Does Meconium Contaminated Amniotic Fluid Affect Intestinal Wall Thickness and Functional Outcome in Patients with Anterior Abdominal Wall Defects?

Melanie Kapapa, Teresa Rieg[1], Alexandre Serra

Department of Surgery, Division of Pediatric Surgery, University Ulm Medical Centre, Eythstrasse, Ulm, [1]Department of Gynaecology and Obstetrics, Hospital Heidenheim, Heidenheim an der Brenz, Germany

Abstract

Background: Gastroschisis (GS) and omphalocele (OC) are congenital abdominal wall defects, the main difference between is the direct exposure of intestinal loops in amniotic fluid in children with a GS. This leads to a reduced primary closure rate and a higher number of intraoperative abnormalities and post-operative complications. **Aims and Objectives:** We analysed abdominal wall defect patients over an 11-year period, aiming to assess the influence of meconium-contaminated amniotic fluid. This study has different objectives to show the consequence of functional outcome of abdominal wall defects (AWD) children in reliance to colour of amniotic fluid, to assess the effect of reduced bowel exposure time to meconium contaminated amniotic fluid on edematous inflammatory thickening of the bowel loops, to show an positively influence in the number of primary AWD closures, to demonstrate a reduced incidence of post-natal complications and to verify a better outcome of OC children because of failing exposure to amniotic fluid. **Methods:** A retrospective, observational case–control design was used to compare GS (n = 36) and OC (n = 18) children. Physical data, colour of amniotic fluid, pre- and perinatal problems, operative complications and surgical technique, post-operative complications, duration of intensive care unit (ICU) stay, mechanical ventilation, parenteral nutrition, commencement of oral feeding and total hospital stay were collected. Data were analysed with descriptive methods, t-test and non-parametric tests such as Wilcoxon and Kruskal–Wallis were performed in addition to the analysis of variance, including *post hoc* testing accepting a confidence interval of 95% ($P < 0.05$) by using IBM SPSS software, version 23 (IBM, Illinois, USA). **Results:** Rate of meconium-contaminated amniotic fluid is significantly higher in GS compared to OC ($P < 0.001$), delivery problems such as congenital infections are also significantly higher ($P < 0.001$), this yields in significantly more bowel loops anomalies and problems during surgery ($P < 0.036$) but had no significant influence on primary abdominal wall closures rate ($P = 0.523$). The post-surgical outcome of OC was significantly better as compared to GS. Within the GS, those with swollen intestines had significantly longer ICU stays ($P = 0.045$) due to extended mechanical ventilation ($P = 0.007$), parenteral nutrition ($P = 0.011$) and delayed initiation of oral feeding ($P < 0.001$. Same results were found for the duration of ICU stay ($P = 0.008$), mechanical ventilation ($P = 0.006$), parenteral nutrition ($P = 0.011$) and delayed initiation of oral feeding ($P < 0.001$) in secondary closures as compared to primary abdominal wall closures in the GS group. **Conclusions:** Worsen functional short-term outcome of GS children was directly addicted to meconium contamination of amniotic fluid due to swollen intestines and because of this more post-surgical problem including significantly extended hospital stays were observed.

Keywords: Abdominal wall defects, gastroschisis, omphalocele, outcome

Introduction

Congenital anterior abdominal wall defects (AWD) include severe abnormalities of the anterior abdominal wall such as gastroschisis (GS) and omphalocele (OC). In GS, the intestines are directly prolapsed and exposed to the surrounding amniotic fluid[1] and as pregnancy progresses, this exposure causes the

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Address for correspondence: Dr. Melanie Kapapa, Department of Surgery, Division of Pediatric Surgery, University Ulm Medical Centre, Eythstrasse 24, 89075 Ulm, Germany.
E-mail: melanie.kapapa@uniklinik-ulm.de

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formation of an inflammatory layer on the intestines, leading to thickening of the intestinal wall, decreased intestinal motility and potentially intestinal obstruction through a reduced intraluminal diameter caused by thicker intestinal walls.[2] GS is rarely associated with other distant malformations, yet can lead to intrauterine and postnatal complications such as bowel dysfunction, bowel atresia, bowel necrosis and/or short-bowel syndrome.[3,4] Children with OC have normally no direct exposure of their intestines and other prolapsed organs to the amniotic fluid, but OC is often associated with congenital heart diseases or genetic disorders.[5-7] Numerous studies have already tried to understand which factors influence the pre-, peri- and post-natal outcome in AWD infants, aiming to establish an optimal time of delivery, especially in GS neonates.[8,9]

Methods

Design

The present study was designed as a retrospective, observational case–control supported trial, enrolling children with either GS or OC. The local ethics committee approved this study (No. 29/11). Information was gained by recorded in-hospital files and surgical reports.

Inclusion criteria

AWD new-borns treated surgically during the study period at the department of pediatric surgery of the tertiary hospital were included.

Exclusion criteria

We excluded syndromic anomalies such as multiple midline anomalies (e.g., Cantrell's Pentalogy) and body wall-limp defect complexes.

Patients

The International Classification of Diseases (ICD-9 and-10) was used to identify all patients with diagnostic code Q79.3 for GS and Q79.2 for OC. During the survey period of the study 27.438 (twenty-seven thousand and four hundred thirty-eight) deliveries occurred, there from 36 new-borns with GS and 18 new-borns with OC. Four OC (n = 4) patients died (e.g., of heart failure) in older age.

Data collection

All parents were initially contacted by phone. After written informed consent to participate the data was collected: Physical data (gestational age, birth weight and height) through in-hospital files, colour of amniotic fluid, gestational week of first ultrasound detection of GS (duration of bowel contact), pre- and perinatal problems (early rupture of amniotic membranes, congenital infection and prolapsed organs), operative findings (meconium contamination and or fibrin coated intestines, edematous intestines, stenosis, perforation and surgical complications (partial resection and ileostomy) and surgical technique for AWD correction, post-operative complications (bowel movement and mechanical ileus), duration of intensive care unit (ICU) stay, mechanical ventilation, parenteral nutrition, also time to the initiation of feeding and total hospital stay directly from AWD patients' medical records and additionally from surgical reports.

Statistics

The recorded data were initially analysed with descriptive methods and clearly outlined. The mean, standard deviation, median and range were reported in the case of quantitative parameters, absolute and relative frequencies for the qualitative parameters. Exploratory tests between interesting subsets were selected based on the underlying parameters. Given the size of the subsets, the t-test and non-parametric tests such as Wilcoxon and Kruskal–Wallis were performed in addition to the analysis of variance, including *post hoc* testing. Ordered logistic regressions for univariate and multivariate group differences and analyses of covariance were performed. Significance was established as $P \leq 0.05$. All statistical tests were analysed using the IBM SPSS software, version 23 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

Results/Procedure

Physical data

The mean age of delivery of GS children was 35.6 (27–38) pregnancy weeks, whereby 78.8% of these children were preterm and 21.2% term new-borns (P = 0.036). OC patients were on average 36.6 (27–41) weeks at delivery. Average of GS delivery age was significantly lower (P = 0.027) as compared to OC. The birth weight showed no significant difference, despite the height at birth which was significant lower (P < 0.05) [Table 1].

Color of amniotic fluid

In 95.5% of GS deliveries the colour of the amniotic fluid was documented as compared to 88.9% of OC deliveries. Clear amniotic fluid was found in 24.9% of GS, as compared to 83.3% in OC group (P < 0.001), which could be influenced by intrauterine stress. In GS group, 69.4% had meconium contaminated amniotic fluid, compared to 5.5% in OC group (P < 0.001), in 5.7% the colour of amniotic fluid was not documented [Table 1].

Bowel loop abnormalities

In 24.9% of GS dilated bowel loops were detected through prenatal ultrasound, compared to none in OC group (P = 0.016), at delivery in 69.4% meconium contaminated bowel loops were present in GS, as against 5.5% in OC group (P = 0.145). Problems with enteral feeding were found in 50% of GS and in 33.3% of OC group (P = 0.025) additionally bowel movement problems till discharge and mechanical ileus are present in 24.9% of GS, but none in OC group (P = 0.021) [Table 2].

Abnormalities during surgery

We found edematous/swollen small intestines in 50% of GS and in 5.5% of OC group (P = 0.001), in GS fibrin-coated bowel loops were striking in 38.8% (P = 0.002), a stenosis was present in 11.1% (P = 0.212), an ileostomy has to be performed in 30.5% (P = 0.010), a bowel perforation with consequence of partial bowel resection in 22.2% (P = 0.032) of the group, whereas nothing of these was found in

OC group. Overall abnormalities were found significantly more often in GS group (91.6%; *P* = 0.036) as compared to OC group (83.3%) [Table 2].

Technique for abdominal wall closure

Primary closure could be performed in 66.6% of GS and 77.7% of OC group (*P* = 0.523), secondary closure in 33.3% of GS and 22.2% of OC (*P* = 0.523). Within the secondary closures, the need of using a non-meshed Neuro-Patch® to closure was 2.7% in GS as compared to 5.5% in OC (*P* = 0.511), using silo-bag till final closure in 22.2% in GS compared to 16.6% OC (*P* = 0.277). A combination of both techniques (silo-bag followed by patch) was performed in 8.3% in GS, but it was not necessary in OC [Table 2].

Clinical progress on intensive care unit

The duration of stay on ICU was 23.34 days for GS and 20.22 days for OC (*P* = 0.201), days of ventilation in GS 12.69 days compared to 7.89 days in OC group (*P* = 0.021), the initiation of enteral nutrition after primary closure began after 12.80 days compared to 5 days in OC group (*P* < 0.001), the total parenteral nutrition period was 42.46 days in GS and 19.89 days in OC group (*P* < 0.001). The total hospital stay duration till discharge was 55.6 days in GS group as compared to 31.7 days in OC group (*P* = 0.034) [Table 3].

Clinical progress primary versus secondary abdominal wall closure in gastroschisis

The duration of ICU stay was 13.88 days in primary closures of GS, as compared to 44 days in secondary closures (*P* = 0.008) of GS. The duration of ventilation was 6.21 days in primary closures, in comparison to 26.82 days in secondary closures (*P* = 0.006). Initiation of enteral feeding could be started after 7.92 days in primary closures, as against to 23.45 days in secondary closures (*P* < 0.001). The duration of total parenteral nutrition was 30.96 days in primary closures, in contrast to 67.55 days in secondary closures. The total duration of hospital stay till discharge was 43.17 days in primary closures, in contrast to 82.73 days in secondary closures (*P* = 0.034) [Table 3].

Clinical progress swollen versus normal small intestines in gastroschisis

In 25 GS new-borns meconium-stained amniotic fluid was present and resulted to swollen intestines in 18 of them. The duration of ICU stay was 26.5 days in GS with clinically swollen small intestines, compared to 20 days in those with normal non-swollen intestines (*P* = 0.045). The duration of ventilation was 14.89 days in GS with clinically swollen small intestines, in comparison to 10.35 days in those with normal non-swollen intestines (*P* = 0.007). Initiation of enteral feeding could be started after 15.83 days in GS with clinically swollen small intestines, as against to 9.59 days in GS with normal non-swollen intestines (*P* = 0.002). The duration of total parenteral nutrition was 40.28 days in GS with clinically swollen small intestines, in contrast to 36.29 days in GS with normal non-swollen intestines. The total duration of hospital stay till discharge was 61.22 days in GS with clinically swollen small intestines, in opposition to 49.65 days in GS with normal non-swollen intestines (*P* = 0.034) [Table 3].

Discussion

In the present study, GS new-borns were delivered on average after 35.6 gestational weeks and 36.6 gestational weeks in the OC group. The rate of pre-terms (<37 gestational weeks) was significantly higher in our GS group as compared to OC. Our data show delivery before 37. Pregnancy weeks did not result in disadvantages for the AWD patients and/or in significant differences in the short-term outcome due to prematurity, which further emphasizes and corroborates the notion that shortly after the sonographic detection of the first

Table 1: Physical data (gestational age. birth weight). Colour of amniotic fluid and problems at delivery in gastroschisis and omphalocele newborns

	Gastroschisis (*n*=36)	Omphalocele (*n*=18)	*P* OC vs. GS
	Physical data		
Gestational age (weeks)	35.6 (27-38)	36.6 (27-41)	*P*=0.027
Preterm (<37. gestational weeks)	*n*=26 (78.8%)	*n*=7 (21.2%)	*P*=0.036
Term (>37. gestational weeks)	*n*=10 (47.6%)	*n*=11 (52.4%)	non-significant
Birth weight (gram)	2438g (1550-3080g)	2790g (980-3960g)	*P*<0.05
Height at birth (cm)	46.2cm (42-53cm)	48.8cm (37-58cm)	
Color of amniotic fluid [%]			
No comment	*n*=2 (5.5%)	*n*=2 (11.1%)	non-significant
Clear	*n*=9 (24.9%)	*n*=15 (83.3%)	*P*<0.001
Meconium contaminated	*n*=25 (69.4%)	*n*=1 (5.5%)	*P*<0.001
Problems at delivery/postnatal [%]			
Early rupture of amniotic membranes	*n*=5 (13.8%)	*n*=4 (22.22%)	*P*=0.404
Congenital infection (CrP; Il-8)	*n*=19 (52.77%)	*n*=1 (5.5%)	*P*=0.001
Prolapsed organs	*n*=36 (100%)	*n*=10 (55.5%)	*P*<0.001
Small intestines	*n*=34 (94.44%)	*n*=7 (38.88%)	*P*<0.001
Small intestines & liver	*n*=1 (2.77%)	*n*=11 (61.11%)	*P*<0.001
Liver			

Table 2: Abnormalities of bowels prenatal and postnatal. During surgery and technique for abdominal wall closure

	Gastroschisis (*n*=36)	Omphalocele (*n*=18)	*P* OC vs.GS
Bowel loops abnormalities [%]			
Dilated intestinal loops via prenatal ultrasound	*n*=9 (24.9%)	*n*=0 (0.0%)	*P*=0.016
Meconium contaminated bowel loops at delivery	*n*=25 (69.4%)	*n*=1 (5.5%)	*P*=0.145
Bowel movement problems till discharge	*n*=9 (24.9%)	*n*=0 (0.0%)	*P*=0.021
Mechanical ileus till discharge	*n*=9 (24.9%)	*n*=0 (0.0%)	*P*=0.021
Problems with enteral feeding	*n*=18 (50.0%)	*n*=6 (33.3%)	*P*=0.250
Abnormalities during surgery [%]	*n*=33 (91.6%)	*n*=15 (83.3%)	*P*=0.036
Edematous/swollen small intestines	*n*=18 (50.0%)	*n*=1 (5.5%)	*P*=0.001
Ileostomy	*n*=11 (30.5%)	*n*=0 (0.0%)	*P*=0.010
Stenosis of bowel loop	*n*=4 (11.1%)	*n*=0 (0.0%)	*P*=0.212
Bowel perforation/-partial resection	*n*=8 (22.2%)	*n*=0 (0.0%)	*P*=0.032
Fibrin-coated small intestines	*n*=14 (38.8%)	*n*=0 (0.0%)	*P*=0.002
Technique for abdominal wall closure			
Primary closure of abdominal wall	*n*=24 (66.6%)	*n*=14 (77.7%)	*P*=0.523
Secondary closure of abdominal wall	*n*=12 (33.3%)	*n*=4 (22.2%)	*P*=0.523
Using patch	*n*=1 (2.7%)	*n*=1 (5.5%)	*P*=0.511
Using silo-bag	*n*=8 (22.2%)	*n*=3 (16.6%)	*P*=0.277
Using silo-bag followed by patch (combination)	*n*=3 (8.3%)	*n*=0 (0.0%)	non-significant

Table 3: Comparison of gastroschisis and omphalocele in postsurgical outcome: Duration on ICU. ventilation time. Parenteral nutrition. Beginning of enteral feeding. Hospital stay till discharge

Duration in days (d)	Gastroschisis (*n*=36)	Omphalocele (*n*=18)	*P* OC vs. GS	mean	SD
Stay on ICU	23.34	20.22	*P*=0.201	22.28	±30.450±20.25
Ventilation	12.69	7.89	*P*=0.021	11.06	2±9.371±36.69
Initiation enteral nutrition after primary closure	12.80	5.0	*P*<0.001	10.15	3±46.138
Total parenteral nutrition	42.46	19.89	*P*<0.001	34.79	
Hospital stay till discharge	55.6	31.7	*P*=0.034	47.49	

dilated bowel loops a planned delivery should be performed, regardless of the possible immaturity of the new-born. We therefore fully support an optimization of the time of delivery based on the clinical findings of ultrasound, advocating that the delivery should take place shortly after the initial signs of intestinal wall edema and damage are present in GS children.[10-12] Documentation of amniotic fluid colour was present only in 94.3% of GS and 88.8% of OC deliveries; GS had significantly more often meconium contaminated fluid. A constant irritation of the exposed bowel loops by eliminated meconium intensifies the defecation thus creating a self-perpetuating, deleterious cycle in particular GS new-borns much more than in OC new-borns, an in utero defecation is a well-known sign of foetal distress.[13] In terms of timing of abdominal wall closure, it seems a consensus that the operation should take place as soon as possible after delivery, which we were able to accomplish in 89% of GS and 77% of OC patients. This is important, since Baird *et al*. showed that surgery within the first 6 h of life is associated with a significantly lower rate of wound infection,[14] which was unfortunately still high in our study in GS children (52.77%), but not in OC children (5.5%). Time of exposure to meconium-filled amniotic fluid and potential bacterial translocation may explain this discrepancy. We could verify Velemínský and Tosner[15] who found no correlation between a specific bacterial steam and early rupture of membranes. Early rupture of amniotic membranes was not significantly more frequent in GS as compared to OC in this study, despite significantly higher rate of congenital infections in GS new-borns, which was in our opinion caused by damage of intestinal walls though meconium contaminated amniotic fluid. We found no correlation for higher risk of GS after mothers' urinary tract infection like Yazdy *et al*. published.[16] However, we found no correlation between early rupture of membranes with prematurity in both groups. As expected small intestines were always prolapse in GS, just as additionally liver was significantly more frequent in GS, compared to OC. As already known the size and number of prolapsed organs as well as rigidity of intestines as a sign of inflammation had direct influence on primary closure rate.[17] We observed in 24.9% of GS dilated intestinal loops through prenatal ultrasound, most of them had meconium contaminated amniotic fluid. These children had significantly more bowel movement problems and mechanical ileus till discharge. Hence, we completely support Moir *et al*., who showed that in cases of an intestinal thickening seen on ultrasound an earlier delivery leads to less intestinal damage, less secondary closure, reduced wound complications, shorter parenteral nutrition, shorter time to full enteral nutrition and earlier discharge from the hospital.[17] Serra *et al*. confirmed these results and showed that GS new-borns delivered before the 37th week had faster enteral nutrition, shorter hospital stays and fewer complications.[18] Overall, conclusion was that specific sonographic criteria and early elective cesarean lead to better surgical outcome without significant secondary disadvantages due to preterm delivery.[17] Puligandla *et al*. showed prolonged oral nutrition in the preterm and longer duration of hospital stay in later deliveries,[19] which in GS leads to longer directly exposure of the intestines to amniotic fluid thus establishing a direct correlation between gestational age and the degree of intestinal dilation.[20] Furthermore, meconium staining is uncommon before the 37th week gestational age. In addition, we had confirmed that GS new-borns had significantly often edematous bowel loops at surgery (50%), which can lead to difficult reposition of the prolapsed intestine and lower number of primary closures due to the thickening of the intestinal wall[21] and in more surgical procedures, prolonged parenteral nutrition and increased risk of sepsis or liver damage.[22] Similarly, Long *et al*. showed that GS patients had prolonged parenteral nutrition and increased mortality due to intestinal failure (but no differences in the number of operations) when intestinal dilation >20 mm was detected on ultrasound,[23] we verify these results with our study. Independent of gestational age at delivery, GS had more frequently edematous, swollen intestines and needed more often an ileostomy, intestinal decompression or partial intestinal resection compared to OC. These alterations dependent in the present study on the colour of the amniotic fluid at birth, results in significantly elevated dilation with fibrin covered small intestinal loops-consequence were poorer outcome parameters. In terms of timing of abdominal wall closure, it seems a consensus that the operation should take place as soon as possible after delivery, which we were able to accomplish in 66.6% of GS and 77.7% of OC patients. Baird *et al*. showed the importance of fast surgery within the first 6 h of life, because it was associated with significantly lower rates of congenital and wound infection,[14] which was unfortunately still high in our study in GS children (52.77%) but not in OC children (5.5%). Time of exposure to meconium-filled amniotic fluid and potential bacterial translocation may explain this discrepancy of outcome. In the present study, the abdomen could be closed primarily in 66.6% of GS and 77.7% of OC new-borns, rates were comparable to literature,[24,25] we found no significantly advantages in secondary closures between silo-bag or patch. Our results support the statement of Maksoud-Filho *et al*., who found no distinction between primary closure, silo-bag or patch in terms of mortality, there was an extended parenteral nutrition and hospital stay in GS and OC children who were not primary closed.[26] However, a consensus about the advantages and disadvantages of different abdominal wall closure and techniques does not exist.[27] Regarding the surgical techniques employed, we confirmed the accepted notion that primary closure is always desirable in AWD, since it leads to shorter mechanical ventilation and intensive-care stay, shorter parenteral nutrition and earlier begin of oral feeding. Huh *et al*. showed that new-borns with dilated bowels at birth had significantly more often bowel-associated complications and delayed enteral feeding and hospital discharge.[28] We can support these results completely since in our cohort the ventilation time and discharge of OC children occurred significantly earlier than GS children, particularly in those with dilated intestines at birth. Moreover, the delay in the beginning of enteral feeding and longer parenteral feeding leads to affected liver enzymes and hospital stay, those factors carry considerable psychological strain for parents and result in higher costs due to prolonged need of intensive care.[29,30] We could show significant differences between primary and secondary abdominal wall closures inside the GS group. Every parameter was significantly shorter, respectively, better in primary closures: ICU stay, ventilation time, beginning of enteral nutrition, length of parenteral nutrition and total hospital stay. These results were shown as well by Maksoud-Filho *et al*. and Huh *et al*.[26,28] However, overall stands the capital importance of surgeons` clinical view to ponder chances and danger of compartment syndrome to make the best decision for every child individually, not just following written recommendations. Inside the GS group, we could show significant differences between swollen and normal small intestines. GS patients with meconium-contaminated amniotic fluid and fibrin-covered bowels had a lower rate of primarily abdominal wall closure and poor post-operative outcome, with longer periods of mechanical ventilation and parenteral nutrition, ultimately leading to prolonged discharge and much higher costs. Long *et al*. and Piper and Jaksic confirmed these results.[21,23] Every parameter was significantly shorter, respectively, better in normal intestines: ICU stay, ventilation time, beginning of enteral nutrition, length of parenteral nutrition and total hospital stay. Because of our results, we advocate to prevent such situations with swollen rigid intestines, difficult to handle in surgery. The initial damage could not be withdrawn and al the following complications are predictable and often preventable.

Conclusions

The establishment of an ideal delivery time in GS has been extensively discussed and remains controversial.[9,31] Due to the possibility of primary caesarean section, the delivery time can be freely selected, which make the decision even more challenging.[32,33] We could show that functional outcome of AWD children was reliable to colour of amniotic fluid as a sign of contamination. We were able to prove evidence that primary AWD closures were influenced positively and the incidence of postnatal complications were reduced in children with less edematous inflammatory thickening of the bowel loops. This could be easily be influenced by shortening bowel exposure time to meconium contaminated amniotic fluid with optimal planned delivery time. Our data showed that delivery before the 37th pregnancy week does not result in disadvantage due to prematurity for AWD patients, neither in significant differences in short-term outcome. We conclude that the primary prognostic parameter for short-term outcome is the level of damage and swelling of the intestines at the time of the initial surgery. Therefore, it is crucial to establish guidelines for the timing of delivery in AWD and most importantly in GS patients to preventing these complications, which in our opinion should be focused on the diagnosis of bowel damage on ultrasound irrespectively of gestational age. Our data showed that in OC new-borns should not be lumped together, they had better outcome because of failing exposure to amniotic fluid.

Limitation-selection

Strength of our study was complete and extensive neonatal outcome information because of rigorous postnatal outcome evaluation, which was possible because of our multidisciplinary prenatal care team. Strength was high rate of participation and a study period covering late pregnancy, delivery information, surgically conspicuousness and short-term outcome including whole paediatrics ICU stay data until discharge. However, our study is not without limitations. Only life birth AWD patients were included, we were unable to determine associations to stillbirth. Another was the existence of a single centre hospital observation, but we offer the long-term experience of an interdisciplinary team in a maximum care hospital.

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Conflicts of interest

There are no conflicts of interest.

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