH is a rare disease, which survival rate has increased from 50% to above 75% in the last decades. At long-term follow-up, CDH survivors can develop several morbidities, which include persistent/recurrent pulmonary hypertension, bronchopulmonary dysplasia, gastrointestinal morbidities, orthopedic, neurological and neurodevelopmental disorders. While it is difficult to predict all the needs for a long term CDH survivor, a team including a cardiologist, a pneumonologist, a gastroenterologist, a neurologist, and an orthopedist can provide the needed expertise as CDH patients reach adulthood. Short bowel syndrome (SBS) is a consequence of an initial disorder that requires massive intestinal resection. Typical neonatal conditions that can cause SBS include necrotizing enterocolitis and midgut volvulus. Patients with SBS are dependent on total parenteral nutrition which is not devoid of complications such as catheter related infections, parenteral nutrition-associated liver failure, and venous thrombosis. These patients often suffer from intestinal dysmotility that predisposes to luminal bacterial overgrowth and sometimes sepsis. It is therefore clear that long term follow-up of these patients is crucial, with careful transition when they reach the adult age. Purposely, intestinal failure teams have been developed, which include a pediatric surgeon, a gastroenterologist, a nutrition expert, an endocrinologist, an hepatologist, and last but not least a dedicated nurse. Transplantation teams may be included in the team. Anorectal malformations (ARM) are a broad spectrum of anomalies involving the anus and rectum. Often also the urogenital tract is involved in the anomaly and the innervation of the perineal region may be deficient. Long-term morbidity of patients with ARM may involve bowel function with constipation or incontinence, bladder control, renal function, and sexual function. Therefore, a team including a general or colorectal surgeon, a gastroenterologist, a urologist, a nephrologist and a gynecologist for female patients, should be able to provide the necessary transition care. These three examples clearly show the need for dedicated transition care programs that should be extended also to all the other congenital anomalies treated in the neonatal period susceptible to develop long-term morbidities.

### Declaration of interest

The Authors declare that there is no conflict of interest.

### References

- Grosfeld JL, O'Neill JA Jr, Fonkalsrud EW, Coran AG (Eds.). *Pediatric surgery*, 6<sup>th</sup> ed. Philadelphia: Mosby-Elsevier, 2006.
- Hirose S, Farmer DL, Lee H, Nobuhara KK, Harrison MR. The ex utero intrapartum treatment procedure: looking back at the EXIT. *J Ped Surg*. 2004;39:375-80.
- Bouchard S, Johnson MP, Flake AW, Howell LJ, Myers LB, Adzick NS. The EXIT procedure: experience and outcome in 31 cases. *J Ped Surg*. 2002;37:418-26.
- Flageole H, Evrard VA, Piedboeuf B, Laberge JM, Lerut TE, Deprest JA. The plug-unplug sequence: an important step to achieve type II pneumocyte maturation in the fetal lamb model. *J Pediatr Surg*. 1998;33:299-303.
- Jani JC, Nicolaidis KH, Gratacós E, Valencia CM, Doné E, Martínez JM, Gucciardo L, Cruz R, Deprest JA. Severe diaphragmatic hernia treated by fetal endoscopic tracheal occlusion. *Ultrasound Obstet Gynecol*. 2009;34(3):304-10.
- Ure BM, Suempelmann R, Metzelder MM, Kuebler J. Physiological responses to endoscopic surgery in children. *Semin Pediatr Surg*. 2007;16:217-23.
- Bishay M, Giacomello L, Retrosi G, Thyoka M, Garriboli M, Brierley J, Harding L, Scuplak S, Cross KM, Curry JJ, Kiely EM, De Coppi P, Eaton S, Pierro A. Hypercapnia and acidosis during open and thoracoscopic repair of congenital diaphragmatic hernia andesophageal atresia: results of a pilot randomized controlled trial. *Ann Surg*. 2013;258:895-900.
- Gauderer MW. Experience with a nonlaparoscopic, transumbilical, intracavitary pyloromyotomy. *J Pediatr Surg*. 2008;43(5):884-8.
- Bianchi A, Sowande O, Alizai NK, Rampersad B. Aesthetics and lateral thoracotomy in the neonate. *J Pediatr Surg*. 1998;33(12):1798-800.
- Maitra S, Baidya DK, Pawar DK, Arora MK, Khanna P. Epidural anesthesia and analgesia in the neonate: a review of current evidences. *J Anesth*. 2014;28(5):768-79.
- Geze S, Imamoğlu M, Cekiç B. Awake caudal anesthesia for inguinal hernia operations: successful use in low birth weight neonates. *Anaesthesist*. 2011;60(9):841-4.
- Somri M, Gaitini LA, Vaida SJ, Malatzkey S, Sabo E, Yudashkin M, Tome R. The effectiveness and safety of spinal anaesthesia in the pyloromyotomy procedure. *Paediatr Anaesth*. 2003;13(1):32-7.
- Zani A, Eaton S, Hoellwarth ME, Puri P, Tovar J, Fasching G, Bagolan P, Lukac M, Wijnen R, Kuebler JF, Cecchetto G, Rintala R, Pierro A. International survey on the management of esophageal atresia. *Eur J Pediatr Surg*. 2014;24(1):3-8.
- Ryan DP. Laryngotracheoesophageal cleft repair. In: Grillo HC (Ed.). *Surgery of the Trachea and Bronchi*. Hamilton, ON: BC Decker Inc, 2004, pp. 675-80.
- Bagolan P, Valfrè L, Morini F, Conforti A. Long-gap esophageal atresia: traction- growth and anastomosis – before and beyond. *Dis Esophagus*. 2013;26(4):372-9.

16. Friedmacher F, Puri P. Delayed primary anastomosis for management of long-gap esophageal atresia: a meta-analysis of complications and long-term outcome. *Pediatr Surg Int.* 2012;28(9):899-906.
17. Mahalik SK, Sodhi KS, Narasimhan KL, Rao KL. Role of preoperative 3D CT reconstruction for evaluation of patients with esophageal atresia and tracheo-oesophageal fistula. *Pediatr Surg Int.* 2012;28(10):961-6.
18. Atzori P, Iacobelli BD, Bottero S, Spiridakis J, Laviani R, Trucchi A, Braguglia A, Bagolan P. Preoperative tracheobronchoscopy in newborns with esophageal atresia: does it matter? *J Pediatr Surg.* 2006;41(6):1054-7.
19. Sroka M, Wachowiak R, Losin M, Szlagatys-Sidorkiewicz A, Landowski P, Czauderna P, Foker J, Till H. Foker technique (FT) and Kimura advancement (KA) for the treatment of children with long-gap esophageal atresia (LGEA): lessons learned at two European centers. *Eur J Pediatr Surg.* 2013;23(1):3-7.
20. Lopes MF, Catre D, Cabrita A, Pires A, Patricio J. Effect of traction sutures in the distal esophagus of the rat: a model for esophageal elongation by Foker's method. *Dis Esophagus.* 2008;21(6):570-3.
21. Vogel AM, Yang EY, Fishman SJ. Hydrostatic stretch-induced growth facilitating primary anastomosis in long-gap esophageal atresia. *J Pediatr Surg.* 2006;41(6):1170-2.
22. Boyle EM Jr, Irwin ED, Foker JE. Primary repair of ultra-long-gap esophageal atresia: results without a lengthening procedure. *Ann Thorac Surg.* 1994;57(3):576-9.
23. Foker JE, Linden BC, Boyle EM, Marquardt C. Development of a true primary repair for the full spectrum of esophageal atresia. *Ann Surg.* 1997;226(4):533-43.
24. Al-Qahtani AR, Yazbeck S, Rosen NG, Youssef S, Mayer SK. Lengthening technique for long gap esophageal atresia and early anastomosis. *J Pediatr Surg.* 2003;38(5):737-9.
25. Skarsgard ED. Dynamic esophageal lengthening for long gap esophageal atresia: experience with two cases. *J Pediatr Surg.* 2004;39(11):1712-4.
26. Foker JE, Kendall TC, Catton K, Khan KM. A flexible approach to achieve a true primary repair for all infants with esophageal atresia. *Semin Pediatr Surg.* 2005;14(1):8-15.
27. Kunisaki SM, Foker JE. Surgical advances in the fetus and neonate: esophageal atresia. *Clin Perinatol.* 2012;39(2):349-61.
28. Nasr A, Langer JC. Mechanical traction techniques for long-gap esophageal atresia: a critical appraisal. *Eur J Pediatr Surg.* 2013;23(3):191-7.
29. Kimura K, Nishijima E, Tugawa C, Matsumoto Y. A new approach for the salvage of unsuccessful esophageal atresia repair: a spiral myotomy and delayed definitive operation. *J Pediatr Surg.* 1987;22(11):981-3.
30. Dessanti A, Caccia G, Iannuccelli M, Dettori G. Use of 'Gore-Tex surgical membrane' to minimize surgical adhesions in multistaged extrathoracic esophageal elongation for esophageal atresia. *J Pediatr Surg.* 2000;35(4):610-2.
31. Gough MH. Esophageal atresia-use of an anterior flap in difficult anastomosis. *J Pediatr Surg.* 1980;15(3):310-1.
32. Brown AK, Gough MH, Nicholls G, Tam PHK. Anterior flap repair of esophageal atresia: a 16-year evaluation. *Pediatr Surg Int.* 1995;10:525-8.
33. Castanon M, Prat J, Saura L, Muñoz ME, Corradini M, Morales L. Lessons we've learned in the treatment of long gap esophageal atresias. *Cir Pediatr.* 2006;19(2):95-100.
34. Morabito A, Plummer NT, Bianchi A. Clinically significant gastro-oesophageal reflux following oesophageal flap repair for oesophageal atresia and tracheo-oesophageal fistula. *Pediatr Surg Int.* 2006;22(3):240-2.
35. Bagolan P, Iacobelli BD, De Angelis P, di Abriola GF, Laviani R, Trucchi A, Orzalesi M, Dall'Oglio L. Long gap esophageal atresia and esophageal replacement: moving toward a separation? *J Pediatr Surg.* 2004;39(7):1084-90.
36. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. *BMJ.* 2001;323(7308):334-6.
37. [http://www.chped.it/?page\\_id=33](http://www.chped.it/?page_id=33), accessed on September 14, 2015.
38. Reiss I, Schaible T, van den Hout L, Capolupo I, Allegaert K, van Heijst A, Gorett Silva M, Greenough A, Tibboel D; CDH EURO Consortium. Standardized postnatal management of infants with congenital diaphragmatic hernia in Europe: the CDH EURO Consortium consensus. *Neonatology.* 2010;98(4):354-64.
39. Van den Hout L, Tibboel D, Vijfhuizen S, te Beest H, Hop W, Reiss I; CDH-EURO Consortium. The VICI-trial: high frequency oscillation versus conventional mechanical ventilation in newborns with congenital diaphragmatic hernia: an international multicentre randomized controlled trial. *BMC Pediatr.* 2011;11:98.
40. Binks JA, Barden WS, Burke TA, Young NL. What do we really know about the transition to adult-centered health care? A focus on cerebral palsy and spina bifida. *Arch Phys Med Rehabil.* 2007;88:1064-73.
41. Hewitt M, Greenfield S, Stovall E (Eds.). *From cancer patient to cancer survivor: lost in transition.* Washington, DC: National Academies Press, 2005.