**Introduction**

The two most common congenital abdominal wall defects are gastroschisis and omphalocele. Both have reported incidences around 1 in 4,000 live births, however the incidence of omphalocele identified on second-trimester ultrasound is as high as 1 in 1,100 highlighting the significant rate of associated intrauterine fetal demise (1-4). In contrast, the incidence of gastroschisis specifically has increased world-wide over the last few decades. This increase is not entirely understood, though socioeconomic status and environmental factors have been postulated as potential contributors (5). Both omphalocele and gastroschisis are commonly diagnosed prenatally, and each has an associated spectrum of postnatal outcomes that can range from a brief neonatal intensive care unit (NICU) stay to life-long functional limitations or even death. Outcomes for neonates with gastroschisis are generally dependent on the characteristics of the abdominal wall defect and underlying bowel viability, while omphalocele outcomes are determined by both defect size and the presence of other associated anomalies (5-8). Because of the dependence on prenatal diagnostics and the broad spectrum of postnatal...
outcomes associated with these defects, gastroschisis and omphalocele are excellent examples of fetal anomalies that require multidisciplinary and translational approaches to patient care. This review focuses on recent advancements, novel techniques, and current controversies related to the prenatal diagnosis and management of gastroschisis and omphalocele.

**Gastroschisis**

**Background**

The abdominal wall defect of gastroschisis occurs to the right side of the umbilicus and is by definition lacking a protective covering over the herniated abdominal contents. Though not entirely understood, it is thought to be due to a disruption in migration of the lateral ventral body folds early in embryonal development, creating a para-midline defect. In normal development, the elongating intestine herniates outside of the abdominal cavity around the sixth week of gestation, and then over the next four weeks undergoes a process of midgut rotation with return of the intestines to the abdomen (2). However, if the abdominal wall fails to form completely, the intestine can remain herniated into the amniotic cavity.

Gastroschisis is not frequently associated with other anomalies. Postnatal outcomes are related to degree of intestinal injury and subsequent gastrointestinal complications. Broadly, gastroschisis can be divided into two types—simple and complex. Complex gastroschisis is defined as any associated intestinal atresia, necrosis, perforation, or volvulus, while simple gastroschisis lacks any intestinal complications (4-6). Complex gastroschisis is associated with a higher mortality rate, prolonged hospital stays, increased infectious complications, and greater risk of intestinal failure (2). Another predictor of mortality and worse postnatal outcomes is the presence of liver herniation in gastroschisis. Retrospective review of gastroschisis patients at a single institution over a 15-year period found a 6% rate of liver herniation, which was associated with 57% mortality and poor outcomes overall (9). The prenatal workup and management of pregnancies complicated by gastroschisis include predictive risk stratification and close monitoring for fetal distress or demise.

**Prenatal diagnosis, surveillance, and prognosis**

Gastroschisis is currently diagnosed prenatally in over 90% of cases (10). Identification of free-floating intestines outside of the abdominal cavity to the right of a normally-inserted umbilical cord on prenatal ultrasound is diagnostic. Prenatal diagnosis most frequently occurs during the second trimester, though has been reported as early as the twelfth week of gestation. A diagnosis of gastroschisis made during the first trimester must be interpreted with caution and confirmed later in gestation, however, as normal visceral rotation may not be completed until the end of the first trimester (11). Once gastroschisis has been identified, referral to a multidisciplinary fetal center is recommended for close fetal surveillance, delivery planning, and high-level neonatal care. Though no specific guidelines for prenatal gastroschisis surveillance exist, a recent North American Fetal Therapy Network (NAFTNet) survey assessed current monitoring practices for gastroschisis among participating maternal-fetal medicine (MFM) specialists (12). In stable patients, antenatal testing with a combination of nonstress test, biophysical profile, and sonographic amniotic fluid index most commonly began at 32 weeks gestation and was repeated weekly. The necessity of such close surveillance is related to the high incidence of spontaneous intrauterine fetal demise, which has been prospectively identified as 4.5% in fetuses with gastroschisis compared to 0.6% in non-anomalous fetuses and may be increased throughout the third trimester (13-15). Further, intrauterine growth restriction is common in gastroschisis and should be monitored closely during gestation (12).

Another contemporaneous reason for focused and repeated prenatal evaluation of fetuses with gastroschisis is attempted antenatal prediction of complex gastroschisis and associated adverse neonatal outcomes. This predictive ability is necessary for MFM specialists to provide recommendations regarding delivery planning, and for more accurate prognostication and counseling of families. Multiple recent studies have evaluated different antenatal sonographic factors with discrepant results, often due to small sample sizes and inconsistent definitions/documentation. The factors identified on multi-institutional review and meta-analyses that correlate with complex gastroschisis include intra-abdominal bowel dilation (especially when repeatedly present during fetal development) and polyhydramnios (10,16). Further, gastric dilation, increased abdominal distention, intrauterine growth restriction, and extra-abdominal bowel dilation identified on antenatal ultrasound were found to be predictive of adverse neonatal outcomes (16,17). More work is needed to prospectively validate these results, and to
determine the predictive value of multiple factors combined.

**Prenatal management**

**Delivery planning**

Another area of controversy in the management of gastroschisis patients is the ideal timing of delivery. Overall the average gestational age at spontaneous delivery in gastroschisis is <37 weeks, and some postulate that late preterm, planned delivery could result in improved outcomes (18). As discussed above, there is a high incidence of spontaneous intrauterine fetal demise in gastroschisis pregnancies compared to non-anomalous pregnancies and this risk may increase approaching term gestation (13,15). Further, gastroschisis is associated with variable degrees of bowel inflammation/thickening termed “matting” that is identified at birth and has been hypothesized to be due to the inflammatory nature of amniotic fluid on exposed bowel (Figure 1). The degree of bowel matting identified at birth has been found to be predictive of worse neonatal outcomes (18). Another consideration when determining the ideal timing of delivery in gastroschisis is the risk of vanishing gastroschisis, or closure of the abdominal wall defect around herniated bowel resulting in devastating midgut necrosis, which may increase as pregnancy progresses. Taking these concerns together, some clinicians advocate for early delivery (<37 weeks gestation) at varying gestational ages for fetuses with gastroschisis in an attempt to minimize fetal demise and neonatal morbidity (19,20). However early delivery is not without its own potential risks, mainly related to the physiologic immaturity associated with preterm birth. Potential risks include increased mortality, respiratory morbidity, neurocognitive deficits, cholestasis, and sepsis (20,21). Further, a recent Canadian Pediatric Surgery Network (CAPSNet) review found that the degree of bowel matting at birth is inversely associated with gestational age in gastroschisis patients, lending more strength to the argument that elective term delivery (≥37 weeks gestation) should be preferred (22). A Cochrane review was unable to draw any conclusions regarding delivery timing for gastroschisis as no large, adequately powered studies were available for review (23). A recent randomized controlled trial (RCT) comparing early delivery (34 weeks gestation) to routine obstetric care was stopped early due to a significantly elevated rate of sepsis in the early delivery group (24). Another RCT is currently underway that will compare delivery at 35 weeks gestation to 38 weeks, and also includes a prospective long-term database and biobank (25). At this time, the published data available do not definitively conclude the ideal timing of delivery in gastroschisis.

The preferred mode of delivery—vaginal versus cesarean section—for fetuses with gastroschisis has also been controversial. However, most data comparing the two delivery methods support the hypothesis that vaginal delivery is as safe as cesarean section in gastroschisis patients, and a recent meta-analysis failed to demonstrate a difference in outcomes between the two methods of delivery (26). Currently accepted practice is to proceed with vaginal

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**Figure 1** Pictorial representation of the spectrum of bowel inflammation or “matting” (none, mild, or severe) that can be seen in gastroschisis patients. Used with permission from The Canadian Pediatric Surgery Network website (http://www.capsnetwork.org/portal/ForAbstractorsSiteInvestigators/EducationfortheGSBowelInjuryScore.aspx)
delivery unless there is another indication for cesarean.

**Novel therapies**

With advancements in fetal surgery and the ability to perform in utero procedures during gestation, several innovative therapies have been introduced over the last decade with the goal of improving outcomes in gastroschisis after delivery. A common theme to this work is the hypothesis that reducing the degree to which herniated bowel is in contact with amniotic fluid will improve its function after birth. Both animal and human studies have identified high levels of inflammatory mediators such as ferritin and cytokines (interleukin-6, interleukin-8, tumor necrosis factor) as well as digestive compounds (e.g., lipase and bile acids) in the amniotic fluid of pregnancies complicated by gastroschisis (27,28). Further, this inflammatory milieu is believed to be the cause of the characteristic bowel matting identified after birth. The degree of bowel matting, in addition to the presence or absence of intestinal atresia, perforation, or necrosis, has been used to generate a “gastroschisis prognostic score” (GPS) postnatally (18). The GPS is a predictive marker for increased risk of mortality and morbidity, and higher GPS scores have been shown to correlate with poor outcomes in gastroschisis patients (18,29).

One attempt at minimizing the inflammatory effect of amniotic fluid was the amnioexchange procedure. Amnioexchange involves removal of amniotic fluid during gestation and replacement with the same volume of sterile saline (30). Animal models demonstrated a significant decrease in the presence of inflammatory mediators following amnioexchange, and so the procedure was attempted on human fetuses with gastroschisis. Unfortunately, the RCT was stopped early due to a higher fetal mortality rate in the amnioexchange arm, and interim results demonstrated that although there was an initial decrease in inflammatory and digestive compounds present within the amniotic fluid following the procedure, this effect was lost over time (31). Amnioexchange is not currently recommended as a potential treatment option for gastroschisis.

Another novel approach to prenatal treatment of gastroschisis is fetoscopic intervention via either intestinal coverage with a synthetic bag (similar to silo placement) or closure of the defect in utero. A fetal lamb model has been developed to test this innovative approach (32). Early studies demonstrated proof of concept, with reduced inflammatory “peel” formation identified in fetal lambs that had complete coverage of their iatrogenic gastroschisis defects compared to those that had no or partial coverage (33). Attempts at fetoscopic bag coverage and closure have so far been technically unsuccessful, however open fetal repair was successful in two lambs and both fetuses survived to term (34-36). This novel technique is still being developed and has exciting potential implications for future prenatal management of gastroschisis.

The newest approach to prenatal gastroschisis coverage involves the use of mesenchymal stem cells. This technique is termed transamniotic stem cell therapy, or TRASCET (37). The theory behind TRASCET is that through augmentation of the biologic role of native stem cells within the amniotic fluid, targeted tissue repair can be achieved. Intra-amniotic delivery of amniotic fluid-derived mesenchymal stem cells (aMSCs) has been demonstrated to successfully induce partial or complete coverage of experimental myelomeningocele defects (37). The same theoretical benefit is now being explored for gastroschisis defects as well, with early results demonstrating site-specific homing of aMSCs to areas of intestine exclusively exposed to amniotic fluid following TRASCET (38). These examples of novel prenatal interventions for gastroschisis show great promise for the future management of these patients.

**Omphalocele**

**Background**

In contrast to gastroschisis, the omphalocele defect occurs at the abdominal midline and involves the umbilical ring, resulting in a 3-layer sac encasing the herniated abdominal contents. This sac consists of an inner layer of peritoneum, middle layer of Wharton’s jelly, and outer layer of amnion. Embryologically, omphalocele is thought to be the result of a folding defect that occurs as the bowel is returning to the abdominal cavity during normal development (1). The omphalocele defect can range widely in size and type of abdominal viscera present within the sac depending on when during gestation the arrest in bowel rotation occurs. Postnatal outcomes in infants with omphalocele are predominantly dependent on other concurrent anomalies or comorbidities associated with larger-sized defects. Concurrent congenital anomalies can be present in up to 40–80% of omphalocele cases and most commonly include chromosomal (15–57%), cardiac (11–23%), genitourinary
(6–21%), musculoskeletal (21%), gastrointestinal (7–19%), and neurologic (4–8%) abnormalities (39-41). Omphalocele can also be associated with certain genetic syndromes, such as Beckwith-Wiedemann, pentalogy of Cantrell, and cloacal extrophy. A recent review of respiratory comorbidities in omphalocele patients identified respiratory insufficiency as an independent predictor of mortality. Specifically, underlying pulmonary hypoplasia and pulmonary hypertension, which are typically seen with large defects that restrict thoracic domain and alter diaphragmatic function, are associated with worse long-term outcomes in omphalocele patients (8). Comprehensive prenatal workup of both the omphalocele itself as well as any associated anomalies or comorbidities is critically important to continued surveillance, prognostication, counselling, and ultimate management.

Prenatal diagnosis, screening, and prognosis

Similarly to gastroschisis, omphalocele is typically diagnosed on prenatal ultrasound. Diagnostic findings include herniated abdominal contents along the abdominal midline (epigastric, umbilical, or hypogastric locations) covered by a three-layer sac (1,42). The timing of prenatal diagnosis for omphalocele has shifted over the last two centuries from near-universal identification within the second trimester to almost half being identified during the late first trimester (11–14 weeks gestation) (42,43). As mentioned earlier, there is an increased incidence of prenatal demise also associated with omphalocele. This significant prenatal mortality is likely due to a combination of spontaneous abortions and elective pregnancy terminations, especially when other significant anomalies are concurrently identified (7,41,42). Once a diagnosis of omphalocele is made, referral to a fetal care center is recommended to establish a multidisciplinary team of obstetricians, pediatric surgeons, and neonatologists. This team will determine a plan for prenatal surveillance, delivery, and postnatal care based on the characteristics of the omphalocele defect and any associated anomalies.

Comprehensive prenatal ultrasonography along with fetal echocardiogram allow for evaluation of other structural defects and are critical components of the prenatal workup for omphalocele. In addition, fetal karyotyping is offered to provide information on associated chromosomal anomalies. The most common of these include Trisomies 18, 13, and 21; Turner syndrome; and triploidy (41). One study found the elective pregnancy termination rate to be 74% (compared to an 18% rate of spontaneous fetal demise) in pregnancies complicated by omphalocele in addition to a known chromosomal abnormality (41).

Prenatal ultrasound is being increasingly used as a means to assist in prognostication depending on specific sonographic characteristics of the omphalocele defect. In general, omphaloceles are classified as either small, giant, or ruptured (Figure 2). The smallest and least morbid defects are sometimes referred to as hernias of the umbilical cord, in which the lateral body folds seem to form correctly during embryologic development, however a portion of small bowel fails to return to the abdominal cavity via the intact umbilical ring. This results in a small hernia located at the base of the umbilical cord at birth (44). These minor defects (described as less than 1.5–4 cm depending on the source) are infrequently associated with other congenital anomalies and do not contain any portion of liver, thereby distinguishing them from larger omphalocele defects in which the abdominal wall musculature is disrupted to a greater degree and higher morbidity is expected (2,44,45). Ruptured omphalocele, though rare, is associated with the highest morbidity, and is defined by disruption of the protective omphalocele sac (46). It can be difficult to distinguish a ruptured omphalocele from gastroschisis, however the presence of an intact umbilical cord remote from a right-sided abdominal wall defect is diagnostic of gastroschisis.

Current controversy exists over the appropriate definition of giant omphalocele. The utility of distinguishing between
small and giant omphaloceles relates to delivery planning, prognostication, and postnatal repair of the defect. Larger omphalocele defects put infants at higher risk of other associated medical comorbidities, such as pulmonary hypoplasia, chronic lung disease, feeding difficulties, prolonged hospital stays, and increased mortality (47,48). Giant omphaloceles are independently associated with higher morbidity and worse long-term outcomes than small omphaloceles, generally due to lack of abdominal domain and associated pulmonary insufficiency that are common with larger defects (8,49). Classic consensus recognized small omphaloceles as having a defect size <5 cm at birth without any portion of the liver present within the omphalocele sac. Defects greater than 5 cm with liver at least partially protruding were generally considered “giant” and closure was typically delayed (48). However, controversy exists regarding the specific size cut-off of 5 cm (as outcomes likely depend more on the relative volume of the omphalocele contents in relation to the size of the abdominal cavity) as well as the amount of protruding liver necessary to make a diagnosis of giant omphalocele (50-52). Further, using a size cut-off for diagnosis limits the ability to identify giant omphaloceles prenatally as the size of the fetal abdomen (and by extension the size of the omphalocele defect) changes over the course of gestation.

In general, small omphaloceles can be closed primarily after birth while giant omphaloceles require delayed or staged closure to prevent poor outcomes associated with inadequate abdominal domain (2). The main concerns associated with immediate primary closure of larger omphalocele defects are abdominal compartment syndrome due to inadequate abdominal domain, hepatic artery compression following reduction of an extracorporeal liver, and lack of adequate skin coverage. Staged closure techniques for giant omphalocele include placement of fascial bridging mesh with serial mesh excisions, silo placement followed by serial reductions, raising of skin flaps, and vacuum-assisted closure (2). Another contemporary option for giant omphalocele repair is delayed closure following a period of escharification. This option is colloquially termed the “paint and wait” approach, as a number of different agents can be “painted” onto the omphalocele sac (including silver sulfadiazine, povidone-iodine solution, topical antibacterial ointments, and silver-impregnated solutions), allowing for escharification and epithelialization of the sac and eventual repair of the resulting ventral hernia at a later date (2,53). A recent area of study has focused on identifying prenatal factors in omphalocele pregnancies that predict type or timing of postnatal surgical closure. The fetal omphalocele ratio is the proportional measurement of omphalocele circumference (or diameter alternatively) to either abdominal circumference or head circumference identified on prenatal ultrasound, and has been demonstrated in various iterations to predict type of surgical closure (primary vs. staged/delayed) and outcomes in multiple cohorts (Figure 3) (47,48,54-56). The underlying principle of these ratios is to determine the “viscero-abdominal disproportion” between the contents of the omphalocele sac and the fetal abdomen (47,48). These measurements are already being utilized at some fetal centers to aid in prenatal prognostication and family counseling for pregnancies complicated by omphalocele.

Fetal magnetic resonance imaging (MRI) is another diagnostic tool that may have utility in the prenatal workup of omphalocele. Respiratory insufficiency related to low lung volumes and associated pulmonary hypoplasia in the setting of large omphalocele defects is a major contributor to infant morbidity and prolonged hospital stay. Contemporary data has shown that low observed/expected ratios of fetal lung volume identified on MRI are predictive of increased postnatal mortality, morbidity, and hospital length of stay (57,58).

**Prenatal management**

In comparison to gastroschisis, the delivery recommendations
for omphalocele are somewhat less controversial. First and foremost, the family should meet with members of the multidisciplinary fetal care team to discuss findings identified on prenatal workup and to determine if continuation of the pregnancy is desirable. In the setting of other associated structural or chromosomal anomalies, the decision to electively terminate an omphalocele pregnancy can be as high as 75% (41).

If delivery planning is desired, the ideal timing of delivery should be determined. Currently there are no data to suggest that preterm delivery is advantageous for omphalocele, unless there is another indication for earlier delivery (42). Route of delivery, however, is dictated by the size of the omphalocele sac and whether or not the liver is located extracorporeally. In general, studies that have compared outcomes following vaginal delivery and cesarean section have combined all sizes and types of omphaloceles and have been limited by small sample sizes (59). These data demonstrated no associations between mode of delivery and postnatal outcomes. However, in very large defects, cases of sac rupture during vaginal delivery have been reported (46,59,60). Because of these findings and the concern for hepatic compression when a significant portion of the liver is extracorporeal, most clinicians recommend cesarean delivery in the setting of giant omphalocele.

Conclusions

Gastroschisis and omphalocele are common congenital abdominal wall defects. Though they represent different embryological outcomes, both rely on accurate prenatal diagnosis and referral to a multidisciplinary fetal center. The prenatal management strategies of gastroschisis and omphalocele are nuanced and continually evolving with new technology and large-scale data. Though definitive treatment for congenital abdominal wall defects currently remains in the postnatal realm, advancements in fetal surgery may one day change that.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Eric B. Jelin and George B. Mychaliska) for the series “Fetal Surgery” published in Translational Pediatrics. The article was sent for external peer review organized by the Guest Editors and the editorial office.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tp-20-94). The series “Fetal Surgery” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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