

Meconium contaminated amniotic fluid leads to intestinal wall thickness and affects the functional outcome of abdominal wall defects

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Abstract

Background: We analysed abdominal wall defect patients over an 11-year period, aiming to assess the influence of meconium-contaminated amniotic fluid . Meconium-contaminated amniotic fluid leading to intestinal wall thickness and impairs surgical and functional outcome.

Methods: A retro- and prospective, observational case- control design was used to compare gastroschisis (n=36) and omphalocele (n=18) children. Physical data, color of amniotic fluid, pre- and perinatal problems, operative complications and surgical technique, postoperative complications, duration of ICU stay, mechanical ventilation, parenteral nutrition, begin of oral feeding and total hospital stay were collected. Data was analyzed with descriptive methods, t-test and non-parametric tests such as Wilcoxon and Kruskal-Wallis were performed in addition to ANOVA, 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, delivery problems are also significantly higher, this yields in significantly more bowel loops anomalies and problems during surgery but had no significant influence on primary abdominal wall closures rate. The post-surgical outcome of OC was significantly better compared to GS. Within the GS, those with swollen intestines had significantly longer ICU stays due to extended mechanical ventilation, parenteral nutrition and delayed initiation of oral feeding. Same results were found for secondary closures compared to primary abdominal wall closures in 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 stay were observed.

Background

Congenital 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 formation of an inflammatory fibrotic layer in the intestines, leading to thickening of the intestinal wall, decreased intestinal motility and potentially intestinal obstruction (2). GS is rarely associated with other 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) (6) (7). Numerous studies have already tried to understand which factors influence the pre-, peri- and postnatal outcome in AWD infants, aiming to establish an optimal time of delivery especially in GS neonates (8) (9). This study has different objectives: [1] to show the consequence of functional outcome of AWD children in reliance to color of amniotic fluid, [2] hypothesizing that shortening bowel exposure time to meconium contaminated

amniotic fluid reduce edematous inflammatory thickening of the bowel loops, [3] influence number of primary AWD closures positively, and [4] reduces incidence of postnatal complications. We expected [5] better outcome of OC children because of failing exposure to amniotic fluid.

Methods

Design

The study was designed as a prospective, 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 newborns treated surgically during the study period at the Department of pediatric Surgery at Ulm University 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 internal 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 deliveries occurred, therefrom 36 newborns with GS and 18 newborns 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, color of amniotic fluid, pre- and perinatal problems (early rupture of amniotic membranes, congenital infection, prolapsed organs), operative complications (meconium contamination and or fibrin coated intestines, edematous intestines, stenosis, perforation, partial resection, ileostomy) and surgical technique for AWD correction, postoperative complications (bowel movement, mechanical ileus), duration of 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 analyzed 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 ANOVA, 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 analyzed using the IBM SPSS software, version 23 (IBM, Illinois, USA).

Results

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 newborns ($p = 0,036$). OC patients were on average 36,6 (27–41) weeks at delivery. Average of GS delivery age was significantly lower compare to OC ($p = 0,02$). The birth weight showed no significant difference despite the height at birth ($p < 0,05$) (Table 1). Again, the exposure to the meconium-filled amniotic fluid seems to be the decisive factor for the outcome of GS regardless of birth age.

Color of amniotic fluid

In 95,5% of GS deliveries the color of the amniotic fluid was documented compared to 88,9% of OC deliveries. Clear amniotic fluid was found in 24,9% of GS, compared to 83,3% in OC group ($p < 0,001$). In GS group 69,4% had meconium contaminated amniotic fluid, compared to 5,5% in OC group ($p < 0,001$) (Table 1).

Problems at delivery

Early rupture of the amniotic membranes was documented in 13,88% of GS group and in 22,2% of OC group ($p = 0,404$). GS mothers had congenital infections in 52,77%, compared to 5,55% in OC group ($p = 0,001$). The prolapsed organs were such as small intestines in 100% of GS, in OC 55,5% ($p < 0,001$), small intestines and liver in GS 94,44%, in OC 38,88% ($p < 0,001$) and liver alone 2,77% in GS and 61,11% in OC group ($p < 0,001$) (Table 1).

Bowel loop abnormalities

In 24,9% of GS dilated bowel loops were detected via 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, while nothing of these was found in OC group. Overall abnormalities were found significantly more often in GS group (91,6%; $p = 0,036$) 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 patch to closure was 2,7% in GS 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 ICU

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 compared to 31,7 days in OC group ($p = 0,034$) (Table 3)

Clinical progress primary vs. secondary abdominal wall closure in GS

The duration of ICU stay was 13,88 days in primary closures of GS, 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 ($p = 0,000$). 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 4)

Clinical progress swollen vs. normal small intestines in GS

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 4)

Discussion

Physical data

In the present study GS newborns 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 compared to OC. Our data shows that delivery before 37.pregnancy weeks did not result in disadvantages for the AWD patients and/or in significant differences in short-term outcome due to prematurity, which further emphasizes and corroborates the notion that shortly after the sonographic detection of the first dilated bowel loops a planned delivery should be performed, regardless of the possible immaturity of the newborn. 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.

Color of amniotic fluid

Documentation of amniotic fluid color was present in 94,3% of GS and 88,8% of OC deliveries, GS had significantly more often meconium contaminated fluid. Since many authors interpret the defecation in utero as a physiological process (10), it is clear that the constant irritation of the exposed bowel by eliminated meconium only intensifies the defecation thus creating a self-perpetuating, deleterious cycle in particular GS newborns much more than in OC newborns. It is well known that meconium contamination affects the neonatal middle ear and the outcome pulmonary aspiration and tracheal suctioning (11).

Problems at delivery

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 hours of life is associated with a significantly lower rate of wound infection (12), 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 Veleminsky et al. (13), 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 compared to OC in this study, despite significantly higher rate of congenital infections in GS newborns, 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 Yasdi et al. published (14). But 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 (15).

Bowel loop abnormalities

We observed in 24,9% of GS dilatated intestinal loops via prenatal ultrasound, these children had significantly more bowel movement problems and mechanical ileus till discharge. So 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 (15). Serra et al. confirmed these results and showed that GS newborns delivered before the 37th week had faster enteral nutrition, shorter hospital stays and fewer complications (16). Over all conclusion was that specific sonographic criteria and early elective cesarean lead to better surgical outcome without significant secondary disadvantages due to preterm delivery (15). Pulingandla et al. showed prolonged oral nutrition in preterm and longer duration of hospital stay in later deliveries (17), 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 (18).

Abnormalities during surgery

Additionally, we had confirmed that GS newborns 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 (19) and in more surgical procedures, prolonged parenteral nutrition and increased risk of sepsis or liver damage (20). 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 >20mm was detected on ultrasound (21), 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 color of the amniotic fluid at birth, results in significantly elevated dilation with fibrin covered small intestinal loops- consequence were poorer outcome parameters.

Technique for abdominal wall closure

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 hours of life, because it was associated with significantly lower rates of congenital and wound infection (12), 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 newborns, rates were comparable to literature (22), (23), we found no significant 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 (24). Yet a consensus about advantages and disadvantages of different abdominal wall closure and techniques does not exist (25). 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.

Clinical progress on ICU in GS vs. OC

Huh et al. showed that newborns with dilated bowels at birth had significantly more often bowel-associated complications and delayed enteral feeding and hospital discharge (26). 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 (27), (28).

Clinical progress primary vs. secondary abdominal wall closure in GS

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. (24), (26). But 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.

Clinical progress swollen vs. normal small intestines in GS

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 postoperative outcome, with longer periods of mechanical ventilation and parenteral nutrition, ultimately leading to prolonged discharge and much higher costs. Long et al. and Piper et al. confirmed these results (21), (19). 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 all the following complications are predictable and often preventable.

Conclusion

The establishment of an ideal delivery time in GS has been extensively discussed and remains controversial (9, 29). Due to the possibility of primary cesarean section, the delivery time can be freely selected, which makes the decision even more challenging (30, 31). We could show that functional outcome of AWD children was reliable to color 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 newborns 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 pediatrics ICU stay data until discharge. However, our study is not without limitations. One limitation was that only life birth AWD

patients were included. We were unable to determine associations to stillbirth. Another was the existence of a single center hospital observation, but we offer the long-term experience of an interdisciplinary team in a maximum care hospital.

List Of Abbreviations

AWD- abdominal wall defect

GS- gastroschisis

ICU- intensive care unit

OC- omphalocele

Declarations

Acknowledgements

This paper was presented, in parts, as an E-poster presentation at the 2nd International Neonatology Association Conference (INAC) on 15th- 17th July 2016 in Vienna, Austria and won the 2nd E-Poster Prize of this conference.

Ethics approval and consent to participate

The study was designed as a prospective, observational case-control supported trial; enrolling children with either GS or OC, parents participated voluntarily and the consent was written. The local ethics committee the Ethics Committee of the University of Ulm approved this study (Registration No. 29/11). The Ethics Committee of the University of Ulm is registered in accordance with § 41a Medicines Act registered at the Federal Institute for Drugs (BfArM).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

Not applicable, no funding.

Authors' contributions

MK organized the study and was contributor in writing the manuscript. TR contacted the parents, organized the database and analysed the data. AS supervised the project, interpreted the data and edited the manuscript. All authors read and approved the final manuscript.

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This paper was presented, in parts, as an E-poster presentation at the 2nd International Neonatology Association Conference (INAC) on 15th- 17th July 2016 in Vienna, Austria and won the 2nd E-Poster Prize of this conference.

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Tables

Due to technical limitations, Table 1 is only available as a download in the supplemental files section.

Table 2 Abnormalities of bowels prenatal and postnatal, during surgery and technique for abdominal wall closure

	gastroschisis (n=36)	omphalocele (n=18)	p-value vs. GS	OC
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 [%]				
edematous / swollen small intestines	n=33 (91,6%)	n=15 (83,3%)	p=0,036	
ileostomy	n=18 (50,0%)	n=1 (5,5%)	p=0,001	
stenosis of bowel loop	n=11 (30,5%)	n=0 (0,0%)	p=0,010	
bowel perforation/ -partial resection	n=4 (11,1%)	n=0 (0,0%)	p=0,212	
fibrin-coated small intestines	n=8 (22,2%)	n=0 (0,0%)	p=0,032	
technique for abdominal wall closure				
primary closure of abdominal wall	n=14 (38,8%)	n=0 (0,0%)	p=0,002	
secondary closure of abdominal wall	n=24 (66,6%)	n=14 (77,7%)	p=0,523	
using patch	n=12 (33,3%)	n=4 (22,2%)	p=0,523	
using silo-bag	n=1 (2,7%)	n=1 (5,5%)	p=0,511	
using silo-bag followed by patch (combination)	n=8 (22,2%)	n=3 (16,6%)	p=0,277	
	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

	gastroschisis (n=36)	omphalocele (n=18)	p-value OC vs. GS	mean	SD
Duration in days (d)					
stay on ICU	23,34	20,22	p=0,201	22,28	±30,450
ventilation	12,69	7,89	p=0,021	11,06	±20,252
initiation enteral nutrition after primary closure	12,80	5,0	p<0,001	10,15	±9,371
total parenteral nutrition	42,46	19,89	p<0,001	34,79	±36,693
hospital stay till discharge	55,6	31,7	p=0,034	47,49	±46,138

Table 4 Comparison of gastroschisis with swollen vs. non-swollen small intestines and primary vs. secondary closure of abdominal wall 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)				p-value
	primary closure (n=24)		secondary closure (n=12)		
	mean	SD	mean	SD	
stay on ICU	13,88	±21,24	44,0	±41,86	p=0,008
ventilation	6,21	±13,05	26,82	±28,88	p=0,006
initiation enteral nutrition	7,92	±4,57	23,45	±9,76	p=0,000
total parenteral nutrition	30,96	±33,55	67,55	±44,30	p=0,011
hospital stay till discharge	43,17	±48,00	82,73	±51,51	p=0,034
	swollen intestines (n=18)		normal intestines (n=18)		
	6 (33,3%)		18 (100%)		p=0,003
primary closure (n)	mean	SD	mean	SD	
stay on ICU	26,5	±25,66	20,0	±38,07	p=0,045
ventilation	14,89	±15,60	10,35	±26,38	p=0,007
initiation enteral nutrition	15,83	±7,59	9,59	±10,99	p=0,002
total parenteral nutrition	40,28	±34,99	36,29	±45,78	p=0,011
hospital stay till discharge	61,22	±34,32	49,65	±59,62	p=0,089

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1.pdf](#)