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# Abdominal wall defects: Prenatal diagnosis, newborn management, and long-term outcomes

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ABSTRACT

Omphalocele and gastroschisis represent the most frequent congenital abdominal wall defects a pediatric surgeon is called to treat. There has been an increased reported incidence in the past 10 years mainly due to the diffuse use of prenatal ultrasound. The early detection of these malformations, and related associated anomalies, allows a multidisciplinary counseling and planning of delivery in a center equipped with high-risk pregnancy assistance, pediatric surgery, and neonatology. At present times, closure of defects, even in multiple stages, is always possible as well as management of most of cardiac-, urinary-, and gastrointestinal-associated malformations. The progress, herein discussed, in the care of newborns with abdominal wall defects assures most of them survive and reach adulthood. Some aspects of transition of medical care will also be considered, including fertility and cosmesis.



## Introduction

Omphalocele and gastroschisis are the two most common congenital abdominal wall defects, and their repair and management need multidisciplinary expertise. The increased possibility to detect them at early stages during pregnancy allows planning the best prenatal and postnatal management in a center with pediatric surgery, neonatology, and high-risk pregnancy assistance. The common goal of closure of defect, either primary or staged, is herein discussed together with the dissimilar and peculiar aspects each malformation has. Finally, early and long-term outcomes are considered, in light of the general favorable prognosis and survival into adulthood.

## Omphalocele (exomphalos)

### *Definition and pathogenesis*

Omphalocele (from ancient Greek: *omphalos* = umbilicus; *cele* = hernia) is a congenital defect of the abdominal wall, located by the umbilical ring, consisting of an evisceration of internal organs in a sac covered by a three-layered membrane made of peritoneum, Wharton's jelly, and amnion. The sac usually contains the small intestine, liver, spleen, colon, and sometimes the gonads. Exomphalos results from the failure of bowel loops that do not return to the abdominal cavity following the physiological herniation of the umbilical cord between the 6th and 10–11th week of development. The small bowel is usually malrotated or non-rotated, although usually it is morphologically and functionally normal. An omphalocele containing the liver of at least 4.5–5 cm in diameter is defined as a giant omphalocele (GOC). In these cases, the thoracic cavity may also be abnormally shaped and reduced in size. GOC is associated with an underdeveloped abdominal cavity and with a significant visceral–abdominal disproportion, which prevents a safe primary closure. Pulmonary hypoplasia may also be present, associated with pulmonary distress and narrow thorax in chest radiographs. Children with an omphalocele generally have essentially intact abdominal wall muscles, but hypoplastic and laterally displaced rectal abdominal muscles[1] (Table 1).

### *Prevalence*

The prevalence of omphalocele has been estimated to be 1 per 3000–4000 births in Western countries.[2] In Japan, the prevalence during the period 1997–2006 was reported to be 1 per 2500 births by the Japan Association of Obstetricians and Gynecologists Program of Birth Defects Monitoring.[3] At around 14 to 18 weeks of gestation the incidence is 1 case out of 1100 fetuses. A recent study reported a prevalence of one in 381 at 11–14 weeks of gestation.[4] There is a very high rate of termination of pregnancy (30–52%) due to the presence of associated anomalies, and spontaneous abortion.

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**Table 1**
Type of defect, contents, and modality of delivery.

| | | | | |
|---|---|---|---|---|
| Hernia of the cord | | Small bowel/Meckel's diverticulum/omphalomesenteric duct remnant | Vaginal at term | |
| Minor/medium defect | 2–4 cm | Small bowel/liver/stomach | Vaginal/cesarian at term | Intact/ruptured sac |
| Large defect (GOC) | > 4 cm | Liver, spleen, and small bowel | Cesarian at term | Intact/ruptured sac |

A recent article from EUROCAT reports an increasing prevalence of abdominal wall defects that, however, seems to involve only instances of gastroschisis[5] (Table 2).

*Prenatal diagnosis, associated anomalies, and delivery*

Prenatal diagnosis of omphaloceles is usually made by ultrasound screening in the late first trimester to mid-second trimester. In some cases, an elevated maternal alpha fetoprotein level may be detected. Congenital omphaloceles are often associated with other anomalies; chromosomal defects (trisomy 13, 18, or 21) are observed in 30–40% of cases, and multiple anomalies including chromosomal aberrations are observed in 67–88% of cases. Interestingly, multiple associated anomalies appear to be more common with minor omphalocele ( < 4 cm) than giant omphalocele (55% vs. 36%).[6] Associated syndromes such as cloacal exstrophy, Donnai–Barrow syndrome, pentalogy of Cantrell, and Beckwith–Wiedemann syndrome (12%) can also be suspected or identified through a fetal ultrasound. In a study from the Netherlands, only 14% of omphaloceles were effectively isolated lesions. Prenatal screening in omphalocele fetuses needs to have a detailed evaluation of the cardiac system (14–47% of associated anomalies) and of the central nervous system (3–33% of associated anomalies), as severe defects strongly encourage a termination of pregnancy. Nonetheless, one-third of the fetuses considered to present isolated cases end up having multiple associated defects that are only detected postnatally.[7,8] This is an important evidence for high-risk pregnancy teams to discuss with prospective parents of an omphaloceles fetus. Reliable sonographic data and/or MRI evaluation to predict postnatal morbidity and survival rates are being developed.[9,10] A measurement of the lung/thorax transverse area ratio (L/T) may be useful to predict associated pulmonary hypoplasia in giant omphaloceles.[9] Some researchers have studied the ratios between the biggest omphalocele diameter compared with abdominal circumference (O/AC), femur length (O/FL), and head circumference (O/HC), in an attempt to correlate it with postnatal morbidity and mortality. The most useful parameter to predict the need for staged versus primary closure and respiratory insufficiency is probably that of O/HC, as 0.21 or more had 84% sensitivity and 58% specificity in predicting challenging cases.[1]

In the meantime, other studies support the thesis that, in the first trimester, isolated fetal exomphalos with normal nuchal translucency (NT) may be considered "physiological." The midgut is normally herniated within the umbilicus in early embryogenesis but resolves by the 12th week of gestation. Therefore, before this time, a "physiological" exomphalos may be detected in all fetuses. In most cases, the exomphalos will resolve spontaneously as pregnancy progresses, with no adverse sequelae; this is particularly true for exomphalos containing only the bowel.[4]

Currently, there are no specific fetal interventions performed either experimentally or on people for omphaloceles, other than karyotype amniocentesis.

The timing of delivery of an omphalocele is not controversial; most infants are indeed born at term, unless there are complicating features such as polyhydramnios. Preterm delivery is in fact not recommended. In contrast, the route of delivery is not yet a settled issue, with a dispute between vaginal birth and caesarian section proponents. Generally, when the defect is an extra-abdominal liver, the concern for hepatic injury during vaginal delivery encourages resorting to a caesarian section.[1]

**Table 2**
Prevalence of abdominal wall defects in the last 50 years.

| | Omphalocele | Gastroschisis |
|---|---|---|
| Sweden, 1965–1976 | 1/5000 | 1/15,400 |
| California, 1968–1977 | 1/4000 | 1/20,000 |
| Spain, 1976–1981 | 1/6600 | 1/25,000 |
| Finland, 1970–1979 | 1/5100 | 1/9200 |
| Literature review, 1985–2003 | 1/4–7000 | 1/10–20,000 |
| EUROCAT, 1999–2008 | 2.19/10,000 | 2.98/10,000 |

*Treatment*

*Perinatal care*

In the delivery room, the initial management of an infant with omphalocele requires a careful assessment of the cardiopulmonary condition, since these children may have unsuspected pulmonary hypoplasia that requires immediate intubation and ventilation. A thorough search for associated anomalies should then be undertaken. The high risk of associated cardiac defects demands a directed cardiac evaluation, including auscultation, four-limb blood pressures, and peripheral pulse examination. Once stabilized, a more detailed evaluation can be pursued with an echocardiography. Likewise, an abdominal ultrasound should be obtained to evaluate the possibility of associated renal anomalies. Neonatal hypoglycemia should alert the physician to the possibility of Beckwith–Wiedemann syndrome (EMG syndrome: exomphalos, macroglossia, and gigantism), which occurs in 12% of omphaloceles.[6] When planning the delivery of infants with omphalocele, risks arising from associated anomalies have to be properly taken into consideration. Adequate intravenous access should be obtained in order to begin fluid resuscitation. Infants with omphalocele with an intact sac do not have as significant fluid and temperature losses as those with gastroschisis; nonetheless, losses are higher than for infants with an intact abdominal wall. To minimize losses, the omphalocele itself can be dressed with saline-soaked gauze and an impervious dressing. A nasogastric or orogastric tube should be inserted and placed on suction or gravity drainage. In case of a ruptured omphalocele, the initial management of the viscera should be the same as that recommended for infants with gastroschisis.

*Surgical treatment: General considerations*

Over the past five decades, the surgical management of omphalocele has evolved, to the point that now the ultimate goal of surgical intervention is to provide complete fascial and skin closure without causing excessive intra-abdominal pressure or abdominal wall tension. The improved safety of techniques and of supportive care is now allowing us to make a step further from the modern ideal of a single-stage reduction and defect closure adding to it an enhanced cosmetic outcome. The levels of safety of reduction and closure techniques are related to the level of intra-abdominal pressure (IAP) and therefore to the degree of visceral–abdominal disproportion, which in turn, influences the risk of complications and thus the ultimate outcome of the intervention. Therefore, it is important to minimize intra-abdominal hypertension (IAH) in order

to avoid the abdominal compartment syndrome (ACS). Margins are defined by a measured IAP greater than 15 mmHg for IAH and greater than 20 mmHg for ACS. The effects of IAH are essentially hemodynamic and ventilatory.[6] Reduced cardiac output, as well as reduced splanchnic perfusion pressure, will lead to oliguria and gut mucosal acidosis. Furthermore, hypoventilation compounds will have hemodynamic effects, which in turn will lead to ACS and to potentially devastating complications, such as renal failure, sepsis, bowel ischemia, and wound dehiscence. Bowel ischemia may develop into necrotizing enterocolitis (NEC), which may cause a loss of bowel during surgery, resulting in a short bowel that will directly affect the outcome of the intervention. Wound complications including dehiscence, sepsis, and enterocutaneous fistula can lead to significant morbidity and dreadful cosmetic outcomes. IAP-related measuring parameters at time of primary reduction and at closure, under general anesthesia, have generally been used to guide the type of reduction in gastroschisis; however, they can also be applied to exomphalos.

Usually the most diffused method, although not universally accepted, is the measurement of the intravesical pressure; nonetheless, there are also less invasive methods, including end-tidal $CO_2$, airway pressures, and pulse oximetry.[6] It is important to check for the presence of malrotation in order to prevent devastating midgut volvulus either in pediatric or adult age. At the Great Ormond Street Hospital, they suggest to ascertain the presence of intestinal malrotation by upper gastrointestinal contrast study either before or after definitive closure of the defect. They also recommend performing a prophylactic laparoscopic Ladd's procedure at a later stage in patients with intestinal malrotation.[11,12]

*Surgical treatment: Primary closure*

In general, the surgical management of a small- to medium-sized omphalocele defect (2–4 cm) is fairly standard: a primary closure with a good surgical outcome. In these cases, survival and morbidity depend on associated defects. Interestingly, small defects, especially the ones in a central location (as opposed to those in hypogastric or epigastric locations), have a higher incidence of associated anomalies and chromosomal disorders. Infants with larger defects who survive at birth do not usually have associated lethal defects, and they represent some of the most challenging problems for pediatric surgeons and neonatologists.[1] In a survey carried out by a group of Dutch surgeons, the authors of a report discussing the closure of giant omphaloceles (1967–2009) were asked whether they were still performing the same procedure, or if they had modified their techniques. They concluded that over a 30-year period, there has not been an entirely accepted technique to treat giant omphalocele, and that in general, two methods have persisted: staged or delayed closure of the defect. However, the study did not address the issue considering the aforementioned heterogeneity of definition of a giant omphalocele, similarly to what happens for prenatal ultrasonographic definition issues. Some authors base their considerations only on size; others take into account the presence or absence of liver, and some use an estimate of the amount of intestinal contents (all or partial). In some cases, the combination of liver and intestines has also been taken into consideration. Such heterogeneity hindered the possibility of successfully combining literature in order to obtain a shared consensus. In addition to delayed repair or staged methods, there are several reports describing successful primary closures of giant omphaloceles shortly after birth. In a report from London, 12 of 24 cases of large defects had an immediate repair performed without consequences, and, in comparison to the other cases, these had shorter ventilator requirements and time to attain full feeds. However, this trial cannot represent a real prospect as for immediate repair there was a significant selection bias toward full-term and normal birth weight neonates. Furthermore, the definition of "large" was not uniformly applied.[14,15]

*Surgical treatment: Staged delayed*

Non-operative techniques have in common the use of a topical agent that allows an eschar to form over the intact amnion sac, which epithelializes over time, leaving a ventral hernia that will likely require repair later in life. This method is employed when the surgeon considers the defect too large or the baby too small to allow a safe primary repair, or if the neonate has significant concurrent cardiac or respiratory issues that would preclude an attempt at surgical closure.[15] This is not a new concept, as it has been evolving since Gross' time, when in 1948 he described it using skin flaps, and considering that others have used alcohol as a topical agent since 1899.[16] Concerns regarding large isolated defects derive from the fact that an initial repair without adequate abdominal domain for the organs would result in potentially life-threatening abdominal compartment syndrome, or in the inability to provide skin coverage, therefore this approach is not considered ideal. Earlier reports describing the use of mercurochrome, alcohol, and silver nitrate as eschar-producing agents were very effective but also associated with toxicity and therefore abandoned. Subsequently, there have been reports of a number of other topical agents used, including silver sulfadiazine, povidone–iodine solution, silver-impregnated dressings, neomycin, and polymyxin/bacitracin ointments.[15,16]

Eschar and epithelialization may take 4–10 weeks to complete, and in some cases, patients may complete the process after hospital discharge. There are also reports combining the use of a previously listed agent together with compression dressing, which helps to reduce the contents in the abdomen and thus facilitates closure. The repair is performed via either primary fascial closure, autologous repair with component separation, or using a mesh repair.[13] The number of patients in each report is small, and, without prospective studies, failures are usually not reported. Innovative techniques have also been used to recreate the abdominal domain also using tissue expanders in the abdomen that gradually increase in size. While the initial reports of Gross' staged operation had significant mortality and morbidity, current results are much better, with very few deaths reported.[17] In some "small" cases, there is no need for surgical closure, as the defect contracts and closes similarly to an umbilical hernia; however, most patients will eventually require closure of a ventral hernia defect, which is usually performed between 1 and 5 years of age. In 1967, Schuster[18] described the use of a silicone plastic "silo" to provide staged reduction for children with omphalocele. The sac was excised, and the silo was sewn to the rectus fascia and over the top of the viscera. Some surgeons created a short circumferential skin flap so that the silo was sewn only to the fascia; others instead attached the Silastic to the full thickness of the abdominal wall. Some surgeons have recently recommended the use of preformed spring-loaded silos in this setting, but this may not be successful due to the relatively large size of the defect that prevents the silo from remaining in place. Another option for moderate-sized omphaloceles with a relatively thick sac is to use the sequential ligation of the sac itself for a gradual reduction of the viscera. Serial reductions, similar to those for gastroschisis, are performed on a once- to twice-daily schedule, until definitive closure can be obtained. At this point, the infant is returned to the operating theater for the definitive closure of the defect. If at this time, the fascial edges cannot be approximated, prosthetic closure can be utilized.

*Techniques for giant omphaloceles*

Other special techniques have been created for giant omphaloceles, such as bipedicled skin flaps obtained with longitudinal

incisions along the margins of the rectus abdominis muscle. This may represent a good alternative solution to achieve a complete, tension-free, midline closure.[19] More recently, the component separation technique (CST) has also been described, which is based on the enlargement of the abdominal wall surface by translation of the muscular layers without compromising the innervation and blood supply of the muscles. The arterial blood supply of the abdominal skin runs mainly via the intercostal arteries and the perforating branches of the epigastric artery, as well as through the branches of the pudendal artery.[13] The developers of this technique have also presented the long-term positive results of this method.[6,20]

*Long-term follow-up and quality of life*

Provided that there are no significant structural or chromosomal abnormalities, most infants with a small omphalocele recover well and do not present any long-term issues. However, this may represent as few as 10% of all omphaloceles diagnosed with prenatal ultrasound. A number of long-term medical problems occur in patients with large omphaloceles. These include gastroesophageal reflux, pulmonary insufficiency, recurrent lung infections or asthma, and feeding difficulty with failure to thrive, reported in up to 60% of infants with giant omphalocele. Many of these children may initially require gastrostomy feeding, although some studies report that these difficulties seem to resolve by childhood, with height and weight measurements becoming similar to those of their peer group. The management of severe gastroesophageal reflux can be difficult, especially in children being managed with escharotic therapy, for whom a fundoplication may be technically challenging if not impossible. These children may be better served by the use of a naso- or gastrojejunal tube. A third of patients with omphalocele report intermittent abdominal pain persisting into young adulthood. The respiratory insufficiency associated with giant omphaloceles may be secondary to abnormal thoracic development with a narrow thorax and small lung area leading to pulmonary hypoplasia. However, a study looking at the long-term cardiopulmonary consequences of large abdominal wall defects reported normal lung volumes and oxygen consumption on long-term follow-up, although exercise tolerance was slightly reduced.[21] In the long-term follow-up, the most widespread concern for patients with omphalocele is cosmesis, with nearly one-half of patients expressing dissatisfaction for the lack of an umbilicus and for the large abdominal wall scar. Predictably, these complaints were expressed more by those patients who had giant omphaloceles at birth, rather than by those with minor omphaloceles. Nonetheless, recent studies showed how this aspect did not affect the overall quality of life, and different techniques of umbilical reconstruction have been proposed mainly by plastic surgeons that are, usually, performed at request of the patient.[22,23] The authors of the study conclude that after a high level of medical intervention in early life, minor and GOC patients report similar long-term results with the exception for cosmetic problems, which are more serious in GOC. However, this issue did not influence the quality of life in either group, which is comparable to that of healthy young adults. With the latter positive prospective in mind, expectant parents with fetal diagnosis of omphalocele and parents of newborns with omphalocele should be informed that the high burden of surgical interventions their child will need is likely to result in good health condition in the long-term, especially if there are no associated anomalies.[6,24] Some of these patients could require additional surgery for adhesive bowel obstruction, and a small number, not treated for malrotation, could develop devastating midgut volvulus with subsequent short bowel syndrome.[6] A recent study from Netherlands indicates that after a high level of medical intervention in early life, minor and giant OC patients report similar long-term results, and the quality of life in both groups is comparable to that of healthy young adults.[24] For the surviving patients affected by Beckwith–Wiedemann syndrome (EMG syndrome: exomphalos, macroglossia, and gigantism), a regular follow-up must be organized to do an early diagnosis of Wilms or Hepatoblastoma tumor, frequently associated to this syndrome.[26]

## Gastroschisis

*Introduction*

Gastroschisis (from ancient Greek *gastro* = stomach and *schisi* = split or open) is a full-thickness defect of the abdominal wall, usually located to the right of the normal umbilical cord. It is considered a rare malformation with a prevalence recently published between 1.10/10.000 and 5.1/10.000[25] while in the past decades it was reported around 0.7/10.000.[26] This apparent rising prevalence may be due to more accurate screening of pregnancies, improved technologies, and increased environmental factors.[27]

Different theories regarding the pathogenesis of gastroschisis followed each other in the past (in utero rupture of umbilical cord hernia,[28] weakness on the right side of the umbilical cord,[29] persistence of right umbilical cord, and disruption of right omphalomesenteric artery[30]). More recently, Stevenson et al.[31] hypothesized gastroschisis may be the result of failure of the yolk sac and vitelline structures to be included into the body stalk. Several studies reported an increased incidence among young mothers, primiparas or primigravidas; low socioeconomic status and poor maternal diet[32,33]; mothers exposed to specific medications (decongestants, such as phenylpropanolamine and pseudoephedrine; analgesic, such as salicylates, ibuprofen, and acetaminophen)[34,35]; and cigarette smoking.[36,37] These sympathomimetics support a vascular aspect theory. Also, genetic polymorphisms of specific genes involved in angiogenesis, wound repair, inflammation, and blood vessel integrity had been associated to an increased incidence of gastroschisis in case of cigarette smoking.[35] The association between gastroschisis and genitourinary infection, a risk factor for venous thromboembolism, prior to conception until the end of the first trimester has been reported as a further possible risk factor.[38] Finally, an interesting three-part hypothesis has been proposed that links the early estrogenic thrombophilia, racial differences in thrombosis, and thrombotic by-products interfering with early developmental signaling with the incidence of gastroschisis.[39] In this theory, different interconnected aspects are in charge such as the high levels of estrogen in young mother with low body mass index, the lower frequencies of thrombotic known genes in blacks, and palmitic acid by-products of thrombosis affecting cell signaling.

*Prenatal diagnosis and management of pregnancy*

The prenatal diagnosis of gastroschisis is possible from the end of the first trimester, after the physiological closure of the abdominal wall around 10 weeks of gestation. At this time, the midgut should have completed rotation and fixation intra-abdominally and the abdominal wall be entirely formed. In case of gastroschisis, at ultrasound, loops of bowel are detected outside the abdominal cavity, herniated through a small para-umbilical wall defect, floating in the amniotic fluid, without any covering membrane. This last feature, absence of covering membrane, together with evidence of a small defect (usually 2–3 cm) and herniated loops, allows one to differentiate gastroschisis from

**Table 3**
Differences between omphalocele and gastroschisis.

| | Omphalocele | Gastroschisis |
|---|---|---|
| Incidence | Stable | Increasing |
| Maternal age | 30 years | 22 years |
| Gestational age | Term | 34 weeks |
| F:M | 1.5:1 | 1:1 |
| Site | Umbilical defect | Lateral defect (right) |
| Sac | Always | Never |
| Malrotation | Possible | Possible |
| Associated anomalies | Frequent | Rare |
| Intestinal atresia | Rare | Up to 10% |

omphalocele (Table 3). In omphalocele, indeed, the defect is usually greater (5 or more centimeters), centrally located, loops and liver may be herniated, and a covering membrane is always present. Other differential diagnosis with gastroschisis include hernia of the cord, which is a small central defect containing loops covered by membrane; the very rare entity called limb-body wall complex, which involves thoraco-abdominoschisis and limb defects; and more destructive abdominal defects such as bladder and cloacal exstrophy, which will be treated in a separate section.

Once gastroschisis has been identified, a multidisciplinary counseling, including obstetricians, pediatric surgeons, and neonatologists is mandatory. A program of bi-monthly sonographic surveillance is established with the aim to check amount of amniotic fluid, appearance of herniated loops, and possible development of intra- and extra-abdominal bowel dilatation. The pregnancy of a fetus with gastroschisis can go on with both polyhydramnios and oligohydramnios. Polyhydramnios, together with progressive intra-abdominal bowel dilatation, is considered highly predictive of bowel atresia.[40] On the other hand, some reduction of amniotic fluid is often detected at the end of the second trimester, but severe oligohydramnios (AFI $<$ 2 cm) is a rare and, potentially, fatal event. In case of oligo-anhydramnios, the repeated infusion of saline solution has been proved to be beneficial.[41,42] The practice of amnioinfusion requires expertise and a center with neonatal intensive care and pediatric surgery available. A simple and innocuous method to correct the tendency to oligohydramnios seems to be the maternal oral hydration.[43] It has been suggested, indeed, that a glass of water per hour while awake would significantly increase the amount of amniotic fluid.

Bowel dilatation of the extruded intestinal loops is common and variable in these fetuses and is related to the restriction at the level of the abdominal defect. Different is the occurrence of bowel dilatation of the intra-abdominal portion of intestine. According to recent reports, the onset and progression of intestinal dilatation is strongly suggestive of intestinal atresia[40] or poor postnatal outcome.[44–46] Fetuses with intra-abdominal bowel distension, especially if persistent and progressive, tend to be born earlier than those without detection of bowel dilatation; to have a lower birth weight; less likely to undergo to a primary repair, therefore to require multiple operations; longer administration of parenteral nutrition; and ultimately, longer hospital stay.

A significant number of newborns with gastroschisis are small for gestational age (SGA) with normal Doppler sonography of umbilical and middle cerebral arteries.[47,48] The deflection of intra-uterine growth is usually detected at the end of the second trimester or beginning of the third, when the fetus begins actively to swallow the amniotic fluid, which is thought to partially contribute to fetal growth.[49] The fetus with gastroschisis is, indeed, in a condition of intestinal subocclusion due to both herniation of loops, which can be variously damaged, and their constriction at the level of the defect. The result is a reduced assumption and absorption of nutrients from the amniotic fluid. Moreover, it is thought that some nutritive factors are lost from the extruded intestine into the amniotic fluid, and this may further contribute to slowing the fetal growth.[50]

Fetal karyotyping is not usually indicated, as to date, neither genes have been identified as responsible for the occurrence of gastroschisis nor recognized syndromes.[51] Recent articles have calculated the risk of family recurrence between 2.4%[52] and 2.5%[53] with a trend toward underestimation. This aspect should be considered in view of the fact that the affected patients survive at birth and more and more often reach the reproductive age.

Finally, a few associated malformations have been reported, mainly intestinal atresia (around 10% of cases)[40]and cardiac, renal, musculoskeletal, and central nervous system anomalies.[54]

### *Prenatal therapy*

At the beginning of the century, a series of experimental and clinical articles came out proposing a procedure to reduce the concentration of inflammatory markers present in the amniotic fluid, likely derived both from urine, intestinal content and exposed intestine of fetuses with gastroschisis,[55–57] which is the amnioexchange. It consists in the replacement of the amniotic fluid with an equal amount of sterile warm saline or Ringer's lactate solution. A similar procedure, but with different indications, is the amnioinfusion, which is performed in case of severe oligohydramnios and consists in the infusion of appropriate amount of warm saline solution required to achieve a normal AF volume. A few years ago, our center undertook a study on eight women carrying a fetus with gastroschisis who accepted to undergo the amnioexchange procedure.[58] The results were quite disappointing both in terms of reduction of macroscopic intestinal damage, amount of neutrophil infiltration and level of proinflammatory cytokines, and ultimately, postnatal course. Therefore, the recommendation is still to avoid such an invasive and useless procedure. In case of severe oligohydramnios, however, amnioinfusion has proved to be a life-saving maneuver with a worthwhile risk-to-benefit ratio.

### *Route and time of delivery*

It is a common experience that fetuses with gastroschisis go into spontaneous preterm delivery more often than in the general population.[48,59,60] Another common observation, also in our series, is that if the onset of labor starts spontaneously before 37–38 weeks, the loops tend to be more damaged and the amniotic fluid stained as in cases of fetal distress. It is possible the condition of intestinal occlusion is more severe in these cases and the fetus keeps vomiting the gastrointestinal contents into the amniotic fluid, thus increasing the amount of factors and inflammatory mediators.[58] This group of patients is more likely to undergo staged closure.[60]

Fetal distress, the presence of intra-amniotic inflammatory factors, and alteration of amount of amniotic fluid may all trigger the onset of labor. The average gestational age at birth is 36 + 2–3/7 weeks.[44,60,61–63] However, about half of the pregnancies continue beyond 37–38 weeks. The best route and time of delivery, in these cases, is not known as contradictory reports have been published. Some authors who believe the amniotic fluid has a harmful effect on the herniated bowel advocate an early delivery at 36–37 weeks, or even earlier, either with C-section or induced labor.[64,65] Others, instead, have reported no benefits in terms of first feeding and full feeds, length of hospital stay, and weight at discharge when babies with gastroschisis are born preterm.[48,66–69] Those authors who do not advise early delivery tend to encourage normal vaginal labor, whereas those who advocate the preterm birth are also inclined to recommend C-section, both for obstetrical reasons (the labor may not begin before term) and surgical aspects (the extruded gut may

be further ruined during vaginal delivery). At our center we still prefer a planned C-section at 37 weeks, although the lack of randomized studies does not allow, at the moment, to identify any possible advantages if the baby is born preterm. Finally, location of delivery seems to have some importance in terms of reduction of complications if the patients are delivered in a perinatal center with a neonatal intensive care unit and pediatric surgery availability.[70]

### *Neonatal therapy*

The optimal surgical management of a neonate born with gastroschisis is still undefined, but presently the survival is expected to exceed 95%[46] if patients are treated in pediatric centers. This percentage can drop to about 70% if intestinal atresia, volvulus, or perforation occurs[71,72] Molik et al. published an article to highlight two possible scenarios a pediatric surgeon can deal with simple and complex gastroschisis. In the former, and more common situation, primary reduction is expected to be accomplished in 70% of cases with quicker start of feeding and achievement of full feeds, lower complication rate, and shorter hospital stay. In complex cases, which is when atresias, stenosis, perforations, or volvulus occurs, all parameters are worse, including mortality,[72] After 10 years, Cowan et al. proposed a "gastroschisis prognostic score (GPS)" that correlates the bowel appearance at birth with clinical outcome in a large population-based group of gastroschisis (Table 4). The score is based on presence of bowel matting, necrosis, atresia, or perforation evaluated within 6 h from birth. The score allows the reliable identification of groups at high-risk for mortality and morbidity and, as a consequence, to plan the best counseling and therapies.[61]

Quick protection of extruded bowel is mandatory at birth by means of sterile wet sponges and aluminum foil, cling-film, or plastic bag, together with the right flank decubitus in order to limit a possible vascular damage. The definitive covering, either primary or staged, should be undertaken within the next 4–7 h.[73,74] Besides coverage or reduction of the intestine, a central line needs to be inserted at the time of first repair or within a few days. Even if loops are apparently little damaged, in fact, still many days are usually required for peristalsis to be actively functioning, and in the meantime, the infant needs to be totally or partially supported by parenteral nutrition.

If the herniated loops look almost normal, without matting and peel, it is possible to perform the reduction at the bedside,[75] preferably under mild sedation with midazolam[73] and after decompression of the recto-sigmoid with washouts. This procedure requires a trained pediatric surgeon, time and patience, and the experience to understand when it is safer to "convert" to the traditional surgical reduction. The major risk is, indeed, to force a fragile intestine into a small abdominal cavity, thus directly injuring the loops and creating the conditions for the development of the abdominal compartment syndrome.

If the loops are edematous and covered by an inflammatory peel, still the primary reduction may be feasible, but under general anesthesia, enlarging the defect and, again, avoiding excessive compression of the intestine. Different methods to record the abdominal pressure have been adopted in the past,[76,77] and the measurement via a transurethral urinary catheter seems to be the most reliable.[78] Conversely, in about one-third of cases, the herniated loops are very edematous, covered by a thick peel and tightly matted together, then a staged reduction is advisable. Under general anesthesia, an extracorporeal bag (either silastic, goretex, or others) is sutured around the enlarged defect, or inserted within the abdomen in case of preformed spring-loaded silo, and hung from the roof of the crib or isolette so the intestine can then return to the abdomen spontaneously or by daily gentle pressure. It usually takes 7–10 days for the loops to return into the abdomen, after which the baby is brought back into the operating theater to remove the bag and close the abdominal wall. It is not necessary to keep the infant intubated and/or sedated while the bag is in place, not even during daily manual reduction. It has to be mentioned the preformed spring-loaded silo, although attractive for the ease of use and avoidance of general anesthesia, do carry risks and complications such as enlargement of fascial defect (44% of cases), silo replacement (15%), need of mesh at time of abdominal closure (19%),[79] and according to some recent surveys, does not seem to ensure advantages over traditional primary closure.[80]

At the time of primary inspection, it is possible to encounter fibrous obstructing bands that can be easily lysed/removed; intestinal atresia, usually along the midgut; perforation; or necrosis. The reported percentage of bowel atresia varies between 10–15%[1,40,81] and 26–28%.[72,82] If an atresia is present, or suspected, one of the best choice is still to return the loops in the abdomen, in order to give the bowel time to recover, and deal with the atresia a few weeks later.[1,83] In case of perforation or necrosis, the best/optimal treatment is driven by bowel appearance: if inflammation is minimal resection and anastomosis can be undertaken, conversely it would be safer to resect the damaged loop and create a temporary stoma.[81]

### *Post-operative outcome*

The post-operative course largely depends on the severity of intestinal damage and the occurrence of complications.[61,72,81,84] Patients with simple gastroschisis who undergo primary closure, either manually at bedside or surgically in the operating room, are still expected to experience a period of adynamic ileus due to the characteristics of malformation and the use of paralytic post-operative drugs. This period may vary between one or more weeks during which the neonate is entirely supported by total parenteral nutrition administered via a central venous line. Minimal enteral feeding should be started as soon as the bilious-gastric drainage begins to diminish in order to enhance peristalsis, avoid the villous atrophy and, possibly, reduce intestinal stasis, overgrowth, and bacterial translocation.[85]

Length of hospital stay, in this group of patients, can be up to a month, after which, neither particular restrictions are required nor differences in diet weaning. Some authors suggest the administration of low dose of oral antibiotics one week per month, or according to different protocols, in the first year of life as prophylaxis for intestinal infections.[86]

Patients who, instead, undergo a staged closure of their defects, for intestinal atresia, perforation, or necrosis (also consequent to excessive abdominal pressure during primary closure), experience a very different outcome. They often require multiple operations and the management of a central line with administration of parenteral nutrition that may be prolonged and continued at home.[83]

Finally, the rarest, but worst, category/group of patients are those affected by short bowel syndrome, consequent to either extensive bowel necrosis that occurred during gestation or during the initial inexpert reduction of loops. In this small subset of patients, the parenteral nutrition needs to be maintained for many

**Table 4**
Gastroschisis prognostic score (GPS).

| | | | |
|---|---|---|---|
| Matting | None (0) | Mild (1) | Severe (4) |
| Atresia | Absent (0) | Suspected (1) | Present (2) |
| Perforation | Absent (0) | – | Present (2) |
| Necrosis | Absent (0) | – | Present (4) |

months, years, or lifetime with all the well-known related consequences (catheter's infections and malfunction, diet restrictions, growth delay, and reduced social and scholastic activities) that contribute to a poor quality of life.

### *Long-term follow-up and quality of life*

Nowadays, the outcome of the majority of patients affected by gastroschisis is considered good in terms of growth in 75% of cases[87]; the neurodevelopmental outcome seems comparable to gestational age-matched control,[88] and there is possibility of reproduction and improvement in overall quality of life.[89] The minority of cases affected by short bowel syndrome is totally or partially dependent on TPN.[90] Two-thirds of these unfortunate patients will be eventually weaned off TPN, but the risk of malabsorption and nutritional deficiencies ought to be considered and corrected throughout their life. Some of them, instead, will remain dependent on TPN and still represent the main cohort of candidates for intestinal transplantation. Finally, some newer aspects, although still little documented, are arising along with the fact that patients with gastroschisis survive into adulthood. One of these is the incidence and morbidity of intestinal adhesions estimated as frequent as 27% in gastroschisis, with a mortality rate for bowel occlusion of 15% and an incidence of chronic abdominal pain more frequent in these patients than in healthy peers.[89,91] In the gynecology literature, there is concern about the impact of adhesions among fertile women; over 30% of women operated on reproductive tract required re-admission for adhesions,[92] but pregnancy is described in patients previously affected by gastroschisis, meaning both reproductive system and abdominal capacity seem adequate.[89] Testicles herniated from the defect at birth and relocated into the abdomen at first operation may descend into the scrotum spontaneously in 50% of cases.[93,94] Also, the ability to participate in sports is reported as comparable to healthy peers.[21] The last concern is cosmesis. It has been reported, indeed, 60% of patients without an umbilicus would experience some psychological stress.[89,95] For this reason, different techniques of umbilical reconstruction are available, mainly performed by plastic surgeons at a later age.[22,23]

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