

Past and Present in Omphalocele Treatment in Romania

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Rezumat

Tratamentul omfalocelului în România ieri și astăzi

Introducere: Omfalocelul este o malformație congenitală a cărei pronostic s-a îmbunătățit foarte mult în ultimul timp, cu o rată a supraviețuirii de 80-90% în țările dezvoltate. În România, la momentul actual nu există nici un studiu extensiv asupra incidenței, tratamentului și supraviețuirii pacienților cu acest defect al peretelui abdominal anterior.

Material și metode: Studiul analitic retrospectiv a fost efectuat pe o perioadă de 23 de ani asupra a 105 copii cu omfalocel, analizând diagnosticul antenatal, condițiile de transfer către spitalul nostru, vârsta copilului la internare, afecțiunile asociate, managementul medical și chirurgical, complicațiile postoperatorii și la distanță, perioada de spitalizare.

Rezultate: Rata scăzută a diagnosticului antenatal (13,3%), asocierea cu frecvență ridicată a malformațiilor congenitale (71,4%) și a anomaliilor cromosomiale (27,6%), condițiile inadecvate de transport și întârzierea acestuia către centrul specializat de chirurgie pediatrică, împreună cu rata crescută a sepsisului (37,1%) au condus spre o rată a mortalității ridicată (54,3%).

Concluzii: Perioada de spitalizare semnificativ mai mică și rata supraviețuirii mai mare, în ciuda complicațiilor medicale aparent mai frecvente pledează pentru tratamentul chirurgical

al omfalocelului, atunci când acesta nu este contraindicat de prezența hipoplaziei pulmonare severe, defectelor cardiace, imaturității sau altor anomalii congenitale grave, cazuri în care este indicat tratamentul conservator.

Cuvinte cheie: omfalocel, defect de perete abdominal, mortalitate

Abstract

Background: Omphalocele is a congenital abnormality whose prognosis has improved significantly over the last few decades, reaching a survival rate of 80-90% in developed countries. Currently, in Romania no comprehensive study on the incidence, treatment, and survival of patients with this defect of the anterior abdominal wall has been carried out.

Methods: This retrospective analytical study was conducted over a period of 23 years and included 105 children with omphalocele. Prenatal diagnosis, referral to our hospital, children age upon admission, associated diseases, medical and surgical management, early and late postoperative complications, and the length of hospital stay were analysed. **Results:** The low rate of antenatal diagnosis (13.3%), the high frequency of associated congenital malformations (71.4%) and chromosomal abnormalities (27.6%), inadequate and delayed transport to a specialized pediatric surgery center together with an increased rate of sepsis (37.1%) resulted in a high mortality rate (54.3%).

Conclusions: The significantly reduced length of hospital stay and higher survival rate despite the apparently more frequent medical complications plead for the surgical treatment

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of omphalocele whenever not contraindicated by the presence of severe pulmonary hypoplasia, cardiac defects, immaturity and other severe congenital anomalies, when conservative treatment is indicated.

Key words: omphalocele, abdominal wall defect, mortality

Introduction

The first description of omphalocele was given in 1634 by Ambroise Paré who in his "The Workes of that Famous Chirurgion" highlighted the severity and grim prognosis of this malformation (1), and credit for the first successful closure of an omphalocele was given to Hey in 1803 (2). The goal of treatment is to return the intestinal loops to the abdomen and to close up the opening in the abdominal wall, in many cases with small and medium-sized omphalocele this being possible per primam. Mobilization of skin flaps from the flank to cover an omphalocele was first described in detail by Gross in 1948 (3). Given the risk of bleeding, infection, and skin necrosis this method is currently used only in combination with other techniques. In 1814, Scarpa noted that omphalocele is often associated with other congenital anomalies and that a large omphalocele is usually fatal because the return of the loops to the abdomen is impossible. In other cases, the newborn associates severe pulmonary hypoplasia, cardiac defects, immaturity, or other congenital abnormalities that contraindicate surgery. Nonoperative treatment of omphalocele was first described in 1899 by Ahlfeld, who used alcohol as antiseptic and escharotic agent (4). The technique became popular in 1963 when Grob described the topical use of 2% mercurochrome solution for promoting progressive epithelialization (5). The result is a ventral hernia that requires elective repair surgery usually at the age of approximately one year (6). In 1967, Schuster proposed a staged closure of omphalocele, the promoter of "silo" method, using two Teflon® sheets (7). In 1969, Allen and Wrenn's modification of this technique involved a single circular Dacron-reinforced silastic sheet sutured to the abdominal wall defect (8). The now available prefabricated silos can be placed without the need for fascial sutures (9) and sometimes even for anesthesia, thus the abdominal compartment syndrome being avoided; this tipped the balance towards staged closure of anterior abdominal wall defects against primary closure in an increasing number of centers throughout the world (10). Two other important advances in the medical management of these children had a significant impact in the last 30 years, namely the use of post-operative paralysis and ventilatory support in the neonatal intensive care unit (11) and the introduction of total parenteral nutrition (12). Since the 1970s, prenatal ultrasound diagnosis of congenital anterior abdominal wall malformations further increased the survival rate. In recent decades, we have witnessed a dramatic increase in the survival rate of children with these conditions, 10% in 1960 to approximately 90% in

1980-1990 (13). Newborn babies with omphalocele associated with severe chromosomal or structural abnormalities have a poor prognosis, requiring an open discussion with the parents and neonatologist before initiating an aggressive treatment. In Romania, currently there is no comprehensive study on the incidence, treatment, and survival of patients with anterior abdominal wall defects; this study aims to address at least part of these deficiencies.

Material and Methods

We performed an analytical retrospective study covering a period of 23 years, January 1990 – September 2012 of all children with omphalocele admitted to the Pediatric Surgery Unit of the Iași „Sfânta Maria” Emergency Children Hospital. Data were collected from medical records, 8 patients being excluded from the study due to damaged or incomplete records. Prenatal diagnosis, surgical referral, children's age upon admission, associated diseases, medical and surgical management in the specialized center, early and late post-operative complications, and length of hospital stay were analysed. Data were expressed as mean \pm standard deviations or as frequencies. The threshold of statistical significance was $p \leq 0.05$. To perform a pertinent statistical analysis of the obtained data sets specialized software, such as SPSS, Statistica and Microsoft Excel were used. The study was approved by the hospital ethics committee, meeting the requirement for research bioethics and ethics. One hundred and five patients were analysed: small and medium-sized omphalocele - 68 cases, giant omphalocele - 30 cases, and ruptured omphalocele - 7 cases. Overall survival rate was 45.7%. Chromosomal abnormalities were confirmed in 29 patients (27.6%): Down syndrome - 7 cases, trisomy 18 - 7 cases, trisomy 13 - 3 cases, trisomy 1 - 1 case, Widemann - Beckwith syndrome - 2 cases, and other genetic abnormalities - 9 cases. Chromosomal abnormalities were detected in almost half (42.1%) of the deceased patients with 85% of them also presenting other associated congenital malformations, compared with 10.4% and 56.3%, respectively in the survivors ($p = 0.024$). Of the 105 patients, 71.4 % had one or more associated congenital abnormalities. The size of the anterior abdominal wall defect was on average 6.20 ± 3.24 cm in the survivors and 7.01 ± 3.96 cm in the patients who died, difference statistically insignificant ($p = 0.252$). The special requirements for transportation of a newborn with anterior abdominal wall defect to a specialized pediatric surgery center were met in only 78% of cases; 12.5 % of the survivors and 30% of the newborns with omphalocele who died were inadequately transported. All 7 cases of ruptured omphalocele had a poor outcome. Area of residence of omphalocele patients was urban in 38% of the cases; the parents of 9 of the 14 children prenatally diagnosed with this condition (13.3% of all patients) lived in urban areas, statistically significant association ($p = 0.030$). The average age upon admission was 10.33 hours, but when surviving and deceased newborns were analysed separately there was a significant 9.45 hour difference between them in favor of the deceased: 15.46 ± 31.0 versus: 6.01 ± 6.5 hours, respectively

($p = 0.043$). The explanation could be that the deceased patients were more severe cases, and thus more rapidly referred to pediatric surgery. When analysing the age upon admission of the prenatally diagnosed patients we found a difference of about 6 hours ($p = 0.023$) in their favor compared to the post-natally diagnosed newborn babies (5.10 versus 11.14 hours). After admission to the neonatal intensive care unit, the newborn with omphalocele underwent thorough clinical and laboratory assessment aimed at determining and later on correcting the hydroelectrolyte, acid-base, and thermal imbalances, and detection of associated abnormalities and malformations; a broad-spectrum antibiotic prophylaxis was initiated and based on test results and omphalocele size an appropriate treatment protocol was established. According to this protocol, 58 patients (55.2%) underwent surgery: resection of omphalocele membrane, reintegration of intestinal loops into the peritoneal cavity, primary closure of the abdominal wall defect, umbilicoplasty - 49 cases (Fig. 1), defect coverage with skin flap from the flanks (Gross technique) - 5 cases, reintegration of the viscera through a two-stage resection of avascular membrane (Fufezan technique) - 2 cases, staged reintegration of the intestinal loops into the abdomen, according to Schuster technique - 2 cases (Fig. 2). In only two patients, in which a primary closure of the defect was performed, the intraabdominal pressure was measured by a mercury manometer, the pressure being within normal range. In the other patients, the possibility to reintegrate the abdominal viscera and tension-free closure was assessed subjectively by each surgeon, and objectively by measuring ventilatory pressures and arterial oxygen saturation during surgical maneuvers. Expansion of the abdominal wall defect was required in 12 cases (for liver reintegration), and in 18 patients other concomitant surgeries were performed. Thus, in 8 children the persistent omphaloenteric duct or Meckel diverticulum was resected with primary ileo-ileal anastomosis; in two patients with jejunoileal atresia and in other two with ileal perforation resection and primary anastomosis were performed; in a patient with esophageal atresia and associated high anorectal malformation thoracotomy, cervicostomy and gastrostomy, laparotomy and colostomy were performed; in one patient a persistent urachus was resected, and in 3 patients with bladder exstrophy a bladder plate closure with pubic osteotomy in two of them were also performed. In one of the two patients with cloacal exstrophy (OEIS complex) bladder plate closure, ileostomy, pubic osteotomy and closure of pubic symphysis were performed, the other patient dying before surgery. Of these 18 patients requiring concomitant surgery only 8 survived. Six (10.34 %) of the 58 operated patients presented postoperative complications requiring surgical reinterventions. Survival rate in the group of operated patients was 50%. The course according to the type of the first surgery was as follows: 25 of the 49 newborns with reintegration of the viscera into the abdomen and primary closure of the defect survived; both patients in which Schuster method and both patients in which an umbilical cord patch were used did not survive. Two patients initially treated by Gross technique required surgical reintervention at the age of 1.5 years

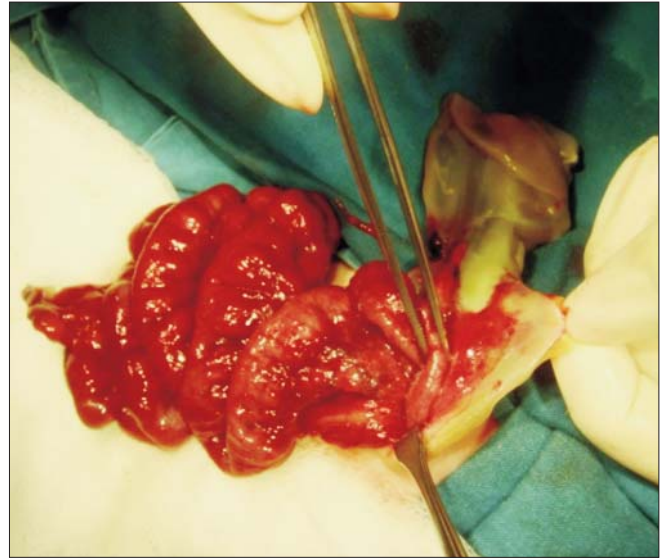


Figure 1. Omphalocele membrane resection and primary reintegration of the intestinal loops



Figure 2. Staged reintegration of the intestinal loops with the help of a sterile urine bags

and 2 years, respectively, consisting in the surgical repair of the right rectus abdominis muscles dehiscence, 2 of the remaining 3 patients survived but were lost to follow up after the age of two and one patient died two days postoperatively. The small number of patients treated by the last three methods does not allow us to statistically compare the data and draw reliable conclusions on the effectiveness of one surgical method over another. Forty-seven patients with omphalocele were treated conservatively because of the severe associated malformations that contraindicated surgery (5 cases), chromosomal abnormalities incompatible with life (2 cases), or large-sized omphalocele (40 cases). Conservative treatment relied on Grob method. Within 2-4 weeks, the marginal epithelialization process has advanced, covering the abdominal viscera with newly formed skin, changing the omphalocele into a ventral hernia (Fig. 3). Of the 47 omphalocele patients treated



Figure 3. Ventral hernia resulting from the conservative treatment of a giant omphalocele

conservatively only 19 survived (40.4%); 10 patients needed surgical reintervention to repair the rectus abdominis muscle dehiscence around the age of 2 years (8 cases), 11 months (1 case), and 16 years (1 case). In 8 patients the left hepatic lobe, firmly adherent to the skin, required careful dissection and hemostasis (Fig. 4), but without notable postoperative complications. Of the remaining 9 patients 5 were lost to follow up, in 2 the abdominal wall defect closed spontaneously and did not require surgery, and 2 were operated in another pediatric surgery center. Comparatively analysing the groups of surviving patients in terms of the length of hospital stay, a significantly shorter stay was found in patients who underwent surgery compared to those treated conservatively: 14.20 ± 6.73 days versus 37.63 ± 26.36 days at first admission ($p = 0.001$) and 17 ± 11.02 days versus 53.05 ± 33.82 days overall ($p = 0.0002$). However, the surgically treated patients started enteral feeding later, on average on day 3.9, and received total enteral nutrition on day 9.2 compared to 2.6 days and 8.3 days, respectively in the conservatively treated patients, difference statistically insignificant ($p=0.07$ and $p=0.54$, respectively).

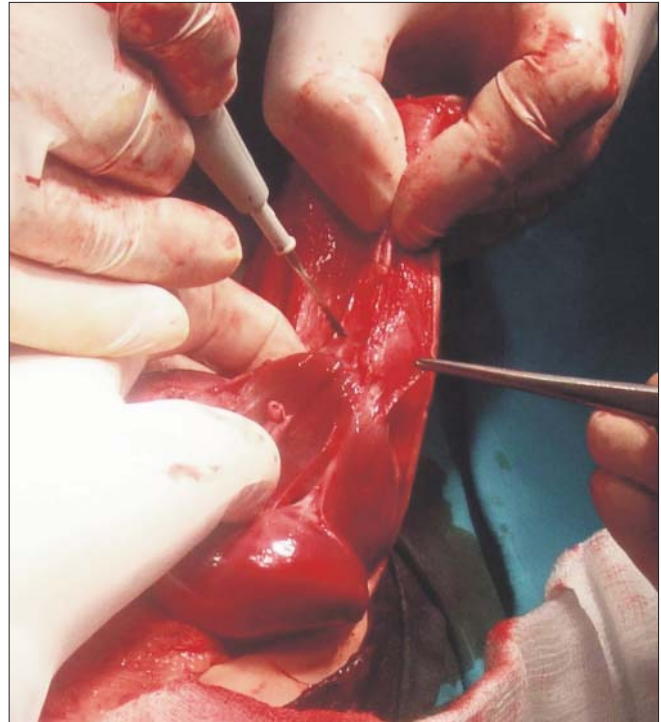


Figure 4. Dissection of adhesions to the liver

The frequency of medical complications in relation with the type of treatment is shown in Table 1. Although all patients received since admission at least one broad spectrum antibiotic, 16.6 % of survivors and 54.3 % of the deceased had developed hospital-acquired severe sepsis (37.1 % of total). Once all 29 surgically treated patients received enteral nutrition exclusively and in the 19 conservatively treated patients the omphalocele sac was satisfactorily covered by newly formed epithelium, the survivors were discharged home and scheduled for follow up visits at 2 weeks, then 3 month and 6 months, or in emergency in case of complications. Only 31 of the surviving 48 children with omphalocele returned for at least one follow up visit, 28 of them having favorable outcome and reaching normal height and weight for age by the age of 6-7 months. The other 3 patients had episodes of gastrointestinal intolerance, constipation or intestinal obstruction caused by adhesions and bands (none required surgical reintervention) resulting in a moderate weight-height deficit. Of these, two children had Down syndrome.

Discussions

Newborn babies with omphalocele represent a significant proportion of the patients with a prolonged hospital stay in

Table 1. Frequency of complications according to treatment type

| Treatment | Anemia | Thrombocytopenia | Bronchopneumonia | Enterocolitis | Sepsis | Mortality |
|--------------|--------|------------------|------------------|---------------|--------|-----------|
| Surgical | 48.2% | 41.3% | 36.2% | 23.4% | 39.6% | 50% |
| Conservative | 26.7% | 27.6% | 29.7% | 5.1% | 34.0% | 59.6% |

neonatal intensive care units. Comparatively analysing the groups of surviving omphalocele patients in terms of the length of the first hospital stay and total length of hospital stay we found a significantly shorter stay in the surgically treated compared with conservatively treated patients ($p = 0.001$ and $p = 0.0002$). Surviving surgically treated patients started enteral feeding a little later, differences being statistically insignificant. Medical complications occurred more frequently in the surgically treated group (Table 1), but survival rate was higher in this group of patients compared with those treated conservatively: 50% and 40.4%, respectively. Moreover, most conservatively treated patients will require additional follow-up of ventral hernia, multiple check-ups, and at least one more surgery to repair the ventral abdominal muscle dehiscence and the esthetic and functional deficit. In a 1997 study on 31 surgically treated patients with omphalocele Dunn reported a mortality rate of 10% and an average hospital stay of 52 days (range 3 to 496 days), depending on the severity of associated congenital anomalies and the degree of visceroperitoneal disproportion (14). In a 2006 article Lee et al. pleaded for conservative treatment only in patients with giant omphalocele and severe chromosomal, heart or lung abnormalities, and repair of remnant ventral hernia by the age of 6 to 12 months (6). The authors reported a median length of hospital stay of 20 days, range 5 - 239 days (compared to 30 days, range 7 - 112 days in our study), the median age until the initiation of total enteral nutrition of 8 days, range 4 - 80 days (compared to 7 days, range 3 - 23 days), and a mortality rate of 13.3% (compared to 59.6%). The length of hospital stay depends on the association of other congenital malformations, abdominal wall closure method, and postoperative complications. In small omphaloceles without associated abnormalities the primary closure of the abdominal wall results in a shorter length of stay, of only a few days, as opposed to a very long stay, sometimes for several months, in the case of giant omphaloceles initially treated conservatively by the use of escharotic agents. All these results plead for the surgical treatment of omphalocele, at least when not contraindicated by the presence of severe chromosomal abnormalities, lung hypoplasia or some heart defects that contraindicate general anesthesia, postnatal mortality being closely related to their presence. A recent study conducted in Germany revealed an 81% rate of associated anomalies in omphalocele and of only 28% in gastroschisis. Mortality rate in this group of patients was 0% for gastroschisis and 8% for omphalocele (15). The mortality rate of congenital anterior abdominal wall defects has significantly decreased, but these very good results are recorded in developed countries where the prenatal diagnosis rate exceeds 60% (69% for omphalocele and 88% for gastroschisis in Germany), thus allowing birth planning and optimal medical and surgical management (15). However, in developing countries the mortality rate is still high, reaching 20% for omphalocele and up to 80% for gastroschisis (16). Long term prognosis of children with omphalocele depends on the presence and severity of chromosomal abnormalities and associated malformations present with a frequency of up to 72% (17,18) (71.4% in our study). The high mortality rate in the present study is also accounted for by

the association of other severe congenital malformations (statistically significant difference between deceased and survivors) and absence of prenatal diagnosis, 27.6% of the children in our study presenting associated chromosomal abnormalities. Their prenatal diagnosis could lead to a parental decision to terminate pregnancy and thus to a lower postnatal mortality rate. A concordance in the characteristics of omphalocele patients admitted to and treated in our clinic and those in other studies was noticed, only the survival rate being significantly lower due to some negative factors such as the absence of prenatal diagnosis, delayed and improper transportation, delayed correct treatment, and high rate of sepsis. Babies with prenatally diagnosed omphalocele are born in a specialized center, the medical team being ready to provide the highest level of immediate care for the newborn, thus improving the prognosis. In the present study we found a significant association ($p = 0.030$) between the rate of prenatal diagnosis and living in an urban environment, in rural areas the poor living conditions leading to a low rate of presentation to a doctor and hence of disease diagnosis. When age upon admission of the prenatally diagnosed patients was analysed, we found a significant difference of about 6 hours ($p = 0.023$) in their favor compared to those without prenatal diagnosis. If a prenatal diagnosis was not made and the child with anterior abdominal wall defect was born in a hospital that cannot provide an adequate level of care, the medical team has to follow a protocol for postnatal referral, as described by Stringer in 1991 (19). Unfortunately, this protocol has not always been followed, 30% of the deceased patients being inadequately transported to our unit, this having a negative impact on the survival rate. In addition, improper handling and transport of the newborn with omphalocele can lead to ruptured membranes, another negative prognostic factor (all 7 patients with ruptured membranes have died). Giant omphalocele is difficult to treat, the conservative treatment not being free of serious complications such as sepsis, rupture of membranes and evisceration, damage to the intestinal loops or liver, bleeding. The very long hospital stay of these patients may also be a problem, and many of these children die before complete epithelialization (20). The surgical treatment of giant omphalocele has to face the visceroperitoneal disproportion. The small, underdeveloped peritoneal cavity may cause compression of abdominal contents, ventilatory disturbances, compression of the inferior vena cava and mesenteric vessels with decreased venous return, impaired hepatic and renal circulation with the risk of developing an abdominal compartment syndrome (21,22). If the wall defect is closed using a "silo-bag", the progressive return of intestinal loops into the abdomen can be guided with a pulse oximeter placed directly on the prosthetic bag, actively monitoring the degree of loops oxygenation and detecting early a possible abdominal pressure (23). In the last two decades, prefabricated silastic bags (spring loaded silo) have been used routinely, and seem to be the method of choice in the treatment of large omphaloceles. Multiple retrospective studies analyse the differences in outcome of

primary closure versus the „silo” method, most documenting better outcomes after primary closure. These results may represent selection biases because the patients treated by Schuster method were actually those who had severely impaired intestinal loops or associated other defects that contraindicated general anesthesia, these being responsible for the worse results and not the surgical technique itself. Prospective studies on larger series of patients are required for developing criteria of optimal therapeutic decision making (24). Unfortunately, due to the high cost, the silo-bags are not available in our clinic, so that for the Schuster method we had to use other types of prosthetic materials, with questionable results (Fig. 2). The small number of patients treated by the Schuster method did not allow us to compare the data statistically in view of drawing reliable conclusions on the effectiveness of one surgical method over another. The frequency of complications in the treatment of anterior abdominal wall defects decreases as the medical-surgical team gains experience and the structure of neonatal intensive care units is improved. Infectious complications are responsible for the increased morbidity and mortality of patients with anterior abdominal wall defects (25), but are not closely related to the initial status of the patient or used therapeutic method. In conservatively treated giant omphaloceles there is a risk of omphalocele membrane infection with multiresistant hospital germs, the necrosis and rupture of this membranes being the most severe complication. The risk of local infection is also high if prosthetic materials are used, especially if the closure is under tension with the risk of sheet dislocation or subsequent surgical wound dehiscence. In 1976, Rubin reported in a series of 55 cases of omphalocele and gastroschisis treated by the Schuster method an infection rate of 60% with a mortality rate of 28%, mainly due to *Candida*, closely related to how long the prosthetic material is used (26). Although upon admission all our patients received at least one broad-spectrum antibiotic, 37.1% of all children and 54.3 % of the children who died had developed severe nosocomial sepsis. Many of these infections can be avoided by strictly observing the rules of perioperative asepsis and antisepsis and systematically administering antibiotic therapy, initially broad-spectrum and subsequently targeted, and protective antifungal therapy when antibiotic therapy is long-term. In the absence of severe heart or lung malformations and chromosomal abnormalities, most of these children will live a normal life (27). A 2001 study concluded that the abnormalities and malformations associated with anterior abdominal wall defects are the main factors that may affect long-term quality of life (28). Over 90% of the children with anterior abdominal wall defects without associated abnormalities and malformations will have a normal physical, psychological and intellectual development and perfectly integrated into society at adulthood. Parents should be advised regarding the need for long-term follow up of the patient, but also reassured about the favorable prognosis in terms of growth and development of most children with such

problems. Currently, survival and quality of life of children with omphalocele has improved dramatically due to the more and more widespread use of prenatal diagnosis and significant progress in terms of medical and surgical management of these patients.

Conclusions

Comparing the results of our study with data in the literature, we believe that a closer monitoring of pregnancy, increasing the prenatal diagnosis rate and implicitly of therapeutic abortion in case of severe chromosomal abnormalities, a faster referral and adequate transport of the newborns with anterior abdominal wall defects, and also a more aggressive surgical approach (possibly by the Schuster method) would result in increased survival. More studies on congenital malformations in general and on their diagnosis and treatment, the causes of such high morbidity and mortality in our country are needed because these malformations are an important factor of neonatal mortality.

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