Strategies and trends in the treatment of (giant) omphalocele

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STRATEGIES AND TRENDS IN THE TREATMENT OF (GIANT) OMPHALOCELE

Strategieën en trends met betrekking tot de behandeling van (giant) omphalocele

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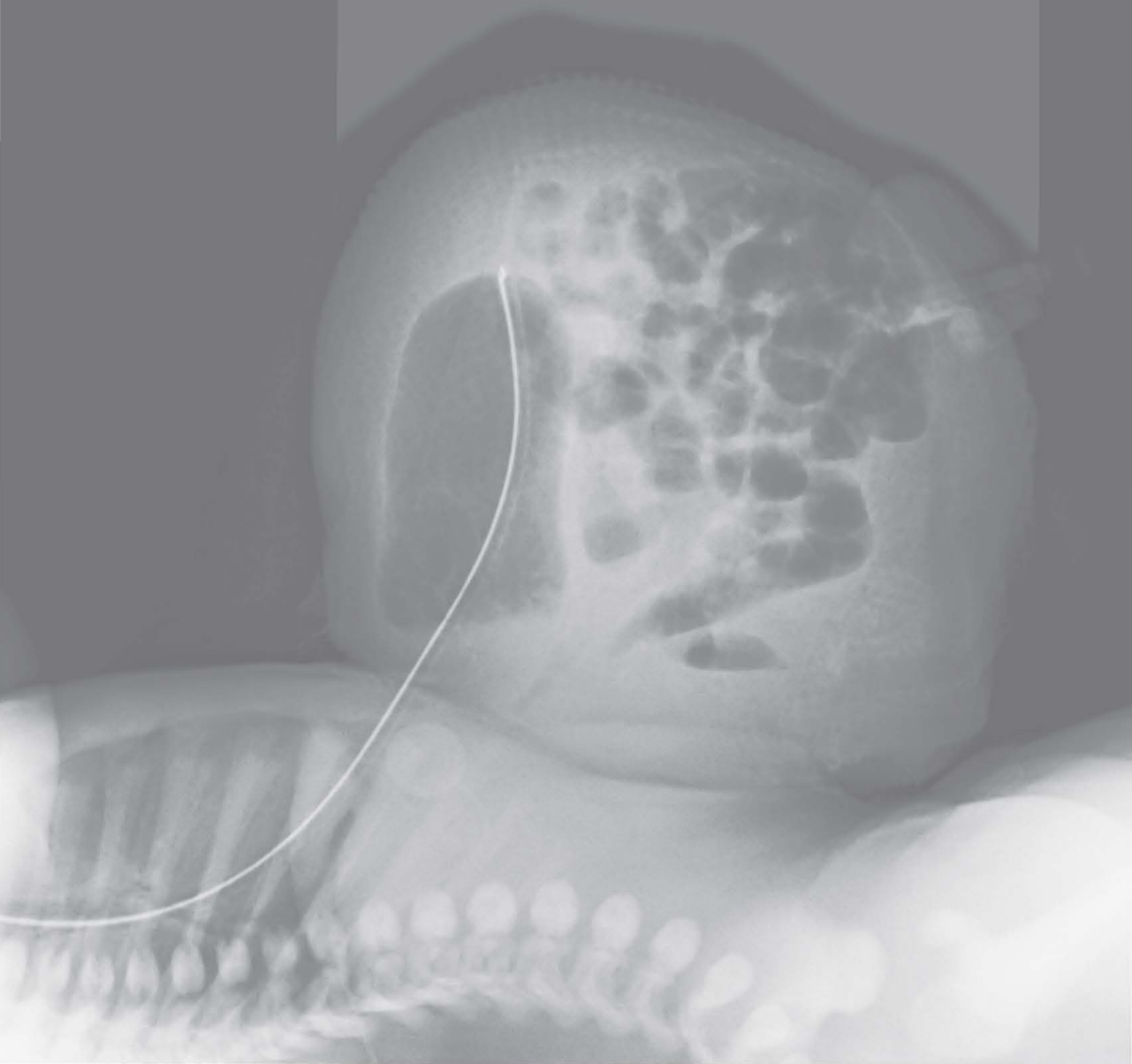
CHAPTER 1

Introduction and outline of the thesis



1. HISTORICAL BACKGROUND AND DEFINITION

It was the 17th-century French surgeon Ambroise Paré who first described omphalocele [1]. At that time, the outlook for survival was dismal, but things have changed for the better. Omphalocele (OC) is now defined as a congenital abdominal wall defect at the site of the umbilical ring with evisceration of the visceral organs as a sac covered by a three-layered membrane of peritoneum, Wharton's jelly and amnion. The sac usually contains small intestine (midgut) only, but occasionally liver, spleen, colon or gonads are eviscerated as well. The intestines are usually malrotated or nonrotated, though generally they are morphologically and functionally normal. The omphalocele may be either liver-containing, and then reach a size of at least 5 cm in diameter ('giant omphalocele'(GOC)), or non-liver containing mostly up to 5 cm in diameter ('minor omphalocele'). In case of GOC, the thoracic cavity may also be abnormally shaped en reduced in size [2]. GOC are associated with an underdeveloped abdominal cavity and a high degree of visceroabdominal disproportion that prohibits safe primary closure. Pulmonary hypoplasia may also be present, as demonstrated by pulmonary distress and a narrow thorax on a chest radiograph. In general, children with an omphalocele have essentially intact abdominal wall muscles, but the rectal abdominal muscles are hypoplastic and displaced laterally.

2. EMBRYOLOGY, EPIDEMIOLOGY AND ASSOCIATED ANOMALIES

During the 4th to 5th week of development, the flat embryonic disk folds in four planes: cephalic, caudal, and right and left lateral. Each fold converges at the site of the umbilicus, thus obliterating the extraembryonic coelom. The lateral folds form the lateral portions of the abdominal wall and the cephalic and caudal folds make up the epigastrium and hypogastrium. At this time rapid growth of the intestines and liver occurs. During the 6th week of development (or eight weeks from the last menstrual period), the abdominal cavity temporarily becomes too small to accommodate all of its contents, resulting in protrusion of the intestines into the residual extra-embryonic coelom at the base of the umbilical cord. This temporary herniation is called physiologic midgut herniation and is sonographically evident between the 9th to 11th postmenstrual weeks. The midgut rotates as it re-enters the abdominal cavity so that the small intestine and colon come into their eventually correct anatomical positions. The intestine migrates to its normal intraperitoneal position beyond the 12th week, so after this period a midgut herniation is no longer physiological. The mechanism responsible for the return of the intestine into the abdomen is disputed; contributions from the growth of the abdominal wall, the regression of the mesonephros, the relative shrinkage of the liver and the retraction of the mesentery have been proposed.

The exact pathogenesis of omphalocele is still speculative [3]. A simple midline OC develops if the extra-embryonic gut fails to return into the abdominal cavity and remains covered by a three-layered membrane of peritoneum, Wharton's jelly and amnion, into which the umbilicus inserts. In contrast to fetal bowel, the fetal liver does not migrate outside of the abdominal cavity and is therefore never present in physiologic midgut herniation. However, if the lateral folds fail to close, a large abdominal wall defect will remain through which the abdominal cavity contents, including the liver, may herniate. The result is a GOC [4].

The incidence rate of OC is approximately 1 in 5000 live births and has been stable over the last decades. The male-to-female ratio is 1:1. It is usually sporadic, although some familial cases, consistent with X-linked, recessive and autosomal dominant pedigrees, have been reported [5, 6]. The incidence of OC has also been found to vary among maternal age, geographic locations, urban versus rural setting and ethnic groups [7]. The maternal age distribution tends to be U-shaped (<20 years and > 40 years), being more frequent at both age extremities with a shallow trough in between [7]. The median maternal age of OC is 29. There is no link between the occurrence of abnormal karyotype and maternal age. OC is more likely present in black infants compared to white and Hispanic infants. Infants of Asians and Pacific Islanders have the highest risk for omphalocele (3-4 times that of white infants). Infants of rural residents are more likely to be born with OC than infants of city dwellers, suggesting an influence of environmental factors [7, 8].

OC is often associated with major structural and/or chromosomal anomalies that may determine the prognosis and/or mortality. These include cardiac (16-47%), gastro-intestinal (gastro-esophageal reflux) (40%), genitourinary (40%), central nervous defects, pulmonary hypoplasia and musculoskeletal anomalies (10-30%). Cardiovascular anomalies are particularly common, e.g. tetralogy of Fallot (33%) and atrial septal defect (25%) [9]. More than half of patients with OC and congenital heart disease have multiple congenital anomalies or a specific syndrome [10]. Syndromic associations have been found with the VACTERL association, Beckwith-Wiedemann syndrome (12%), EEC syndrome, OEIS, and Pentalogy of Cantrell. Uncommon associated syndromes are Reiger's syndrome and Prune-Belly syndrome.

From 8-69% of cases of OC have been found associated with chromosomal abnormalities [7, 11-13]. Most frequent are trisomies 13, 18, 21, triploidy and Turner syndrome. Chromosomal abnormalities are more likely if the OC is small and does not involve herniation of the liver [14-16].

3. PRENATAL DIAGNOSIS AND MANAGEMENT

Prenatal diagnosis creates a potential opportunity to counsel the parents and to discuss options for perinatal management, depending on the type and severity of the defect and the nature of co-morbidity, if any. These options range from termination of the pregnancy in very severe and complex cases, to normal delivery with postnatal surgical repair. Moreover, timing and/or mode of delivery may be altered to minimize postnatal morbidity and mortality.

Ultrasonography allows accurate prenatal diagnosis of OC. Another indicator is elevated maternal serum α-fetoprotein level [17], which, however, may also be associated with other congenital lesions such as gastroschisis, open neural tube defects, intrauterine death, duodenal atresia, congenital nephrosis and Turner Syndrome. OC cannot be reliably diagnosed earlier than approximately after 10th postmenstrual weeks, because bowel within the umbilical cord is a normal phenomenon between 9 and 11 weeks. The sensitivity of ultrasonography and screening is estimated at 80% [18, 19].

The prognosis is related to the presence of associated chromosomal and structural anomalies and the size of the defect. It is therefore important to obtain as much information as possible using additional investigations including; amniocentesis (chromosomal, molecular and α-fetoprotein), fetal echocardiography and sometimes MRI [20, 21]. Life-threatening co-morbidity may be reason to consider termination of the pregnancy. In all cases, it is imperative that the parents are counseled by a multidisciplinary team and take part in this difficult decision-making process. This team should consist of an obstetrical, surgical, neonatological and pediatric specialist [22, 23]. For those women continuing their pregnancies, the best mode of delivery is still debated [24-28]. The sac of the OC may rupture in utero, during labor, or after delivery. Prenatal rupture of the sac has been reported to occur in 10-18% of cases. The eviscerated intestine may then be covered by a thick, matted exudate, which is apparently caused by exposure to amnion fluid as is often seen in gastroschisis. Rupture of the sac at time of delivery is reported in only 4% of cases. Fetuses with a minor OC can be delivered vaginally without undue risk. Randomized studies so far have not shown a difference in outcome between vaginal or caesarean delivery. In case of GOC, however, most clinicians prefer caesarean section because of the potential risk of damage of the fetal liver during birth. All infants with OC should be delivered at a perinatal center where neonatal and pediatric surgical expertise is immediately available. This permits early diagnosis and management of previously unrecognized anomalies, as well as appropriate evaluation and surgical treatment of the abdominal defect.

4. IMMEDIATE POSTNATAL MANAGEMENT

A nasogastric tube should be placed to prevent vomiting and aspiration. The nasogastric tube will keep the stomach decompressed, thereby preventing intestinal distension and facilitating reduction of the viscera. In case of serious respiratory distress, the infant needs to be intubated and ventilated. Fluid resuscitation must be initiated immediately by placing an intravenous catheter in an upper limb because some degree of compression of the inferior vena cava may occur when visceral reduction is performed. A Foley catheter is inserted into the bladder to monitor urine output and to monitor intra-abdominal pressure. Neonates with OC experience abnormal fluid and heat losses. Immediate fluid resuscitation should consist of rapid infusion of 20ml/kg of crystalloid solution. The rate of infusion should be guided by the baby's clinical condition as determined by hemodynamics and urinary output. Further guidance is obtained by measuring the electrolytes, calcium, glucose, hematocrit, and base deficit. Blood glucose levels must be monitored as well, especially if there is any suggestion of macroglossia, which in Beckwith-Wiedemann syndrome is associated with refractory hypoglycaemia [29]. Finally, because the intestine or amnion sac is easily contaminated, antibiotics (cephalosporin) are given at low threshold if signs of infection or sepsis become present.

Fluid resuscitation requires monitoring of the condition of the herniated intestine and avoiding hypothermia. The eviscerated mass should be carefully wrapped and supported with sterile dry gauze. The OC should be supported to avoid traction to the mesentery. The infant is placed under a radiant heater immediately after birth and is subsequently put in a heated incubator.

After these immediate resuscitative measures, careful screening for associated anomalies is performed. A plain chest X-ray may be helpful to identify cardiac and diaphragmatic defects or aspiration. Ultrasound of the heart and kidneys, and genetic counselling will follow. If the patient is born in a regional hospital, transfer to a tertiary neonatal care centre is always recommended.

In case of a minor OC, primary closure of the abdominal wall defect is performed. In GOC, the amnion sac is covered, wrapped and suspended; whereafter different surgical strategies are possible.

5. PRIMARY CLOSURE OF MINOR OMPHALOCELES

Primary fascial and skin closure is recommended for OC < 5 cm in diameter; this strategy is associated with minimal complications. The amnion sac can be removed entirely or left to cover the intestine. The umbilical vessels and urachus are carefully ligated. The abdominal contents are examined and if needed, the abdominal cavity is manually

enlarged by stretching. The defect may be extended 2 to 3 cm at its superior and inferior borders to obtain a more tension free closure of the fascia. Hereafter skin flaps are raised and the fascia is closed with absorbable sutures. Closure of the skin should also include umbilicoplasty. Good cooperation between anaesthetist and paediatric surgeon is of importance. The anaesthetist should monitor intraoperative airway pressure, pulmonary compliance and hemodynamic state and should alert the surgeon if visceral reduction causes respiratory, metabolic or hemodynamic compromise. Airway pressure should not exceed 25 mm Hg and indirect measurement of intra-abdominal pressure (IAP) should not exceed 20 mm Hg [30].

Primary closure is beneficial in that it lowers the incidence of sepsis and reduces mortality [31]. On the other hand, aggressive attempts at primary closure of larger defects can greatly increase abdominal pressure (abdominal compartment syndrome). This could result in impaired ventilation (high peak pressures and rising CO_2), diminished perfusion of the viscera and kidneys (oliguria and acidosis) and inferior vena cava syndrome with reduced venous return (hypotension). The whole cascade can lead to bowel perforation and necrotizing enterocolitis, or eventually even to bowel loss [23, 32]. Thus it is extremely important to monitor the diuresis, laboratory values (creatinin, urea, blood gas) and venous stasis of the legs. For all these reasons, primary closure should be withheld in GOC.

6. TREATMENT OF GIANT OMPHALOCELE

In general there are two different approaches in the treatment of GOC. The common approach in the United States is staged closure with the use of "silo" or patches. This approach seeks to reconstruct the abdominal wall and close the defect as soon as possible, with or without biodegradable or prosthetic materials. In contrast, most European centers aim at primary nonoperative management with delayed closure of the abdominal wall defect after epithelialisation of the OC. Choosing the best treatment of GOC and its timing remains challenging. So far, there is not yet level 1 or 2 evidence; treatment therefore is largely determined by defect size, associated anomalies, and local protocols.

A. Primary nonoperative treatment ("Paint and Wait") / delayed closure

There are two indications for nonoperative management of GOC. First, other life-threatening co-morbidities such as severe cardiac disorders, chromosomal syndromes, or acute respiratory distress syndrome, which raise the risk of repeated surgical interventions to an unacceptably high level. Second, the degree of visceroabdominal disproportion almost always makes it difficult or impossible to close the defect primarily.

The goal of primary nonoperative treatment is to bridge the period, usually 6-12 months, until reconstruction of the abdominal wall can be undertaken. The abdominal cavity develops with the child's growth, so that the relative size of the omphalocele decreases and the abdominal-visceral disproportion normalizes.

1. Epithelialization

Primary nonoperative treatment involves treatment of the sac with an agent to promote eschar formation, allowing granulation and epithelialisation of the OC. In 1899, Ahlfeld first reported successful escharotic treatment of intact omphaloceles with alcohol dressings [33]. Grob described the use of 2% mercurochrome solution for topical application on the OC sac [34]. This topical application has remained popular, although several studies reported toxic systemic mercury levels [35-37]. Application of 0.5 % mercurochrome in 65% alcohol resulted in less toxic levels [38, 39]. Safe use of this agent requires strict monitoring of mercurochrome levels in the blood and urine [38]. Other topical agents are silver nitrate solution, silver sulfadiazine (Flamazine), 70% alcohol and povidone iodine [40-44]. Silver nitrate solution, being hypotonic, may cause loss of body sodium. In contrast, silver sulfadiazine was found to be safe and effective [40, 41, 45]. Application of povidone iodine can induce hypothyroidism [46-48]. Currently, wound dressings based on alginates or other materials often replace these agents. They can be kept in place for several days. Hanging of the dressings is recommended until fully epithelialisation occurs, usually between two and three months after the initial treatment.

2. Delayed closure

The following techniques for delayed closure have been described.

- The Lazaro da Silva's technique consists of the bilateral longitudinal fibroperitoneal-aponeurotic transposition, resulting in three different layers of closure [49]. The ventral hernia is corrected at the age of approximately two years, when the hernial sac is thick enough to serve as a substrate for the reconstruction of the abdominal wall.
- The principle of external pressure compression using helmet device is to place a sphygmomanometer cuff on top of the hernia and compress the hernia contents by controlled inflation of this cuff daily [50]. Reduction of the ventral hernia is achieved after several months after which primary hernia repair is achieved. Preoperative elastic bandaging after epithelialisation for several weeks facilitates primary closure of large ventral hernias [51].
- The use of tissue expanders after initial nonoperative treatment is described by De Ugarte et al. [52]. The tissue expanders are placed within the intramuscular layers of the abdominal wall, allowing creation of an outer layer composed of skin and internal and external oblique muscles. After removal of the tissue expanders a

silo is still necessary to allow reduction of the viscera before the skin and muscle flaps can be closed over the defect. Intraabdominal placement of tissue expanders after epithelialisation was described by Martin et al. [53]. The goal is to increase the intraabdominal domain in weeks without respiratory compromise and visceral ischemia.

B. Operative treatment

The goal of operative treatment is to provide complete fascial and skin closure without causing subsequent injury due to excessive intra-abdominal pressure or abdominal wall tension. Several techniques – either primary or staged – have been described.

1. Primary closure with biodegradable / prosthetic materials in GOC

In case the defect cannot be closed primarily, fascial closure is performed using a variety of prosthetic materials or biodegradable materials [54-63].

a) Prosthetic materials

Available prosthetic materials include Goretex, Dacron, Marlex, Teflon [58-61]. As a downside of the use of these materials, they may be associated with high mortality and morbidity such as persistent infection and fascial-prosthesis separation. The patches then need to be removed, resulting in ventral hernias that need reoperation.

b) Biodegradable materials

Since the late 1950s, biomaterials such as solvent-dried dura have been used successfully as patches in OC [56]. However, after the outbreak of Creutzfeld-Jacobs disease in the late 1990s these patches were presumed unfit for human usage [64, 65]. They were largely replaced with bovine pericard patches, which had been successfully used in cardiac surgery. Another fascial substitute used in abdominal wall reconstructions in adults and infants is human acellular allograft of dermis (Alloderm) and acellular xenograft biomaterials such as porcine dermal collagen or porcine small intestinal submucosa (Surgisis) [54, 55, 66, 67]. These acellular hypoallergenic sheets are designed to allow interstitial ingrowth of fibroblasts and vascular tissue. Little is known about the long-term results of all biomaterials mentioned above. Notably the incidence of reherniation can be expected to be very high. Visceral coverage with absorbable mesh followed by skin flaps or split skin grafts minimizes ongoing pulmonary morbidity [62, 68].

2. Staged closure in GOC

Staged repair of GOC has become the treatment of choice in many pediatric surgical centers in the United States. Regrettably, the final stage is still problematic with regard to the use of prosthetic materials, multiple operations, or tissue expanders to restore

the abdominal wall integrity to decrease the intra-abdominal pressure. The following techniques have been described.

a) Skin flaps

In 1948, Gross described staged closure by advancing skin flaps to cover the defect without opening the amnion sac. This technique achieved skin coverage by lateral mobilization of extensive skin flaps for the initial covering, resulting in a ventral hernia that should be corrected later in life [69].

b) Silo/silastic sheet

In 1967, Schuster modified Gross's procedure by suturing temporary Teflon mesh or Silastic mesh to the rectus sheath and covering the defect with skin flaps [70]. Over the first postoperative days, the skin is periodically opened and the mesh gradually tightened until the viscera are reduced into the abdomen and the midline fascia can be closed primarily. The amnion sac is left intact. The disadvantage of this technique is the need to reopen the incision, removal of mesh, loss of integrity of the fascial edges and multiple re-operations.

In 1969, Allen and Wrenn introduced the silastic silo sutured at the fascial edges around the base of the defect in gastroschisis and ruptured OC [71]. The silo is suspended above the baby allowing gravity to pull the viscera back into the abdominal cavity. The silastic silo can be sutured to the fascial edges or to the skin at the skin-amnion junction. The latter suturing method does not require incision to skin and exploration of the fascial edges. Sequential manual reduction or ligation of the sac is performed with or without general anesthesia. A possible complication of silo placement is infection of the fascia with disruption of the suture line, in which case closure of the abdominal wall is difficult or impossible. The amnion sac can be removed or be left intact. Currently most surgeons leave the amnion sac intact to avoid trauma, adhesions and subsequent adhesive bowel obstruction [72-77]. Instead of using a silastic silo, sequential sac ligation has been described using the amnion sac itself [78-80].

c) External compression/ active enlargement abdominal cavity

Avoiding infection of the fascia with disruption of the suture line due to silastic silo, delayed external compression reduction (DECRO) is an alternative method for relatively rapid closure of the defect [81, 82]. A sterile umbilical tape is tied around the umbilical cord clamp to hold the sac into the air allowing gravity to help reduce the abdominal contents. The sac is covered with vaselin gauze to keep the membrane moist. Gauze is wrapped around the sac and behind the lumbar area. Next, an elastic bandage is wrapped around the sac making the top part tighter than the bottom. The taped umbilical cord

is suspended and the dressings are daily changed. Progressive external compression by elastic bandaging was described by Belloli et al.[83].

Active enlargement of the abdominal cavity by using the silo technique in combination with external continuous contraction of the abdominal wall was described by Patkowski et al. [84]. The sac is suspended using a system with active external traction with a force amounting to 30-40% of the baby's weight. In this way earlier reduction is possible.

Intraperitoneal tissue expanders have been used to create an adequate peritoneal domain to the point that the viscera could be reduced in one operation with abdominal wall closure [85-87].

Using a multi-detecting CT scan, the volume of the extraperitioneal volume can be calculated as a reasonable projection of the volume needed for the tissue expander. The tissue expander is removed when the calculated volume is exceeded by a margin of 20 to 25 percent [86]. Nevertheless, the abdominal wall of some patients treated with intraperitoneal tissue expanders could not be closed primarily [86, 87].

7. OUTCOME AND LONG-TERM FOLLOW-UP

Prior to the 1970s, up to 80% of neonates died from starvation and associated complications in the postoperative period as a result of prolonged intestinal ileus. The development of parenteral nutrition and staged methods of closure in the late 1970s helped to improve survival. Mortality and morbidity rates in children with (giant) OC are still high (10-46%) [2, 88], even up to 80% in case of chromosomal abnormalities, which are more common in minor OC [89].

Long-term results of OC correction have been little studied. Research mainly focused on cosmetic aspects and gastrointestinal disorders [90-92]. The two available studies on morbidity and quality of life revealed normal growth and development of children without additional severe congenital anomalies. Most children participated in normal activities and education without problems or reduction in quality of life [93, 94]. These studies included both OC and gastroschisis. So far, the literature does not contain a study concentrating on the long-term outcome and quality of life in children with OC.

AIMS AND OULINE OF THE THESIS

The treatment, outcome and quality of life of (giant) OC depend on multiple factors. Expectant parents with fetal diagnosis of OC and parents of newborns with OC should be well informed by their counselors concerning the long-term outcome. Based on the

literature above we performed some retrospective studies and a prospective study to add to the knowledge on (giant) OC. In this thesis, we developed a new innovative technique for delayed closure in giant OC. Among the aspect studied were quality of life, morbidity and long-term follow-up and outcome.

Aims of the studies:

PART 1 Retrospective studies

- Quality of life in minor and giant omphalocele.
- Incidence of adhesion related morbidity in omphalocele and gastroschisis.
- Position of the liver and visceral organs in giant omphalocele later in life.

PART 2 Operative techniques

Evaluation of several operative techniques in giant omphalocele.

- Component Separation Technique (Ramirez) in giant omphalocele.
  1. Case report
  2. Cohort study: early and late results
- Functional and motor development and long-term outcome after the Component Separation Technique in children with giant omphalocele

PART 3 Summary and conclusions

OUTLINE

PART 1

Before the 1970s, up to 80% of neonates with OC died of starvation and its associated complications in the postoperative period, and/or of the co-morbidity. New developments in treatment and neonatal care after 1970 have led to higher survival rates in this patient group. Nevertheless, morbidity and mortality are still high in GOC (up to 30%).

Prenatal ultrasonography can detect OC during the second trimester. Upon this early diagnosis it is essential to inform parents concerning morbidity, mortality and expected quality of life. We therefore retrospectively evaluated long-term morbidity and quality of life in paediatric patients treated for OC, distinguishing between those with minor vs. GOC in **chapter 2**.

Children treated for gastroschisis and OC seem to be particularly at risk of developing adhesions-related morbidity. Small bowel obstruction occurs two to three times more often in these children compared to children undergoing abdominal procedures for other abdominal complaints. In **chapter 3,** short and long-term adhesion-related

morbidity and mortality in a large group of patients with congenital abdominal wall defects were evaluated, with a focus on incidence and risk factors.

GOC is defined as a congenital abdominal wall defect larger than 4 cm in which the liver partly extrudes into the OC. There is little information on the position and size of the liver later in life. When the liver is located in an abnormal position and/or closure of the abdominal wall is incomplete, there may be an increased risk of liver rupture in case of abdominal trauma or in acute operations. In **chapter 4** the results of a long-term follow up study with ultrasonography in GOC compared to controls is described, focussed on the eventual position of the liver and other visceral organs.

PART 2

The main problem in the treatment of GOC is to achieve closure of the abdominal defect without creating increased abdominal pressure, so as to prevent compromised cardiovascular and respiratory function. A broad range of surgical techniques has been described in the literature. There is no consensus, however, on the 'gold standard' procedure. We therefore asked paediatric surgeons who had published results of surgical treatment of abdominal wall defects to complete a questionnaire asking if the operative methods described were still in use, or whether they had been modified over the years or had been replaced with other operative techniques. The results of this survey are described in **chapter 5**.

Furthermore, we reported our experience with a new technique for delayed closure in giant omphaloceles using the component separation technique (CST), earlier described by Ramirez. We described the first successfully treated patient in a case report **(chapter 6)**, and next performed a prospective follow up study of all our patients treated with this technique. The early and late outcomes are described in **chapter 7.** In **chapter 8**, we evaluated the long-term outcome of functional and motor development and abdominal muscle quantity in GOC after the CST.

PART 3

Chapter 9 and **chapter 10** summarize results and conclusions.

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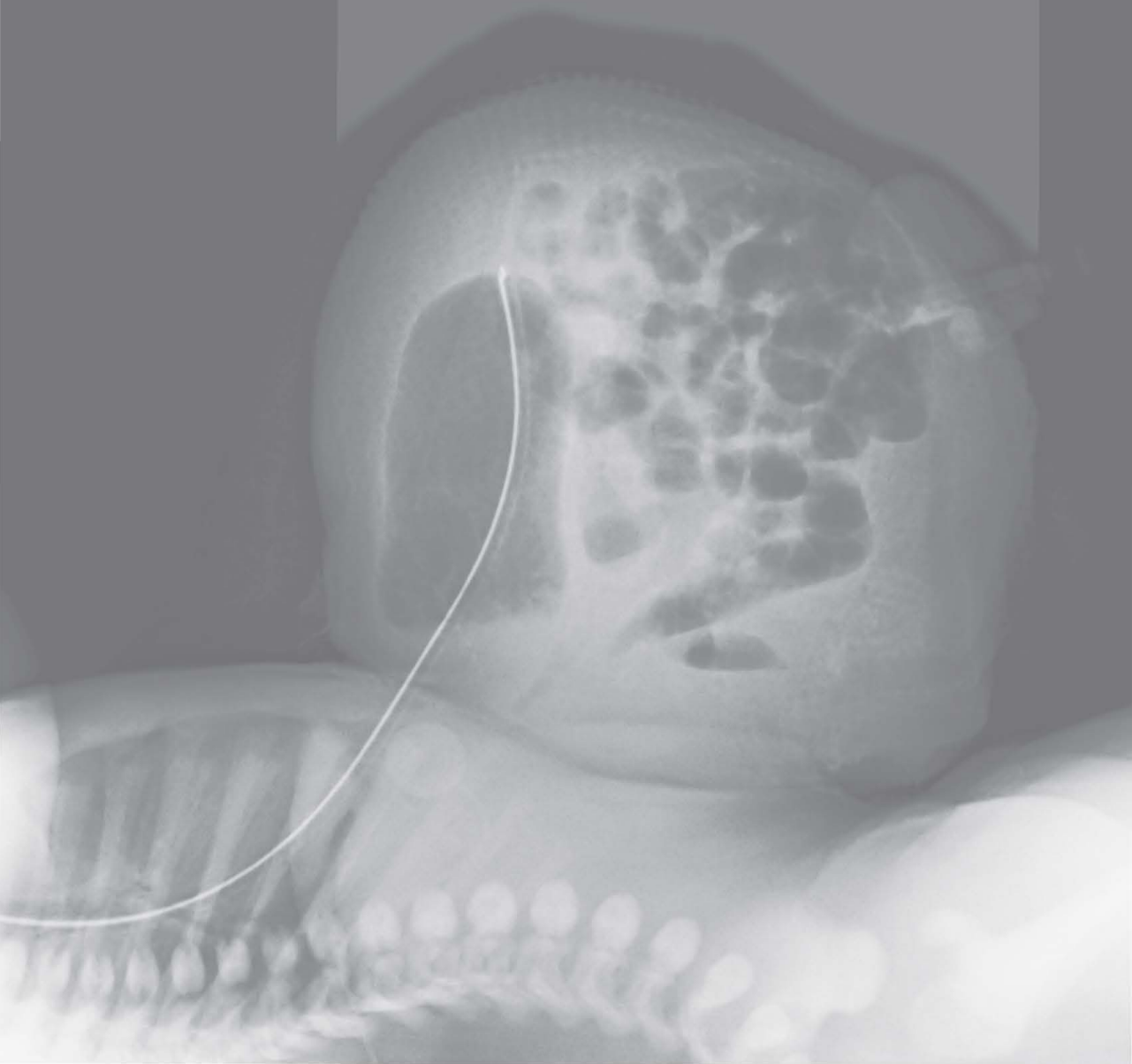
PART 1

retrospective studies



CHAPTER 2

Minor and Giant Omphalocele: Long-term Outcomes and Quality Of Life

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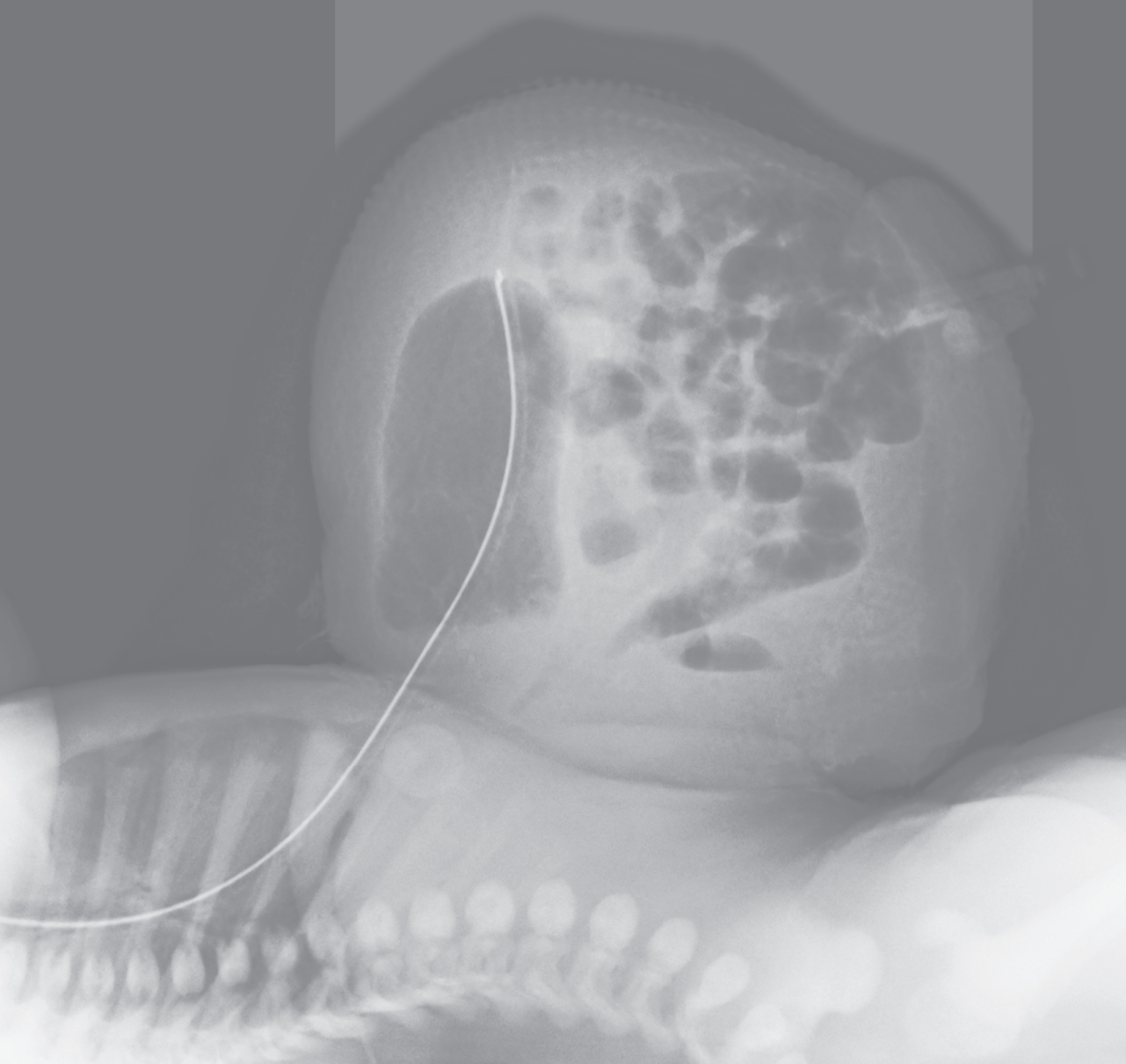

ABSTRACT

Background: Long-term outcome and quality of life in omphaloceles (OC) studies are mainly focused on cosmetic disorders with the abdominal scar and gastrointestinal disorders. The aim of this study was to compare long-term mortality, morbidity, and quality of life between patients with minor and giant OC s.

Methods: Records of 89 minor and 22 giant OC children were reviewed. A questionnaire on general health was sent to all patients. A second questionnaire concerning quality of life and functional status; Darthmouth COOP Functional Health Assessment Charts/ WONCA (COOP/WONCA) was sent to all patients aged 18 years or older and a peer control group.

Results: Of the surviving patients (69 minor OC, 20 giant OC), 12 were lost to hospital follow-up. The first questionnaire was returned by 64 (83%) of 77 patients. There were no significant differences in gastrointestinal disorders. Cosmetic problems were experienced significantly more in giant OC. The results of the COOP/WONCA charts indicated a good to very good quality of life in both groups comparable to the control group.

Conclusions: Our study indicates that after a high level of medical intervention perinatally, quality of life is good to very good in both groups and comparable to healthy young adults.

INTRODUCTION

Omphalocele (OC) is a congenital abdominal wall defect (CAWD) at the site of the umbilical ring with evisceration of the bowel covered by a three-layered membrane of peritoneum, Wharton's jelly and amnion. It is associated with other congenital anomalies in up to 77% of patients. Omphalocele can be approximately divided into two groups: minor and major (giant). In minor OC the abdominal wall defect is relatively small (≤ 4 cm) and can generally be managed by primary closure. Giant OC is defined as abdominal wall defect of at least 5 cm and liver included[1-4]. It is associated with an underdeveloped abdominal cavity and a high degree of visceroabdominal disproportion that prohibits safe primary closure.

Prior to the 1970s, up to 80% of neonates died from starvation and associated complications in the postoperative period as a result of prolonged intestinal ileus [5-8]. The development of total parenteral nutrition (TPN) and staged methods of closure in the late 1970s contributed to an increased rate of survival. Morbidity and mortality are still high in OC (up to 30%) and in case of chromosomal abnormalities, which are more common in minor OC, these are even higher [9]. Koivusalo showed in patients born up to 1980, that after the first year the morbidity and quality of life are similar in comparison with the general population[10]. In the area of prenatal sonography OC can be detected at the second trimester ultrasonography scan. A diagnosis of OC is almost always followed by amniocentesis and chromosome analysis. A Norwegian study reported more than 50% pregnancy terminations in case of chromosomal anomalies[11]. Even in case of isolated omphalocele, termination is still high (37%)[11,12]. However, the question arises if this should be advocated for all patients with an omphalocele or is there a need to differentiate between minor and giant omphaloceles?

Long-term outcome seems to be the most important issue for parents[13]. Upon this early diagnosis, it is essential to inform the parents concerning morbidity, mortality and quality of life later in life.

The aim of our study was to retrospectively evaluate the long-term morbidity and quality of life in a group of pediatric patients treated for OC and to compare the outcomes of patients with a minor versus a giant OC.

PATIENTS AND METHODS

Between 1971 and 2004, 111 patients with OC were treated at the Radboud University Medical Centre in Nijmegen, the Netherlands. All medical records were reviewed. Minor OC was defined as abdominal wall defect 4 cm or less; giant OC was defined as abdominal wall defect of at least 5 cm and liver included.

Patients were treated either surgically, receiving standardized perioperative care, including mechanical ventilation and TPN if necessary, or nonoperatively by covering the OC after birth with dry sterile dressings until fully epithelialized. In case of infection of the OC, specific wound dressings available at that time were used. Nonoperative treatment was performed in case of contraindications for surgical repair or in case of a giant OC in which epithelialization was the primary goal. Those who survived in the nonoperated group were not operated upon later in life for correction of the abdominal wall.

To evaluate long-term outcomes, a questionnaire on general health and nonoperative and postoperative outcomes was sent to all surviving patients. Parents completed the questionnaire for patients younger than 8 years and assisted children between 8 and 12 years. Those older than 12 years completed the questionnaire themselves or with support of their parents. The questionnaire consisted of 4 sections: health/disease, gastrointestinal and urogenital disorders, cosmetic results, and social functioning (Table 1).

The Darthmouth COOP Functional Health Assessment Charts/WONCA (COOP/WONCA) was sent to all young adults aged 18 years or older. This questionnaire, validated for adults, represents functional status and quality of life and appears to have low susceptibility to cultural differences [14]. The COOP-WONCA charts were initially developed and tested by the Dartmouth COOP Project and were translated and further tested in collaboration with the World Organisation of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA). The COOP/WONCA charts measure 6 core aspects of functional status: physical fitness, feelings, daily activities, social activities, change in health and overall health. Each item is rated on a 5-point ordinal scale ranging from 1 ('no limitation at all') to 5 ('severely limited'); 'for change in health' score 1 indicates 'much better' and score 5 'much worse'[14-18].

For peer group reference, the COOP/WONCA charts were also completed by a control group of healthy young adults (n = 100). The control group consisted of males and females aged between 18 and 25 years, chosen at random from the patient registers

Table 1. Questionnaire; divided into 4 sections.

Section	Questions
Health/disease	General health, stature and weight, use of medication, pulmonary complaints, operations or hospitalization after initial treatment
Gastrointestinal disorders	Incidence and frequency of chronic abdominal complaints, abdominal pain, constipation, diarrhea, nausea, vomiting, bowel habit, and use of a special diet
Cosmetic results	Previous ventral hernia and surgery, presence or absence of umbilicus. The abdominal scar and umbilicus: cosmetic problems, cosmetic surgery performed; or wish for cosmetic surgery to improve the results
Social functioning	Subjects as relationship related problems, choices with regard to school and profession, type of education undertaken, present profession, and any sporting activities.

of two general practitioners in the Netherlands, with one located in a city of 120,000 inhabitants and the other in a small country town.

This study was approved by the Institutional Review Board of the Radboud University Nijmegen Medical Centre.

Statistical analyses were performed using SPSS 16.0 (SPSS Inc, Chicago, Ill) A χ^2 test was used to analyze the statistical difference between compared groups. A *P* value of less than .05 was considered statistically significant.

RESULTS

The OC patient group (n=111) consisted of 89 (80%) minor OC and 22 (20%) giant OC. Associated congenital anomalies were identified in 57 (51%) patients, including Beckwith Wiedemann syndrome (n=12), trisomy 13, 18 and 21 (n=9), cardiovascular disorders (n=9), pentalogy of Cantrell (n=5), pulmonary hypertension (n=3) and pulmonary hypoplasia (n=3), VACTERL (Vertebral anomalies, Anal atresia, Cardiovascular anomalies, Tracheoesophageal fistula, Esophageal atresia, Renal or radial anomalies, preaxial Limb anomalies) association (n=1), OEIS (Omphalocele, Exstrophy of the cloacae, Imperforate anus, Spinal abnormalities) (n=1). These congenital anomalies were clearly more present in minor OC (55 % vs. 36%).

Of the 111 patients with omphalocele, 22 (20%) patients died: 7 patients in less than 36 hours because of multiple congenital anomalies, 12 died within 1 year (5 congenital anomalies, 2 pulmonary hypoplasia, 3 pulmonary hypertension, 1 sepsis, 1 acute respiratory distress syndrome), and 3 died after 1 year but before 8 years (2 aspiration, 1 postoperative sepsis). Only 2 of the 22 (9%) deceased patients had giant OC, one due to pulmonary hypoplasia. There was no significant difference in mortality between the two groups *(P* < .16). The deceased patients were excluded from further evaluation.

Of the 89 surviving patients, 20 (22%) were giant OC and 69 (78%) minor OC. The overall median hospital stay was 12 days (range, 2-226 days).

The questionnaire on general health and post-operative outcomes was sent to 77 of the 89 surviving patients (12 lost to hospital follow-up). The response rate was 64 (83%) of 77 patients, of which 16 (25%) patients were giant OC. The median age of the patients at the time of the survey was 11.3 years (range, 1-25 years) for giant OC and 16.7 years (range, 3-32 years) for minor OC.

Questionnaire outcomes for:

(1) Health/disease: Re-admission to hospital occurred 32 times in 11 (69%) giant OC and 48 times in 33 (69%) minor OC. The most frequent operations were inguinal hernia correction (n=20) and for ear-nose-throat problems (n=13) (tonsillectomy, paracen-

tesis and ear tubes, nasal polyps). Other operations included: surgery for associated anomalies, fundoplication, small bowel obstruction, correction of malrotation, orchidopexy, hernia cicatricialis, cosmetic surgery of the abdominal wall, abdominal scar and creating a new umbilicus, hip operation, and eye operation.

Medication was still used by 20 patients (31%) (6 giant OC (37%), 14 minor OC (29%)). The most frequent being pulmonary medication (3 giant OC (19%), 8 minor OC (17%)) or medication for chronic constipation (2 giant OC (13%), 2 minor OC (4%)).

At re-admission and/or operation the age of the patient varied from 1 month to 23 years.

(2) *Gastrointestinal disorders (GI):* GI disorders are given in figure 1. A quarter (n=4) of the giant OC and 15% (n=7) of the minor OC mentioned GI disorders with a frequency of more than four times a month. Abdominal pain was reported in 33 % of minor OC and in 19% in giant OC. This was not significant ($P = .27$). Special diet because of allergies was used in 13% giant OC versus 4 % in minor OC (ns, $P = .23$).

(3) *Cosmetic results:* Cosmetic problems with abdominal scar were present in 7 (44%) of 16 giant OC (median age 12 years; range, 2-20 years) and in 9 (19%) of the 48 minor OC (median age 19 years; range, 1-29 years) responders, all of who desired a correction by cosmetic surgery. These cosmetic problems were significantly more present in giant OC ($P < .05$). Three patients had already undergone cosmetic surgery to improve the scar and one patient had reconstruction of the umbilicus.

Of the 6 (3 males and 3 females) (38%) giant OC with an umbilicus, 2 (33%) patients expressed satisfaction. Of the 21 (13 males and 8 females) (44%) minor OC with an umbilicus, 14 (67%) patients expressed satisfaction. This was not significant between the two groups ($P = .14$). All giant OC without an umbilicus (n=10) indicated dissatisfaction with missing the umbilicus ($P < .001$), with one third desiring reconstructive surgery. In the group of 27 minor OC without an umbilicus, 10 (37%) indicated dissatisfaction with missing the umbilicus of whom 9 desired reconstructive surgery.

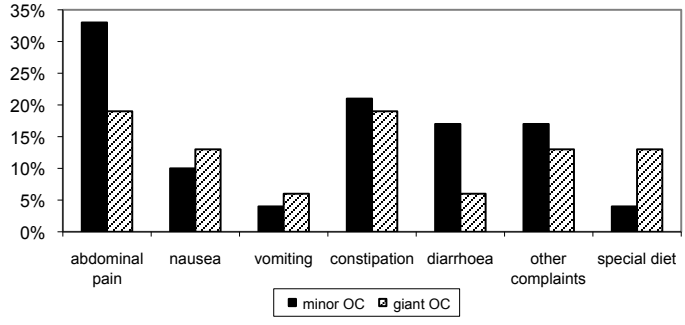

Figure 1. Long-term abdominal complaints in patients with minor and giant omphalocele. No significant differences were found between the two groups

(4) Social functioning: Of the 64 patients (30 males, 34 females), 13 (5 giant OC, 8 minor OC) were primary school pupils, 6 (6 minor OC) attended special schools, 23 (5 giant OC, 18 minor OC) were in secondary education/high school, and 9 (2 giant OC, 7 minor OC) attended or had studied at university and 9 (1 giant OC, 8 minor OC) were permanently employed. Thirteen patients were in day care.

Only 3 (2 giant OC, 1 minor OC) patients ever had the feeling that their abdominal defect prevented particular choices with regard to school and profession. The abdominal wall defect influenced relationships in 10 patients (1 giant OC, 9 minor OC) (concerns about relationship, teasing). Fifty-one patients participated in sporting activities.

COOP/WONCA questionnaire

The COOP/WONCA questionnaire was sent to 23 patients aged 18 years or older and returned by 21 (2 giant OC, 19 minor OC) patients) (response rate 92 %), consisting of 10 females (median age 26 years; range, 18-28.5 years) and 11 males (median age 20 years; range, 18-23.3 years). Six responders (1 giant OC, 5 minor OC) had associated anomalies (2 cheilo-gnatopalato-schisis, Cantrell, BW-syndrome, cardiac disorder, skeletal anomalies). Figure 2 shows the mean scores for each COOP/WONC chart according to giant and minor OC. The median scores were similar for each chart. For both giant OC and minor OC, feedback indicated no change in state of health (scale 3) during the last two weeks. Overall health was generally rated good in the giant OC to very good in the minor OC. Physical and emotional health did not appear to limit social activities in both groups: minor OC scored no problems on feelings and daily activities, while giant OC were only

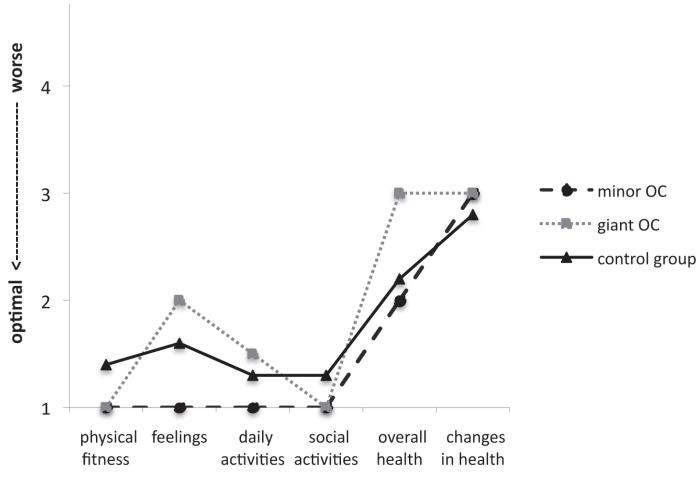

Figure 2. Mean scores COOP/WONCA charts (minor OC vs Giant OC vs control group)

slightly bothered on feelings and daily activities. The responses given in the questionnaire by our patient group indicate that associated anomalies did not influence quality of life.

Of the COOP/WONCA charts sent to 210 young adults (age/gender matched) for the control group, 100 were returned (response rate 48%). Compared to the patient group, there were no clear differences in the scores for each chart. The minor OC even scored slightly better than the control group.

DISCUSSION

New developments in treatment and neonatal care after 1970 have led to higher survival rates of neonates with OC, which could be of influence on the quality of life in OC. Our retrospective long-term follow-up study, a first to be performed in a large group of children with OC exclusively, found that OC (minor and giant OC) patients as young adults (≤ 28.5 years) achieve a state of health and quality of life comparable to that of general population peers. The only significant difference was the presence of cosmetic problems in giant OC.

Main causes for readmission to hospital of our patients were general surgical procedures unrelated to the pre-existing omphalocele. Gastrointestinal disorders were common in our series (40%). Up to 30% of the patients mentioned periods of chronic abdominal pain with no significant difference between minor and giant OC. Lindham et al [19] reported similar results (27%), although their patient group was younger (8.8 years). This indicates that chronic abdominal pain is not restricted to childhood but plays an important role even in (young) adulthood.

Cosmetic issues with the abdominal scar and absence of the umbilicus appear to be important from the responses given by more than half of our patient group with ages between 20 and 30 years. Preservation of the umbilicus at primary closure might give superior cosmetic results and patient satisfaction[10]. However, almost all the patients with a giant omphalocele were not satisfied with the cosmetic result compared to one third of the patients with a minor OC, independent of preservation of the umbilicus. Overall the satisfaction with the cosmetic result was significantly better in the minor OC group.

Studies by Tunell et al [20] and Koivusalo et al [10] present results of long-term morbidity and quality if life in patients with gastroschisis and OC born between the periods 1948 and 1980 and 1975-1984, respectively. Both studies concluded that most patients (median follow-up was 26.5, (range, 17-48 years) and 14.2 years (range, 10-20 years), respectively) with abdominal wall defects are healthy adults with few or no factors restricting their activities or decreasing their quality of life. Our study involving patients

treated from 1971 through 2004, shows general agreement with these two studies in that we found a good to very good quality of life in young adults with OC but then exclusively in minor and giant omphalocele patients, and a quality of life as good as our aged matched control group. We compared the educational level of our study group with the Dutch national population and concluded that no difference existed, with respectively 43% and 34% having attended or studied at university[21],

Our study indicates that after a high level of medical intervention in early life, minor and giant OC patients report similar long-term results except for the cosmetic problems mentioned more serious in giant OC. However, this did not influence quality of life in either group and is comparable to that of healthy young adults. With the latter positive prospect in mind, expectant parents with fetal diagnosis of OC and parents of newborns with OC should be informed that the high burden of (surgical) interventions their child will need to undergo will likely yield a good health status in the long-term, especially when there are no associated anomalies.

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CHAPTER 3

The incidence and morbidity of adhesions after treatment of neonates with gastroschisis and omphalocele; a 30-year review

Floortje C. van Eijck, René M.H. Wijnen, Harry van Goor

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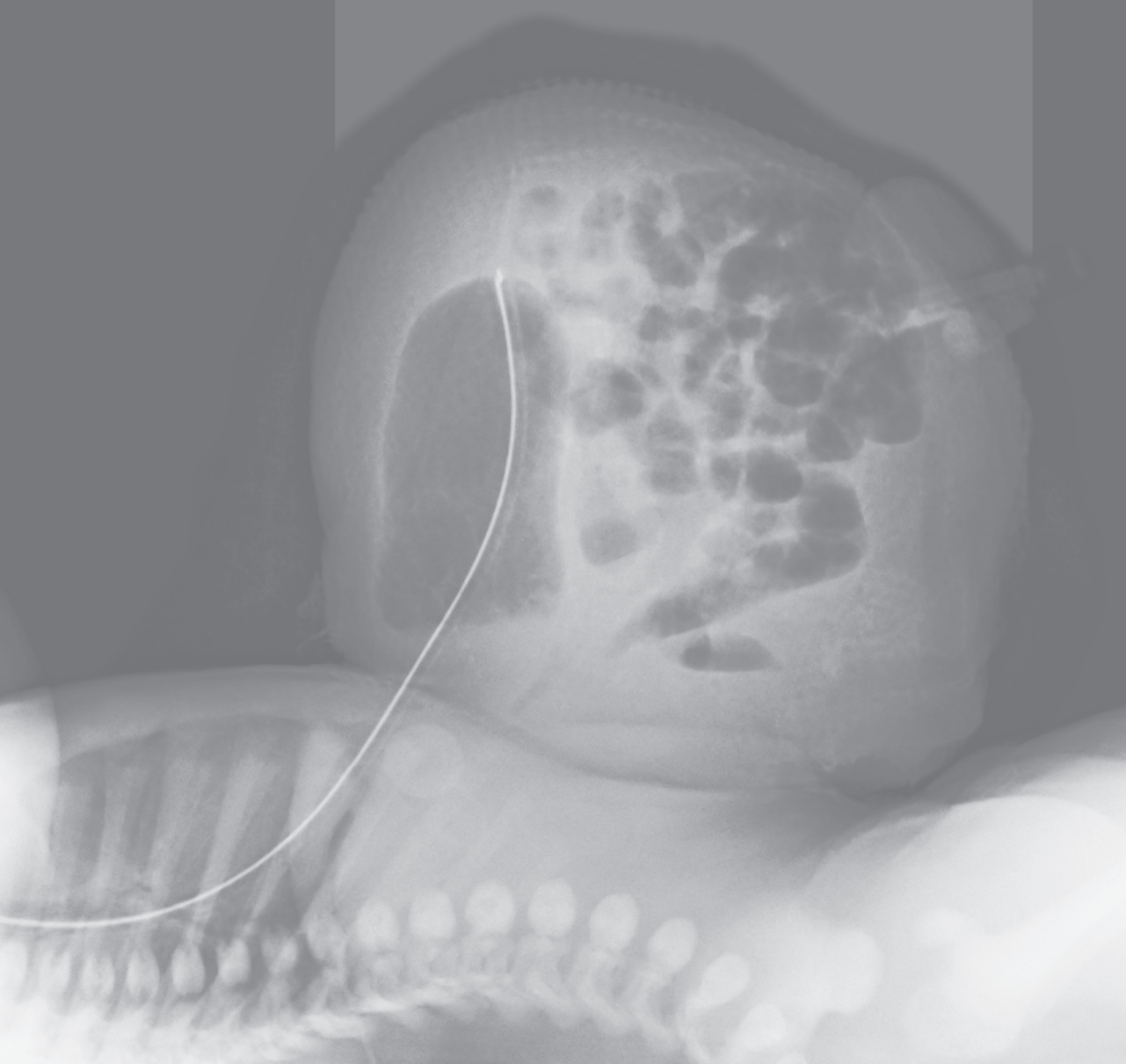

ABSTRACT

Background: Adhesive small bowel obstruction (SBO) is a feared complication following correction of abdominal wall defects in neonates. Knowledge of its incidence and potential risk factors in a well-documented group with strict follow-up is needed to guide preventive measures.

Methods: Records of 170 neonates with abdominal wall defects, 59 gastroschisis (GS) and 111 omphalocele (OC), were reviewed focussed on SBO. Risk of SBO was calculated, and potential risk factors were analysed. Long-term complaints possibly associated with adhesions were assessed through questionnaire.

Results: One hundred forty-seven neonates were operated, 12 were treated nonoperatively and 11 patients died shortly after birth. Defects were primarily closed in 128, 7 neonates needed prosthetic mesh and 12 had a silastic sac inserted. Twenty-six (18%) neonates had SBO, 14 (25%) of 55 with GS and 12 (13%) of 92 with OC ($P = .06$). Of the 26 with SBO, 23 (88%) needed laparotomy. Four patients died because of SBO. Most episodes (85%) were in the first year. Sepsis and fascia dehiscence were predicting risk factors for SBO. Abdominal pain and constipation were frequent long-term complaints not significantly associated with SBO.

Conclusions: Adhesive SBO is a frequent and serious complication in the first year after treatment of congenital abdominal wall defects. Sepsis and fascial dehiscence are predictive factors.

INTRODUCTION

Postoperative adhesions have great impact on morbidity and mortality, including small bowel obstruction (SBO), inadvertent enterotomy during subsequent operations and female infertility [1-3]. Adhesions are associated with chronic abdominal and pelvic pain and constipation [4-6]. Adhesive SBO occurs in two third within 1 to 2 years after surgery; however, it has been reported even 25 years after initial surgery [3,7,8] .

General interest in intraabdominal adhesion formation has increased among surgeons and gynaecologists because of new developments in adhesion prevention [9-11]. Most epidemiologic studies have focussed on incidence, risk factors and clinical and economic consequences of post-surgical adhesion formation in adult populations [3,6,12]. Data of postsurgical adhesion formation in children are scarce despite the fact that children have a longer life time risk for development of adhesion related complications [13,14].

Children treated for congenital abdominal wall defects seem to be particularly at risk developing adhesion-related morbidity. Small bowel obstruction, for example, occurs 2 to 3 times more often in comparison with children undergoing other abdominal operations [13-17]. Paediatric patients might benefit from adhesion preventive measures. However, more accurate data on incidence and short- and long-term adhesion-related morbidity and mortality in a large group of patients are needed before a plea for routine adhesion prevention can be made. We therefore undertook a retrospective analysis in a large well-documented group of paediatric patients treated for gastroschisis (GS) and omphalocele (OC) focussed on incidence, risk factors, and morbidity of adhesion formation.

PATIENTS AND METHODS

Medical records of consecutive neonates having GS or OC treated in our department between 1971 and 2004 were reviewed. One paediatric surgeon meticulously listed relevant demographic and peri-operative data of all these neonates during the entire 30 years period in the records. The following demographic and operative data were extracted: gestational age, sex, type of abdominal wall defect, and other congenital malformations. Treatment was divided into nonoperative and operative. Initial operative treatment was divided into primary closure, insertion of prosthetic mesh and temporary closure using a silastic sac. Major systemic and abdominal postoperative complications were noted including infant respiratory distress syndrome (IRDS), sepsis, cause of death, anastomotic leakage, need for reoperations, fascial dehiscence, and the occurrence of SBO. Small bowel obstruction was defined based on history (pain, nausea, vomiting and cessation of stool production), physical examination (abnormal bowel sounds, abdominal distension) and abdominal radiography (dilated loops of small bowel, air-fluid levels). Findings

had to be positive in at least 2 of 3 categories. Small bowel obstruction was considered adhesive if adhesive bands were divided relieving distended bowel at laparotomy.

Potential risk factors for SBO were analysed including sex, gestational age, type of abdominal wall defect, giant omphalocele, type of treatment, type of operation, number of reoperations, need for bowel resection at initial surgery, inadvertent enterotomy at initial and subsequent laparotomies, and major postoperative complications.

Long-term morbidity focussed on consequences of postoperative adhesions was obtained by data from medical records and a questionnaire sent to all surviving patients. This included hospital readmission for abdominal complaints, abdominal operations, SBO, chronic abdominal pain, and chronic constipation.

Statistical analysis

The Kaplan-Meier method was used to calculate the probability of developing SBO. This method calculates incidence curves over time by using follow-up data from all individuals in the cohort, regardless of duration of follow-up. End points of follow-up were first occurrence of SBO, death, loss to follow-up, and end of the observational period. The log rank test was used to determine potential risk factors for developing SBO. The Student-*t* test was used for analysing gestational age as potential risk factor. A multivariate modelling approach (Cox proportional hazards) was used to identify any variable that predicts SBO. Analysis of long-term morbidity (chronic abdominal pain and constipation) related to SBO was performed using the Fisher's Exact test. A *P*-value less than .05 was considered statistically significant.

RESULTS

1. Patients

One hundred seventy neonates were identified with a congenital abdominal wall defect. Their demographic data are shown in Table 1. One hundred forty-seven underwent surgery and 12 were not operated on awaiting closure by primary epithelialization. Eleven patients died within 36 hours after birth because of multiple congenital defects and were excluded for further evaluation. Median follow-up of the remaining 159 patients was 87 month (range, 5 days-32.5 years).

2. Non operative group

Of 12 patients, 2 had a giant omphalocele (defined as abdominal wall defect > 4 cm and liver included). Eight (67%) patients died (all in OC group), three following severe sepsis and five as a result of other congenital disorders. Four patients survived. No patient in this group had SBO with a median (range) follow-up of 4 month (range, 6 days-26 years).

Table 1. Demographic data of 170 neonates with congenital abdominal wall defect treated between 1971 and 2004.

	Omphalocele	Gastroschisis	Total
Total	111	59	170
Sex male	56	40	96
female	55	19	74
Mean (range) gestational age (wk)	38.4 (31-42)	36.5 (32-42)	
Other congenital anomalies [a] (%)	34 (31%)	1 (2%)	35 (21%)
Operative group (%)	92 (83%)	55 (93%)	147 (86%)
Nonoperative group (%)	12 (11%)	0 (0%)	12 (7%)
Mortality [b] within 36 h (%)	7 (6%)	4 (7%)	11 (6%)
Mortality after 36 h	19 (17%)	9 (15%)	28 (16%)

[a] Beckwith Wiedeman syndrome, Trisomie 13/18/21, Pentalogy of Cantrell, VACTERL association, OEIS syndrome (Omphalocele, Exstrophy of the cloaca, Imperforated anus, Spinal abnormalities) [b] Patients were excluded for further evaluation

3. Operative group

Primary closure was performed in 128 (87%) neonates, prosthetic mesh insertion in 7 and silastic sac coverage in 12 patients. Sixteen (11%) patients died (9 GS, 7 OC) and time of death varied between 2 days and 7.5 years. Syndrome-related mortality occurred in 6 of 7 patients with OC. Four patients, all with gastroschisis, died because of bowel ischemia. Two patients died because of sepsis, 2 due to respiratory failure and 2 patients died because of aspiration at the age of 5 and 7.5 years.

Small bowel obstruction occurred in 26 (18%) of 147 patients, 14 (25%) of 55 with GS and 12 (13%) of 92 with OC ($P = .06$). Of 12 SBOs in OC, 7 occurred in giant omphaloceles (n=23). In 23 (88%) of 26, adhesive SBO was confirmed at laparotomy. The median time to develop SBO after the first operation was 39.5 days (range, 8 days-13 years). Sixteen patients (62%) had SBO within the first 3 months after initial operation and in 85 % within the first year. In-hospital SBO occurred in 17 (66%) patients and out-hospital SBO (readmitted after primary discharge) in 9 (33%) patients between 5 months and 13 years. Cumulative hazard to develop SBO as calculated by the Kaplan-Meier method is 0.27 and 0.10 within 6 months, 0.27 and 0.12 within 1 year and 0.27 and 0.13 within 2 years for GS and OC, respectively (Figure 1).

Three patients with SBO were successfully treated nonoperatively. Laparotomy was done in 23, and in those, SBO was due to adhesive bands. Eight (35%) patients needed small bowel resection and 4 of them had to undergo a second look to check bowel vitality. Of 26 patients, 4 (15%) died after operative treatment for SBO; 1 patient because of postoperative sepsis after repeated relaparotomies for ischemic bowel, 1 because of diffuse intravascular coagulopathy, 1 as a result of an anastomotic leak and 1 patient with lung hypoplasia because of pulmonary failure.

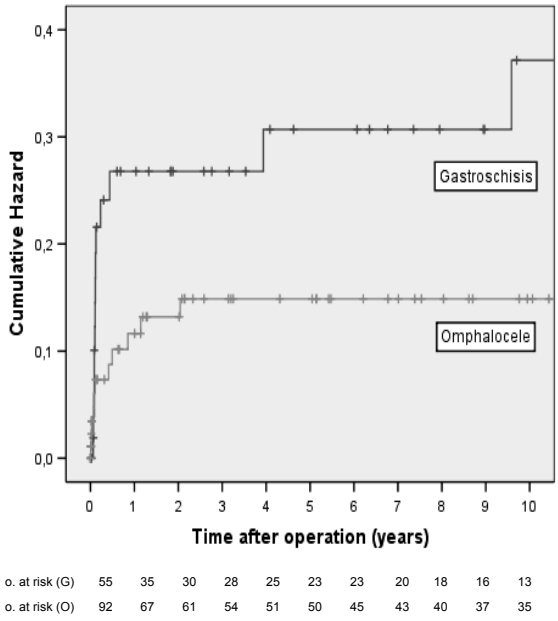

Figure 1. Cumulative incidence of SBO using the Kaplan-Meier methods for time-related incidences

Results of univariate analysis are shown in Table 2. Incidence of SBO was significantly higher in patients who had fascia dehiscence ($P < .01$), anastomotic leakage ($P = .01$) and sepsis ($P = .01$) and tended to be higher in the GS group (25%) than in OC group (11%) ($P = .06$). At multivariate analysis, sepsis and fascial dehiscence were independent predictors of SBO (Hazard ratio 2.66 (95% CI: 1.03-6.85) and 14.71 (95% CI: 2.33-92.97), respectively).

The response rate of the questionnaire was 102 (76%) of 135 patients. Operation for SBO was the second most common operation in the follow-up of children after correction of congenital abdominal wall defects. Chronic abdominal pain and constipation occurred in 30 (30%) and 20 (20%) of the 102 patients, respectively, and were not correlated to occurrences of SBO (6/30 and 4/21 patients, respectively, ($P = .27$ and $P = .38$). Follow-up by questionnaire revealed SBO in 2 patients, who both have had surgery in another hospital.

Table 2. Univariate analysis of potential risk factors for SBO in the operative group (n=147).

	No SBO	SBO	Total	*P*
GS	41	14	55	.06
OC	80	12	92	
Male/female	68/53	15/11	83/64	.72
Mean gestational age	37.9	37.2		.19 [a]
Type of correction				.66
Primary closure	108	20	128	
Silastic sac	9	3	12	
Prosthetic mesh	5	2	7	
Small bowel resection at first operation	7	3	10	.23
1 or more re-operations	31	12	43	.06
Postoperative complication				
IRDS	5	2	7	.36
Fascia dehiscence	0	2	2	<.01
Anastomotic leakage	3	2	5	.01
Sepsis	32	13	45	.01
Chronic abdominal pain	23	6	29	.27 [b]
Chronic obstipation	16	4	20	.38 [b]

A log rank test was used, [a] *t* test, [b] Fisher's Exact test

DISCUSSION

The present study demonstrates that the risk of adhesive SBO after operation for congenital abdominal wall defects is considerably high and that SBO is associated with marked morbidity and mortality particularly in the first year of life. Fascial dehiscence and sepsis predicted SBO in this series. SBO did not correspond with chronic abdominal complaints such as pain and constipation, which are present in 20% to 30%, respectively, of patients years after abdominal wall reconstruction.

This is the first study reporting on SBO exclusively in neonates treated for gastroschisis and omphalocele. Previous studies showed results of all neonatal surgeries, making accurate and long-term analysis of incidence and risk factors for SBO in this distinct relatively small subgroup difficult [13,14,18]. Studying neonates with gastroschisis and omphalocele was chosen for 2 reasons. First, these neonates undergo extensive peritoneal manipulation for abdominal wall closure and often need repeated laparotomy or insertion of prosthetic mesh, which are key factors inducing adhesion formation. Second, new techniques for abdominal wall closure and modern antiadhesive products give promising results in adults but need to be validated in neonatal laparotomy with high risk of adhesion-related morbidity [19,20].

The calculated incidence of SBO within 1 year was 12% in the OC group and 27% in the GS group increasing to 15% vs 37%, respectively, after 10 years. Both incidences are considerably

higher than previously reported and may be explained by the completeness and accuracy of data and almost 10-year median and 30-year maximum follow-up in comparison with other series [13,14,18,21]. Wilkins and Spitz, who reported 15% SBO after gastroschisis, had a 10.5 year follow-up and only 58% reply on questionnaires. Choudry and Grant reported a 6% and 0% incidence after gastroschisis and exomphalos, respectively, with a short median follow-up of 39 months. In a population-based analysis of children younger than 5 years with a 4-year follow-up, Grant and coworkers found a 6.3% cumulative incidence of SBO after abdominal wall surgery directly related to adhesions and 14.2% incidence of SBO possibly related to adhesions. Long follow-up, however, is not the only explanation since the majority of SBO (85%) developed within the first year of life. The early occurrence of SBO is in concordance with other studies regarding adhesive bowel obstruction following neonatal laparotomy but has recently been challenged by Grant and coworkers [13,14,18,21]. They relate the highest incidence in the first year to the preponderance of short-term follow-up in most studies; however, this does not hold through for the observation in our study. The population-based study including a small proportion of neonates in a group of children younger than 5 years of age does not allow for proper conclusions on incidences of early SBO. The reason why SBO develops early in neonates after laparotomy has not been accurately addressed, but findings from our study and that of Choudry suggest repeated laparotomies within a short period of time, extensive intraperitoneal tissue handling and abdominal and systemic infections (sepsis, wound dehiscence, anastomosis leakage) to play a role. Dissecting adhesions during relaparotomy rapidly induces adhesion reformation that can be very dense. The early reformation, which is more difficult to prevent than de novo adhesion formation, is attributed to increased levels of fibrinolytic inhibitors and transforming growth factor in adhesive bands [22]. Operative procedures in adults with extensive tissue dissection also seem to induce early adhesive morbidity [23]. We previously reported a 11% calculated risk within 1 year to develop SBO after (sub) total colectomy, a surgical procedure with extensive dissection [12]. For other procedure with less peritoneal injury such as appendectomy and hysterectomy, time interval seem to be significantly longer and adhesive SBO may occur for the first time even 25 years after surgery.

The incidence of adhesive SBO tended to be higher in gastroschisis than in omphalocele. Several theories are conceivable regarding the massive adhesion formation propensity of GS correction beside extensive tissue manipulation. First, bowel is exposed to amnion fluid causing toxic and inflammatory reaction of the serosal lining [15,16]. Second, intestine sustains injury during labour and desiccation in air. Third, newborns with GS often present hypoperistaltism and malabsorption [24]. Bowel paralysis mechanically increases adhesion formation because early fibrinous bands are not detached by peristaltic movements. The less adhesiogenicity of laparoscopic surgery has been in part attributed to early restoration of bowel function.

There may be criticism that the obstruction is interpreted as adhesive but in fact was prolonged postoperative ileus. Touloukian et al [24] showed a mean period of bowel paralysis after gastroschisis correction of eight days. However, the mean time interval to SBO was 39,5 days in the present study, and only one patient developed SBO within 4 days. In addition, adhesive SBO was confirmed by laparotomy in almost all cases, making misinterpretation of obstructive symptoms unlikely.

Fascial dehiscence and sepsis predicted SBO. Conceivably, secondary healing of the fascia is accompanied by granulation tissue covering the viscera, ultimately leading to adhesive bands to the ventral abdominal wall. Intraabdominal sepsis in particular aggravates the inflammatory response in the abdominal cavity inducing diffuse adhesions. Both locations of adhesions are known to cause SBO [12]. Because of the small number of neonates who underwent small bowel resection at initial surgery, we could not confirm bowel resection as important risk factor for SBO in contrast to others [21].

Early morbidity following SBO was significant and related mortality was 15 %, underlining the great impact of adhesions in sick children and this vulnerable patient group in particular [14]. We have a strong impression that the surgical community underestimates the great impact of adhesive SBO on morbidity and mortality. In our series, mortality following SBO was higher than mortality after surgery for neonates with GS and OC. In adult population, SBO-related mortality varies between 2% and 10% and equals the mortality rate of major abdominal surgery such as pancreaticoduodenectomy or open aortic aneurysm repair [25-27]. Questionnaires were used to investigate long-term complaints possibly related to intraabdominal adhesions and SBO experienced earlier. About 1 out of 4 patients had chronic abdominal complaints, which is significantly higher in comparison with the healthy population. Proper explanations here for are lacking, but the importance of long-term quality of life studies in patients who underwent major neonatal surgery was stressed [28]. Results from the present study confirm the hypothesis that neonates with a congenital abdominal wall defect have a high risk for adhesive SBO and could benefit from adhesion prevention. There are new developments aiming at reduction of intestinal injury or prevention of adhesion formation. The use of amnion exchange during pregnancy may reduce bowel damage and subsequent SBO [29]. Waiting for complete epithelialisation in giant omphaloceles before operation might reduce serosal injury and limit adhesiogenic areas. The component separation technique is a promising technique to primarily close the abdominal wall defect without tension and avoiding insertion of foreign material [30]. Recently, Inoue et al [20] reported a significant reduction in incidence and severity of postoperative adhesions and mean relaparotomy operation time with the use of hyaluronate-based barrier membrane in a series of 122 neonates, infants, and children.

Based on these results, we plan a multicenter study aiming at reduction of adhesion-related morbidity using adhesion reduction products at initial laparotomy in neonates with congenital abdominal wall defects.

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CHAPTER 4

Has the liver and other visceral organs migrated to its normal position in children with Giant Omphalocele? A follow-up study with ultrasonography

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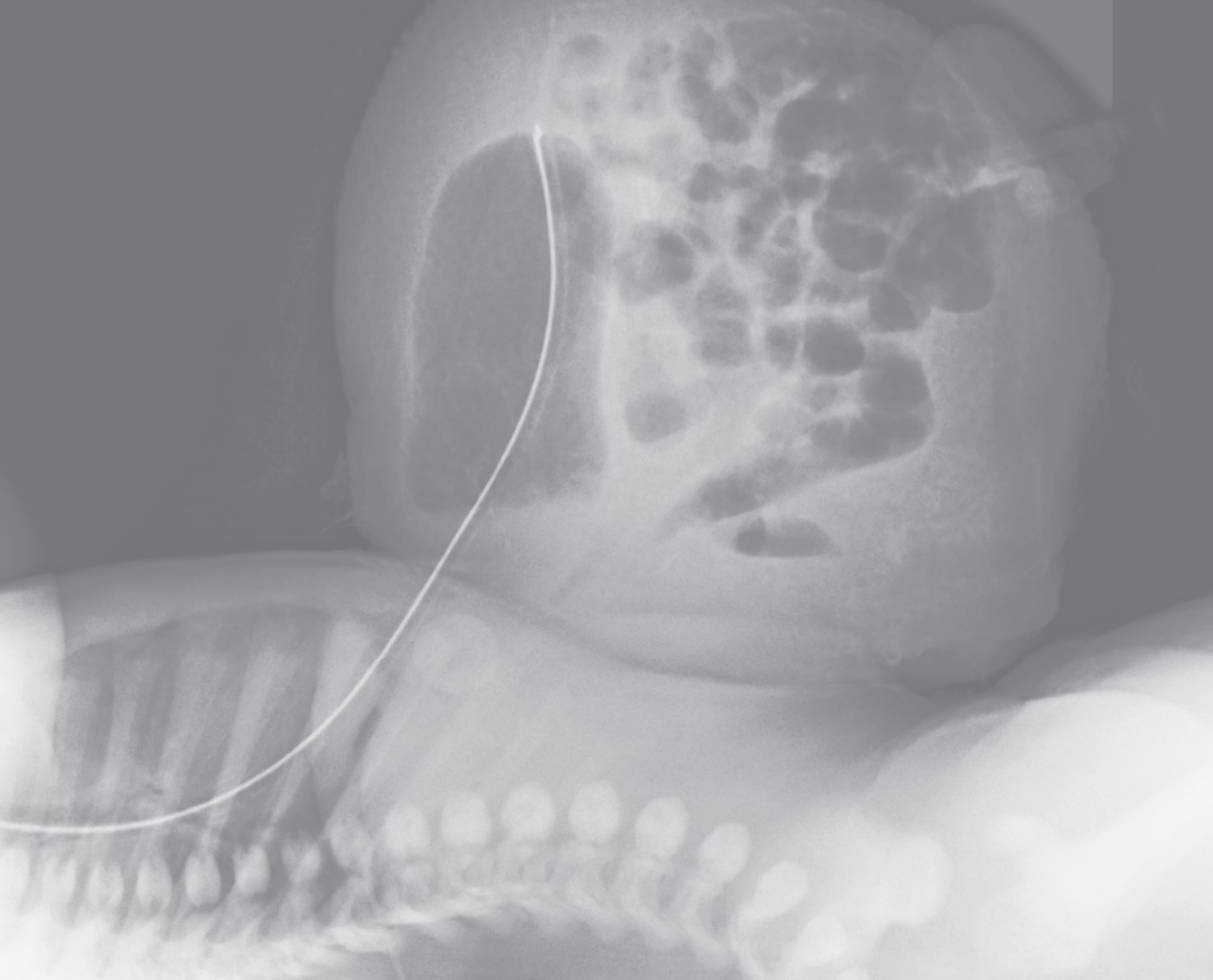

ABSTRACT

Background: There is little information on the position and size of the liver later in life in patients with giant omphalocele. This study evaluates whether, on the long run, in patients born with a giant omphalocele, the liver and other solid organs reach their normal position, shape and size.

Methods: Seventeen former patients with a giant omphalocele, treated between 1970 and 2004, were included. Physical examination was supplemented with ultrasonography for ventral hernia and precise description of the liver, spleen and kidneys. The findings were compared with 17 controls matched for age, gender and body mass index.

Results: An abnormal position of the liver, spleen, left kidney and right kidney was seen in eight, six, five, and four patients, respectively. An unprotected liver was present in all 17 patients and in 11 controls, the difference being statistically significant (P=0.04). In ten of the 11 patients with an incisional hernia, the liver was located underneath the abdominal defect.

Conclusions: In all former patients with a giant omphalocele an unprotected liver and in the majority of them also an incisional hernia was found. The liver and sometimes also the spleen and the kidneys do not migrate to their normal position. Exact documentation and good information are important for both the patient and their caretakers in order to avoid liver trauma.

INTRODUCTION

An omphalocele (OC) is a congenital abdominal wall defect at the umbilicus, which can in most cases be closed primarily. More difficult is a giant omphalocele (GOC), defined as an abdominal wall defect larger than 4 cm and the liver partly extruded in the omphalocele.

Neonates with GOC often have a small underdeveloped peritoneal cavity with a high degree of viscera-abdominal disproportion that can prohibit save primary closure. Placing the abdominal contents under pressure leads to an abdominal compartment syndrome with reduction of cardiac output, hypotension and hampered renal perfusion and often leads to postoperative respiratory failure by the elevation of both diaphragms. Therefore primarily non-operatively approach is recommended by several authors, leaving the organs up front in an uncorrected position. Secondarily, the defect can be closed by several different techniques, with reposition of the liver and bowel into the abdominal cavity [1,3,4,6-8,11,16]. There is little information on the position and size of the liver later in life in patients with GOC [17]. In case the liver is ventrally (medial) located, there is an increased risk for liver rupture in case of an abdominal trauma. In addition, for acute abdominal operations and in case of pregnancy, the position of the liver could be important. The aim of this study is to investigate if the liver and other solid organs eventually migrated to their normal position, regaining their normal shape and size. Furthermore, special attention was paid to the presence of the natural protection of the liver by the chest wall and the strength of the abdominal wall in case of an 'unprotected' liver.

PATIENTS AND METHODS

Between 1970 and 2004, 22 (9 males, 13 females) surviving patients with GOC were treated at the Radboud University Nijmegen Medical Centre. All patient records, operative reports and office notes were retrospectively reviewed.

Patients were treated either surgically or conservatively. Initial operative treatment was divided into primary or staged closure of the abdominal wall defect. Initial non-operative treatment consisted of covering the omphalocele after birth with dry sterile dressings until it was fully epithelialized and liver and bowel were partly migrated into the abdomen by gravity. Later in life the abdominal defect was either closed or an incisional hernia was accepted.

The addresses of the patients were traced and they were subsequently asked in writing to participate in this study. After informed consent was obtained, the patients were seen at the outpatient clinic. Patient's characteristics, medical history, use of medication,

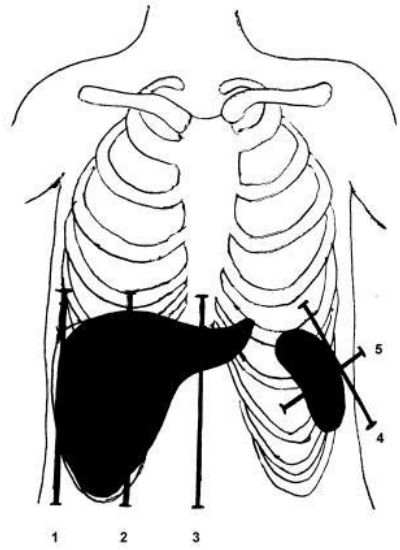

Figure 1. Section planes of liver and spleen.
1= anterior axillary line (AAL),
2= medioclavicular line (MCL),
3= sternal line (STL),
4= longitudinal section,
5= transverse section

and physical examination, anthropometry (weight, height, Body Mass Index (BMI)) and a digital picture of the abdomen (anterior, lateral) were collected. The sonographic measurements of organ size were perfomed with a real-time parallel ultrasound **(**Toshiba Aplio XG, using a curved 3.5 MHz and linear 8.0 MHz probe**).** All patients were investigated in supine position. Determination of liver size was calculated by measuring the craniocaudal liver extension in three standardized section planes: anterior axillary line (AAL), medioclavicular line (MCL) and sternal line (STL) (Fig.1) [5].

Index liver size (ILS) was calculated by the following formula: ILS = $(AAL^2 + MCL^2 + STL^2) \cdot 0.2618$ [5]. The grade of unprotected liver was defined as the number of cm of the liver beneath the chest boundary at section planes AAL, MCL and STL. The spleen size was measured by the largest section area in the longitudinal and transverse plane (fig 1.). All measurements were repeated 3 times and the mean score was recorded as the absolute value. The position of the liver (normal/abnormal position; unprotected liver yes/no; number of cm beneath ribcage at section planes AAL, MCL, STL; thickness of abdominal wall (mm) of unprotected liver), position spleen, kidneys and the presence of an incisional hernia were recorded.

For peer group reference, the results were compared with a control group (after informed consent), matched for gender, age and BMI. Significance testing for discrete variables was performed with the Fisher's exact test when appropriate. Student T-test was used for comparing means. Reported P values are two-sided. $P<0.05$ was considered statistically significant. All analyses were two-sided and conducted using SPSS software (version 16.0 SPSS, Inc., Chicago, Illinois, USA).

RESULTS

Of the 22 patients, 18 patients in the age from 3 to 29 years could be traced, of whom one did not want to participate in the study. The remaining 17 could be included and underwent physical and ultrasonographic examination. Patient's demographics and those of control group showed 12 females and 5 males in both groups. Median age was 13.3 vs 15 years (range 4-30) and median BMI was 18.4 vs 17.1 respectively (range 13-32). Physical examination did not correlate well with ultrasonography. Only in 4 patients the liver was palpated during physical examination in contrast to ultrasonography of which all patients had a partly unprotected liver (beneath chest boundaries). Hernia of the abdominal wall was detected during physical examination in 9 patients vs. 11 hernias that were detected during ultrasound. No correlation was found between patients treated for GOC with primary vs staged closure and presence of hernia (7/12 vs 3/4). In ten out of 11 patients with an incisional hernia the liver was located underneath the abdominal defect which explained the absence of protrusion of small bowel or fat tissue through the abdominal wall defect during physical examination. The results of the measurements and observations of ultrasound are shown in Table 1. The size of the liver (ILS) was larger in the GOC group (P=0.01). In contrast, the spleen size was equal in both groups.

Table 1. Results measurements ultrasound (median) in 17 patients born with giant omphalocele and 17 controls

		Patient (range)	Control (range)	Sign.
Position spleen	Normal	11	17	P=0.018[a]
	Abnormal	6	0	
Spleen volume (cm3)		37.4 (6-101)	44 (21-93)	P=0.58[b]
Position kidney left	Normal	12	17	P=0.044[a]
	Above spleen	5	0	
Position right kidney	Normal	13	17	P =0.10[a]
	Above liver	4	0	
Position liver	Normal	9	17	P=0.03[a]
	Abnormal	8	0	
Unprotected liver AAL (cm)		0 (0-6)	1.6 (0-5)	P=0.72[b]
Unprotected liver MCL (cm)		5.1 (4-22)	0 (0-7)	P=0.017[b]
Unprotected liver STL (cm)		8.6(0-25)	4.4 (0-8)	P=0.000[b]
Index of liver size (ILS)		139 (59-341)	103 (35-180)	P=0.012[b]
Liver totally covered by ribcage		0	6	P=0.044[a]
Thickness abdominal wall at unprotected liver (mm)		4.5 (3-19)	9.5 (0-25)	P=0.31[b]
Incisional Hernia	Yes	11	0	P=0.000[a]
	No	6	17	
Size hernia (cm2)		29 (5-153)	-	

[a] Fisher's Exact test, [b] Student's *t*-test

Abnormal position of liver, spleen, left and right kidney was observed in eight, six, five and four patients, respectively. Unprotected liver (cm) under the chest boundaries at STL and MCL was significantly more often seen in the GOC group as compared to the control group (Fig 2). In two patients, the liver was located in the lower abdomen reaching into the pelvis. In these two, one kidney was located cranial from the liver. In one patient the gallbladder was located at the ventral aspect of the liver.

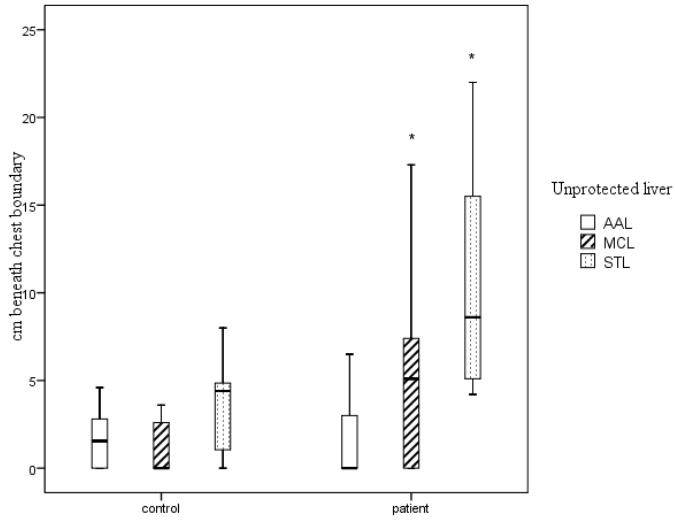

Figure 2. Unprotected liver beneath chest boundary: patient vs control
Box represents: upper border (first quartile), lower border (third quartile), black bold line in box represents the median. The asterisk represents the significant difference between patient vs control

DISCUSSION

The treatment of GOC is still under discussion. In the last decades several surgical techniques have been described. Primary closure with acceptance of high abdominal pressure gives rise to circulatory problems. Also staged closure techniques, like silastic silo, skin flap closure can lead to pulmonary or circulatory problems [1,2,6,7,9,12,16]. Independent of the definitive treatment of closure of the abdominal wall, the position of the liver and of other visceral organs in patients born with GOC differs from the normal position and it is unclear if the position changes during life. To our knowledge, this is the first study, which demonstrates a persistent abnormal position of liver, kidneys and spleen in most GOC.

In two patients, the liver was even located in the lower abdomen and pelvis. Incisional hernias were present in 11 patients, of which the liver was located in front of the defect

in ten, sealing off the defect to such extent that no complaints or symptoms were present. This explains the absence of protrusion of small bowel and/or fat tissue at physical examination.

Zaccara et al [17] studied the shape and position of liver and spleen in patients with abdominal wall defects (gastroschisis and omphalocele). They found larger index liver size and spleen volume in comparison with normal healthy persons as published by Dittrich et al [5]. Over the last decennia welfare, and most of all food intake habits, have changed anthropometry, which makes it quite difficult to compare these results with data that were obtained 20 years earlier. In our study we used for peer group reference a control group matched for gender, age and BMI. There was no difference in spleen volume between the patient group and controls.

Zaccara et al. found a normal position of liver and spleen in patients with abdominal wall defects. In contrast, our study detected an abnormal position of the liver and spleen in eight and six patients, respectively. This difference can be explained by the heterogeneity of the group. In gastroschisis the liver is not included in the defect. Furthermore, it is unclear if the liver was included in the omphalocele in all patients of their series, and not only in GOC.

The high incidence of abdominal wall hernias in our patient group can be explained by high tension still present during primary or staged closure of the abdominal wall. This could plead for initial non-operative treatment after birth and secondary closure if disproportion of the abdominal wall and visceral organs has decreased. Secondary closure using the component separation technique shows promising results with no incisional hernia after a median follow up of 23.5 month [14].

A striking finding was the liver beneath the abdominal wall defect in ten of the 11 patients that theoretically may be quite vulnerable for blunt abdominal trauma. However, literature of traumatic liver rupture in GOC is scarce and therefore no evidence is available as to what should be the best treatment option for this specific group.

Even if no herniation was detected, an unprotected liver beneath the ribcage was significantly more present in the patient group as compared to the controls. Studying the ultrasound data, it seems that the volume of the liver is significant larger, and is located more medial and caudal in comparison with the control group. This explains the significant higher grade of unprotected liver.

In literature there is only one paper describing a perforation of small intestine inside an undetected internal hernia sac after blunt trauma at the age of 40 years [13]. Even in patients with ventral hernia, intestinal perforation after blunt injury seems to be rare [10,15].

In case of acute abdomen or caesarean birth knowledge of an abnormal position of the liver or of other abdominal organs may be of importance for the choice of the surgical access to the abdomen to prevent damage to the liver and other abdominal organs.

Therefore good documentation and information of the parents may be of pivotal importance for both patient and surgeon and recommendation of a pre-operative ultrasound should be given. The question remains to what extent we have to advise exclusion of contact sports and other risk behaviour, since information of true increased incidence of blunt trauma in these patients is not available in the literature. However, good information of potential risks to the patients is part of good clinical practise.

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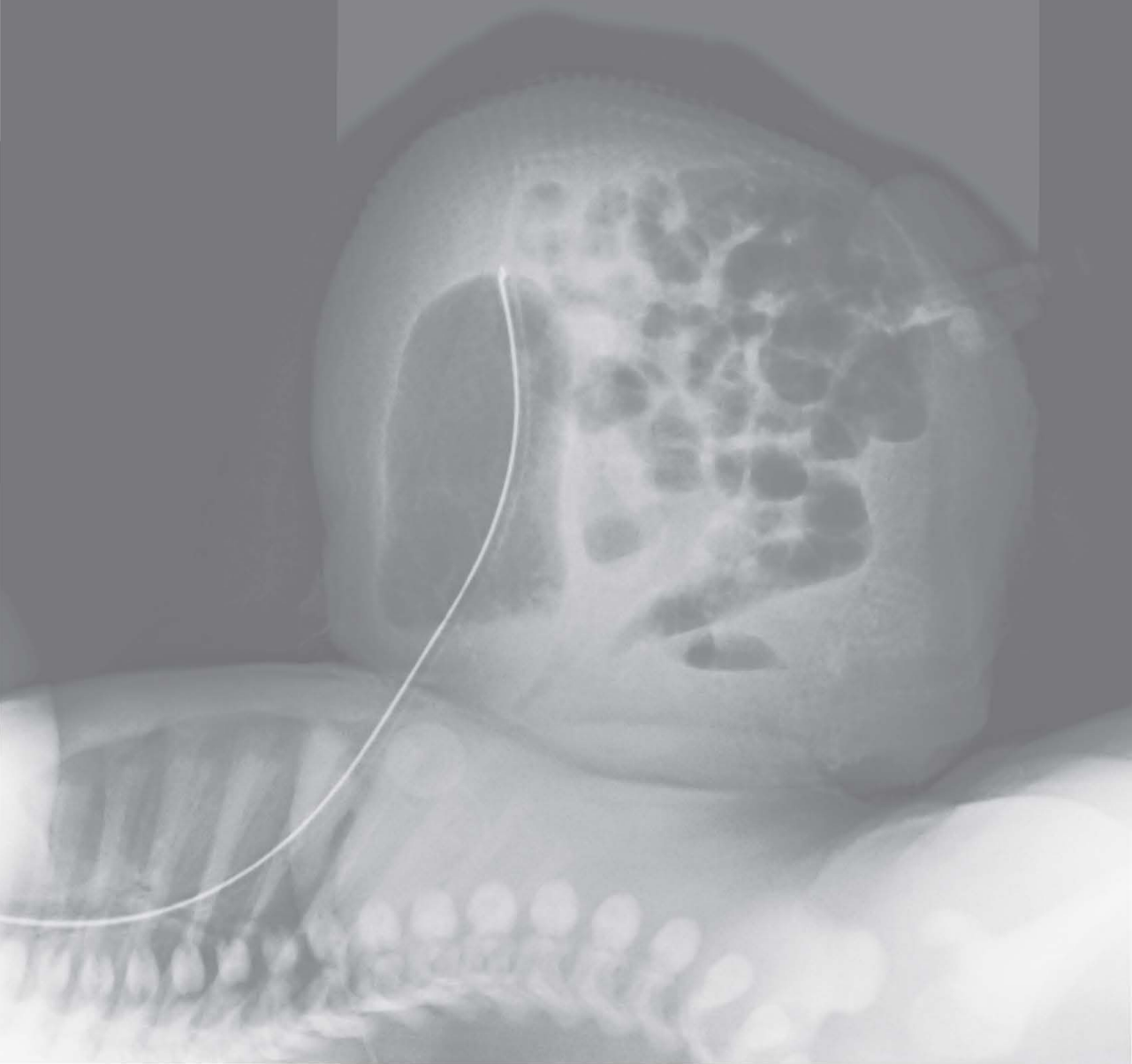
PART 2

surgical techniques



CHAPTER 5

Past and current surgical treatment of giant omphalocele: outcome of a questionnaire sent to authors

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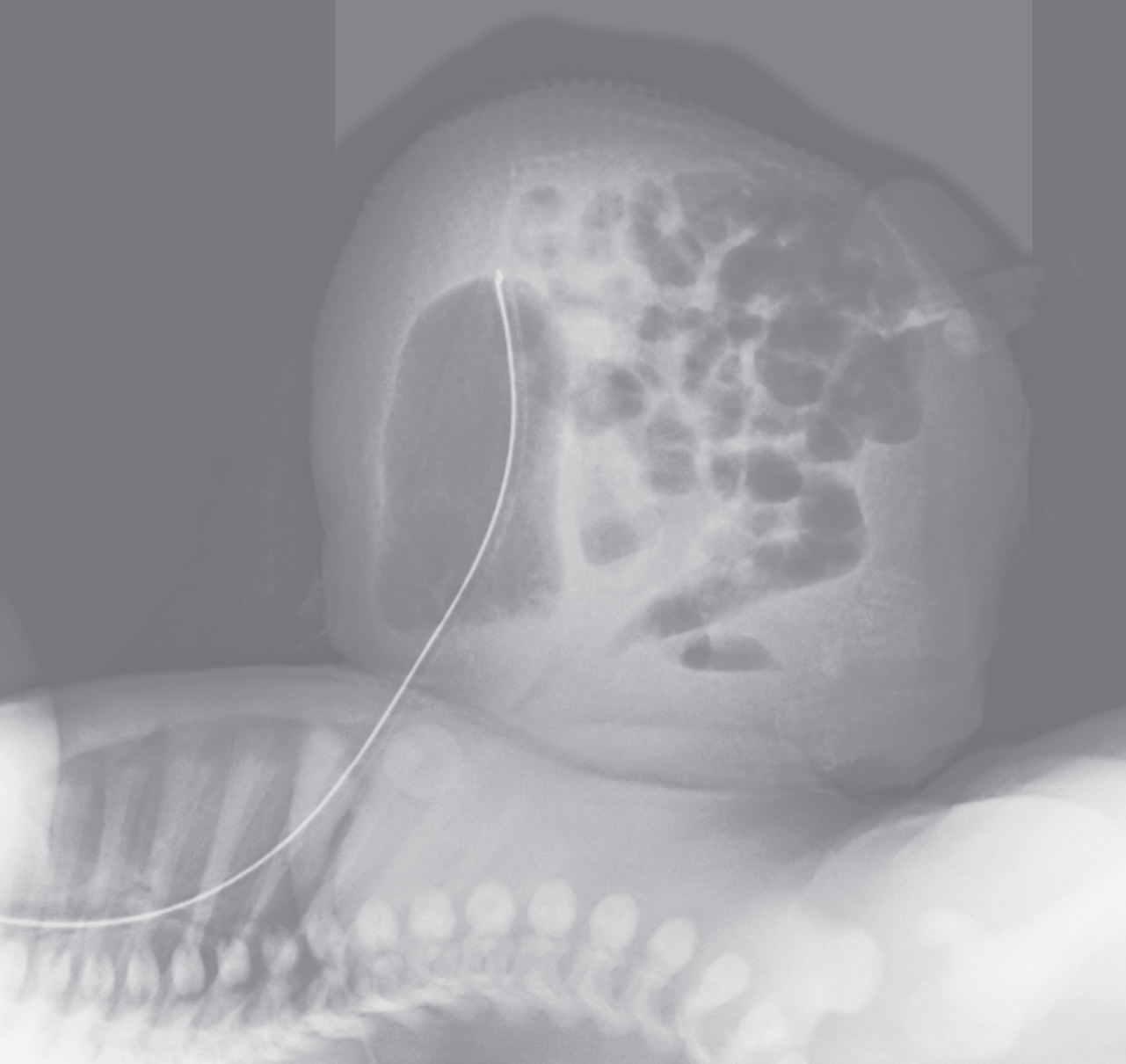

ABSTRACT

Purpose: Operative treatment of giant omphalocele (OC) is still a challenge for pediatric surgeons. We were interested to ascertain whether published operative techniques for giant OC once advocated by their authors, were still being used by these authors and whether the techniques had been modified or even abandoned for other techniques.

Methods: Relevant studies concerning the treatment of giant OC were identified by an electronic search. Publication date of the articles was from 1967-2009. A questionnaire was sent to the first author, or co-author unless contact details were unavailable. The described surgical techniques were categorized into: primary closure, staged closure and delayed closure.

Results: Almost half of the authors (42%), independent of the initial technique used (primary, staged, or delayed closure), changed or stopped using their technique after the publication of the article. The change was not to one particular proven better technique. Herniation rate was lower in delayed closure (9% delayed vs 18% staged vs 58 % primary).

Conclusions: The results of the questionnaire did not show a generally accepted treatment after more than 30-year of innovations in the treatment of patients with a giant omphalocele. There are generally two main treatment modalities: staged closure and delayed closure. Because of the lack of large patient numbers and late follow-up, long-term results of the published techniques are needed and randomized multicenter trials based on these outcomes are recommended. Until then, we remain dependent on expert opinions.

INTRODUCTION

The surgical management of omphalocele (OC) has evolved over the past 5 decades. The definitive goal of surgical intervention is to provide complete fascial and skin closure without causing excessive intra abdominal pressure or abdominal wall tension. In giant OC, primary closure is usually not feasible. Operative treatment of giant OC is still a challenge for pediatric surgeons, which is reflected by the broad range of approaches described in the literature. Most of these publications are case reports or describe a small number of patients, without long-term follow-up.

We attempted to ascertain whether published operative techniques for giant OC once advocated by their authors were still being used by these authors and whether the techniques had been modified or even abandoned for other techniques. In this study, we focused on the closure techniques and not on the treatment of associated comorbidities.

This study presents the results of a questionnaire concerning the currently preferred method of treatment by pediatric surgeons who had previously published their technique of choice.

PATIENTS AND METHODS

Potentially relevant studies concerning the treatment of giant OC were identified by an electronic search. Giant OC was defined as abdominal wall defect ≥ 5 cm and protrusion of liver in the sac. The period of publication of the articles ranged from 1967 to 2009. The e-mail addresses of authors were obtained from the articles, member lists of national associations for pediatric surgeons or google.com. A questionnaire regarding treatment of giant OC was preferentially sent to the first author or, unless contact details were

Table 1. Questionnaire treatment giant omphalocele

1.	Are you still using this technique for closing giant omphalocele? a) If yes, is it modified? How is it modified? b) If no, what technique are you using now?
2.	What are the advantages of your current technique?
3.	What are the disadvantages of your current technique?
4.	Which postoperative complications do you encounter?
5.	How many patients (%) developed a ventral hernia during follow up?
6.	How many minor omphaloceles (abdominal wall defect ≤ 4 cm) are treated in your hospital every year?
7.	How many giant omphaloceles (abdominal wall defect ≥ 5 cm and protrusion of the liver) are treated in your hospital every year?
8.	What are your criteria for primary non-operative treatment?
9.	What is your preferred non-operative treatment?

unavailable, to coauthors. Current hospital, country and profession were noted. The questionnaire consisted of 9 questions (Table 1). We choose to email this short questionnaire to maximize the response.

The described surgical techniques were categorized according to the literature as: primary closure (defined as primary closure of the defect in one operation, with or without extra corporal material, shortly after birth)[1-10]; staged closure (closure of the abdominal wall defect in more than 1 operative procedure) [11-35]; delayed closure of the abdominal wall after epithelialization of the OC sac (36-48).

RESULTS

Forty-eight articles were included in our study [1-48]. Of these, the email addresses of the authors of 10 articles could not be traced [7,9,12,13,26,29,34-36,42]. Eight of the 10 articles were published before the era of email announcement in the articles [7,9,12,29,34-36,42]. The questionnaire was sent to the remaining 38 authors or coauthors. The questionnaire response rate was 24/38 (63%). Among the published material of the nonresponders, 7 articles were case reports ($n \leq 3$ patients). Two non-responders evaluated a large group of patients ($n > 22$) in their publications [32,48]. Two of the 24 responders, Adzick and de Lorimier [19], were the authors of a similar paper. The 24 responding authors consisted of 21 pediatric surgeons, 1 trauma surgeon, 1 pediatric urologist and 1 plastic surgeon. All were still active in clinical practice.

The management of giant OC using a single technique was described in 21 articles. Primary closure was reported in 4 articles, staged closure in 11 and delayed closure in 6. A comparison of 2 treatments was described in 3 articles: primary/staged or delayed/staged [2,6,37]. The results of the questionnaire are outlined in Table 2.

Ten authors (42%) modified their technique over time. One author stopped using the originally described technique [20], while the other 13 authors were still in favor of their reported technique.

1. Primary closure

The main advantage given by the authors for primary closure was a successful abdominal wall closure and skin closure in a single procedure. However, most of the patients needed artificial substitutes for temporary closure of the abdominal wall. Substitutes for closure of the abdominal wall defect consisted of biomaterials (alloderm, bovine pericard patch (Tutopatch), Surgisis, Permacol) [4,5] or artificial patches (Teflon, polypropylene, Gore-Tex). Only Rodgers [3] changed materials, namely from Teflon to Gore-Tex patches. Maksoud-Fihlo [6] modified the original technique leaving the membrane

Table 2. Results of the questionnaire

Ref	Technique	Author	Year of publication	N patients	Same technique.	Changes of the technique	Advantage	Disadvantage	Complications	% hernia
2	Primary/ staged	Davenport	2005	13/11	Yes	-	Early abdominal wall closure	High quality of intensive care necessary	Resp. complications, woundinfection, septicaemia	0 0-60%
6	Primary/ staged	Maksoud-Filho	2006	22/11	Mod	Leaving the membrane intact and covering it with mesh	No contact with the bowel, less perforation	Dressing changes for months, sometimes skin grafting	Local infection. Prolonged ileus	100
3	Primairy+ mesh	Rodgers	1979	4	Mod	Gore-tex instead of Teflon	Creation of a secure anterior abdominal wall with complete skin closure in one procedure.	Foreign material + removal years later	Herniation around margin of the patch in 2 patients	50
4	Primary + bioabsorbable	Alaish	2006	1	Yes	-	Achieves 2-layer closure; no mesh used.	Cost of alloderm; potential for alloderm to attenuate	None	0
10	Primary + bioabsorble	Kapfer	2006	3	Yes	-	NA	NA	NA	NA
5	primary + bioabsorbable	Saxena	2006	8	Yes	.	Avoidance of venous kinking	2-3 surgical interventions	None	100
19	Staged	de Lorimier	1991	6	Yes	-	No protrusion of the liver, kinking of IVC, exposure of the bowel to adhesions	Prolonged paralysis and ventilation	Sutures pulling away from the skin/amnion junction	17
19	Staged	Adzick	1991	6	Mod	2 Teflon meshes sutured to each fascia	Easy, amnion stays intact, reduction of the OC in 2-3 week time.	None	-	< 5

Table 2. Results of the questionnaire (continues).

Ref	Technique	Author	Year of publication	N patients	Same technique.	Changes of the technique	Advantage	Disadvantage	Complications	% hernia
18	Staged	Harjai	2000	1	Mod	Sometimes Dual-meshes	It can take care of any giant OC	After 5 to 7 days it comes out,due to excessive tension	Local disruption and infection.	18
21	Staged	Kiely	2005	12	Yes	-	It works well nearly all giant OC	Not successful in severe lung hypoplasia	Occasional infection beneath the mesh	0
22	Staged	Sigalet	2003	4	Mod	Surgisis instead of polyglycan mesh	Prevents excessive pressure on the diaphragm, no mech. Ventilation	Multiple reoperations	Wound infection, SBO	75
17	Staged	Patkowski	2005	8	Yes	-	Early closure, simple and effective, minimal bowel compression	Muscle paralysis, mechanical ventilation	One case of mechanical bowel injury	12
16	Staged	Zama	2004	4	Yes	-	Early complete closure of the abdominal wall	Scarring of the grafts	None	-
14	Staged	Krasna	1995	10	Mod	?	No compression of abdominal contents	Longer hospital stay	None	0
20	Staged	van der Zee	1993	1	No	-	Less morbidity/ mortality	Recurrent local infections	None	0
15	Staged	Kane	2006	2	Mod	Endoscopic assistance with placement of the tissue exp.	Control and calculation of the amount of expansion, less invasive	Prolonged treatment, often requiring synthetic (alloderm) fascial closure.	Skin necrosis. Also have impending exposure of expander during expansion period	100
23	Staged	Luks	2009	2	Yes	-	Avoid long-term hernia; allows better, cleaner planes, more resilient abdominal cavity.	Some pressure on venous return of lower extremities, mild-moderate edema of scrotum/perineum	None	0

Table 2. Results of the questionnaire (continues).

Ref	Technique	Author	Year of publication	N patients	Same technique.	Changes of the technique	Advantage	Disadvantage	Complications	% hernia
37	Delayed/ staged	Nuchtern	1995	7/15	Yes	-	Early feeding and discharge, avoid mech. ventilation	Prolonged treatment	Sometimes the amnion ruptures and needs to be repaired.	0-50
38	Delayed closure	Beasley	1986	4	Mod	Application of tegaderm or opsite	Maintain sterile abdominal contents, controlled reduction. inspection of bowel for viability possible.	Difficult reduction when the neck is relatively narrow	ischemic small bowel in 1 patient	0
40	Delayed closure	Bax	1984	16	Yes	-	Slow return of the liver into the abdomen	Long hospital stay, infection, septicaemia, ventral hernia	Infection, sepsis	NA
41	Delayed closure	Wakhlu	2000	42	Yes	-	Easy, consistent results.	Long scar line	None	0
48	Delayed closure	Ledbetter	2006	22	Mod	Timing if closure	Easy, no cardiopulmonary compromise, shorter hospital, stay, early feeding	Prolonged time to heal, potential "hernia incarcartation".	Occasionally the sac will tear	0
46	Delayed closure	Pereira	2004	11	Yes	-	Utilization of the hernial sac, reconstruction of the original place the rectus abdominal muscles, without tension.	18 % IC admission	None	27
47	Delayed closure	van Eijck	2008	10	Yes	-	No ardiopulmonary compromise, restore of anatomical abdominal wall	None	Partial skin necrosis	0

intact and covering this with a mesh. Kapfer [10] has not treated other OC patients since the publication of his article.

Overall disadvantages of primary closure with a patch were the costs, eventual removal of a foreign material and poor skin quality. The mean herniation rate was 58% (range 0-100%, median: 50%). The mortality rate was only reported by Maksoud-Fihlo et al [6] and Kapfer and Keshen [10], which were 11% and 33% respectively. This mortality was not related to associated malformations but probably because of the operation.

2. Staged closure

The main advantage of staged closure given by the authors was early closure of the defect and minimal compression of the abdominal contents. All but one (which makes use of tissue expanders) of the staged techniques described a gradual reduction of the external peritoneal viscera with increasing intra abdominal pressure causing a slow improvement in peritoneal volume. After reduction of the viscera using a silastic silo (either leaving the amnion intact [14,19,21] or by resection [16,18] of the amnion), the fascia is closed with either prosthetic or absorbable patches, or skin flaps or grafts. Disadvantages of staged closure were as follows: occasional necessity for synthetic or biological mesh, prolonged muscle paralysis, mechanical ventilation and local infections. The mean incidence of postoperative ventral hernia was 18% (range 0-75%, median: 12%). No mortality was mentioned as postoperative complication except in the study by Nuchtern et al [37] who described a mortality of 27 %.

Adzick [19] modified the technique described by Shuster [29] by suturing 2 Teflon meshes to each fascia, after which sequential reduction was performed. Sigalet [22] reverted to using Surgisis instead of polyglycan mesh for eventual closure of the defect. Harjai [18] currently uses dual-meshes as well as the silastic patch originally advocated. The silastic patch, which Harjai and Krasna [14] sutured to the abdominal wall, is most often used as a temporary solution and is eventually removed.

The use of tissue expanders to create adequate enlargement of the peritoneal cavity was reported in 3 articles [15,20,23] and resulted in a mean incidence of ventral hernia of 33% (range 0-100%); (n=5 patients). No mortalities were reported. Although the advantage of these expanders is a controlled amount of expansion, a disadvantage is the frequent requirement of a synthetic substitute for closure of the defect. Van der Zee [20] no longer uses tissue expanders to enlarge the abdominal cavity. Kane [15] now places more tissue expanders with endoscopic assistance. Luks [23] still uses the original technique.

3. Delayed closure

The initial treatment of this group was nonoperative topical therapy leading to promote epithelialization of the OC and subsequent delayed closure of the abdominal wall [36-48].

The advantages of epithelialization mentioned by the authors were as follows: easy management and early feeding after birth [38,40]. In addition, the avoidance of increased abdominal pressure reduces the need for mechanical ventilation. Prolonged duration of healing with an increased hospital stay, daily dressings and wound infections were the drawbacks of this method [38,40]. Beasley [38] changed the management of the OC sac from topical mercurochrome to application of an Opsite dressing and external compression followed by surgical closure once the sac contents have been largely reduced [39]. Bax closes the defect after 6-12 month by primary closure of the fascia and skin.

The other delayed closure techniques [41, 46-48] come from recent articles with larger numbers of patients (n = 10-22 patients). No cardiopulmonary compromise was seen in delayed closure of giant OC. However, 18% needed admission to the intensive care unit postoperatively in the group treated by Pereira et al [46]. According to the authors, a shorter hospital stay and closure of the abdominal wall without tension was achieved. However, if the period of epithelialization is included in the hospital stay, the hospital stay is longer. No hernias were observed by Ledbetter [48] van Eijck et al [47], Beasley and Jones [38] and Wakhlu and Wakhlu [41], whereas Pereira described a ventral hernia in 27% of patients during follow up. Minor complications were reported, such as a tear of the sac by Ledbetter, and partial skin necrosis by van Eijck. Ledbetter was the only author to change the time for starting with external compression. Correction of ventral hernia was performed at approximately age 2 years by Pereira et al to ensure adequate thickness of the hernial sac for utilization as a substrate for the construction of the abdominal wall. Ledbetter combined primary epithelialization and gradual reduction of abdominal contents after stabilization of associated comorbidities, after which delayed repair was planned. Of these, 25% still required implantation of mesh for definitive closure. Wakhlu and Wakhlu also needed a mesh in 20 % of their cases whereas van Eijck et al only required temporary application of a small goretex patch in the cranial part of the wound in one patient and Pereira et al required no artificial patches for defect closure. Only Wakhlu and Wakhlu reported a mortality rate of 19%; in contrast there were no reported mortalities by the other authors.

Wakhlu [41] treated an exceptional number of 20 giant OC per year. The median number of minor and giant OC for all authors was 6 and 2 per year respectively, per author. The latter numbers correspond with middle sized and large pediatric surgical centers.

The authors who used operative treatment were asked if they had indications for initial non-operative treatment. Criteria for non-operative treatment mentioned by the authors were as follows: severe associated anomalies, cardiorespiratory insufficiency, giant OC, or primary closure, which was deemed impossible.

The current choices for preferred topical applications on the umbilical sac to prevent infections during the epithelialization of the OC are: Silvadine (n=6), povidone iodine (n=1), mercurochrome (n=2), flamazine (n=3), alchohol (n=1), Opsite (n=1), compression dressings (n=2), and mepefix (n=1). Seven authors gave no response or had no experience with nonoperative treatment.

DISCUSSION

This study gives an updated overview of data concerning the different treatment modalities of giant OC published during the last 4 decades. The main goal was to investigate if the treatment described by the authors is still used by these authors today, and if so why or whether, modifications were made over time or these techniques have become redundant. We focused on the closure technique specifically and not on the treatment of associated comorbidity such as gastroesophageal reflux and other problems.

The response rate for the questionnaire of 63% may be considered acceptable for this type of study.

Performing primary closure without using biodegradable or artificial substitutes to close the abdominal wall defect is rarely ever possible in truly giant OC. Using grafts for closure has the disadvantages of cost and the potential need for removal of the patches during follow-up. A high herniation rate of 58 % (mean) was reported, which suggests the need for hernia correction later in life. The use of biodegradable patches would seem to be a good option, however the chance of developing ventral hernias at the location where the scaffold has resolved is still unknown [4,10]. Which biodegradable patches are the most promising has to our best knowledge as yet not been established. However, current knowledge indicates the use of patches prohibits anatomical correction of the abdominal wall by bringing the fascial layers (and thus the muscular layers) together [46,47].

Staged closure consists of gradual reduction of the external peritoneal viscera with increasing intra abdominal pressure causing a slow increase of volume of the peritoneal cavity. Many different techniques have been described in literature to accomplish closure of this defect. Often, temporary applications of prosthetic patches are necessary to accomplish this task, and multiple operations are needed. However, the (mean) ventral hernial rate of 18 % after staged closure was considerably lower than in primary closure, but is still high. Of the authors, 50% have modified their technique after their initial publication.

The aim of tissue expanders is to create adequate enlargement of the peritoneal cavity without using the viscera as the source of expansion [15,20,23]. In this study, the patients in whom tissue expanders were applied can be regarded as a subgroup. The advantage

of tissue expanders is the controlled amount of expansion but the disadvantage is a herniation rate of 33 %. There is still little experience with this technique and long-term results are not available. The use of external traction devices may be worthwhile in case of prematurity and amnion sac rupture.

Delayed closure is performed after primary epithelialization of the OC has been achieved and the abdominal cavity has gained sufficient volume. The most favored topical agent for primary epithelialization was silver sulfadiazine, which is a safe and effective topical agent [36,37]. There is no evidence as to which agent is the best and should be used for epithelialization of the OC sac. No cardiopulmonary compromise was seen in the delayed closure group. The mean herniation rate was 9 % and the lowest compared to the other groups.

Almost half (42 %) of the authors, independent of the initial technique used (primary, staged, delayed), changed or stopped using their technique after the publication of their paper. However, all authors except one (van der Zee, [20]) revised their current treatment instead of changing to another.

The results of this questionnaire demonstrate the difficulty that pediatric surgeons have in determine the best management of giant OC. Furthermore, the low incidence of giant OC does not allow a prospective evaluation of the different treatment modalities for which larger cohort of patients would be necessary.

In general, there are 2 main treatment modalities: staged closure, with the advantage of early closure of the defect and the disadvantages of temporary use of artificial patches and multiple operations; and delayed closure after the abdominal cavity has gained sufficient volume, with the advantages of a low herniation rate and a single operation and the disadvantages of daily dressings during epithelialization and longer hospital stay.

The results of the questionnaire did not show a consensus for a generally accepted treatment method after more than 30 years of innovations in the management of patients with a giant OC.

Because of the lack of large numbers of patients and long-term follow-up studies currently, the choice in selecting the method of treating patients with giant OC is mainly based on training and personal experience of the surgeon and comorbidities of the patient.

Long-term results of the published techniques are needed, and based on these outcomes, randomized multicenter trials are recommended. Until then, we remain dependent on expert opinion.

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CHAPTER 6

Secondary closure of a giant omphalocele by translation of the muscular layers: a new method

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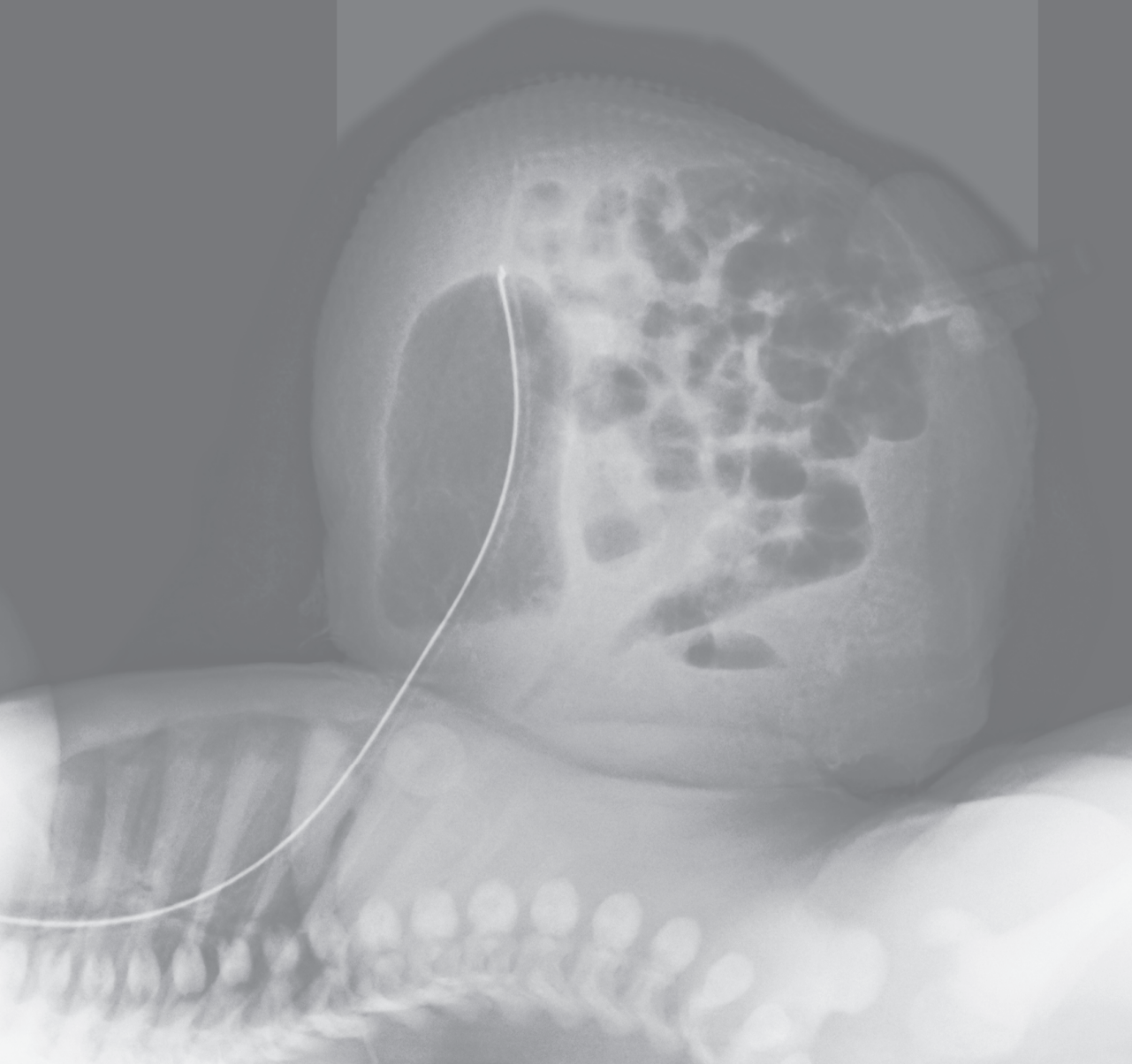
Pediatric Surgery Int. 2005; 21: 373-376



ABSTRACT

The current report describes a case of an infant girl with a giant omphalocele in whom a new surgical technique was used for closing the abdominal wall after epithelialization of the omphalocele for 16 months. The technique used was translation of the muscular layers of the abdominal wall. The functional and cosmetic results appear superior compared with other suggested treatments used for this abdominal wall defect.

INTRODUCTION

Omphaloceles are characterized by a central defect at the site of the umbilical ring. The size of this abdominal wall defect varies from 4 cm to 12 cm. The sac usually contains stomach and intestinal loops, and in half of cases, the liver is also included. Regardless of the defect's size, the abdominal musculature is normally developed, and the rectus muscles are intact at the margins of the defect. Treatment depends on the size of the defect; small and moderate omphaloceles are often primarily closed, but this is not feasible for giant omphaloceles. Giant omphaloceles are associated with a small, underdeveloped peritoneal cavity with a high degree of visceroabdominal disproportion that prohibits safe primary closure. Several techniques have been introduced in the last decades, such as closing with dura, silo prostheses, skin flaps, different kinds of meshes, and the use of tissue expanders [1–6]. The disadvantages of most of these techniques are the risk of a large ventral hernia and the use of prosthetic materials. In adults, reconstruction of large midline abdominal wall hernias that cannot be closed primarily poses a similar problem. Several techniques have been advocated to repair these defects. In 1990, Ramirez et al. developed a technique for reconstructing abdominal wall defects without the use of prosthetic material [7]. The technique is based on enlargement of the abdominal wall surface by translation of the muscular layers without compromising the innervation and blood supply of the muscles. This technique has been modified and used in larger series by others [8–11]. We used this technique for treating a giant omphalocele. This is the first case report that describes this technique in an infant with a giant omphalocele.

CASE REPORT

During the mother's first pregnancy, a prenatal ultrasound showed a giant omphalocele at 27 weeks of gestation. Because of a breech presentation combined with the prenatally diagnosed omphalocele, the infant was delivered by planned caesarean section at 39 weeks. Her Apgar score was 9 at 1 min, and birth weight was 2,720 g. The giant omphalocele had a diameter of 12 cm, and bowel and liver were included. The omphalocele was banded circumferentially with dry wraps and elastic bandages. The infant needed lowflow oxygen for 2 days. Because of a high insensible water loss, we started with an intravenous fluid infusion of 100 ml/kg/day at day 0 with increasing amounts of fluid in the following days. Except for a malrotation, there were no other associated malformations. An initial nonoperative management was decided upon because of the large defect and the ability of the amnion to support epithelial proliferation and migration from the skin edges. During the period of epithelialization (Fig. 1), three episodes of

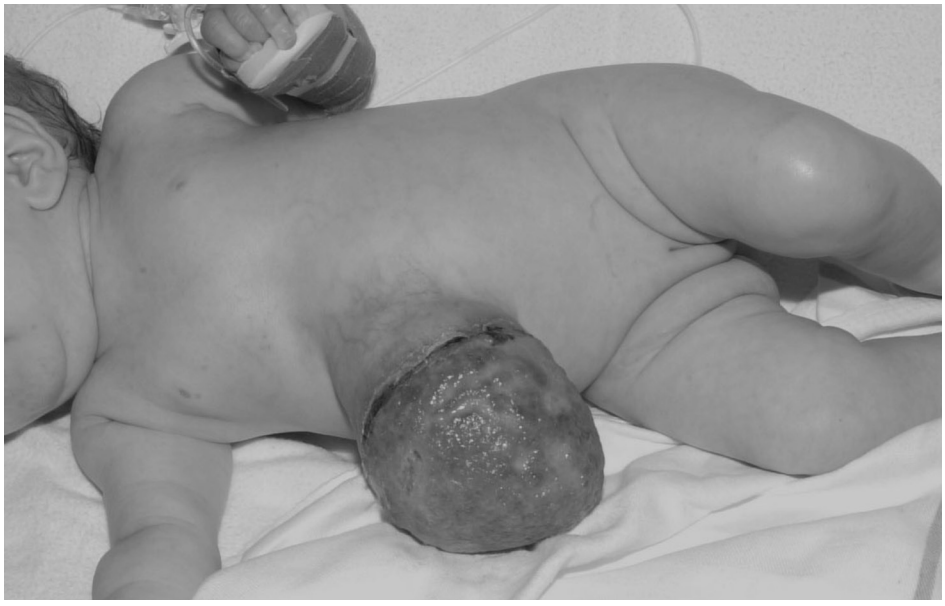


Figure 1. Giant omphalocele 2 weeks after birth, with partial epithelialization of the sac

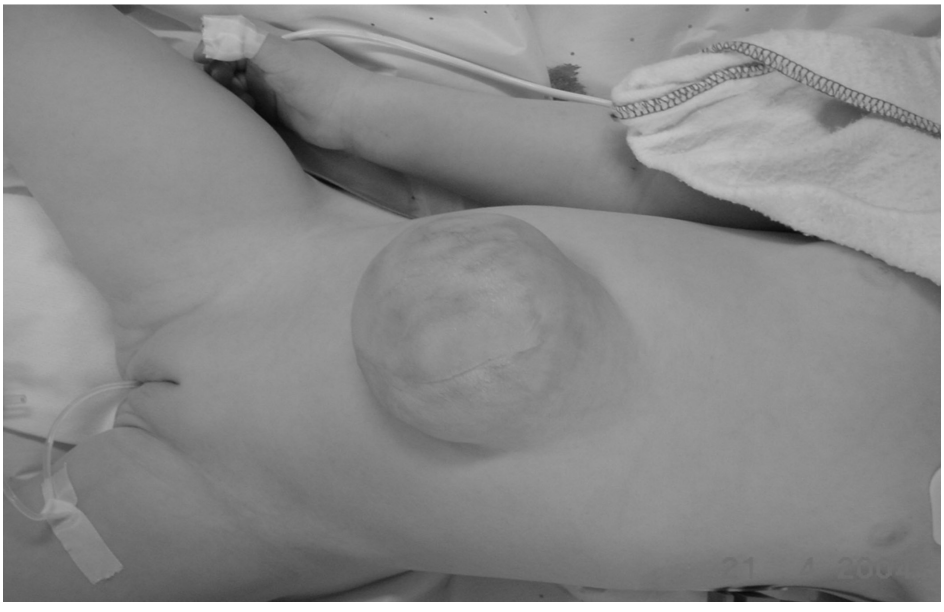


Figure 2. Ventral hernia of the abdominal wall caused by a giant omphalocele, after epithelialization at 16 months, just before surgical treatment

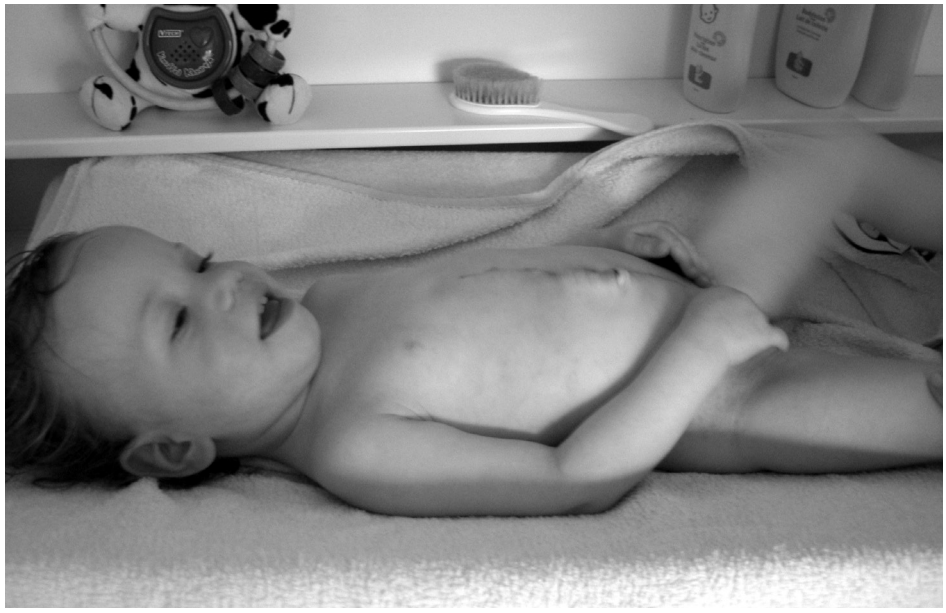


Figure 3. Results after translation of the muscular layers 2 months after operation

sepsis occurred, which were treated with antibiotics. Tube feeding was started on day 3, and full enteral (tube) feeding was reached at day 7.

When the omphalocele was fully epithelialized at 2 months, the baby was discharged; her weight was 4,200 g. Closure of the abdominal wall was planned for the age of 16 months; at that time, the child weighed 8.2 kg (Fig. 2). A translation of the abdominal muscular layers on both sides was performed, and the nonrotation was operated by dividing duodenum bands and broadening the mesentery of the small bowel; an appendectomy was also done. Two subcutaneous drains to prevent seroma were placed, and an umbilicus was created. Postoperatively, the child was treated with intravenous morphine for 1 day, and feeding was started on day 2. She was discharged on postoperative day 6. After 2 months of follow-up at the outpatient clinic, the abdominal wall proved to be sufficient, and the wounds had healed by primary intention (Fig. 3).

SURGICAL TECHNIQUE

The technique used is based on enlargement of the abdominal wall surface by translation of the muscular layers without compromising the innervation and vascularization of the muscles (Fig. 4). The arterial blood supply of the abdominal wall is mainly via the intercostal arteries and the perforating branches of the epigastric artery. The abdominal

cavity is entered via an incision just lateral from the scar tissue of the skin on the omphalocele. The liver and bowels are dissected free from the skin. Thus, the lateral border of the rectus abdominal muscle can be identified properly, from the inside of the abdomen. The skin and subcutaneous fat are dissected free from the anterior rectal sheath and the aponeurosis of the external oblique muscle to about 3– 5 cm lateral of the lateral border of the rectus sheath. The aponeurosis of the external oblique muscle is incised 1-2 cm laterally of the lateral border of the rectus ab- dominis muscle. The aponeurosis of the external oblique muscle is transected longitudinally over its full length.

Transection includes the muscular part of the external oblique muscle on the thoracic wall. In this way, the rectus abdominis muscle can be shifted medially at a maximum in the upper abdomen. The external oblique muscle is separated from the internal oblique muscle in the avascular plane between both muscles up to the midaxillary line. Mobilization is essential because the fibrous interconnections between both muscles prevent optimal median shift of the rectus abdominal muscle. The abdominal wall is closed in the midline with a running suture of a nonabsorbable or slowly absorbable suture material, taking big "bites" of fascia. If further mobilization of the rectus abdominis is warranted, the posterior rectus sheath can be transected longitudinally over its full length. Suction drains are placed subcutaneously, and the subcutis and skin are closed.

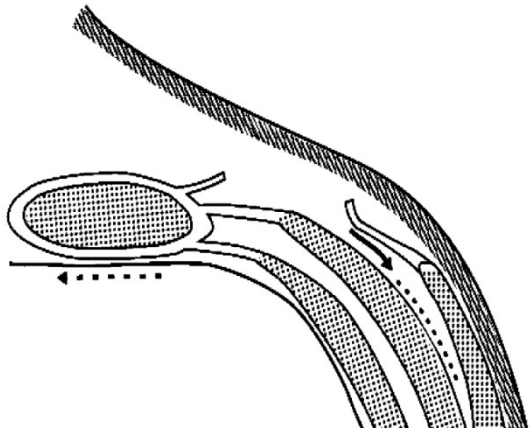


Figure 4. Schematic drawing of the separation of the external oblique muscle from the internal oblique muscle in the avascular plane between both muscles up to the midaxillary line

DISCUSSION

Staged repair of a giant omphalocele is in many centers the treatment of choice, but final closure still gives problems with the use of prosthetic materials, plural operations, or tissue expanders to restore abdominal wall integrity to decrease the intra-abdominal pressure. A residual ventral hernia often results. Collagen-based biomaterials have been

applied for abdominal wall defects in adults and children, but in the long term, degradation of the patches may result in reherniation [12].

De Ugarte et al. reported a case with tissue expanders in the abdominal wall instead of the intra-abdominal cavity. Between the internal oblique and transverse abdominis muscles, a space was created [6]. This was advocated to be a safe and anatomically logical approach for reducing the degree of visceroabdominal disproportion. However, the neurovascular bundle runs between the internal oblique and the transverse muscle and may easily be damaged, resulting in denervation of the abdominal wall muscles. With the component separation technique, the abdominal wall surface is enlarged by translation of the muscular layers without damaging the innervation and blood supply of the muscles. However, because the perforating branches of the epigastric artery are transected, the skin's blood supply is at risk because it then solely depends on the intercostal arteries and branches of the pudendal artery. Furthermore, it is essential to properly identify the plane between the internal and the external oblique muscle because transection of the internal oblique muscle may result in abdominal wall rupture, as the transverse muscle is too weak to resist the intra-abdominal pressure. The reherniation rate varies from 0–30% in adult series. Most herniations are located in the upper abdomen and need no operation. How this will develop in children operated for a giant omphalocele with this technique will be further studied.

Despite these pitfalls, the component separation technique is an outstanding procedure for closing the skin-covered giant omphalocele. It provides a way to enlarge the abdominal cavity with a cosmetically pleasing and strong abdominal wall with no prosthetic materials and a normal abdominal cavity; moreover, these results can be achieved in only one surgical procedure.

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CHAPTER 7

Closure of giant omphaloceles by the abdominal wall Component Separation Technique in infants

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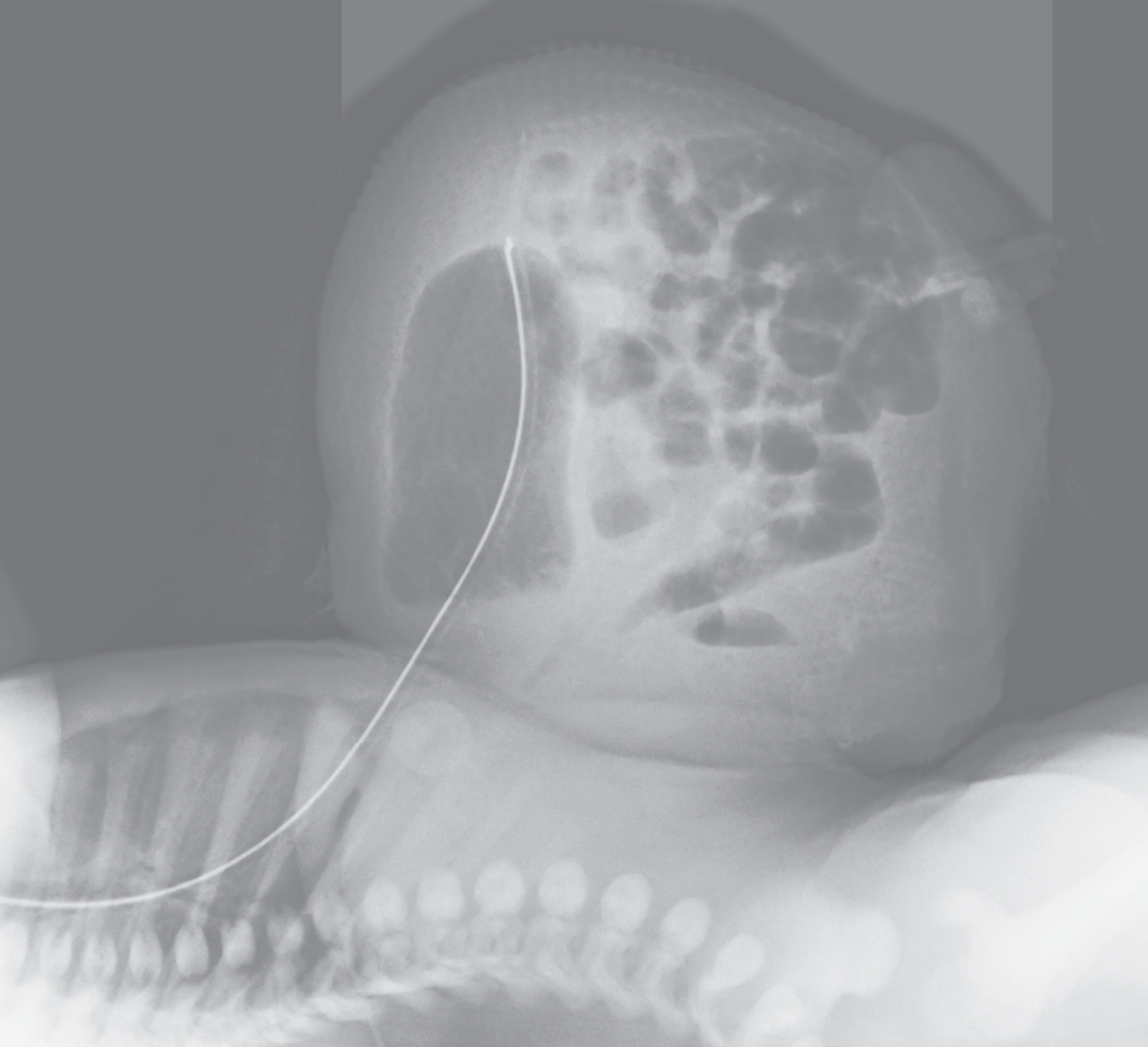

ABSTRACT

Background: Several techniques have been described to repair giant omphaloceles. There is no procedure considered to be the criterion standard worldwide. The aim of the present prospective study was to analyze the early and late results of secondary closure of giant omphaloceles using the Component Separation Technique (CST) in infants.

Methods: From January 2004 to January 2007, 10 consecutive pediatric patients with a giant omphalocele were treated at our department. Initially, patients were treated conservatively. After epithelialization of the omphalocele, the abdominal wall was reconstructed using CST. Patients were monitored for complications during admission, and all patients were seen for follow-up.

Results: Component Separation Technique was performed at median age of 6.5 months (range, 5-69 months). The median diameter of the hernia was 8 cm (range, 6-9 cm). There was no mortality. The postoperative course was uneventful in 7 patients. Complications were seen in 3 patients (infection, skin necrosis, and haematoma). Median hospital stay was 7 days. After median follow-up of 23.5 months (range, 3-39 month), no reherniations were found.

Conclusions: The CST is a safe 1-stage procedure for secondary closure in children with a giant omphalocele without the need for prosthetic material and with good clinical outcome.

INTRODUCTION

Giant omphalocele is defined as a congenital periumbilical abdominal wall defect containing the liver and having a diameter of at least 5 cm [1-3]. It is associated with an underdeveloped abdominal cavity and a high degree of visceroabdominal disproportion that prohibits save primary closure. These factors determine the decision process of treatment. Primary closure is often impossible and may lead to hypotension, decreased cardiac output, and respiratory failure. Operative treatment of these abdominal wall defects is still challenging for paediatric surgeons, which is seen in the broad range of therapies described in literature such as bridging the defect with dura mater, alloderm grafts, silo prostheses, skin flaps, prosthetic meshes, 2 bipedicled flaps, the use of tissue expanders, and the delayed staged repair [2,4-12].

The disadvantages of most techniques are the risk of developing a large ventral hernia, multiple operations and the use of prosthetic materials. However, staged closure can carry the same risk as primary closure by placing the abdominal contents under pressure [2].

Accordingly, nonoperative treatment by primary epithelialization of the omphalocele is a good alternative although there is a higher sepsis frequency, and ventral hernia correction is needed later in life [7]. In a previous case report, we reported a new technique for secondary closure of the abdominal wall in a child with a giant omphalocele [13]. The technique is based on enlargement of the abdominal wall surface by translation of the muscular layers without compromising the innervation and blood supply of the muscles [14].

The current prospective study describes this new technique in detail and presents the first results with follow-up in 10 consecutive infants with giant omphalocele.

PATIENTS AND METHODS

The case record forms of 10 consecutive children (4 boys and 6 girls) with a giant omphalocele in whom a reconstruction of the abdominal wall was performed between January 2004 and January 2007, were analysed. Giant omphalocele was defined as abdominal wall defect larger than 5 cm, containing a major portion of the liver and a large disproportion of the abdominal cavity. After birth, all neonates were treated in conformance with the Dutch consensus protocol on abdominal wall defects [15]. In short, after birth, the omphalocele was covered with dry sterile dressings. After 1 to 2 weeks, the omphalocele was sufficiently strong to allow a daily bath. Hospital discharge occurred when the patient showed good physical condition, and the omphalocele was (almost) fully epithelialized. Hereafter, definitive closure of the abdominal wall was planned, when

the disproportion between the abdominal cavity and the omphalocele was sufficiently reduced. This occurs mostly within the first 6 months and is based on clinical observation. All patients were operated on upon general anaesthesia and received cefazolin 25 mg/kg and metronidazole 8 mg/kg intravenously as prophylaxis. Postoperatively, all patients received adequate analgesic medication by epidural catheter or by continuous intravenous morphine.

Surgical technique [16]

The component separation technique (CST) is based on 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 is mainly via the intercostal arteries and the perforating branches of the epigastric artery and branches of the pudendal artery.

The patient lies in a supine position. After incision of the skin just lateral of the scar tissue on the omphalocele, the abdominal cavity is entered. The liver and bowels are dissected free from the skin and ventral abdominal wall. In this manner, the lateral border of the rectus abdominal muscle can be identified properly from the interior of the abdomen (Fig. 1a). The skin and subcutaneous fat are dissected free from the anterior rectal sheath and the aponeurosis of the external oblique muscle, to 3 to 4 cm lateral

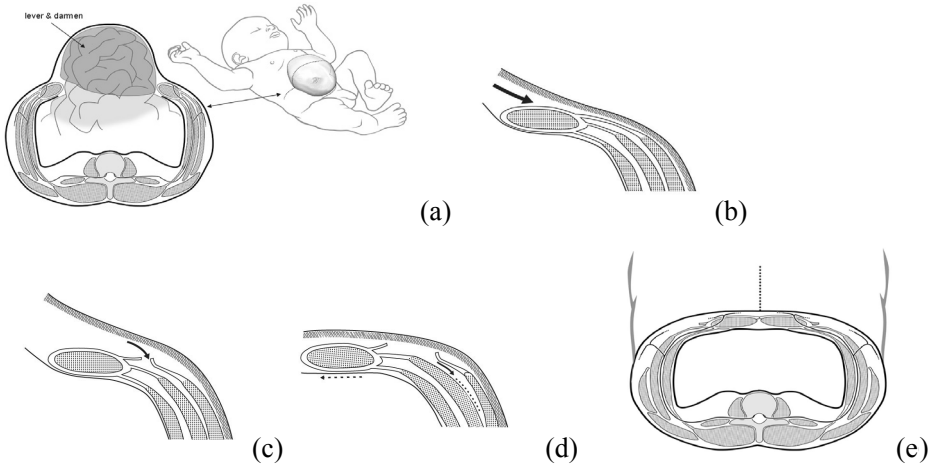

Figure 1. The description of the components separation technique in children with a giant omhalocele:
(a) a new born after epithelialization of the giant omphalocele.
(b) Dissection of the skin and subcutaneous fat from the abdominal wall muscles.
(c) Incision of the aponeurosis of the external oblique muscle 1 cm lateral of the rectus sheath.
(d) Separation of the external and internal oblique muscles.
(e) After closure of the abdomen, the external oblique muscle is retracted laterally.

of the rectus sheath (Fig. 1b). The aponeurosis of the external oblique muscle is incised approximately 1 cm of the lateral border of the rectus abdominis muscle (Fig. 1c).

The aponeurosis of the external oblique muscle is transected longitudinally over its full length. Transection includes the muscular part of the external oblique muscle on the thoracic wall. The attachment to the ribs must be dissected free to mobilize the rectus abdominis muscle to a maximum. Subsequently, the external oblique muscle is separated from the internal oblique muscle in the avascular plane between both muscles up to the midaxillary line (Fig. 1d). Mobilization is essential because the fibrous interconnections between both muscles prevent optimal median shift of the rectus abdominal muscle. In this way, the rectus muscle can be shifted medially 5 cm at each side. The abdominal wall is closed in the midline with a running suture of a nonabsorbable or slowly absorbable suture material (PDS 2.0). The subcutis and skin are closed, and an umbilicus is created. After closure of the abdomen, the external oblique muscle is retracted laterally (Fig. 1e).

RESULTS

The abdominal wall of 10 children with a giant omphalocele was reconstructed with CST (Table 1). The first patient underwent CST at the age of 14 months. The second and oldest patient was 69 months, with an uncorrected ventral hernia at the beginning of this study. The following patients were operated between 5 and 10 month after birth. Likewise, time of operation could depend on associated disorders or logistics. Eight of the 10 patients had other congenital anomalies: cardiovascular disorders (n=5), urogenital disorders (n=4), tethered cord (n=1), chromosome 9p-syndrome (n=1), congenital dysplasia of the hip (n=2) and vertebral anomalies (n=1). Two patients were operated on short after birth: one because of a ruptured omphalocele and the other for a midgut volvulus 4 days after birth. In both patients, only skin covered the defect.

In 8 patients, the omphalocele epithelialized in a mean period of 2 months. Patients were operated on after a median period of 6.5 months (range, 5-69 months) after birth. At the time of CST, the median diameter of the defect was 8 cm (range, 6 - 9 cm), which was, measured peroperatively. The abdominal diameter at the umbilical level showed little variation among the patients (range 36-41 cm) and was not correlated with patient age and size. The median operation time was 157 minutes (range, 120-302 minutes). The operation of 302 minutes was induced by concomitant procedures, such as extensive adhesiolysis, resection of Meckel's diverticula, Nissen fundoplication, and application of gastrostomy catheter. Other concomitant procedures were developing of malrotation and appendectomy (n=8), correction of a hydrocele (n=1). In one patient, the abdominal wall defect could not be closed during CST procedure because of excessive tension during closure of the midline. The residual defect was bridged by a small e-PTFE patch

Table 1. Patients characteristics with Giant OC at time of secondary closure (n = 9).

Patient no	Sex	Associated anomalies	Age (mo)	Ø Umbilicus (mm)	Length (cm)	Width (cm)	Operation time (min)	Enteral feeding (d)	Hospital stay	Complications
1	F	tethered cord, vertebral anomalies, hip dysplasia, mono- kidney left	69	41	10	6	121	1	6	No
2	F	Open foramen oval	14		12	9	120	3	7	No
3	M	Multicystic dyplastic kidney right, VUR	6	36	9	8	182	1	7	No
4	M	Chromosome 9p-syndrome	5	39	10	6.5	120	2	11	No
5	F	None	6	38	11	6	302	5	23	Infection
6	M	Macroglossy, VUR, GERD	8	38	11	6	144	1	6	No
7	F	mild dysmorph characterise	5	37	8	6.5	188	1	5	No
8	M	VSD	6	37	11	8.5	225	6	13	Hematoma
9	M	VSD	7	40	8	8	165	5	10	Partial skin necrosis
10	M	None	10	41	8	8	150	3	6	No

F indicates female; M, male; VUR= vesico-urethral reflux; GERD= gastro-oesophageal reflux disease

(Goretex), which was removed after period of 4 weeks because of infection. The abdominal wall defect was closed during the same procedure. The median blood loss was 75 ml (range 35-340 mL.). The wide range in blood loss was due to extensive concomitant procedures as described above. In one case, there was perioperative bleeding during adhesiolysis of the liver, with a blood loss of 340 mL.

None of the patients died. The postoperative course was uneventful in 7 patients. Three patients had complications: one patient had a wound infection and a central venous line sepsis, one patient had a skin necrosis in the midline with a diameter of 1 cm, and the other patient had a hematoma which was relieved by needle aspiration, which were successfully treated. The median hospital stay was 7 days (range, 5-23 days). The maximum of 23 days was for one patient with feeding, neurological and social problems. The postoperative recovery of this particular patient was only 7 days. Patients were seen at the outpatient clinic after a median period of 23.5 months (range, 3-39 month). At physical examination no recurrent hernias were found.

DISCUSSION

Component separation technique is a promising technique for repairing giant omphaloceles without the use of prosthetic material.

Regardless of the size of the defect in neonates with an omphalocele, the abdominal musculature is present. The rectus abdominis muscle and the rectus sheath are normally intact. This gives the opportunity to use CST for repair of the abdominal wall in these patients, a technique that was introduced by Ramirez et al [14] in 1990 to repair large midline abdominal wall defects without the use of prosthetic material. The technique is described in detail by Bleichrodt et al [16], and the results of CST in adult surgery are recently reviewed [16,17]. In adult surgery, wound complications occur in 33% of patients and reherniation rates in 30% of patients. Common complications are hematoma, seroma, wound infection, and skin necrosis. The creation of a very large wound surface predisposes to the development of these wound healing disturbances. Moreover, transection of the perforating branches of the epigastric artery interferes with the blood supply of the skin of the ventral abdominal wall because it then solely depends on the intercostal arteries and branches of the pudendal artery. This is of utmost importance in patients in whom the intercostals are not intact as a result of former surgery, for example, a subcostal incision or stoma placement. In these cases, the epigastric perforators must be spared.

The results of our pediatric patient group illustrate the safety and applicability of this technique, although we also observed minor complications such as hematoma, wound infection and small skin necrosis.

Management of giant omphaloceles remains a challenge for paediatric surgeons because of the underdeveloped abdominal cavity, a high degree of visceroabdominal disproportion, and a large abdominal wall defect. The ultimate goal in the treatment of giant omphalocele is primary closure of the abdominal wall defect.

However, reduction of the herniated organs in a 1-stage procedure may lead to high abdominal pressure with compression of the inferior vena cava, liver, and suprahepatic veins and often leads to multi-organ failure and respiratory impairment. One stage closure in giant omphalocele is often impossible because of the reasons mentioned above. Some techniques have been described for repairing the abdominal wall defect with biodegradable materials or with prosthetic materials [9]. Only small series have been described with poor results resulting in high morbidity and mortality, and (recurrent) ventral hernias, and without the normal anatomy of the abdominal wall being corrected during these procedures [9,18-20].

To minimize the morbidity and mortality, many centers have chosen stage repair of giant omphaloceles as the treatment of choice; however, final closure still gives problems with the use of prosthetic materials, multiple operations, or tissue expanders to restore the abdominal wall integrity to decrease the intraabdominal pressure. In 1948, stage closure by advancing skin flaps to cover the defect without opening the amnion sac was firstly described, resulting in a ventral hernia, which required correction later in life [8]. Some years later, sequential reduction of herniated organs using a silastic silo was introduced [4]. However, this may cause fascial infection, and the sutured margin loses integrity, making it difficult to achieve fascial closure. Likewise, location of the liver in the defect makes it difficult to close fascia even after successful visceral reduction [4]. Schuster [11] modified the technique by using a Prolene mesh with sequential reduction of the sac content and amnion inversion [10]. They reported a low infection rate. However, 5 sequential silo reductions were needed with 3 reductions under general anaesthesia. Another stage repair technique is the use of intraperitoneal tissue expanders (IPTE) to increase the abdominal domain to the point that viscera could be reduced in one operation [5,21]. Expansion of the abdominal cavity can increase intraabdominal pressure, impair respiratory function, and cause visceral ischemia. A technique of placing tissue expanders in the abdominal wall instead of the intraperitoneal cavity have been reported [6], whereby a space between the internal oblique and transverses abdominal muscles is created. This was declared to be a safe and anatomical logic approach for reducing the visceroabdominal disproportion. However, the neurovascular bundle runs between the internal oblique and transverse muscle, and can be easily damaged, resulting in denervation of the abdominal wall muscles on theoretical grounds.

To improve the complication rate and reduce multistage operations, we have introduced delayed closure after primary epithelialization of the giant omphalocele. Nonop-

erative management has the general advantage of completely avoiding surgery in the newborn. This approach allows stabilization of underlying comorbidities.

Different delayed closure techniques are reported [2,3,22,23], but there are a number of advantages for using the CST. First, avoiding the use of foreign material results in lower infection rates and reduces the formation of dens adhesions. Especially in contaminated conditions, the CST is extremely useful. Second, the CST has the advantage of minimal advancing skin flaps and thus reducing the infection risk. Third, reconstruction of the normal anatomy of the abdominal wall is achieved and gives excellent functional and cosmetic results. Lastly, in most cases, it is a 1-stage procedure.

The wide variation in surgical timing in our limited patient group is mainly owing to the first 2 patients who were operated on at 14 and 69 months. Thereafter, we operated between 5 and 10 month after birth depending on logistics, time of referring, and associated disorders. Currently, we prefer to correct the abdominal wall with the CST between 4 and 6 months because of the motoric development of the child and based on reaching the optimal ratio between omphalocele and abdominal cavity in this period.

We conclude that this new technique in giant omphaloceles is a safe procedure with excellent cosmetic results. Further research is warranted with long-term observation to determine the long-term effects on herniation and functional aspects.

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CHAPTER 8

Functional, motor development, and long-term outcome after the component separation technique in children with giant omphalocele

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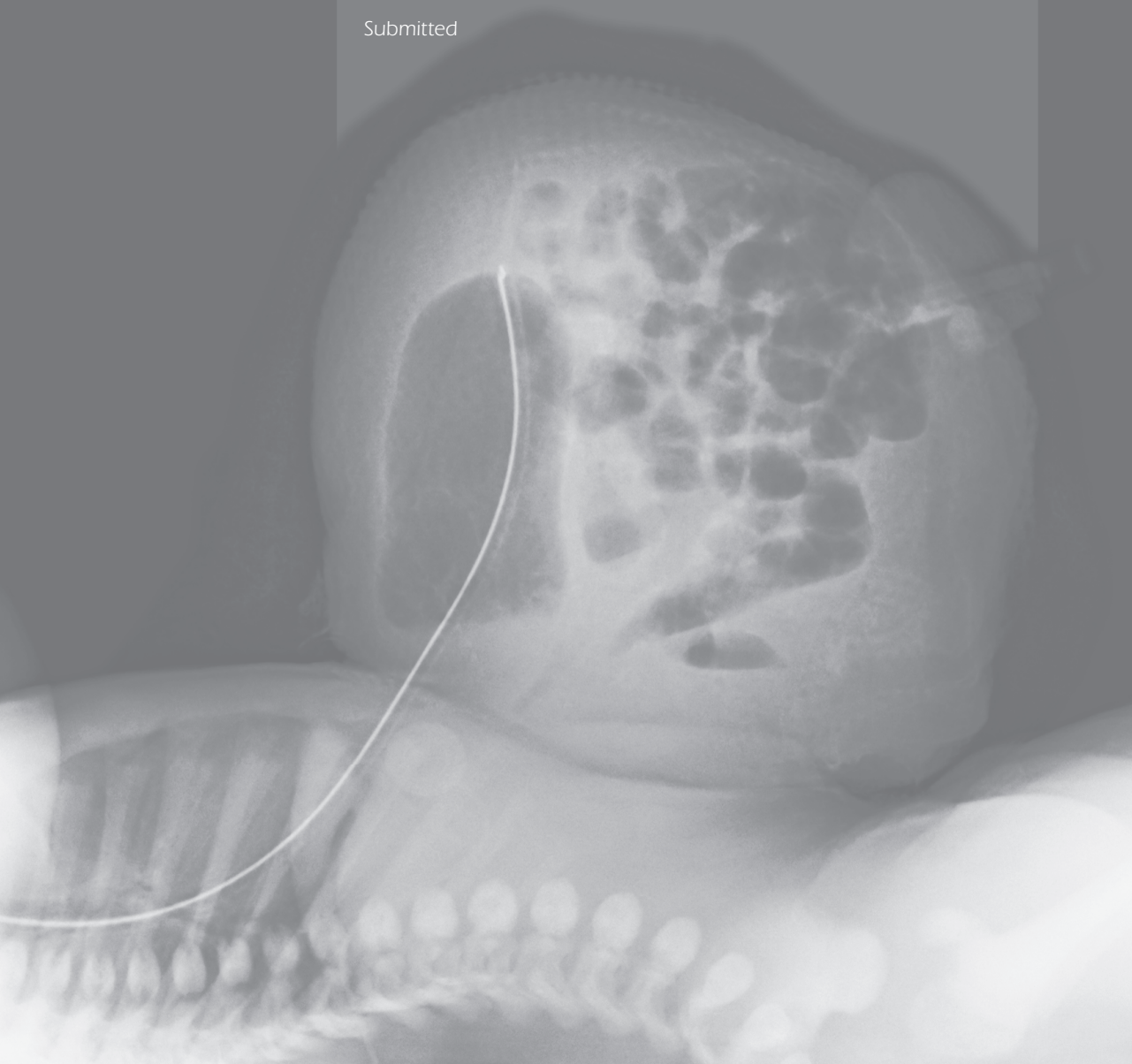

ABSTRACT

Background: The objective of this study was to evaluate the long-term functional and motor development and abdominal muscle quantity in children operated on for giant omphalocele (GOC) with the Component Separation Technique (CST).

Material and Methods: Between January 2004 and July 2007, CST was applied in eleven consecutive infants with GOC. Eight underwent ultrasound of the abdominal wall and muscles; assessment of functional and motor development using the Movement Assessment Battery for Children, 2nd edition (M-ABC-2); and an observational physical examination focused on possible abnormalities in stature and movements related to GOC. Findings were compared with those in age-matched controls. The parents filled in a questionnaire on the children's functioning in daily life.

Results: The median age at evaluation was 59 months (range, 42-141 months) with a median time of follow-up of 54 months (range, 38-84 months). Ultrasound of the abdominal wall muscles showed normal muscle thickness, including the external oblique muscle. In seven of the eight children, a rectus diastasis was seen without any protrusion. The functional and motor development was within the normal range (M-ABC-2) and stature and motor coordination did not differ from those in controls.

Conclusions: After four and a half years these children show normal thickness of all abdominal wall muscles, and motor function within the normal range, despite a rectus diastasis. The Component Separation Technique seems to be a promising closure technique for GOC.

INTRODUCTION

Giant omphalocele (GOC) is a congenital midline abdominal wall defect with herniation of abdominal contents, including the liver, into a membrane-covered sac. Regardless of the size of the defect, the abdominal musculature is present. The rectus abdominis muscle and the rectus sheath are normally intact but lateralized. This makes it possible to repair the abdominal wall with the so-called component separation technique (CST), i.e. after primary epithelialisation of the omphalocele [1]. This technique was introduced by Ramirez et al. [2] in 1990 to repair large midline abdominal wall defects in adults without the use of prosthetic material. It is based on enlargement of the abdominal wall surface by translation of the muscular layers without compromising the innervation and blood supply of the muscles. First, the aponeurosis of the external oblique muscle is incised approximately one centimeter of the lateral border of the rectus abdominis muscle. Next, the aponeurosis of the external oblique muscle is transected longitudinally over its full length. Transection includes the muscular part of the external oblique muscle on the thoracic wall. Finally, the external oblique muscle is separated from the internal oblique muscle in the avascular plane between both muscles up to the midaxillary line. As a result, the external oblique muscle lays lateral to the other abdominal muscles. We have been applying CST in children with GOC and the short-term results were promising. Here we report a long-term follow-up study in these patients, focussing on quantity of the abdominal muscles, and the functional and motor development.

PATIENTS AND METHODS

Between January 2004 and July 2007, CST was applied in eleven children with GOC. We invited all parent couples to participate in this study with their children. Nine parents gave informed consent. One patient and his parent were excluded due to his comorbidities. The following tests and assessments were performed:

1. Questionnaire

The parent(s) completed a questionnaire concerning their child's functional and motor development and possible disabilities and participation problems in daily life (table 1).

2. Muscle and abdominal wall ultrasound

The children underwent a muscle ultrasound study with a Zonare ultrasound device (ZONARE Medical Systems, USA) with a linear 10 to 5 MHz broadband transducer. They were placed in a supine position and relaxation of the muscles was ensured by monitoring the ultrasound image. Measurements were made of the rectus abdominis muscle

Table 1. General questionnaire

1. My child is going to: - Day care - Primary school - Special school - Secondary school
2. My child participates at gym at school: yes/no
3. Frequency gym: 1/2/3 / or more times a week
4. My child has some limitations during gym: yes/no
5. My child has (had) swimming lessons: yes, and certificate A/B/C/no certificate, /no
6. My child has no restriction during swimming lessons: yes/no
7. My child is active in sports: yes /no
8. My child has no restriction during sports: yes/no
9. My child has no problem to: - lay in supine position: yes/no - lay ine position: yes/no - lay on the right side: yes/no - lay on the left side: yes/no
10. My child has no problems in: - running: yes/no - walking up the stairs: yes/no - cycling: yes/no - trampoline jumping: yes/no
11. My child sleeps most of the time on the: - supine - left side - right side - prone - alternating
12. My child needs some adjustments for sitting: No/ yes, for instance:
13. My child has frequently (at least once a week) one or more complaints: - pain - fatigue - nausea - dizziness - sensitive scar - other: - no complaints
14, My child is often ill: - yes, at least every day - couple of days a week - once a month - no, rare
15. My child plays a musical instrument: no/yes, namely:

at an anatomically defined position halfway between the xyphoid bone and the pubic bone. The external and internal oblique muscle and transverse abdominis muscle were measured at the same level as the rectus abdominis but shifted sidewards to the anterior axillary line. Three images were made of each structure. Between each measurement the child was allowed to move and the transducer was repositioned afresh. Muscle thickness

was determined with electronic calipers between the superficial and deep part of the fascia surrounding the muscle. The distance between the medial side of external oblique muscle and the rectus abdominis muscle was measured to evaluate the long-term effect of the separation of the external and internal oblique muscle.

The same ultrasound device was used to detect any ventral hernia or rectus diastasis. A rectus diastasis was defined as space between the rectus abdominis muscle, without protrusion of visceral organs during valsalva maneuver. If a ventral hernia or rectus diastasis was identified, the size was measured. The presence was verified during physical examination.

Analysis of muscle ultrasound results

Muscle thickness was compared to normal values established in 2003 in 45 healthy children between 0 and 16 years (24 boys, 21 girls) [3]. Muscle thickness was transformed into z-scores, obtained by subtracting the normal value from the measured value and then dividing the difference by the SD of the normal value. In effect the z-score expresses the number of standard deviations that the measured values differs from normal. A one-sided t-test was performed to evaluate if muscle thickness was significantly lower than normal. A paired t-test was performed to investigate left to right differences. The level of significance was determined at a p-value below 0.05.

3. Functional and Motor development

All children were assessed by one pediatric physical therapist (LV), who administered the Movement Assessment Battery for Children, 2nd edition (M-ABC-2) [4, 5] and performed an observational physical examination. The examination focused on possible abnormalities in stature and movements related to GOC, including specific skills regarding abdominal muscle function, muscular range of motion in the abdominal and lower extremity regions and qualitative observation of the gross motor performance.

The M-ABC-2 test assesses both gross and fine motor performance, and is the most frequently used standardized test to identify motor problems in children from three to sixteen years of age [4]. The M-ABC-2 is the updated version of the original M-ABC, developed in 1992 [6]. It has good reliability [7-11] and concurrent validity [4, 12]. The child performs eight tasks, divided into three categories: manual dexterity (MD), aiming and catching (AC; ball skills), and balance (BAL) resulting into three component scores and a total test score, which are based on a distribution with a mean of 10 and a standard deviation (SD) of 3 (the so-called 'standard score' for each score). Scores exceeding two standard deviations below mean (<4) point at significant motor coordination difficulties that may require intervention; scores between one and two standard deviations below mean (≥4 & <7) point at a risk of motor coordination difficulties, and are an indication for periodical re-assessment [4]. Raw scores and Component scores are calculated for the three categories separately and for the Total Score.

Physical examination was in six parts:

a. Alignment of the trunk:
Optical determination of (a)symmetry in two planes (in standing and sitting positions).

b. Physical observation of stature in standing and lying positions and testing range of motion (ROM) of the spine, hips and the length of the hamstrings, and calf muscles:
- Stature in standing and in lying position was observed with special focus on the presence of asymmetries;
- Bending and rotating the trunk in all directions was observed and judged as normal when presented as symmetrical, unrestricted range of motion according to the reference values of Bernbeck et al. [13]. Secondly, reaching knee(s) at nose tip was tested and the distance was measured in centimeters.
- A combined ROM of the spine and long lower extremity muscles, especially the hamstrings and calf muscles, was tested with the "Sit & reach test". In a sitting position with extended knees, the child reached with the fingertips to a standardized box with measuring scale (cm). This is a reliable test at six years of age [14-19].

c. Functional activity of the abdominal muscles:
- Total number of sit ups in 30 seconds: in supine position with bended knees, both feet on the surface, and both legs fixed by physical therapist, the child comes to sitting position with the arms reaching forwards [15-17, 19].
- The time needed to raise both extended legs simultaneously ten times, while lying in supine position; reference norms up from nine years of age are available [14, 18].
- To test the oblique abdominal muscles the child, lying in supine position with bended knees, and both feet on the surface, made lateral movements with both bended legs simultaneously, alternating five times to both sides. Performance was measured on an ordinal score based on the degree of sideward rotation of the knees: 70-90 degrees: "good" (2); 40-70 degrees: "fair" (1); 0-40 degrees: "bad" (0).

d. Tightness of the stomach:
The child inflated and deflated the belly to the extreme, and performance was scored on an ordinal scale: "not possible" (0); "slightly possible" (1); "almost normal" (2); "normal" (3).

e. In- and expiration excursion of the chest:
The circumferential difference between maximal inspiration and maximal expiration was measured at xiphoidal level in centimeters.

f. Fundamental motor skills possible affected by GOC:
A qualitative observation was directed at fundamental motor skills: movements were judged as normal when performed symmetrically and as abnormal when asymmetry was observed. The following motor skills were observed: walking, running, walking on tiptoes and heels, hopping, walking stairs, standing on knees, standing on knee and foot, and crouching.

Analysis
The ultrasound results and the M-ABC-2 results are presented as standardized scores. Because of the small sample and the lack of age-related reliability and validity of the other outcome measurements (specific skills), these outcomes are compared with those for age-matched healthy controls for each child. Differences in outcome were tested with non-parametric tests.

RESULTS

Two of the 11 parent couples refused to participate in this study because they expected a high inconvenience for their child. One child with chromosome 9p-syndrome was excluded because he suffered from scoliosis and trigonocephaly. Thus, eight of the eleven children participated in this study; four boys and four girls. The children's median age at time of examination was 59 months (range, 42-141 months) and median time of follow-up after operation of 54 months (range, 38-84 months). One of the eight children (P8) had a congenital tethered spinal cord syndrome and underwent several surgical corrections. Two children had undergone conservative treatment of congenital dysplasia of the hip, but did not show any disability.

1. Questionnaire

Eight parent(s) completed a questionnaire on the child's functional and motor development and any present disabilities. Seven children attended primary school, and one attended day care (P1). Seven joined school gymnastics class once or twice a week. One of the seven children was physically restricted because of hypermobility disorder (P6). Five children took swimming lessons, and two of them had already obtained the first certificate at time of this study (P7-P8). Two children had some difficulty in swimming, due to muscle weakness (P6) and inability to perform breast crawl (P8). The other three were still too young to take swimming lessons (P1-P3). Three children practised some sport (gymnastics, swimming; P6-P8). There were no motor problems as reflected by specifically preferred (sleeping) positions. None of the children showed any difficulty in running, walking, cycling and trampoline jumping. The child with the hypermobility

disorder (P6) needed some seat adjustments at school. In general the children were healthy and rarely ill (less than once a month).

2a. Muscle ultrasound

In the controls, thickness of all examined muscles appeared to increase with age during childhood (table 2). Ultrasound examination of the study children's abdominal wall showed normal thickness of all muscles including the external oblique muscle (table 3). There was no significant left to right differences. The mean distance from the external oblique muscle to the lateral side of the rectus abdominis muscle was 2.4 cm (SD 0.41) on the left and 2.8 cm (SD 0.53) on the right (figure 1).

2b. Ultrasound abdominal wall

In seven children there was no herniation of the abdominal wall on ultrasound images. Diastasis of the rectus abdominal muscle was observed in seven children without any

Table 2. Normal values of muscle thickness and muscle echo intensity of 4 abdominal muscles

Muscle	Muscle thickness (cm, SD)
Rectus abdominis	0.21 + 0.049*age (0.09)
External oblique	0.51 + 0.031*age (0.10)
Internal oblique	0.097 + 0.041*age (0.09)
Transverse abdominis	0.084 + 0.019*age (0.08)

Table 3. Muscle thickness of CST patient

Muscle	Mean Muscle thickness		
	Side	Mean Z-score	SD
Rectus abdominis	Left	0,04	1,03
	Right	0,10	1,70
External oblique	Left	0,50	1,13
	Right	0,60	1,12
Internal oblique	Left	0,14	1,79
	Right	-0,17	1,45
Transverse abdominis	Left	-0,66	0,82
	Right	-0,83	0,78

protrusion of the abdominal contents during valsalva manoeuver. These children's fascia was still strong enough to resist high pressure. A small hernia at the level of the neo umbilicus with only minimal protrusion was detected in one patient.

Physical examination confirmed diastasis of the rectus muscle in of six of the seven children involved, and diastasis in six of the seven children involved.

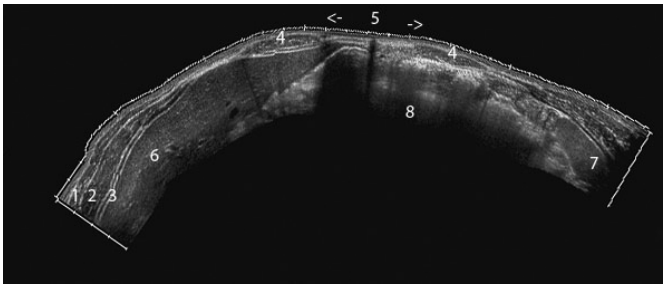

Fig 1. Muscle ultrasound; Relationship regarding each abdominal wall muscle, rectus diastasis

1= external oblique muscle,	5= rectus diastase,
2= internal oblique muscle,	6= liver,
3= transverse muscle,	7= spleen,
4= rectus abdominis muscle	8= stomach, bowel structures

3. Functional and Motor development

Motor development (M-ABC-2 test)

Chi-square testing did not reveal significant difference in motor development between the study children and the reference population ($p > 0.05$). Seven patients scored within the normal range, only P3 scored in the at risk range (table 4).

Alignment and range of motion

The spinal ROM was normal and symmetrical in seven of the children. The other (P8), who had a congenital tethered spinal cord syndrome and surgical correction afterwards, had a slightly asymmetrical position of the sternal bone and a slightly restricted ROM in spinal flexion range of motion. All patients could move firstly one and secondly both knees together to the tip of the nose, indicating normal ROM of the spine and lower extremities, as well as no encumbering influence of the belly in the flexion direction.

Results of the sit and reach test were almost equal for study children and controls and reflected normal ROM of the spine and lower extremity muscles. Only the scores for the over 6-year-olds could be compared with external references. In so doing, scores for two were "good" (P6, P7); score for the third was fair (P8). The three controls older than six years of age all score "good".

Functional muscular activity

Numbers of sit-ups did not differ between the study children and the controls. Three (P1, P2, P8) clearly performed better than their age-match controls. Three (P3, P4, P5) performed equally well. Two (P6, P7) performed slightly worse than the controls, but still acceptable (table 4). There were no group differences for the time needed to symmetrically raise the extended legs ten times from supine position, Three patients

Table 4. Outcome at time of assessment

Patient/ Control	Gender: Boy/Girl	Age (Year, Months)	M-ABC-2: component score (standard score)[1]				Sit and reach test (cm)	Sit ups in 30 sec (times)	Raising legs 10 times (freq)	Oblique abdominal muscle function[2]	Belly thick-thin[3]	In- expiration excursion difference (cm)
			MD	AC	Bal	Tot						
P1	G	3,6	40(17)	15(7)	34(12)	89(13)	28	4	41	2	1	3
C1	*G*	*3,7*					*29*	*0*	*29*	*2*	*3*	*4*
P2	B	4,1	28(9)	22(11)	25(7)	75(9)	31	4	13	1	1	3
C2	*B*	*4,1*					*34*	*0*	*19*	*2*	*3*	*4*
P3	B	4,3	20(5)	17(8)	24(7)	61(5)	23	0	18	1	1	3
C3	*B*	*4,0*					*25*	*0*	*18*	*2*	*3*	*4*
P4	G	4,5	37(14)	16(8)	36(15)	89(13)	40	3	12	2	0	2
C4	*G*	*4,5*					*36*	*3*	*19*	*2*	*3*	*4*
P5	B	5,4	29 (9)	19 (9)	22 (6)	70 (7)	30	8	25	2	2	4
C5	*B*	*5,6*					*26,5*	*10*	*10*	*2*	*3*	*5*
P6	B	6,6	38(15)	23(11)	23(7)	84(11)	28	10	23	2	3	3
C6	*B*	*6,6*					*31*	*14*	*16*	*2*	*3*	*5*
P7	G	7,10	33(11)	20(10)	37(16)	90(13)	27	17	16	2	2	3
C7	*G*	*7,11*					*33*	*23*	*18*	*2*	*3*	*5,5*
P8	G	11,9	37(14)	13(6)	34(12)	84(11)	18	23	12	2	3	4,5
C8	*G*	*11,9*					*32*	*18*	*15*	*2*	*3*	*5*

Table 4. Outcome at time of assessment (continued).

Patient/ Control	Gender: Boy/Girl	Age (Year, Months)	M-ABC-2: component score (standard score)[1]				Sit and reach test (cm)	Sit ups in 30 sec (times)	Raising legs 10 times (freq)	Oblique abdominal muscle function[2]	Belly thick-thin[3]	In- expiration excursion difference (cm)
			MD	AC	Bal	Tot						
			Component score									
			Mean (SD)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*						
			32,8 (6,7)	*18,1 (3,5)*	*29,4 (6,4)*	*80,3 (10,6)*						
			Standard score									
			Mean (SD)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*						
			11,8 (4,0)	*8,7 (1,8)*	*10,2 (4,0)*	*10,3 (3,1)*						
							Mean (SD)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Patients							*28,1 (6,4)*	*8,6 (7,8)*	*20 (9,8)*	*1,7 (0,5)*	*1,6 (1,1)*	*3,2 (0,7)*
Controls							*30,8 (3,8)*	*8,5 (9,1)*	*18 (5,3)*	*2 (0)*	*3 (0)*	*4,6 (0,6)*

Legends:

1. M-ABC-2: MD: Manual Dexterity; AC: Aiming and Catching; Bal: Balance; Tot: Total test score.
2. Belly thick and thin: 0: not possible; 1: slightly possible; 2: almost normal; 3: normal.
3. Oblique abdominal muscle function, rotating the trunk in supine position: 0: bad; 1: fair; 2: good.

(P2,P4,P8) needed a little more time than the controls, two patients (P3,P7) the same time, and three patients (P1,P5,P6) less time (table 4). All patients were capable to tolerate maximum rotation of the trunk by performing lateral movements of both bended legs at a time. Scores for all controls and six patients (P1, P4-P8) were "good"; scores for two patients (P2, P3) were "fair" (table 4).

Tightness of the stomach

Six patients (P1-P5, P7) had problems with inflating and deflating the belly to a maximum. One patient (P4) could not perform this movement at all, three patients (P1-P3) were slightly capable to perform and two patients (P5, P7) almost normal and two had no problems (P6, P8) (table 4). There are no norm-references for this movement.

In- and expiration excursion of the chest

From the measurement of the circumferential difference between maximal inspiration and maximal expiration at xiphoidal level it appeared that all patients' thoracic ROM was slightly but significantly smaller than that of controls (Kolmogorov-Smirnov Z; $p = 0.02$). Their ventilation patterns were normal.

Motor performance

All patients and controls demonstrated normal patterns of walking on tiptoes and heels, walking stairs, standing on knees/ standing on knee and foot, and crouching. Also walking and running was judged normal in all patients, except the one with the congenital tethered spinal cord syndrome (P8), who placed her feet obviously in more exorotation and was inclined to walk a bit on tiptoes. All patients and controls could demonstrate a fluent way of hopping in accordance of their age.

DISCUSSION

Normal functional and motor development was seen in all tested children a mean of four and a half years after CST for the correction of giant omphalocele. Minimal lateralization of the external oblique muscle and a rectus diastasis without protrusion were seen in almost all of them. Alignment, range of motion, functional muscular activity, and quality of motor performance all were normal or almost normal. Nevertheless, most experienced some difficulty in pushing the belly forward and retracting the belly, and they had a slightly lower but significant in-expiration excursion difference at the xiphoidal level. Although these flaws did not appear to have negative functional consequences, we recommend adding endurance tolerance testing to follow-up programmes. These patients after birth show a narrow thorax on chest radiographs and pulmonary hypo-

plasia may be present. Only one patient in our study had needed ventilatory support for a longer time. The others did not show pulmonary distress, and pulmonary hypoplasia can therefore be excluded. Zaccara et al [20] found normal cardio-respiratory function in former patients with gastroschisis or giant omphalocele. They showed normal motor performances in good state of fitness.

Knowledge about the long-term functional and motor developmental outcomes after correction of giant omphalocele would be welcome for parents' counseling and clinical decision-making. So far, there is little such knowledge. A recent study reported mild to profound developmental delays on the short term in 40% of these children [21]. Two (13%) had autism disorder, however, which could have influenced the results. The extent of severe anomalies was not described. In our study the most severe anomaly was a tethered cord syndrome and spine anomalies in one child. Finally, the children in that short-term study were much younger than our study population (median, 12 months vs. 59 month). The former had some multiorgan problems requiring prolonged recovery periods, which might explain their poor neurodevelopmental outcome.

The present long-term study did not reveal any delay in motor development, disabilities in daily practice, nor underdevelopment of abdominal muscles. This suggests that the above-mentioned short-term deficits could be transient. The formation of scar tissue could explain the somewhat poor performance on the belly inflating and deflating test in the present study. On the other hand, this scar tissue makes the fascia of the rectus diastasis strong enough to resist high pressure, on account of which there is no protrusion of abdominal contents, but apparently the tissue is not elastic enough to shorten when the abdominal muscles contract. To reduce the rectus diastasis, the rectus muscle should be more approximated during CST. Another option to minimize diastasis might be to close the fascia of the posterior and anterior rectus muscle separately [22].

A striking finding in our study was that the external oblique muscle was as thick as in controls, while minimal lateralization at the lateral side of the rectus muscle indicated normalization of the external oblique muscle over time.

We are aware that this study has several limitations: First, the study sample is small with a large age range. Second, because the children were still relatively young, muscle function could not be reliably measured. Nevertheless, this study could well serve as a basis for multicenter studies with larger numbers of participants.

In summary, children's muscle thickness of all abdominal wall muscles, and functional and motor development four and a half years after correction of giant omphalocele with the use of the Component Separation Technique did not differ from those in age-matched healthy controls. Most of them showed a rectus diastasis, without clinical protrusion of abdominal contents. So far, we conclude that this remains a promising closure technique for giant omphalocele.

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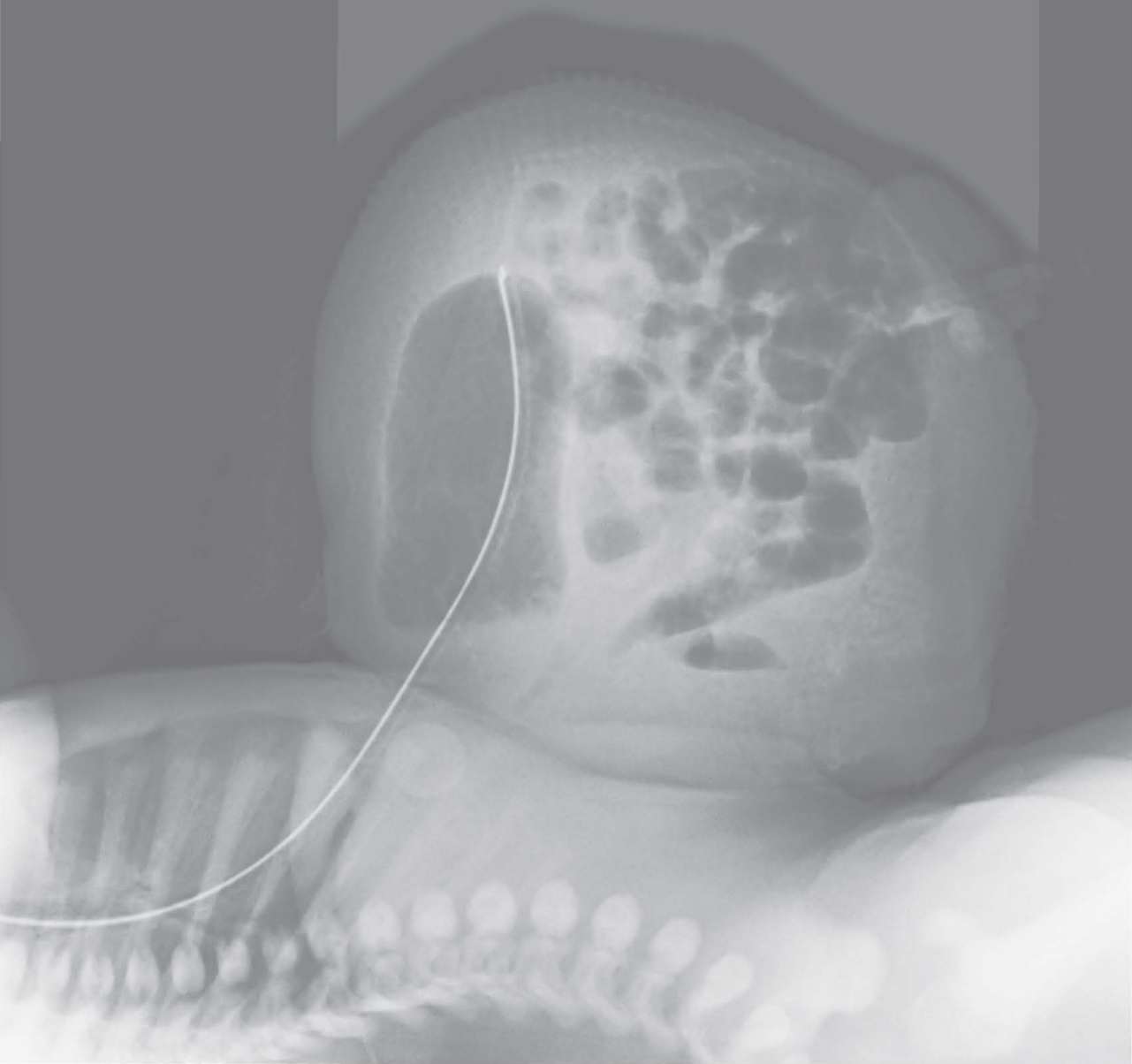
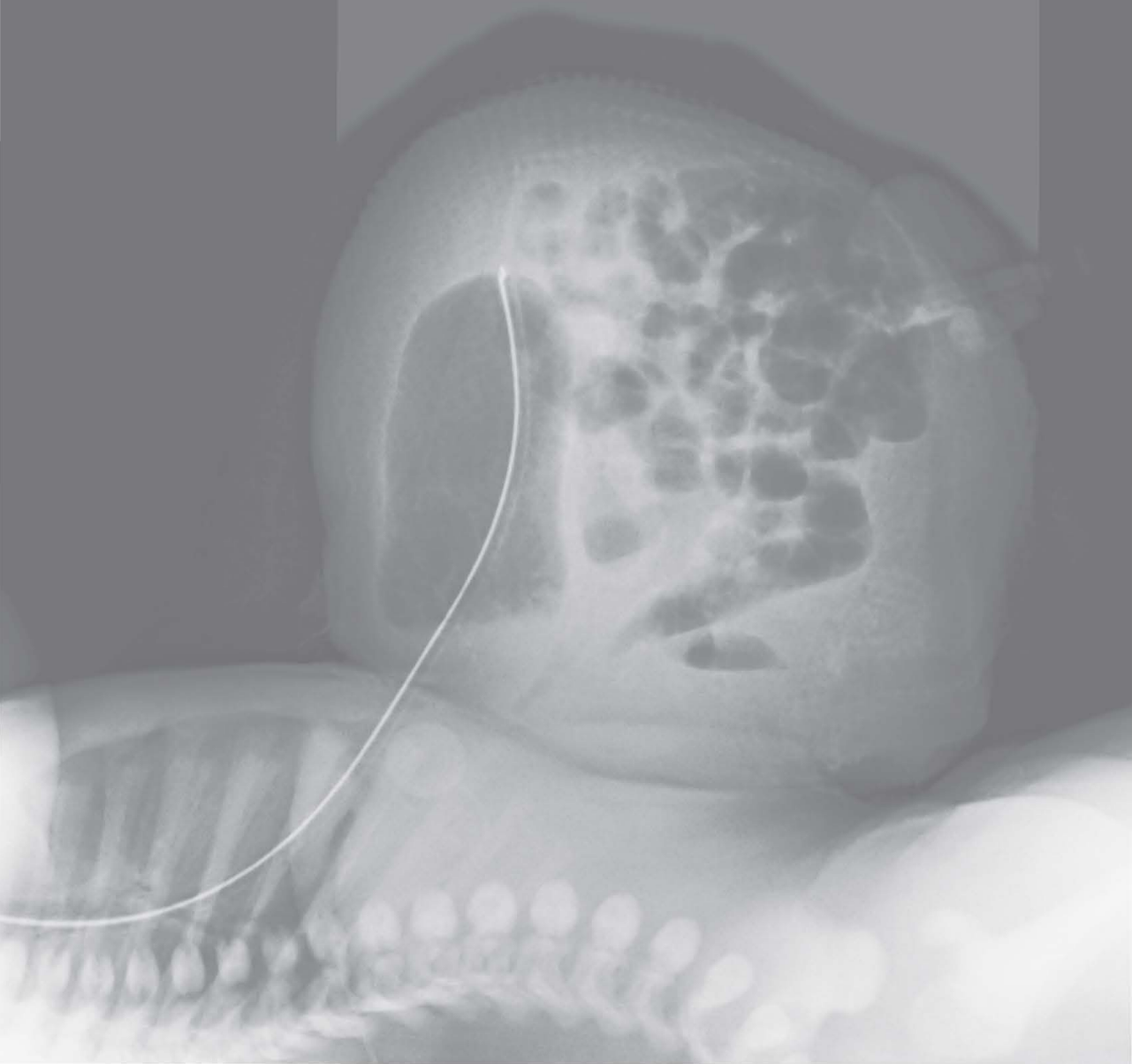
PART 3

Summary & Conclusions



Chapter 9

Summary & Conclusions



SUMMARY & CONCLUSIONS

The subject of this thesis is omphalocele, a congenital abdominal wall defect at the site of the umbilical ring. It is characterised by evisceration of the visceral organs in a sac composed of a three-layered membrane: of peritoneum, Wharton's jelly and amnion. The sac usually contains small intestine (midgut) only, but occasionally also liver, spleen, colon or gonads. Two main types of omphalocele are distinguished: minor and giant. The abdominal defect in the minor type (without eviscerated liver) is up to 5 cm in diameter and in most cases can be closed primarily. The giant type (with eviscerated liver) is larger; primary closure is often impossible because the abdominal cavity may be underdeveloped resulting in a high degree of visceroabdominal disproportion. The newborn may also suffer from pulmonary hypoplasia, as reflected by pulmonary distress and an abnormally shaped, small thoracic cavity. Primary closure of giant omphalocele carries the risk of high abdominal pressure with compression of the inferior vena cava, liver, and suprahepatic veins and often leads to multi-organ failure, respiratory impairment and necrotizing enterocolitis. And then, if the child should have other life-threatening diseases, such as severe cardiac disorders or acute respiratory distress syndrome, repeated surgical interventions bring an unacceptably high risk.

The aim of this thesis, which is built up of two parts, is to add to the knowledge on the treatment and outcome of omphalocele, especially the giant type. **Part one** contains retrospective studies on aspects such as patients' quality of life, incidences of adhesion-related morbidity, and the position of the liver, spleen and kidney in adolescence. **Part two** deals with the surgical technique of closure of the abdominal wall in giant omphalocele.

We attempted to ascertain whether published operative techniques for giant omphalocele once advocated by their authors were still being used and, if so, whether they had been modified. Furthermore, we performed a prospective pilot study with a new innovative technique for delayed closure in giant omphalocele, the component separation technique by Ramirez. The outcome measures were the long-term functional and motor development and the abdominal muscle quantity.

Chapter 1 gives a general introduction and review of therapeutic management in (giant) omphalocele. Three types of surgical techniques are described in the literature:

- primary closure of the defect in one operation, with or without extra corporal material, shortly after birth;
- staged closure of the abdominal wall defect, i.e. in more than one operative procedure;
- delayed closure after epithelialization of the sac and when the abdominal cavity has gained sufficient volume).

PART ONE: CHAPTERS 2, 3 AND 4.

Chapter 2 compares long-term outcomes and quality of life between patients with minor (n=89) and with giant omphalocele (n=22). The medical records were reviewed and a general questionnaire was sent to all surviving patients. A second questionnaire concerning quality of life and functional status (COOP/WONCA charts) was sent to all patients aged 18 years or older. The COOP/WONCA charts were also completed by a control group of 100 healthy young adults aged between 18 and 25 years. These were randomly chosen from the patient registers of two GP practices in the Netherlands, an urban one and a rural one. From the findings of this study we concluded that long-term outcomes and quality of life did not differ between patients with minor and with giant omphalocele. Patients with giant omphalocele reported more cosmetic problems with the abdominal scar and more dissatisfaction with missing the umbilicus. Despite these cosmetic problems, the quality of life in both groups was comparable to that of healthy young adults.

Postoperative adhesions may lead to small bowel obstruction, inadvertent enterotomy during subsequent operations, female infertility, chronic abdominal and pelvic pain, and constipation. Adhesive small bowel obstruction has been observed in two thirds of patients within one to two years after surgery; however, it has been reported even 25 years after initial surgery. Incidences of adhesions reported in the literature range from 1 to 6%; in some groups it may be even higher. Children treated for congenital abdominal wall defects seem to be particularly at risk developing adhesion related morbidity. Small bowel obstruction, for example, occurred two to three times more often in comparison with children undergoing other abdominal operations.

Chapter 3 describes a retrospective analysis in a large well-documented group of paediatric patients treated for gastroschisis or omphalocele. In both conditions, extensive peritoneal manipulation for abdominal wall closure is needed, and often repeated laparotomy and/or insertion of prosthetic mesh as well, which are key factors inducing adhesion formation. In this study we focussed on incidence, risk factors, long-term morbidity, and mortality of adhesion formation.

Data on long-term morbidity related to postoperative adhesions were retrieved from medical records and a questionnaire was sent to the parents of all surviving patients (n=147). Twenty-six (18%) of the neonates suffered from small bowel obstruction and 23 of them underwent laparotomy. Four (15%) patients had died. Most episodes (85%) were in the first year after birth. The cumulative incidence within one year was 12% in the omphalocele group and 27% in the gastroschisis group, increasing to 15% vs. 37%, respectively, after ten years. Sepsis and fascia dehiscence proved predictive for small bowel obstruction. These results demonstrate that adhesive small bowel obstruction

is a frequent and serious complication in the first year after treatment of congenital abdominal wall defects.

In giant omphalocele, also the liver is included in the sac. The intestines are usually malrotated or non-rotated, though generally they are morphologically and functionally normal.

In **Chapter 4** we evaluated whether, on the long run, the liver and other solid organs reach their normal position, shape and size. Normally, the chest wall and a strong abdominal wall protect the liver from trauma and surgery. Physical examination of 17 former patients with a giant omphalocele was supplemented with ultrasonography for ventral hernia and precise description of the liver, spleen and kidneys. The findings were compared with those in controls, matched for age, gender and body mass index.

The liver was defined as unprotected if it was beneath the chest wall at three points: anterior axillary line (AAL), medioclavicular line (MCL) and sternal line (STL). Ventral (medial) or caudal location of the liver was labelled as abnormal position. Location of the kidneys above the liver or spleen was labelled as abnormal position. Abnormal positions of the liver, spleen, left and right kidney were seen in eight, six, five, and four patients, respectively. The children with giant omphalocele have a larger liver than had the controls ($p=0.01$). The liver was partially unprotected in all 17 patients and in 11 of the 17 controls ($p=0.04$). The children with giant omphalocele showed significantly more often unprotected liver under the chest boundaries at STL and MCL than did the controls. The liver was located underneath the abdominal wall defect in ten of the 11 patients with an incisional hernia. Thus, in all former patients with a giant omphalocele an unprotected liver was seen and had not migrated to the normal position. Exact documentation and good information are important for the patient, parents and doctors in order to minimize liver trauma in the future.

PART TWO: CHAPTERS 5, 6, 7 AND 8.

Operative treatment of giant omphalocele is still a challenge for pediatric surgeons, as reflected by the broad range of approaches described in literature during the last decades.

We were interested to ascertain whether published operative techniques (1967-2009) for giant omphalocele once advocated by their authors, were still being used, or whether modifications or even other techniques had been introduced.

Chapter 5 presents the results of a questionnaire concerning the currently preferred treatment of pediatric surgeons who once published their technique of choice. The surgical techniques were categorized into: primary, staged, and delayed closure (see

Chapter 1). Irrespective of the categorization, almost half (42 %) of the authors had modified their techniques after publishing the article or even stopped using them. Overall, a proven better technique had not emerged. The herniation rate was lowest in delayed closure (9% delayed vs. 18% staged vs. 58 % primary). The results of the questionnaire did not show a generally accepted treatment after more than thirty years of innovations in the treatment of patients with a giant omphalocele.

Chapter 6 is a case report on a new technique for delayed closure in giant omphalocele: the Component Separation Technique (CST). It proved successful in this patient, whereupon we initiated a prospective pilot study applying CST in all patients with a giant omphalocele.

Chapter 7 presents the results of this pilot study in ten patients, operated on after a median of 6.5 months (range, 5-69 months) after birth. The postoperative course was uneventful in seven patients. Three patients showed minor complications (infection, skin necrosis and haematoma). None of the patients suffered from reherniation after median follow-up of 23.5 months. This study demonstrates that the CST is a safe one-stage procedure for delayed closure in children with a giant omphalocele without the use of prosthetic material.

In **Chapter 8** we evaluated the long-term functional and motor development and abdominal muscle quantity in patients with giant omphalocele corrected by means of CST. Ultrasonography was performed to detect incisional hernia or rectus diastasis. Functional and motor development were assessed with the Movement Assessment Battery for Children, 2nd edition (M-ABC-2), and the children underwent an observational physical examination with specific focus on possible abnormalities in stature and movements related to giant omphalocele. Findings were compared with those in age-matched controls. The parents filled in a questionnaire on their child's functional and motor development in daily life. Eight of eleven eligible children were included. The median age at evaluation was 59 months (range, 42-141 months) with a median time of follow-up of 54 months (range, 38-84 months). Abdominal wall muscle ultrasound showed no atrophic abdominal muscles. It revealed a rectus diastasis without any protrusion in seven of the eight children. The functional and motor developments were within the normal range (MABC-2) and stature and motor coordination did not differ from those in their peers. This evaluation endorses that CST is a promising surgical technique for giant omphalocele.

CONCLUSIONS

The management of giant omphaloceles remains a challenge for pediatric surgeons. Although the mortality rate is still high (up to 20%) in case of multiple congenital

anomalies, surviving patients with omphalocele achieve a state of health and quality of life comparable to that of general population peers. This is a positive note for parents whose babies are facing a high burden of (surgical) interventions.

Results from our study confirm the hypothesis that neonates with a congenital abdominal wall defect have a high risk for adhesive small bowel obstruction and could benefit from adhesion prevention. Awaiting complete epithelialisation before operation of giant omphalocele might reduce serosal injury and limit adhesiogenic areas. It would be valuable to perform a multicenter study investigating possible reduction of adhesion-related morbidity through the use of adhesion reduction products at initial laparotomy.

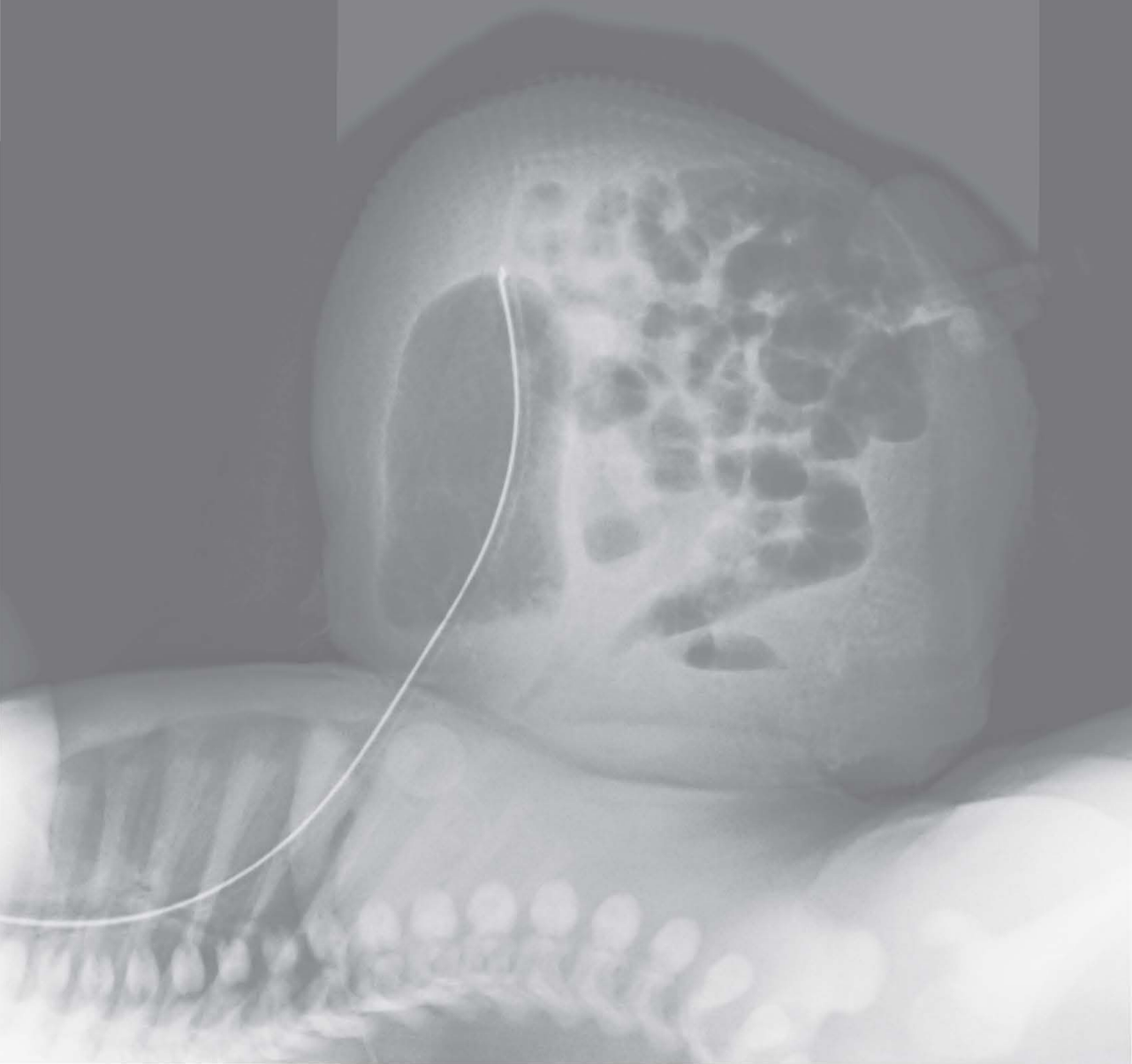
The liver was partly unprotected in all giant omphaloceles evaluated in this thesis. In case of an incisional hernia, the liver was located underneath the abdominal defect. A pre-operative ultrasound study is recommended, therefore. Furthermore, the parents should receive good documentation and information. The question remains whether contact sports and other risk behaviour should be advised against, as there is no indication of more blunt trauma in these patients in the literature.

The results of the questionnaire sent to the authors do not show a consensus for a generally accepted treatment method after more than thirty years of innovations in the management of patients with a giant omphalocele. There are few long-term follow-up studies in large samples, and the surgeon's preferred method is mainly based on training and personal experiences, although taking into account possible comorbidities.

The newly introduced Component Separation Technique seems to have a good outcome. The herniation rate is low, and prosthetic materials are not needed. However, the question remains if delayed closure with this technique is better than immediate staged closure. There is not yet an evidence base; we shall have to await the long-term results of the published techniques. Based on these outcomes, a randomized multicenter trial comparing the staged and delayed techniques is recommended. Until then, we remain dependent on expert opinion.

Chapter 10

Samenvatting en conclusies



NEDERLANDSE SAMENVATTING

Het onderwerp van dit proefschrift betreft een omphalocele; een aangeboren buikwanddefect ter plaatse van de navel. Het kenmerkt zich door evisceratie van darmen, welke bedekt worden door een drielagig membraan: peritoneum (buikvlies), Warton's gelei en amnion. De inhoud van de zak bestaat meestal uit dunne darm. Echter soms liggen ook de lever, milt, dikke darm en eierstokken buiten de buikholte. Een omphalocele kan onderverdeeld worden in twee groepen: minor en giant. Het buikwanddefect bij minor omphalocele (zonder evisceratie van lever) is kleiner dan 5 cm en kan meestal primair gesloten worden. Bij een giant omphalocele (met evisceratie van lever) is het buikwanddefect groter. Bij deze laatste groep is er sprake van een onderontwikkelde buikholte met een grote visceroabominale disproportie, waardoor primair sluiten niet mogelijk is. De pasgeborene kan ook lijden aan longhypoplasie wat zich uit in ademhalingsproblemen na de geboorte bij een reeds afwijkende en kleinere thoraxholte. Agressieve pogingen om een giant omphalocele primair te sluiten kan leiden tot een verhoogde intra-abdominale druk (abdominaal compartiment syndroom) met compressie van de vena cava inferior, lever en suprahepatische venen. Dit leidt vaak tot multiorgaan falen, respiratoire insufficiëntie en necrotiserende enterocolitis. Indien het kind ook andere levensbedreigende ziekten heeft, zoals ernstige cardiale en chromosomale afwijkingen of ARDS ('shocklong'), leiden herhaaldelijk chirurgische interventies tot een onacceptabel hoge morbiditeit en mortaliteit.

Het doel van dit proefschrift, dat opgedeeld is in twee delen is: enerzijds meer inzicht te krijgen in de behandeling en anderzijds de lange termijn resultaten van omphalocele met in het bijzonder de giant omphalocele.

Deel één betreft enkele retrospectieve studies waarin we de kwaliteit van leven, de incidentie van adhesie (verkleving) gerelateerde morbiditeit en de positie van de lever, nier en milt op latere leeftijd hebben onderzocht.

Deel twee gaat over de operatietechnieken van het sluiten van het buikwanddefect bij giant omphalocele.

We hebben geprobeerd te inventariseren welke gepubliceerde operatie technieken voor giant omphalocele momenteel nog gebruikt worden. Een prospectieve pilot studie is opgezet om een nieuwe techniek voor het sluiten van giant omphalocele, de componenten separatie techniek volgens Ramirez te evalueren. De lange termijn resultaten zijn onderzocht door onder andere de buikspierkracht, kwantiteit van de buikspieren en de motorische ontwikkeling te meten.

In **Hoofdstuk 1** wordt een algemene introductie en overzicht van de therapeutische behandeling van (giant) omphalocele gegeven**.** De operatieve behandeling van giant omphalocele wordt onderverdeeld in drie groepen:

- 'Primair' sluiten van het buikwanddefect in één operatie, met of zonder oplosbaar / kunststof materiaal, direct na de geboorte;
- 'Staged' sluiten van het defect in meer dan één chirurgische interventie;
- 'Delayed' sluiten na epithelialisatie van de omphalocele zak waarbij de abdominale disproportie verminderd is.

DEEL ÉÉN: HOOFDSTUK 2, 3 EN 4.

In **Hoofdstuk 2** worden de lange termijn resultaten en de kwaliteit van leven bij patiënten met een minor (n=89) en giant omphalocele (n=22) worden met elkaar vergeleken**.** De statussen werden onderzocht en een algemene vragenlijst werd gestuurd naar alle overlevende patiënten. Een tweede vragenlijst met betrekking tot kwaliteit van leven en functionele status (COOP/WONCA) werd gestuurd naar alle patiënten ouder dan 18 jaar. Deze COOP/WONCA vragenlijst werd ook beantwoord door een controle groep welke bestond uit 100 willekeurig gekozen gezonde mannen en vrouwen tussen de 18 en 25 jaar uit twee huisartsenpraktijken (één stadspraktijk en één dorpspraktijk). De resultaten van deze studie tonen aan dat er, ondanks de hoge medische interventie na de geboorte, geen verschil is tussen de twee groepen (minor en giant) op het gebied van kwaliteit van leven. Echter in de groep van giant omphalocele worden de cosmetische problemen van het litteken en de afwezigheid van een navel vaker genoemd. Ondanks deze cosmetische problemen, is de kwaliteit van leven van omphalocele vergelijkbaar met een gezonde populatie jong volwassenen in Nederland.

Postoperatieve adhesies hebben een grote impact op de morbiditeit en mortaliteit. Dit kan zich uiten in chronische buikpijn, obstipatie, dunne darm ileus, darm resecties of zelfs infertiliteit. Een dunne darm ileus door adhesies, ontstaat in twee-derde van de gevallen binnen het eerste jaar na een buikoperatie. Echter in de literatuur is zelfs 25 jaar na initiële chirurgie een eerste episode beschreven. De incidentie van adhesies na buikchirurgie bij kinderen ligt tussen de 1% en 6%. Echter voor specifieke groepen ligt dit hoger; kinderen met aangeboren buikwand defecten hebben een hoger risico op het ontwikkelen van adhesies in de buik met de daaraan gerelateerde morbiditeit. Een dunne darm ileus treedt twee tot drie keer vaker op bij deze patiëntengroep in vergelijking met kinderen die een andere buikoperatie hebben ondergaan.

Hoofdstuk 3 beschrijft een retrospectieve analyse van een goed gedocumenteerde groep kinderen, die behandeld zijn in verband met aangeboren buikwanddefecten: gastroschisis en omphalocele. Deze twee groepen worden met elkaar vergeleken omdat beide uitgebreide peritoneale manipulaties ondergaan tijdens het sluiten van het de-

fect. Er zijn vaak meerdere relaparotomieen en/of gebruik van een kunststofmat nodig, waardoor de kans op adhesievorming toeneemt.

De incidentie, risicofactoren, morbiditeit en mortaliteit van adhesies (dunne darm ileus) werden geanalyseerd. De lange termijn morbiditeit van postoperatieve adhesies werd verkregen uit statusonderzoek en door een vragenlijst te sturen naar alle ouders van overlevende patiënten (n=147). Zesentwintig (18%) van de neonaten ontwikkelden een dunne darm ileus en 23 van hen ondergingen een laparotomie. Vier (15%) patiënten zijn overleden. De meeste episodes (85%) ontstonden binnen het eerste jaar na de geboorte. De cumulatieve incidentie voor het krijgen van een dunne darm ileus binnen één jaar was 12 % in de omphalocele groep en 27 % in de gastroschisis groep, toenemend respectievelijk naar 15 % vs 37% na tien jaar. Sepsis en fasciedehiscentie bleken voorspellende factoren te zijn voor het ontwikkelen van een ileus. Deze resultaten tonen aan dat een dunne darm ileus een frequente en ernstige complicatie is in het eerste jaar na behandeling van aangeboren buikwanddefecten.

In giant omphalocele bestaat de inhoud van de zak van de omphalocele behalve uit darmen ook uit lever. Er is meestal sprake van een malrotatie of non-rotatie van de darmen.

In **Hoofdstuk 4** hebben we onderzocht of op de lange termijn de lever en andere solide organen hun normale positie, vorm en grootte bereiken. Normaal wordt de lever beschermd tegen trauma en abdominale chirurgie door de borstkas en een stevige buikwand. Het lichamelijk onderzoek bij 17 patiënten met een giant omphalocele werd aangevuld met een echografie van de buik om te kijken of er sprake was van een littekenbreuk. Tevens werd echografisch de positie en grootte van de lever, milt en nieren gemeten. De gegevens werden vergeleken met die van een controlegroep, welke overeenkwam wat betreft leeftijd, geslacht en body mass index.

Een onbeschermde lever werd gedefinieerd als een deel van de lever onder de ribbenboog lag, gemeten op een drietal punten: voorste axillair lijn (AAL), midclaviculair lijn (MCL) en sternum lijn (STL). Een ventraal (mediaal) of caudaal gelegen lever werd gedefinieerd als een afwijkende ligging. Een abnormale positie van nieren werd bevestigd indien deze boven de lever en/of milt lag. Er werd een afwijkende ligging van de lever, milt, linker- en rechternier geconstateerd bij respectievelijk acht, zes, vijf en vier patiënten. Kinderen met een giant omphalocele hadden een grotere lever dan de controle groep (p=0.01). Bij alle 17 giant omphaloceles zagen wij een deels onbeschermde lever versus 11 van de 17 in de controle groep (p=0.04). De mate van onbeschermde lever ter plaatse van MCL en STL was significant groter in de giant omphalocele. Bij tien van de 11 patiënten met een littekenbreuk, lag de lever onder het buikwanddefect. Deze studie toont aan dat de lever onbeschermd ligt in alle voormalige giant omphaloceles en niet naar zijn normale positie migreert. Exacte documentatie en goede informatie is erg

belangrijk voor zowel de patiënt, de ouders als de medici om de kans op een leverletsel in de toekomst te verkleinen.

DEEL TWEE: HOOFDSTUK 5, 6, 7 EN 8.

De operatieve behandeling van giant omphalocele is nog steeds een uitdaging voor kinderchirurgen. Dit uit zich onder andere door de vele operatietechnieken die beschreven zijn in de literatuur. Wij waren benieuwd of de beschreven gepubliceerde operatietechnieken (1967-2009) voor giant omphalocele door de auteurs nog steeds gebruikt worden of dat ze gemodificeerd of gestopt zijn.

Hoofdstuk 5 presenteert de resultaten van een vragenlijst betreffende de huidige voorkeur van de auteurs voor de behandeling van giant omphalocele. De beschreven chirurgische technieken werden onderverdeeld in: primair, staged en delayed (zie hoofdstuk 1). Bijna de helft (42%) van de auteurs heeft de beschreven techniek aangepast of is ermee gestopt na publicatie van het artikel, onafhankelijk van de techniek. Dit resulteerde echter niet in één duidelijk betere operatietechniek. Wel is een kleinere kans op het krijgen van een littekenbreuk bij de delayed techniek (9% delayed vs 18 % staged vs 58 % primair sluiten). Ondanks dertig jaar innovatie tonen deze resultaten geen algemeen geaccepteerde behandeling van giant omphalocele.

Hoofdstuk 6 is een case report over een nieuwe techniek voor uitgesteld (delayed) opereren van een giant omphalocele: de Componenten Separatie Techniek (CST). Na deze eerste succesvolle operatieve behandeling zijn we een prospectieve pilot studie gestart en werden alle giant omphalocele volgens deze nieuwe techniek geopereerd.

Hoofdstuk 7 geeft de resultaten van deze pilot studie weer bij tien patiënten. De mediane leeftijd ten tijde van de operatie was 6.5 maand. Het postoperatieve beloop was ongecompliceerd bij zeven patiënten. Slechts bij drie patiënten werden milde complicaties gezien (infectie, partiële huidnecrose en hematoom). Geen littekenbreuken werden geobjectiveerd na een mediane follow-up van 23.5 maand. Deze studie toont aan dat de CST een veilige uitgestelde methode is om het buikwanddefect in slechts één procedure te sluiten.

In **Hoofdstuk 8** hebben we de functionele en motorische ontwikkeling en de kwantiteit van de buikspieren op de lange termijn geëvalueerd bij onze groep patiënten met een giant omphalocele na correctie met de CST. Met behulp van echografie werd de kwantiteit van alle buikspieren gemeten en de aanwezigheid van een littekenbreuk of rectus diastase. De functionele en motorische ontwikkeling werden getest door gebruik te maken van de Movement Assessment Battery for Children, 2nd edition (M-ABC-2) en door middel van specifieke lichamelijke testen gericht op mogelijke afwijkingen wat betreft houding en beweging gerelateerd aan giant omphalocele. Deze resultaten werden

vergeleken met die van een gezonde controlegroep. De ouders vulden een vragenlijst in met betrekking tot de functionele en motorische ontwikkeling van hun kind. Acht van de elf kinderen na de CST werden geïncludeerd. De mediane leeftijd ten tijde van de studie was 59 maanden (range, 42-141 maanden) met een mediane follow-up van 54 maanden (range, 38-84 maanden). Tijdens echo-onderzoek van de buik werd er geen atrofie van de buikspieren gezien. Bij zeven van de acht kinderen werd een rectus diastase gevonden zonder protrusie van darmen. De functionele en motorische ontwikkeling lag binnen de normale range (M-ABC-2) en de houding en coördinatie verschilden niet van de controle groep. Deze studie bevestigt dat de CST een veelbelovende chirurgische techniek is voor giant omphalocele.

CONCLUSIES

De behandeling van minor en giant omphalocele blijft een uitdaging voor kinderchirurgen. Ondanks dat de mortaliteit nog steeds hoog is (tot 20%) indien er andere bijkomende aangeboren afwijkingen zijn, bereiken kinderen met een omphalocele een gezondheidsniveau en kwaliteit van leven dat vergelijkbaar is met een normale gezonde populatie. Het is belangrijk om ouders tijdens de zwangerschap duidelijk te informeren dat een goede gezondheid en kwaliteit van leven bereikt kan worden. Dit ondanks de vele (chirurgische) interventies die hun kind zal moeten ondergaan.

De resultaten van onze studie bevestigen de hypothese dat neonaten met aangeboren buikwanddefecten een hoger risico hebben op het ontwikkelen van een ileus. Deze groep zou kunnen profiteren van adhesiepreventie. Door eerst de giant omphalocele zak te laten epithelialiseren voordat een definitieve correctie plaats vindt, wordt mogelijk het aantal serosa letsels verminderd en de adhesiogene gebieden beperkt. Het zou waardevol zijn een multicenter studie op te zetten. Dit om een eventuele reductie aan te tonen van adhesie gerelateerde morbiditeit door gebruik te maken van anti-adhesieve producten tijdens de initiële operatie.

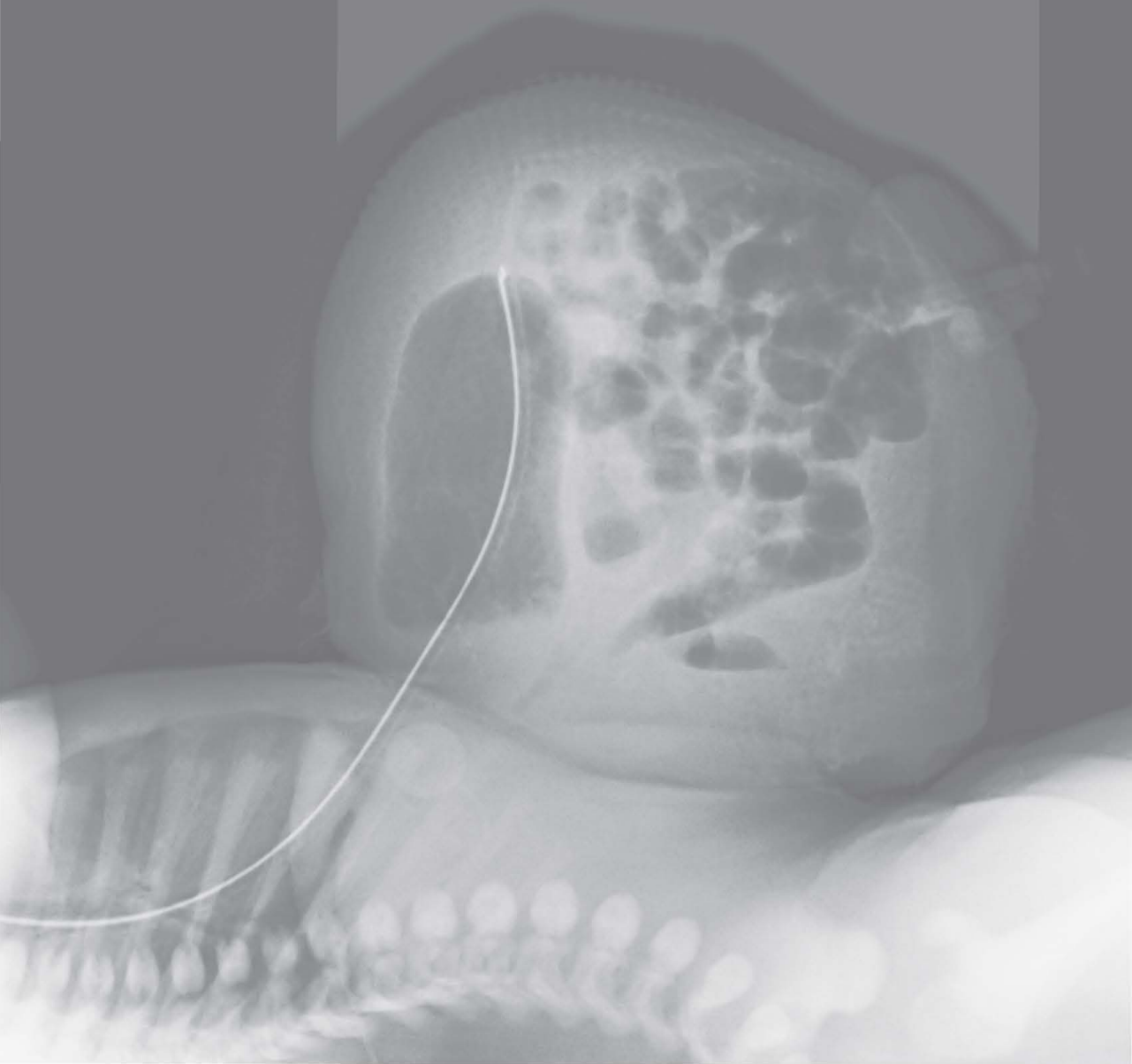
Bij alle giant omphaloceles in dit proefschrift lag een groot deel van de lever onbeschermd. Bij aanwezigheid van een littekenbreuk ligt de lever onder het buikwanddefect. Het is aan te bevelen een preoperatieve echo te maken. Goede documentatie en voorlichting aan de ouders is belangrijk. De vraag blijft in hoeverre we ouders en kinderen moeten adviseren om contactsporten en ander hoog risicogedrag te vermijden, aangezien het toegenomen risico op stomp trauma bij deze patiëntengroep niet voorhanden is in de literatuur.

De resultaten van de vragenlijst aan de auteurs, met betrekking tot hun operatieve behandeling voor giant omphalocele, leveren niet een consensus voor één geaccep-

teerde behandelmethode na meer dan 30 jaar innovatie. Vanwege het gebrek aan grote aantallen patiënten en lange termijn follow-up studies, wordt de keuze voor de bepaalde operatieve behandeling gebaseerd op training en persoonlijke ervaring van de chirurg met inachtneming van de mogelijke comorbiditeit.

De nieuw geïntroduceerde Componenten Separatie Techniek laat goede resultaten zien. De kans op een littekenbreuk is klein en gebruik kunststof materiaal is niet nodig. De vraag blijft of de 'delayed' techniek beter is dan 'staged' techniek. Op dit moment kan er nog geen evidenced based keuze gemaakt worden en zullen we moeten wachten op de lange termijn resultaten van de gepubliceerde technieken. Afhankelijk van deze uitkomsten zal een gerandomiseerde multicenter trial opgestart moeten worden om een 'staged' techniek te vergelijken met een 'delayed' techniek. Tot die tijd blijven we afhankelijk van de expert opinion.

List of publications



LIST OF PUBLICATIONS

1. K.F.M. Joosten, E.D. Kleijn, M. Westerterp, M. de Hoog, **F.C. van Eijck**, W.C.J. Hop, E. Van der Voort, J.A. Hazelzet, A.C.S. Hokken-Koelega. Endocrine and Metabolic Responses in Children with Meningococcal Sepsis: Striking Differences between Survivors and Nonsurvivors. Journal of Clinical Endocrinology and Metabolism 2000, Vol.85, No.10: 3746-3753
2. **F.C. van Eijck**, J.F. Lange, G.J. Kleinrensink. Hartmann's pouch of the gallbladder revisited: 60 years after. Surgical Endoscopy 2007 Jul; 21 (7): 1122-5.
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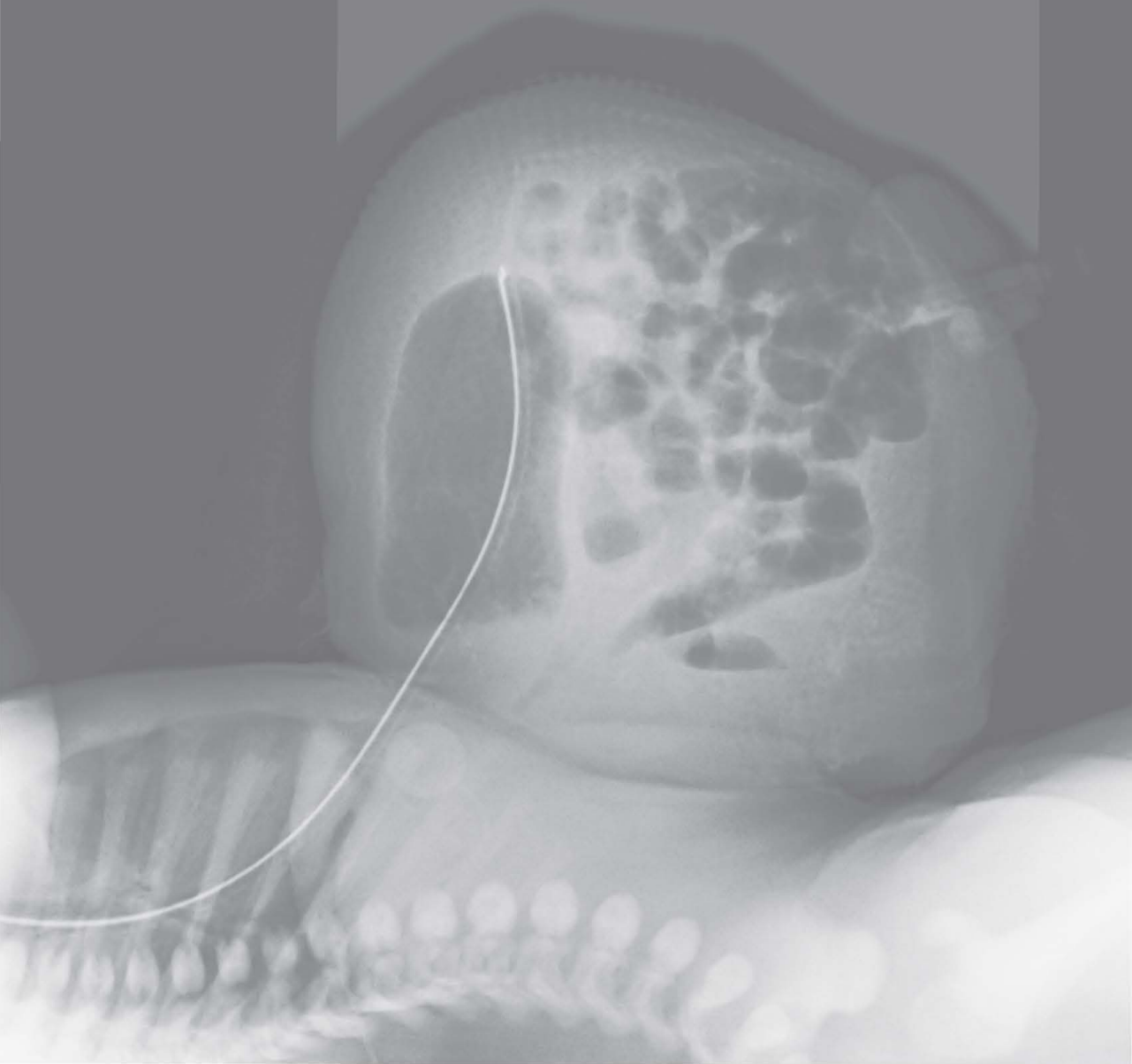
4. **Floortje van Eijck**, Rene M.H. Wijnen, Harry van Goor. The incidence and morbidity of adhesions after treatment of neonates with gastroschisis and omphalocele; a 30-year review. Journal of Pediatric Surgery 2008 March; 43(3): 479-483
5. **Floortje C. van Eijck**, Ivo de Blaauw, Robert P. Bleichrodt, Paul N.M.A. Rieu, Frans H.J.M. van der Staak, Marc H.W.A. Wijnen, Rene M.H. Wijnen. Closure of giant omphaloceles by the abdominal wall Components Separation Technique. Journal of Pediatric Surgery 2008 Jan; 43(1): 246-50.
6. **Floortje C. van Eijck**, Yvonne L. Hoogeveen, Chris van Weel, Paul N.M.A. Rieu, Rene M.H. Wijnen. Long-term results and quality of life in patients with Omphalocele. Journal of Pediatric Surgery 2009 July; 44(7): 1355-1359.
7. **Floortje C. van Eijck**, Willemijn Klein, Carla Boetes, Daniel C. Aronson, Rene M.H. Wijnen. Has the liver and other visceral organs migrated to its normal position in children with Giant Omphalocele? A follow-up study with ultrasonography. European Journal of Pediatrics 2010; 169: 563-567.
8. **Floortje C. van Eijck**, Daniel A. Aronson, Yvonne L. Hoogeveen, Rene M.H. Wijnen. Past and current surgical treatment of giant omphalocele: outcome of a questionnaire sent to authors. In Press, Journal of pediatrics Surgery.
9. **F.C. van Eijck,** L.A. van Vlimmeren, R.M.H. Wijnen, W. Klein, I. Kruijen, S. Pillen, M.W.G. Nijhuis-van der Sanden. Functional, motor developmental, and long-term outcome after the component separation technique in children with giant omphalocele. Submitted.

Dankwoord



DANKWOORD

Mijn proefschrift is af! Het is bijzonder om in Rotterdam te kunnen promoveren.
De cirkel is rond: van Rotterdam, mijn stad, gedurende mijn middelbare school - en studententijd naar Nijmegen voor mijn opleiding tot chirurg en uiteindelijk weer terug naar de basis Rotterdam.

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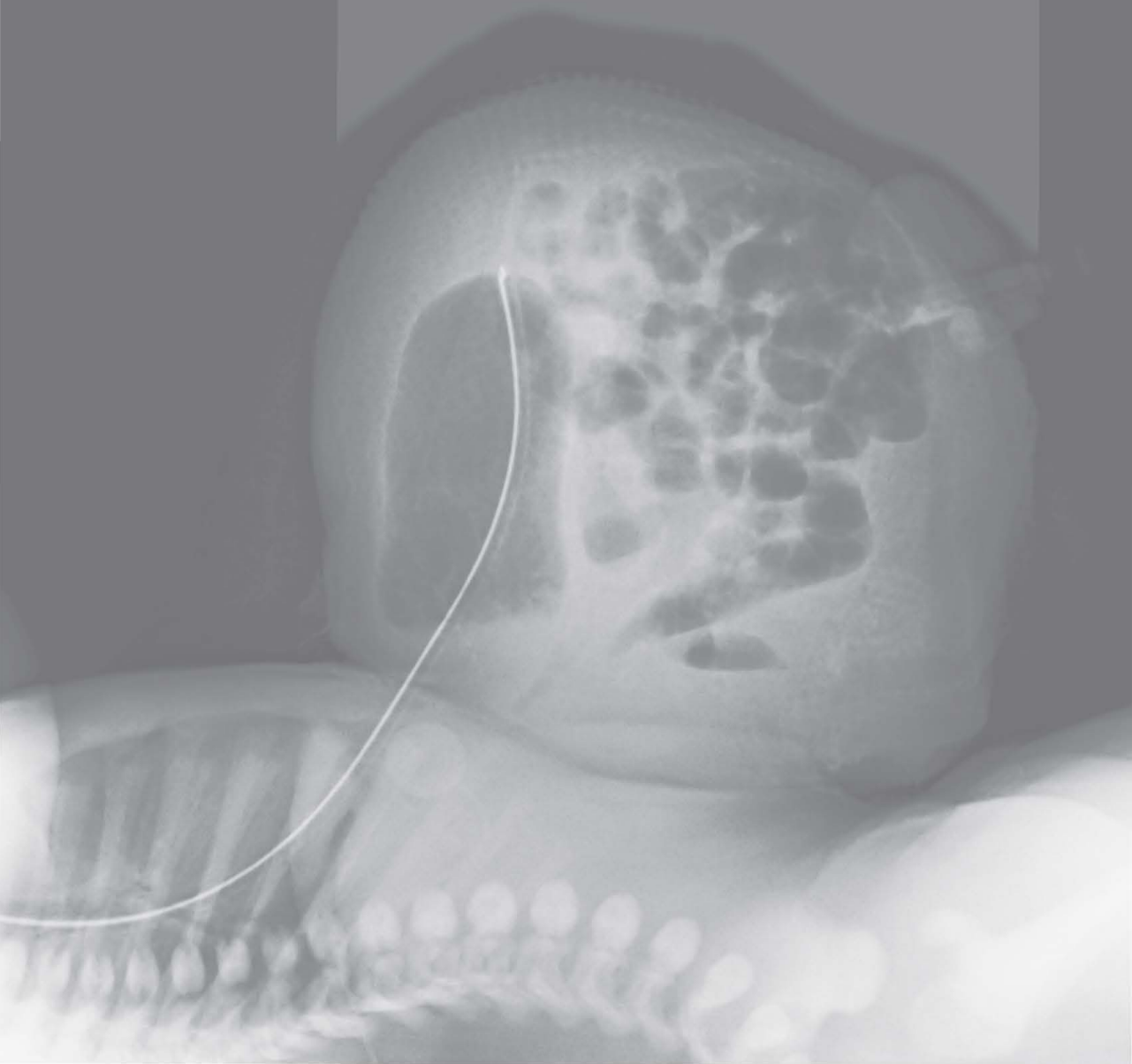
Curriculum Vitae



CURRICULUM VITAE

Floortje Clemens van Eijck werd geboren op 6 mei 1975 te Schiedam. Na het behalen van haar Gymnasium diploma aan het Rotterdamsch Lyceum te Rotterdam in 1993, startte zij haar studie geneeskunde aan de Erasmus Universiteit Rotterdam. Tijdens haar studie roeide zij bij A.R.S.R. Skadi op nationaal en internationaal niveau en behaalde meerdere medailles tijdens wereldkampioenschappen. In 2000 legde zij haar artsexamen af en ging voor 3 maanden stage lopen op de trauma unit van het Groote Schuur Ziekenhuis te Kaapstad, Zuid-Afrika. Nadat zij als arts-assistent niet in opleiding had gewerkt in het voormalige St. Clara Ziekenhuis en het huidige St. Radboud Ziekenhuis, startte zij haar opleiding heelkunde in mei 2003 in het Rijnstate Ziekenhuis te Arnhem (opleider dr. JHG Klinkenbijl). Vanaf mei 2008 tot oktober 2009 deed zij haar differentiatiejaar traumatologie in het Erasmus MC te Rotterdam (opleider prof. dr. JNM IJzermans). Gedurende haar opleiding werkte zij aan de voltooiing van haar proefschrift. Sinds 1 november 2009 werkt zij in Tergooiziekenhuizen te Hilversum/Blaricum als chef de clinique met als aandachtsgebied traumatologie. Zij woont samen met Ian Miller en hun zoon Niels.