Esophageal Perforation and EVAC in Pediatric Patients: A case series of four children
ID: 279

Laura Antonia Ritz*[1;2], Mohammad Samer Hajji[3], Tobias Schwerd[3], Sibylle Koletzko[3], Dietrich von Schweinitz[2], Eberhardt Lurz[3], Jochen Hubertus[2;4]
[1]*Sana Klinikum Lichtenberg, Allgemein- und Viszeralchirurgie, Berlin, Deutschland*, [2]*Kinderchirurgische Klinik und Poliklinik im Dr. von Haunerschen Kinderspital, Ludwig-Maximilians Universität München, München, Deutschland*, [3]*Kinderklinik und Kinderpoliklinik im Dr. von Haunerschen Kinderspital, Pädiatrische Gastroenterologie, München, Deutschland*, [4]*Marien Hospital Witten, Kinderchirurgie, Witten, Deutschland*

Background:
In pediatric patients, esophageal perforation (EP) is rare but associated with significant morbidity and mortality rates of up to 20–30%. In addition to standard treatment options, endoscopic esophageal vacuum-assisted closure (EVAC) therapy has shown promising results, especially in adult patients. Thus far, the only data on technical success and effectiveness of EVAC in pediatric patients were published in 2018 by Manfredi et al. at Boston Children's Hospital. The sparse data on EVAC in children indicates that this promising technique has been barely utilized in pediatric patients. More data are needed to evaluate efficacy and outcomes of this technique in pediatric patients.

Materials and methods:
We reviewed five cases of therapy using EVAC, ArgyleTM Replogle Suction Catheter (RSC), or both on pediatric patients with EP in our institution between October 2018 and April 2020.

Results:
Five patients with EP (median 3.4 years; 2 males) were treated with EVAC, RSC, or a combination. Complete closure of EP was not achieved after EVAC alone, though patients' health stabilized and inflammation and size of EP decreased after EVAC. Four patients then were treated with RSC until the EP healed. One patient needed surgery as the recurrent fistula did not heal sufficiently after 3 weeks of EVAC therapy. Two patients developed stenosis and were successfully treated with dilatations. One patient treated with RSC alone showed persistent EP after 5 weeks.

Conclusion:
EVAC in pediatric patients is technically feasible and a promising method to treat EP, regardless of the underlying cause. EVAC therapy can be terminated as soon as local inflammation and C-reactive protein levels decrease, even if the mucosa is not healed completely at that time. A promising subsequent treatment is RSC. An earlier switch to RSC can substantially reduce the need of anesthesia during subsequent treatments. Our findings indicate that EVAC is more effective than RSC alone. In some cases, EVAC can be used to improve the tissues condition in preparation for a re-do surgery. At 1 year after therapy, all but one patient demonstrated sufficient weight gain. Further prospective studies with a larger cohort are required to confirm our observations from this small case series.

Neuroprotection in Children with Esophageal Atresia - Interdisiplinary Optimization of intra- and perioperative Treatment using cerebral Autoregulation

ID: 324

Simon Scherer*[1], Markus Dietzel[1], Felix Neunhoeffer[2], Frank Fideler[3], Stefanie Hieber[3], Julian Zipfel[4], Martin U. Schuhmann[4]

[1]*Universitätsklinikum Tübingen, Abteilung für Kinderchirurgie mit Poliklinik, Tübingen, Deutschland*, [2]*Universitätsklinikum Tübingen, Kinderklinik, Tübingen, Deutschland*, [3]*Universitätsklinikum Tübingen, Anästhesie, Tübingen, Deutschland*, [4]*Universitätsklinikum Tübingen, Neurochirurgie, Tübingen, Deutschland*

Background:

Despite major advances in diagnosis and surgical therapy, complex congenital malformations in infants still involve a high risk of organ damage like the braun because of hypoxia and ischemia. Due to the condition, neonates often have to undergo severe thoracoscopic surgery, which carries the risk of hemodynamic instability and hypoxia in the perioperative course. We recently showed a correlation with neurological outcome and duration of autoregulation impairment in pediatric patients with traumatic braun injury, and that thoracoscopic surgery has an significant impact on cerebral oxygen saturation.

Materials and methods:

We want to examine in our ongoing prospective pilot study, wether non-invasive measurement of cerebral autoregulation is feasible in clinical practice, Also, if individual blood pressure ranges can be defined in wich cerebral autoregulation is preserved, and if a detection of factors, that influence cerebral autoregulation is possible.

Conclusion:

We believe that neuroprotection of children with esophageal atresia can be significantly improved by perioperative and intraoperative monitoring of cerebral autoregulation. This monitoring allows to detect critical situations in real time, for example, before current monitoring methods such as SpO2 measurement become apparent. Furthermore, the cerebral autoregulation measurement allows an individualization of the therapy measures, for example by specifying target blood pressure ranges in which the autoregulation is maintained.

Patient journey and the underestimated BRUEs in patient after correction of esophageal atresia
ID: 1024

Anke Widenmann-Grolig*[1]
[1]*Stuttgart, EAT e.V., Stuttgart, Deutschland*

Background:
Surgical and gastroenterological complications in esophageal atresia (EA) are well documented in the literature. Although in the long-term follow-up the pulmological issues continue to be relevant, diagnosing and better treatment options are difficult to find for many patients and caretakers as well as for the clinicians. Amongst the clinicians the esophageal atresia is rarely seen as a congenital disease of the esophagus and the pulmonary tract.

Materials and methods:
The findings across all national patient support group have been documented in the Patient Journey developed by the representatives of EAT, the **E**sophageal **AT**resia Global Support Group as EbE (Experts by Experience) within the **E**uropean **R**eference **N**etwork on **I**nherited **C**ongenital **A**bnormalities ERNICA. Devoped by patient representatives in ERNICA there have been several rounds to collect as many parents and patient views as possible. In this process BRUES have been identified as one major challenge in everyday life, especially in the first year.

Results:
The INoEA (International Network of Esophageal Atresia) Care Recommendation gives very detailed and competent consensus statements about how to diagnose and how to treat children born with EA. The dissemination and research on the topic have been agreed in the annual ERNICA conference 2021 in Lille.

Conclusion:
Bringing together the care recommendations of the INoEA experts (Pulmologist and ENT) with the defined needs about BRUES in the first year of life is a valid procedure to get best practice treatment fast to the bedside of the vulnerable patients as the parents are the co-treater on this field.

The Enema for Acute Abdominal Pain in Childhood - Often Curative and without Complications
ID: 836

Benedikt Groß*[1], Jurek Schultz[1], Guido Fitze[1]
[1]*Universitätsklinikum Dresden, Klinik und Poliklinik für Kinderchirurgie, Dresden, Deutschland*

Background:
Up to 15% of school-age patients present to emergency departments with abdominal pain (Sivit, 2004; Jacob and Shavit, 2016). 10-30% of children with acute abdominal pain need surgical interventions (Reust and Williams, 2016). The remaining 70-90% leave the emergency rooms without surgical interventions, many of them after having passed a bowel motion prompted by an enema. Identifying these patients in a preclinical setting could eventually spare them from unnecessary diagnostics and free hospital resources for patients needing surgical therapies.

Materials and methods:
Thus, for 2017 and 2018, we retrospectively analyzed all patients 3-17 years old presenting with acute abdominal pain to our University Hospital. We filtered the records of 1723 patients and investigated if they left the ER without representing for the next 14 days or if they needed admission or surgery. In addition, we reviewed various keywords in the history, initial clinical findings, laboratory and ultrasound results, administration of enemas, further clinical course, and any adverse events.

Results:
Of 1723 pediatric patients with acute abdominal pain, 779 (45%) received an enema. 612 (78.6%) left the emergency department free of complaints after that. However, 167 (21.4%) still had complaints after the enema. Of these, 53 (31.7%) needed surgery. We found no adverse events due to the administration of an enema in our emergency departments.

Conclusion:
Adverse events after enemas are rare but potentially harmful, including bowel perforation, as well as fluid and electrolyte disturbances (Anderson et al., 2019; Ahn et al., 2020). However, these events are found mainly in elderly patients, (pre-term) newborns, or patients with significant comorbidities. None of our 779 patients had any side effects or adverse events after an enema, but 78.6% went home without further pain. In conclusion, the preclinical administration of enemas in selected patients with acute abdominal pain may relieve many patients from their abdominal pain, thus freeing time and resources to treat those with harmful diseases at very little to no risk. However, large prospective trials are needed to test this hypothesis.

Single center experience with biological prosthesis in pediatric surgery
ID: 304

Arne Füldner*[1], Lilli-Malu Tiefel[1], Manuel Besendörfer[1], Vera Schellerer[1]
[1]*Uniklinik Erlangen, Erlangen, Deutschland*

Background:
In pediatric patients, numerous congenital and acquired conditions require tissue replacement or body wall reconstruction by prosthesis, many of them in a contaminated situs. Synthetic, non-absorbable materials have been increasingly replaced in recent years by materials of biological origin, which are designed first to provide mechanical stability and second to serve as a scaffold for the migration of autologous cells.

Materials and methods:
Two different products - SurgiMend© and Tutopatch© - were used in our clinic between 2016-2020. This study evaluates the use of both products in pediatric surgical patients and compares both products in terms of safety and ease of use. For this purpose, clinical and demographic data, including underlying diagnosis, indication for implantation, patch-associated complications, mortality, and costs are collected and compared.

Results:
Indications for patch implantation were A) congenital diaphragmatic hernia (4 patients), B) congenital abdominal wall defects (15 patients) and C) miscellaneous cases of (imminent) abdominal compartment syndrome (18 patients).
Regarding A): Two patients (50%) with patch repair for congenital diaphragmatic hernia had a radiologically proven recurrence in the follow-up, in one case due to colliquation of the implanted patch. Mortality rate in this group was also as high as fifty percent (n=2).
Regarding B): For patients with congenital abdominal wall defect (omphalocele and gastroschisis) patches were not only used in primary repair when the defect was too large for direct closure, but also in secondary repair of occurring diastasis recti. Most patches were implanted in a bridging position between the fascial edges of the rectus muscle with primary skin closure over the patch. Mechanical patch failure occurred in two cases (11%): one patch colliquated intraoperatively and had to be replaced. Another patch colliquation was seen during re-laparotomy for other reasons. Wound infections occurred in four cases (18%), but only in one case the patch had to be explanted. In the follow-up (range 337-1970 days), there was a relevant „bulging“ of the abdominal wall, but no ventral hernia formation was observed.
Regarding C): Underlying diagnosis in this group were necrotizing enterocolitis, intestinal perforation, ileus, Hirschsprung associated enterocolitis and intraabdominal bleeding. About half of the patients had one or more second-look or revision operations and therefore multiple consecutive patch-implantations, thus a total of 36 patches was implanted in 18 patients. All patients were in severe distress and classified with an ASA score ≥ 3 at the time of operation. Coexistent sepsis/SIRS was present at the time of operation in 58% of the cases, peritonitis in 63%. Nearly all patches (91%) in this group were implanted in a contaminated-septic situs, represented by CDC wound contamination classes III and IV. In the majority of the cases, the patch was left open as an „open abdomen“. Accordingly, wound infections occurred in 21 cases (58%). A fistula through the patch developed in one case.
In order to compare SurgiMend© and Tutopatch©, we separately analyzed the occurrence of complications in each group for both products. Overall, patch-associated complications occurred in similar frequency with both products (SurgiMend© 52% vs. Tutopatch©43%). Patch failure was only observed with Tutopatch (7%). Severe enteric adhesions to the patch at the time of explantation occurred more frequently with Tutopatch© (SurgiMend© 27% vs. Tutopatch© 67%).

Conclusion:
For congenital diaphragmatic hernia, the high recurrence rate suggest that absorbable, biological materials are not adequate for this indication. Meanwhile, in congenital abdominal wall defects the materials showed good short- and long-term stability. The rate of patch-associated complications was acceptable, even in the mostly contaminated field of (imminent) abdominal compartment syndrome. In direct comparison, the data favor SurgiMend© over Tutopatch©, which confirms previous results in the experimental setup.

Use of porcine acellular dermal matrix (Fortiva) in combination with vacuum therapy as the primary surgical management for definitive closure in neonates with giant omphalocele. The beginning of a new era? A case series

ID: 420

Julia Kössler-Ebs*[1], Leonie Carstensen[1], Patrick Günther[2]
[1]*Universitätsklinik Heidelberg, Kinderchirurgie, Heidelberg, Deutschland,* [2]*Universitätsklinik Heidelberg, Kinderchirurgie, Heidelberg, Deutschland*

Background:

The closure of a giant omphalocele – defined as an omphalocele larger than 4,5-6cm and containing a major part of the liver – remains a major challenge to the pediatric surgeon due to viscero-abdominal disproportion. Traditionally, giant omphaloceles are treated with a conservative non-operative management followed by delayed closure of the fascia.

Materials and methods:

This case series reports our experience with the use of porcine acellular matrix in combination with vacuum therapy in newborns with giant omphaloceles.
Our method is a two-step concept. During the first surgery the omphalocele sac is resected and the fascia mobilized from the subcutaneous tissue and skin. After the organs are carefully covered with organ foil, a non-absorbable permeable silicone mesh is sewn in at the fascia level using an onlay technique. Subsequently, a vacuum system is applied.
In the following days, the silicone mesh is gathered in the midline every 4-5 days using non-absorbable sutures causing traction on the abdominal wall with approach of fascia and skin. This is done under careful monitoring of the intraabdominal pressure. After sufficient approximation of the fascial edges is achieved, the silicone mesh is removed in a second surgery and an acellular porcine matrix is inserted at the fascial level, also using an onlay technique. Whenever possible, the skin is closed in this step. In some cases, when a skin defect remains, vacuum therapy is applied again onto the acellular matrix. The advantage of this procedure is the faster and early definitive closure of the fascia. The aim is to create a stable abdominal wall, which makes subsequent surgical correction unnecessary.

Results:

During the study period 2016-2021, 5 neonates (2 male/ 3 female) with giant omphaloceles were treated in our department using porcine acellular dermal matrix (Fortiva®) in combination with vacuum therapy as the primary procedure. The indication for primary surgical therapy in these cases was either a ruptured omphalocele sac or the risk of torsion or tipping with impending lack of perfusion of the organs. The mean diameter of fascia defect measured 10.3 ± 2.8 cm. The average gestational age was 37 weeks (range 34 to 39 weeks) with a mean birth weight of 2246g ± 610g. One of the patients had additional pulmonary anomalies.
The first step of the surgical management occurred on average on the 5th day of life (range 1-15). The silicone mesh was sutured in at fascia level with non-absorbable suture material. After an average of 3.5 central gatherings (range 3-6), the fascial edges were approximated, so that the second surgery could be performed 29.2 days (range 21-48) after the first surgery on average. The acellular matrix was also sutured in place with non-absorbable suture material. The median duration of vacuum therapy was 158 days (range 22-257). Complete approximation of the skin was achieved in 2 out of 5 patients.
By applying the described procedure, closure of the defect was achieved in all patients. None of the patients developed wound infection, seroma or foreign material infection. One patient experienced a tear of the silicone mesh, requiring re-operation on day 31th of life. There were no surgery-related deaths, or life-threatening complications. One patient with airway anomalies died of catheter sepsis with ARDS at the age of 7 months in an external hospital.

Enteral feeding was started on average on day 10 (range 7-13) of life and was completed on average on day 70 (range 46-95) of life. The mean length of hospital stay was 145.2±84.8 days.
The mean follow-up was 23.4 months, ranging from 1-59 months. All surviving patients are fed exclusively enterally, with good gastrointestinal passage. The abdominal wall is stable in all patients, there was no indication for closure of an abdominal wall hernia so far.

Conclusion:
This case series shows, that the use of porcine acellular dermal matrix (Fortiva) in combination with vacuum therapy as the primary surgical procedure is feasible in neonates and leads to a stable closure of the abdominal wall in the presence of giant omphaloceles with comparable complication rates to traditional management of the giant omphalocele.

Double duodenal atresia in a premature, low birth weight boy
ID: 741

Alexander Sterlin*[1], Tatjana König[1], Martin Schwind[1]
[1]*Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz, Deutschland*

Background:
Additional intestinal malformation in patients with duodenal atresia is well described in the literature. However, there are only few reports of a combination of annular pancreas and complete duodenal atresia [Quelle 1,2]. Primary operative exploration is crucial to determaning the type of obstruction. We present a case of an uncommon combination of annular pancreas and complete duodenal atresia could not be identified during primary repair in spite of a complete bowel run.

Results:
A 31+5 week preterm and low birth weight infant (1670g) presented with green vomiting and acholic stool. The abdominal X-ray showed a double-bouble sign without intestinal air beyond the duodenum. No other malformations were detected. Laparotomy was performed on the fourth day of life. We found an annular pancreas, which was unusually broad and covered the entire distal duodenum. The jejunum was probed retrogradely passed up to the level of the ligament of Treiz. In order to aviod damage to the pancratic tissue a further dissection was abstained and retrocolic duodenojejunostomy was perfomed. Postoperatively, feeding was commenced without problems on the 3d postoperative day.
On the 11th postoperative day, a cystic mass was detected sonographically in the upper right abdomen and anastomotic leakage and abscess were suspected in MRI, so urgent re-laparotomy was performed. At this point, 11 days after the original procedure, there were severe postoperative inflammation and adhesions. The anastomosis was locaded immediately below the abdominal wall. It was intact and patent. A retroperitoneal cystic mass covered with pancreatic tissue was exposed. After enterotomy, a connection of the duodenal or proximal small bowel lumen could be excluded. However, there was an additional complete atresia of the small bowel proximal to ligament of Treiz. The cystic mass was revealed to be a very short duodenal segment between the annular pancreas and the complete atresia, filled with pancreatic fluid. The original duodenojejunostomy was opened and flipped, in order to anastomose the cyst with the atretic end of the small bowel, and a seperate end-to-side redo-duodenojejunostomy was performed. Sonographic follow-up revealed adequate drainage of the cyst.
Postoperatively, there was an anastomotic leakage, leading to duodeno-cutaneous fistula, which was surgically closed after the initial inflammation subsided.

Conclusion:
Associated intestinal malformation in patients with duodenal atresia can present in unexpected locations. The short doudenal part between two sites of obstruction was detectable only after filling up with fluid. Extesive and widespread pancreatic tissue might be suspect of further underlying malformation. Careful extended exploration might be indicated in order to avoid complicated redo-surgery.

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Identification and characterization of novel candidate genes in familial Hirschsprung disease
ID: 353

Philipp Romero*[1]
[1]*Uniklinikum Heidelberg, Kinderchirurgie, Heidelberg, Deutschland*

Background:
Hirschsprung disease (HSCR), is a rare congenital disorder characterized by aganglionosis due to functional impairment of enteric progenitor cells during embryonic development. Genetic and environmental factors are shaping the phenotype. So far, more than 25 genes have consistently been replicated. Although *RET* is the major disease gene, it accounts for only a fraction of cases. To further dissect HSCR genetics, we investigated an extended family including 18 individuals of three generations and two major branches with four HSCR patients.

Materials and methods:
The individual protein-coding genetic background was assessed by Whole Exome Sequencing (WES) and candidate variants were verified by Sanger sequencing. Validation of candidate genes was performed collecting data on expression, previous disease association, gene function, biological context and mutation prediction. To prioritize candidate gene relevance, a binary scoring system was developed based on validation criteria and verified by established HSCR risk gene variants. Considering the accumulation of genetic variants an individual risk score for each family member has been assessed as well.

Results:
Filtering of the WES data for rare coding variants revealed RET in addition to various novel candidate genes in affected as well as some ‘non-affected’ relatives. To investigate common modifiers, four SNPs in RET and SEMA3A were assessed. SNP carriers were found at higher risk for HSCR and one rare coding RET variant seemed not sufficient for the manifestation of HSCR. Applying our scoring system, the identified novel candidate genes MARCH7 and SLAIN2 displayed even higher scores than RET. Furthermore, all patients demonstrated a considerable higher risk score compared to their non-affected relatives. Of note, two of the parents scored similarly high and reported gastrointestinal complaints. This might be attributed to the genetic burden of gene variants assigned to be relevant in ENS development and function.

Conclusion:
In summary, our results are in line with others, supporting the hypothesis that a certain threshold of gene variants needs to be crossed for the manifestation of the HSCR phenotype, indicating the genetic complexity of HSCR.

Anastomotic leakage following complicated pull-through for Hirschsprung's disease: a failed attempt to avoid protecting ileostomy by endoluminal vacuum therapy
ID: 721

Jan Sabo*[1], Michael Berger[1], Oliver Muensterer[2]
[1]*Uniklinikum Essen, Abteilung Kinderchirurgie, Essen, Deutschland*, [2]*LMU München, Dr. von Haunersches Kinderspital, München, Deutschland*

Background:
Endoluminal vacuum therapy has been recognized to have beneficial healing effects in anastomotic leaks and fistulas, for example in the esophagus or the rectum in adults. The concept of endoluminal vacuum therapy has recently been successfully applied in children, especially in the esophagus. Very little is known if such endoluminal vacuum therapy can be used for anastomotic leakage and breakdown following pull-through procedures for Hirschsprung's disease and if it could potentially avoid a protective ileostomy.

Materials and methods:
Case report of a 13-month-old child with genetically proven Mowat-Wilson Syndrome who underwent complicated pull-through procedure for Morbus Hirschsprung and subsequently developed an anastomotic leakage and partial breakdown of the anastomosis.

Case:
The child was initially treated in another country and the diagnosis of Morbus Hirschsprung was missed. Prior to being referred to our center, the child underwent multiple laparotomies for "small bowel obstruction" and a colostomy of the transverse colon was placed in the left hemiabdomen. We confirmed the suspected diagnosis by rectal biopsy and performed an ostomy takedown and a SILS-assisted pull-through. Because of the prior laparotomies and the localization of the colostomy, the transverse colon had to be used for the anastomosis and was rotated inversely in order to give sufficient length. On postoperative day 7, the child showed anastomotic leakage and partial breakdown of the anastomosis. Endoluminal vacuum therapy was initiated for a total of 10 days in order to avoid a new protective ileostomy, however, there were no signs of healing. The child underwent protective ileostomy and quickly recovered. The ostomy was revised 2 weeks later because it was deemed to proximal, producing high output. The anastomosis continued to heal without stricture and with good sphincter function, and the ostomy was taken down 10 weeks later without further complications. At one year follow up, there is no stricture and the child is well, thriving and able to pass stool daily with laxatives and enemas twice per week only.

Conclusion:
In the case described here, endoluminal vacuum therapy was unsuccessful in treating a partial anastomotic breakdown following pull-through for Morbus Hirschsprung. More experience is required in order to known if such a therapy can help treat anastomotic breakdowns of the rectum in order to avoid protective ileostomy.

Physical self-concept in patients born with Hirschsprung's disease and anorectal malformation.

ID: 735

Mattis Krude[1], Tatjana König*[1]
[1]*Universitätsmedizin Mainz, Klinik und Poliklinik für Kinderchirurgie, Mainz, Deutschland*

Background:

In spite of ongoing medical and surgical advances, children born with anorectal malformation (ARM) or Hirschsprung's disease (HD) need life-long bowel management to treat fecal and urinary incontinence and/ or constipation. The Ritala Score can be used to objectify the severity of symptoms (1). Postoperative outcome, longterm heath-related quality of life (HrQOL) and fecal continence in patients born with ARM are strongly depended on the type of malformation and co-morbidity, (e.g. VACTERL association) (2). In patients with HD, the extent of postoperative constipation, soiling and incontinence and associated HrQOL may differ widely (3). The aim of this study was to determine the impact of the severity of postoperative symptoms on subjectively perceived physical abilities and physical appearence (physical self-concept).

Materials and methods:

In 2020, an anonymous online-survey was conducted among the members of the German ARM and HD patient support group „SOMA. e.V." (www.soma-ev.de). Simultaneously, a control group of children and adolescents without chronic disease was recruited. Patients aged 5-25 years were included and matched 1:1 with controls according to gender and age. All participants older than 18 years were defined as adult and matched with other adults.

The questionnaire for ARM/ HD patients included items regarding the patient history, current health status including fecal incontinence and constipation according to the Rintala Scale (1), and physical self-concept (PSK/ PSK-K). The Rintala Scale includes 7 items (ability to hold back defecation, feeling urge to defecate, frequency of defecation, soiling, accidents, constipation and social problems). The score ranges between 1-20 points, 20 being the most favourable outcome. The physical self-concept was assessed using the validated standardized questionnaires PSK (4) for patients aged 13-25 and PSK-K for patients aged 5-11 years (5). Both, the PSK and the PSK-K consist of seven subscales measuring physical abilities (strength, endurance, speed, flexibility, coordination, and sports competence), and physical appearance (4, 5), each phrased appropriately for the targeted age.

Mean and 95%-confidence intervals (95%-CI) were calculated, non-overlap of 95%-CI marked a statistically relevant difference. A linear regression was performed for Rintala score vs. PSK-K/ PSK, respectively.

Results:

83 patient-control-pairs were matched and analyzed (54 male, 29 female). The mean age was 13,3 years (95%-CI: 12,0-14,7), the mean Rintala score was 12,3 (95%-CI:11,5-13,1). In the patient group, 50% were born with ARM, 25% with ARM and VACTERL and 25% with HD. Overall, 78% had had an ostomy in infancy.

There was no relevant difference in physical self-concept in the PSK-K score for the ages 5-12 years for either dimension or total score. Children born with HD even had a better physical self-concept than controls, while the score of patients born with ARM with or without VACTERL indicated a lower self-concept. However, a relevant negative correlation could be shown only for patients with VACTERL. There was no difference in PSK-K between the genders or children who had or did not have an ostomy in infancy.

In adolescents and young adults (13-25 years), overall physical self-concept was relevantly worse in the patient group compared to controls. The greatest difference could be shown in the dimensions of speed and endurance. No relevant difference in PSK could be shown for patients born with HD, ARM, or ARM with VACTERL and patients who had had an ostomy. In patients, but not in controls, males had a statistically higher self-reported physical self-concept compared to females.

For all ages, there was a linear correlation between a better physical self-concept and a higher Rintala score.

Conclusion:
No statistically relevant difference in self-reported physical self-concept could be shown in younger children (5-12 years) compared to controls. In this age group, PSK-K scores differed between patients with HD, ARM and ARM with VACTERL. For adolescents and young adults, a depressed self-reported physical self-concept could be shown statistically, independent of their type of malformation. Having an ostomy in infancy had no impact on PSK/ PSK-K. However, there was a correlation between a higher self-reported physical self-concept and higher Rintala score in all age-groups.

Formation of ripoptosome complex and influence of the RIP1-kinase in Hirschsprung-associated enterocolitis

ID: 982

Johanna Hagens*[1], Clara Philippi[1], Kim Marili Heuer[1], Magdalena Trochimiuk[1], Laia Pagerols Raluy[1], Konrad Reinshagen[1], Christian Tomuschat[1]

[1]*Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Kinderchirurgie, Hamburg, Deutschland*

Background:

Hirschsprung-associated enterocolitis (HAEC) as one of the major complications in Hirschsprung Disease (HD) is a potentially life-threatening colonic inflammation of unknown course. Receptor-interacting serine/threonine-kinase 1 (RIPK1) is an essential modulator of cell death downstream to the TNFR1 in response to inflammatory stimuli. RIPK1 forms an apoptotic protein complex (ripoptosome), leading to a non-canonical downstream as an alternative to NF-kappa-B signalling. Ripoptosome formation has recently been identified to be dysregulated in IBDs and could possibly explain the intestinal barrier disruption and subsequent bacterial invasion in HAEC. Therefore, we designed this study to investigate the role of RIPK1 for the development of HAEC.

Materials and methods:

Following ethical approval, tissue specimens from human colonic Hirschsprung (n=16) and control samples (n=13) were collected at the time of pull-through surgery in HD- or colostomy closure in non-HD patients. Murine colonic tissue was obtained from *Ednrb*-KO and WT mice which were fed with the RIPK1-inhibitor GSK481 or placebo. Samples were analysed for RIPK1-dependent inflammation using Western Blot (WB) and RT-qPCR. Protein distribution and ripoptosome formation were visualized using confocal and STED microscopy. Organoids cultivated from the human intestinal mucosa were challenged with tumor necrosis factor alpha (TNFα) and investigated for epithelial barrier dysfunction using cell border- and 4 kDa FITC-Dextran labelling for immunofluorescence. Data were analysed by ANOVA with mean ± SD.

Results:

Western Blot and RT-qPCR analysis revealed no significant differences in the expression of the main proteins and genes of the canonical and non-canonical TNFR1-pathway in human tissue. *Ednrb*-KO mice showed a relevant activation of the TNFR1-pathway in the distended bowel state compared to health controls and a prolonged survival after GSK481 treatment compared to the placebo group. Human colonic Hirschsprung organoids responded to the TNFα treatment with increased apoptotic cell death and relevant epithelial barrier dysfunction compared to the untreated and health control groups.

Conclusion:

Here, we report that RIPK1 dysregulation participates in intestinal barrier disruption in Hirschsprung tissue. TNFα disturbed the homeostasis of the epithelial barrier and promoted RIPK1-dependent inflammation in human Hirschsprung organoids but less in healthy controls. Since RIPK1 dysregulation is triggered by chronic nuclear factor (NF)-κB activation, which occurs in human IBD, the study's findings provide further evidence for a link between HAEC and IBD.

MIS-C - Implications for the Pediatric Surgeon: An Algorithm for Differential Diagnostic Considerations

ID: 30

Nora Manz*[1], Claudia Höfele-Behrendt[1], Julia Bielicki[1], Hanna Schmid[1], Matthias Matter[2], Isabella Bielicki[1], Stefan Holland-Cunz[1], Stephanie Gros[1]
[1]Universitäts-Kinderspital Basel, Basel, Schweiz, [2]Universitätsspital Basel, Basel, Schweiz

Background:
Multisystem inflammatory syndrome in children (MIS-C) is a new disease associated with a recent infection with severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). Affected children can present predominantly with abdominal symptoms, fever and high inflammatory parameters that might lead to a consult by the pediatric surgeon and an indication for surgery.

Materials and methods:
Clinical data of three patients with MIS-C that underwent surgery were collected. Histopathological analysis of the appendix was performed.

Results:
We present the clinical course of three children with fever, abdominal pain and vomiting for several days. Clinical examination and highly elevated inflammation markers led to indication for laparoscopy; appendectomy was performed in two patients. Because of intraoperative findings or due to lack of postoperative improvement, all patients were reevaluated and tested positive for MIS-C associated laboratory parameters and were subsequently treated with corticosteroids, intravenous immunoglobulins, acetyl salicylic acid and/or light molecular weight heparin.

Conclusion:
We discuss the implications of MIS-C as a new differential diagnosis and stress the importance of assessing the previous medical history, identifying patterns of symptoms and critically surveilling the clinical course. We implemented an algorithm for pediatric surgeons to consider MIS-C as a differential diagnosis for acute abdomen that can be integrated into the surgical workflow.

Increasing the efficiency of hyperthermic intraperitoneal chemotherapy (HIPEC) by a combination with a photosensitive drug in pediatric rhabdomyosarcoma
ID: 59

Benedikt Richard Wagner*[1], Anna Adamus[1], Mohammad Reza Vahdad[1], Antje Haap-Hoff[2], Benedikt Heinrich[3], Olalla Vazquez[3], Paul Jank[4], Carsten Denkert[4], Guido Seitz[1]
[1]*University Hospital Marburg, Department of Pediatric Surgery, Marburg, Deutschland*, [2]*KARL STORZ SE & Co. KG, Tuttlingen, Deutschland*, [3] *Philipps-University of Marburg, Department of Chemical Biology, Marburg, Deutschland*, [4]*University Hospital Marburg, Department of Pathology, Marburg, Deutschland*

Background:
Cytoreductive surgery (CRS) in combination with hyperthermic intraperitoneal chemotherapy (HIPEC) is an option in advanced peritoneal sarcomatosis. Nevertheless, CRS and HIPEC are not successful in all patients. Therefore, an enhancement of HIPEC using photodynamic therapy might be beneficial. For this approach, we tested a combination of the photosensitizer Hypericin with HIPEC in an animal model.

Materials and methods:
Alveolar rhabdomyosarcoma cells were xenotransplanted into NOD/LtSz-scid IL2Rγnullmice (n=80) inducing intraperitoneal sarcomatosis. All groups received Hypericin (100 µg/200 µl) intraperitoneally with and without cisplatin-based (30 or 60mg/m²) HIPEC (37 or 42°C, for 60 min) (five groups, each n=16). Hypericin-based photodynamic therapy (PDT) of a representative tumor bulk was performed in all groups for ten minutes. Tumor dissemination was documented visually and by using Hypericin-based fluorescence guidance. Tumor and tissue samples, harvested at the end of the perfusion, were evaluated regarding morphology (H&E staining), proliferation (Ki-67 staining) and apoptosis (TUNEL-assay).

Results:
A time dependent Hypericin uptake even in smallest tumor nodes (< 1 mm) was found. Hypericin-based fluorescence guidance detected a higher tumor dissemination compared to the visible tumor spread. Immunohistochemistry revealed a Hypericin penetration across the tumor surface. Hypericin-based PDT without HIPEC induced marginal apoptotic effects only at the tumor surface. Combining Hypericin with HIPEC revealed cisplatin-concentration dependent decrease in proliferation capacity and induction of apoptosis across determined cell layers of the tumor surfaces.

Conclusion:
Hypericin as fluorescent photosensitizer offers an intraoperative diagnostic advantage detecting the exact intraperitoneal tumor dissemination. The combination of Hypericin and cisplatin based HIPEC was feasible in vivo. Effects on tumor proliferation and apoptosis induction across the tumor surface were observed. Further studies combining Hypericin and HIPEC as new therapy approach will follow to establish a clinical application

Blood group AB increases risk for surgical necrotizing enterocolitis and focal intestinal perforation in preterm infants with very low bith weight

ID: 196

Illya Martynov*[1], Wolfgang Göpel[2], Tanja K. Rausch[3], Christoph Härtel[2], Axel Franz[4], Dorothee Viemann[5], Ulrich Thome[6], Martin Lacher[1], Benjamin Ackermann[6]

[1]University of Leipzig, Department of Pediatric Surgery, Leipzig, Deutschland, [2]University Hospital of Schleswig-Holstein, Department of Pediatrics, Kiel, Deutschland, [3]Institute of Medical Biometry and Statistics, University of Lübeck, Lübeck, Deutschland, [4]University Children's Hospital Tübingen, Department of Neonatology, Tübingen, Deutschland, [5]Hannover Medical School, Department of Pediatric Pneumology, Allergology and Neonatology, Hannover, Deutschland, [6]University of Leipzig, Center for Pediatric Research Leipzig, Hospital for Children and Adolescents, Division of Neonatology, Leipzig, Deutschland

Background:

Necrotizing enterocolitis (NEC) and focal intestinal perforation (FIP) are two of the most common emergencies of the gastrointestinal tract in preterm infants with very low birth weight (VLBW, birth weight < 1500 g). Identification of risk factors among these children is crucial for earlier diagnosis and prompt intervention. In this study, we investigated a relationship between ABO blood groups and the risk for surgical NEC/FIP.

Materials and methods:

We genotyped the ABO locus (rs8176746 and rs8176719) in VLBW infants enrolled in a prospective, population-based cohort study of the German Neonatal Network (GNN).

Results:

Of the 10,257 VLBW infants, 441 (4.3%) had surgical NEC/FIP. In univariate analyses, the blood group AB was more prevalent in VLBW infants with surgical NEC/FIP compared to non-AB blood groups (OR 1.51, 95% CI 1.07-2.13, p = 0.017; absolute risk difference 2.01%, 95% CI 0.06-3.96%). The association between blood group AB and surgical NEC/FIP was observed in a multivariable logistic regression model (OR of 1.58, 95% CI 1.10-2.26, p = 0.013) as well.

Conclusion:

In summary, our study suggests that the risk of surgical NEC and FIP is higher in patients with blood group AB and lower in those having non-AB blood groups.

Preclinical evaluation of SLC-0111 in vitro and in the perfusion-based bioreactor slice culture for neuroblastoma.

ID: 201

Remo Bilang*[1], Zihe Huo[1], Claudiu Supuran[2], Nicolas Von der Weid[1], Elisabeth Bruder[3], Stefan Holland-Cunz[1], Ivan Martin[4], Manuele Muraro[4], Stephanie Gros[1]
[1]*UKBB - Universitäts-Kinderspital beider Basel, Basel, Schweiz*, [2]*Department of Neurofarba, University of Florence, Florence, Italy*, [3]*Department of Pathology, Universitätsspital Basel, Basel, Schweiz*, [4]*Department of Biomedicine, Universitätsspital Basel, Basel, Schweiz*

Background:
Neuroblastoma is a rare disease. Thus, possibilities to try new therapeutic options for neuroblastoma in clinical trials are limited. Despite the constant need to improve therapy and outcome for patients with advanced neuroblastoma, clinical trials currently only allow for testing few substances in even fewer patients. This increases the need to improve and advance preclinical models for neuroblastoma to preselect favorable candidates for novel therapeutics. The target for such novel therapeutics could be the carbonic anhydrase IX (CAIX). CAIX is an important membrane-based molecule which allows solid tumors to balance their own microenvironment.

Materials and methods:
For all experiments, the CAIX inhibitor SLC-0111 was used. The inhibitor was applied to three neuroblastoma cell lines SH-EP, LAN1 and SH-SY5Y, as well as to tumor tissue samples of three different patients with different neuroblastomas. To evaluate the expression of CAIX, we performed an immunohistochemical staining on all cell lines as well as on the patient tumor samples. The effect of SLC-0111 was assessed by standard viability assays and by performing isothermal microcalorimetry measurements. Tumor tissue was additionally put inside a perfusion based bioreactor to create a 3D-tissue model for further experiments.

Results:
Neuroblastoma cell lines that express CAIX showed a significant decrease in cell viability under the effect of SLC-0111. Furthermore, these cell lines showed decreased heat expression in the isothermal microcalorimetry, which displays an inhibition of the metabolism. Similar results were observed in patient tumor tissue samples in culture as well as in 3D models.

Conclusion:
The need for developing and improving advanced preclinical testing strategies for potential therapeutics in neuroblastoma is enormous. Here we propose the use of a new patient-derived slice-culture perfusion-based 3D-model in combination with rapid treatment evaluation using isothermal microcalorimetry exemplified on treatment with the novel inhibitor SLC-0111. This approach can facilitate individualization and improve treatment strategies for each patient.

Prevalence and 1-year-survival of selected major birth defects in Saxony-Anhalt, Germany.
ID: 217

Salmai Turial[1], Friederike Stimming*[1], Anke Rißmann[2]
[1]*Universitätsmedizin Magdeburg, Kinderchirurgie, Kindertraumatologie und Kinderurologie, Magdeburg, Deutschland*, [2]*Universitätsmedizin Magdeburg, Malformation Monitoring Centre Saxony-Anhalt, Magdeburg, Deutschland*

Background:
Larger studies in the US and European countries have shown congenital anomalies to be responsible for 30–40% of deaths during infancy. In Europe, nearly 2.4 % of births are affected by a major birth defect. The highest number of deaths in children who suffered from congenital malformations arises in the first year of life. This study aims to present the current data on the prevalence rates and the one-year survival rate for nine selected major birth defects in Saxony-Anhalt, Germany.

Materials and methods:
Data were collected at the Malformation Monitoring Centre Saxony-Anhalt, Medical Faculty Otto-von-Guericke University Magdeburg. To determine the prevalence rates and the survival during infancy statistical analyses were performed in a population-based birth cohort. Nine major birth defects: the hypoplastic left heart syndrome (HLHS), the tetralogy of Fallot (TOF), the transposition of great vessels (TGA), the spina bifida (SB), the congenital diaphragmatic hernia (CDH), the esophageal atresia/fistula (EA), the anorectal malformation (RA), the omphalocele (OM) and the gastroschisis (GAS) were selected for the specific analysis. The case population was divided into the three major groups according to the EUROCAT 1.4 Guide, using the ‘Multiple Congenital Anomaly Algorithm. Total and live birth prevalences were calculated. In addition, a survival analysis of all pregnancy outcomes, including live births and fetal deaths (enclosing stillbirths, spontaneous abortions beginning 16 gestational week or later and termination of pregnancy for fetal anomalies following prenatal diagnosis at any gestational age (TOPFA)) was conducted. Cases were classified as stillbirth if a birth weight of 500g or a gestational age of 24 weeks was achieved.

Results:
In total, 1012 cases of congenital anomaly were registered at the Malformation Monitoring Centre Saxony-Anhalt. The time period of 18 years, from 2000 to 2017, was the subject of data analysis.
Out of 1012 registered cases, 16 spontaneous fetal losses (1.6%), 273 TOPFA (27.0%), 16 stillbirths (1.6%) and 707 live births (69.9%), respectively, were recorded.
The total prevalence rate ranged from 2.5 (CDH) to 5.8 (SB) per 10,000 births. The live birth prevalences were highest for TGA with 4.2 and lowest for OM with 1.2 per 10,000 births. 88.3% of live-born cases survived the first year of life. Survival rates were lowest in HLHS (60.3%) and CDH (70.0%), respectively. The survival of all cases, including fetal losses, the one-year survival was 61.7%, merely.
There was no improvement in survival rate during the study period noted. The one-year-survival was 35.7% for genetic defects, 57.6% for multiple congenital anomalies (MCA), 68.6% for isolated cases, 44.6% for prenatal detected and 85.2% for postnatal identified malformations, respectively. Gestational age less than 31 weeks and birth weight below 1000g affected survival rate adversely. This effect was significant for both the gestational age and the body weight at birth.

Conclusion:
The survival rate of children with congenital malformations in Saxony-Anhalt is comparable to that reported by national and international studies. Malformation monitoring and surveillance programs are beneficial for human genetic counselling and for clinical-decision-making procedures in both antenatal

and neonatal periods. Inclusion of all pregnancy outcomes in malformation registers seems to be important as it influences the total survival rates.

Wnt Receptor Frizzled-4 as a Marker for Isolation of Enteric Neural Progenitors in Children - An up-to-date summary of our work

ID: 317

Simon Scherer*[1], Peter Neckel[2], Steven Warmann[1], Lothar Just[2], Jörg Fuchs[1]
[1]*Universitätsklinikum Tübingen, Abteilung für Kinderchirurgie mit Poliklinik, Tübingen, Deutschland*, [2] *Universitätsklinikum Tübingen, Klinische Anatomie, Tübingen, Deutschland*

Abstract:

Identification and isolation of neural progenitor cells from the human enteric nervous system (ENS) is currently hampered by the lack of reliable, specific markers. We defined the Wnt-receptor frizzled-4 as a marker for the isolation of enteric neural progenitor cells derived from paediatric gut samples. We show that the Wnt-receptor frizzled-4 is expressed in the human colon and in Tunica muscularis-derived enterospheres. To obtain a purified culture, we carried out fluorescence-activated cell sorting using PE-conjugated frizzled-4 antibodies. Frizzled-4^{positive} cells gave rise to neurosphere-like bodies and ultimately differentiated into neurons as revealed by BrdU-proliferation assays and immunocytochemistry, whereas in frizzled-4^{negative} cultures we did not detect any neuronal and glial cells. By using a patch-clamp approach, we also demonstrated the expression of functional sodium and potassium channels in frizzled-4^{positive} cell cultures after differentiation in vitro.

We hypothesize, that neural stem and progenitor cells from the ENS might serve as a source of cells for treatment of neurogastrointestinal disorders, as the expression of this Wnt-receptor correlates with the number of myenteric ganglion cells and decreases from normoganglionic to aganglionic areas of large intestine.

Defining the Optimal Induction Protocol for Experimental Necrotizing Enterocolitis in Murine Animal Models: A Systematic Review and Meta-Analysis

ID: 325

Illya Martynov*[1], Boshen Shu[1], Xiaoyan Feng[1], Johannes Duess[1], Martin Lacher[1], Jan Riedel[1]
[1]*University of Leipzig, Department of Pediatric Surgery, Leipzig, Deutschland*

Background:

Necrotizing enterocolitis (NEC) is one of the most common emergencies of the gastrointestinal tract in preterm infants. Despite extensive clinical and preclinical research, the pathophysiology of NEC remains poorly understood, while abnormal bacterial colonization of the gut, formula feeding, and perinatal hypoxia have been implicated as putative risk factors. To better understand the mechanisms involved in development of NEC and to test potential specific therapeutic strategies that are otherwise not feasible in humans, several animal models have been designed. Although the majority of murine NEC models share similarities in the relevant methodology (lipopolysaccharide (LPS) supplementation or bacterial inoculation, formula feeding (FD), hypoxia, and hypothermia), there are significant differences in NEC severity (e.g. NEC score) and study quality (e.g. reporting of outcomes) between different NEC models. Hence, we conducted a systematic review (SR) and meta-analysis (MA) of all available murine animal models to assess and compare the efficacy, suitability, and appropriateness of different NEC inductions protocols.

Materials and methods:

We conducted a SR of the existing literature on experimental NEC from 01/01/1975 to 31/12/2020 searching the databases of PubMed and Web of Science. After abstraction of all relevant data, we performed a random-effects MA to produce the log odds ratios (OR) estimates. This study is registered with PROSPERO (CRD42021239813).

Results:

The search in PubMed and Web of Science identified 5,229 unique records, of which 4,863 papers were excluded after title and abstract screening. Of 366 remaining articles, 57 (15.6%) were eligible for qualitative synthesis and 47 (12.8%) for quantitative synthesis. To induce NEC, formula feeding (n=46, 97.9%), LPS supplementation (n = 15, 31.9%) or bacterial inoculation (n = 8, 17.0%), hypoxia (n = 47, 100%), and hypothermia (n = 30, 63.8%) were used. The mean sample size of animals in the treatment group (NEC induction) was 20.1 ± 13.6 (range: 5 – 53, n total = 945) and 11.9 ± 4.1 (range: 5 – 22, n total=561) in the control group (breast feed animals). Most of the studies were performed in rats (n = 29, 61.7%) and the remaining in mice (n = 18, 38.3%). Among these studies the incidence of any grade NEC (NEC score from 2 to 4) was 67.5% (637/944) and severe NEC (NEC score from 3 to 4) was 39.2% (322/622). The overall OR for any grade NEC was 3.95 (95% CI 3.51, 4.40), ranging from 1.72 (CI 95%: 0.33, 3.11, any NEC incidence 60.4%, 32/53) to 6.87 (CI 95%: 2.89, 10.85, any NEC incidence 100%, 15/15) and 2.69 (95% CI 2.21, 3.15) for severe NEC with range from 0.07 (CI 95%: - 3.92, 4.05, severe NEC incidence 0%, 0/14) to 4.78 (CI 95%: 1.63, 7.92, severe NEC incidence 80%, 8/10). A sub-metaanalysis of experimental details (e.g. animal age at start of the experiment, frequency of formula feeding, rate of LPS administration, duration of hypoxia or hypothermia) illustrated that there were no key factors leading to higher NEC scores except for protocol duration (2.26 [1.10-3.42] for 48h vs. 4.84 [3.60-6.08] for 72h vs. 4.16 [3.63-4.69] for 96h vs. 3.47 [0.61-6.33] for 120h, p = 0.01). The effect of protocol duration was also observed when performing meta-regression (p = 0.01).

Conclusion:

The findings of this meta-analysis demonstrate that induction protocol using formula feeding, LPS/bacteria, hypothermia, and hypoxia represent a robust animal model for studying NEC. However,

no specific constellation of the experimental setting with regard to frequency or duration of specific regimes was associated with severity of NEC. This might imply that different experimental regimes are the result of experimental adapted refinements by individual research groups following a basic core set-up. Therefore easy adaption of NEC protocols might be challenging and this could explain the difference in NEC severity.

Sacral Nerve Stimulation in Children and Adolescents with Hirschsprung's Disease
ID: 380

Sonja Diez*[1], Annemarie Kirchgatter[1], Arne Füldner[1], Manuel Besendörfer[1]
[1]*Universitätsklinikum Erlangen, Kinderchirurgie, Erlangen, Deutschland*

Background:
Chronic constipation and encopresis following surgical therapy for Hirschsprung´s disease or its short-segment variant are common problems, but treatment options are limited and symptom-based. Sacral nerve stimulation (SNS) has already been established in the treatment of therapy-refractory fecal incontinence and constipation in adults. The aim of the study is to evaluate this innovative therapy in the subgroup of patients with Hirschsprung´s disease.

Materials and methods:
A prospective clinical trial enrolled patients with aganglionic megacolon if the segment of aganglionic megacolon could not be treated with a surgical approach or if symptoms of constipation or encopresis did not respond sufficiently to surgical treatment. A two-step approach was used: First, a temporary electrode is placed at the sacral nerve root S3, and successful stimulation is monitored. Then, a permanent electrode and pacemaker are implanted (Medtronic Inc., Minneapolis, MN, USA). The pacing threshold ranges between 1,5V and 3V with a pulse width of 210 µs and a frequency of 15 Hz. Target variables were defined as defecation frequency, stool consistency, and number of episodes with encopresis. Clinical changes were assessed in all patients using specific questionnaires in regular clinical consultations at 1, 3, and 6 months after implantation of the permanent electrode.

Results:
Temporary electrodes were implanted in 8 patients (median age 8.5 years, range 4-14 years, sex ratio 3 female/5 male). 7 patients showed an immediate improvement of constipation with improvement in defecation frequency and stool consistency and a reduction in encopresis episodes in this initial phase. In one patient, symptoms were completely resolved even after removal of the temporary electrode, bypassing the implantation of permanent electrodes. Treatment was discontinued in further two patients because of an inadequate response. 5 patients underwent implantation of permanent electrodes. Overall, 4/5 of the patients (80%) were satisfied with the therapy and experienced an improvement in their quality of life. After one month of therapy, defecation consistency and frequency improved to normal levels in these 4 patients. Medication with macrogol was reduced or discontinued during treatment. Encopresis occurred in 4/5 patients with an improvement in all 4 patients under SNS therapy. Only one patient still suffers from rare episodes of encopresis and is therefore not completely satisfied with the therapy. Complications such as infections or the early termination of therapy did not occur.

Conclusion:
Preliminary results of the ongoing clinical trial suggest that SNS is a promising and safe treatment for patients with Hirschsprung´s disease. We therefore estimate its value highly in the therapeutic algorithm of Hirschsprung's disease and chronic constipation disorders. However, long-term results must be awaited and should clarify the possible codependency of psychological and neurological pathways.

Sacral Nerve Stimulation in Children and Adolescents with Neurogenic Defecation Disorders
ID: 385

Sonja Diez*[1], Manuel Besendörfer[1]
[1]*Universitätsklinikum Erlangen, Kinderchirurgie, Erlangen, Deutschland*

Background:
Sacral Nerve Stimulation (SNS) has already proven successful in the treatment of therapy-refractory fecal incontinence and constipation in adults and is about to be transferred to the treatment algorithm of chronic constipation disorders in children and adolescents. Neurogenic defecation disorders confront patients with difficult and lifelong symptoms that limit a normal physical and psychosocial development. These patients might benefit from the potential of SNS in the treatment of defecation disorders.

Materials and methods:
In a prospective clinical trial, patients with neurogenic defecation disorders are recruited in a two-step approach: First, a temporary electrode is placed at the S3 sacral nerve root and successful stimulation is monitored. This is followed by implantation of the permanent electrode and pacemaker (Medtronic Inc., Minneapolis, MN, USA). The stimulation threshold ranges between 1,5V and 3V with a pulse width of 210 µs and a frequency of 15 Hz.

Results:
We present three individual cases with neurogenic defecation disorders, in which SNS limited symptoms and supported a normal development.

Case 1: 3-year-old girl with condition after acute bi-clonal lymphocytic leukemia, diagnosed at 10 weeks of age. After chemotherapy and stem cell transplantation, the girl developed chronic constipation in the first year of life. Since the age of 2 years, episodes of 10 days without defecation with symptoms of subileus (significant abdominal pain and vomiting) usually occur. After implantation of SNS, the girl shows regulation of bowel movements to every second day with normal stool consistency.

Case 2: 7-year-old boy with sacral dysgenesis, tethered cord, and anal atresia as part of a VACTERL association. After surgical treatment within the first year of life, the boy shows daily encopresis. After implantation of SNS, episodes of encopresis decrease to 30-50%.

Case 3: 16-year-old girl with surgically covered meningomyelocele and bladder- and rectal dysfunction. Bowel movements are not spontaneous but are performed by the girl’s mother every other day by rectal evacuation. After implantation of SNS and 6 months of training, normal defecation is possible without assistance every third day with normal stool consistency.

Conclusion:
Indications for SNS in children and adolescents are broad. Given the knowledge of the potential impact on neural development, its usefulness in atypical cases might be enormous if lifelong suffering and symptoms can be limited. Certainly, the application of SNS needs to be carefully evaluated in larger population studies.

The urethral plate and underlying tissues; a histological and histochemical study
ID: 619

Michael Sennert*[1]
[1]*Sana Klinikum Offenbach, Offenbach am Main, Deutschland*

Background:
Hypospadias occurs in approximately 1 in 120 live male births, and as many as one-fourth of those born with hypospadias will have some degree of penile curvature. Penile curvature (chordee) also occurs in 4-10% of males born without hypospadias. There is no general consensus in literature regarding the precise definition, etiology, classification or the surgical management of chordee. In addition, very little is known about the nature and histology of the urethral plate and the underlying tissues commonly referred to as chordee. Only two studies focused on severe chordee. The remaining few studies available in literature, obtained small biopsies, mainly from patients with distal hypospadias (usually with no or mild curvature).
In this study, we used histologic and histochemical stains to examine the urethral plate and the underlying tissues in patients with perineal and proximal hypospadias associated with severe chordee (> 30°) that necessitated division and excision of the urethral plate.

Materials and methods:
The urethral plate and the underlying tissue specimens were excised to correct severe chordee in 17 children with proximal and perineal hypospadias with severe chordee. The median age was 20 months (range 8-36). Sections samples were marked and examined from proximal to distal. Specimens were examined histologically using hematoxylin-eosin (HE) and Elastic van Gieson (EvG) stain. Histochemical examination was also performed using smooth muscle actin (SMA) and factor 8 antibodies. For control, samples from four patients with hypoplastic urethra proximal to the meatus including the hypoplastic segments until the normal urethra was taken. In addition, the urethra of an adult patient with penile tumor were used as control.

Results:
The average size of the 17 tissue samples was 1 cm x 1 cm x 0.5 cm in depth. There was a common pattern that was seen in all the 17 specimens with a variable degree of expression. Hematoxylin/eosin (H/E) staining showed that the epithelial lining changed from transitional epithelium at the proximal intact urethra to non-keratinized stratified squamous epithelium at the urethral meatus to keratinized stratified squamous epithelium distally at the urethral plate level. Elastic van Gieson staining showed overall very few elastic fibres that increased slightly in the distal urethral plate. SMA staining showed a circular pattern of smooth muscle cell in the proximal intact urethra that changed to a U-shaped pattern at the level of the meatus, to a triangle shaped pattern just distal to the meatus. The distal urethral plate showed an irregular, disorganized rather flat pattern of the smooth muscles. Factor 8 antibodies staining the blood spaces revealed dysplastic unorganized large blood sinusoids underneath the urethral plate that were different from normal capillaries surrounding the proximal urethra.

Conclusion:
The urethral plate and the underlying tissues in patients with severe chordee has different structure from normal urethra. The lack of elastic fibres may help to explain the rigidity of the ventral penis causing chordee. The disorganized irregular distribution of the smooth muscle fibres is suggestive of the hypoplastic corpus spongiosum. The abnormal large blood sinusoids may explain the poor healing quality of the ventral penis in patients with perineal and proximal patients associated with severe chordee. Further studies are warranted to confirm the findings of the study.

Effect of kigelia africana fruit extract on stage 4 neuroblastoma cell lines
ID: 685

Sofia Ahrens*[1], Birgit Appl[1], Magdalena Trochimiuk[1], Charlotte Dücker[1], Konrad Reinshagen[1], Laia Pagerols Raluy[1]
[1]*Klinik und Poliklinik für Kinderchirurgie, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Deutschland*

Background:
Neuroblastoma (NB) is one of the most common solid childhood tumors with an incidence of 1:100,000 per year in Germany. NB is an embryonal tumor deriving from the neural crest and most frequently developing in either the adrenal medulla or paravertebral sympathetic ganglia thus causing a variety of symptoms, such as abdominal pain, respiratory distress or neurological symptoms. The median age at diagnosis is 17 months. In 50 % of NBs, haematogeneous metastasis has already occurred at diagnosis. Treatment approaches are based on risk-stratification and include tumor resection, (myeloablative-) chemotherapy, radiotherapy and immunotherapy, but the NB still accounts for 12-15 % of cancer related deaths in children. Amplification of MYCN protooncogene is present in about 20 % of neuroblastomas and is one of the strongest predictors of poor prognosis. There are also hints that MYC-proteins influence the tumor immune microenvironment altering the interaction between NB and immune cells. In some cases, NB undergoes spontaneous regression thus suggesting a striking anti-tumor immune response. *Kigelia africana* (KA), a plant belonging to the family of *bignoniaceae*, is used in traditional African medicine for the treatment of a broad variety of inflammatory diseases, cancers and infections. Several compounds such as flavonoids and iridoids have been identified in KA extracts and show a promising potential in cancer treatment by inducing apoptosis and inhibiting growth, proliferation and metastasis in some cancer types. Additionally, the use of some phytochemicals extracted from KA lead to sensitization of cancer cells to chemotherapy in cell cultures. The aim of this study is to evaluate the effect of KA fruit extract on Neuroblastoma cells and the potential immune-mediated anti-tumor activity.

Materials and methods:
Human stage 4 NB cell-lines SK-N-SH and LAN-1 (MYCN amplified) and non-neoplastic cell lines HUVEC (Human Umbilical Vein Endothelial Cells) and PBMC (Peripheral Blood Mononuclear Cells) were treated with KA fruit extract at different concentrations. The solvent of KA extract (propanediol) was used as a control. After several time points, cells were harvested and further processed for the analyses. Cell proliferation and apoptosis as well as levels of secreted cytokines were measured by means of flow cytometry whereas cell viability was assessed by a bioluminescence-based assay. In order to elucidate the mechanism of action of KA on the cells, several proteins involved in survival, tumor growth and metastasis were detected via western blot and immunofluorescence. Subsequently, the potential KA-mediated immunoregulation was examined by analyzing the activation status of immune cell subpopulations by means of mass cytometry. For this purpose, a co-culture of tumor cells and PBMCs was used.

Results:
The study is still ongoing so the results are preliminary.
Our group demonstrated that the viability of KA-treated tumor cells is reduced significantly ($p < 0,05$) in comparison to control (propanediol-treated cells). This effect occurred in a dose- and time-dependent manner. By contrast, KA-treatment shows no modulation of the viability in non-neoplastic cells. Concomitantly, KA-treatment led to a higher apoptosis rate in MYCN non-amplified tumor cells compared to HUVECs and PBMCs. Western blot and immunofluorescence results demonstrated a regulation of NFkB- and FAK activation and EGFR expression in KA-treated tumor cells. Furthermore, we observed an altered immune-population activation pattern in co-cultures incubated with KA extract as well as a modified cytokine secretion response.

Conclusion:
The results demonstrate a cytotoxic effect of KA fruit extract on NB, especially in MYCN non-amplified tumor cells, but not on HUVECs and PBMCs. KA fruit extract regulates the expression and activation of proteins, which play a key role in survival, apoptosis and migration thus confirming anti-cancer and immunomodulating properties in NB. Further research on KA-fruit phytocomposition and its pharmaceutically active substances may help to develop improved therapy strategies against NB.

Quality of life improves following laparoscopic hemifundoplication in neurologically non-impaired children with gastroesophageal reflux disease: A propensity score-matched analysis
ID: 714

Giovanni Frongia*[1]
[1]*Universitätsklinikum Heidelberg, Chirurgische Klinik, Sektion Kinderchirurgie, Heidelberg, Deutschland*

Background:
Quality of life (QOL) data following pediatric fundoplication for gastroesophageal reflux disease (GERD) are rare. Present study assessed the QOL in neurologically non-impaired children before and after laparoscopic hemifundoplication (LHF) in comparison to healthy controls.

Materials and methods:
PedsQL™ questionnaires assessed data on gastrointestinal symptoms (GIS) and general well-being (GWB) were compared in a propensity score-matched analysis (60 patients' pairs for time-point of surgery and 51 for follow-up).

Results:
Preoperatively, the LHF group had more GIS (72.2 ± 53.9 vs. 38.8 ± 31.6; $p < 0.001$) and a lower GWB (16.7 ± 5.5 vs. 23.8 ± 3.5, $p < 0.001$) compared with controls. Postoperatively, GIS decreased significantly (74.3 ± 52.9 vs. 36.3 ± 33.5; $p < 0.001$) and the GWB was significantly higher (16.2 ± 6.0 vs. 20.8 ± 5.8; $p < 0.001$). GIS were similar in the LHF and control groups (39.1 ± 36.4 vs. 40.1 ± 31.0; $p = 0.885$) but GWB was lower in the LHF group than the control group (20.5 ± 6.3 vs. 23.4 ± 3.9; $p = 0.009$).

Conclusion:
QOL significantly improves after LHF in neurologically non-impaired children.

The postoperative C-protein (CRP) value predicts the need for laparotomy following cardiac surgery for congenital heart diesease in children - an analysis of 1013 consecutive cases
ID: 716

Giovanni Frongia*[1]
[1]*Universitätsklinikum Heidelberg, Chirurgische Klinik, Sektion Kinderchirurgie, Heidelberg, Deutschland*

Background:
Gastrointestinal complications with the need of abdominal surgery following cardiac surgery for congenital heart disease are rare but reflect an important cause of morbidity and mortality. Predictors of adverse outcome are not clearly defined and could help to identify patients at risk at an early stage and optimize patients' outcome. The aim of present study was to determine predictors of adverse GIC following cardiac surgery in children.

Materials and methods:
Retrospective analysis of all consecutive children undergoing cardiac surgery for congenital heart disease during a 7.7 years period (2012-2019) at a tertiary center. Predictors of abdominal surgery were identified within 30 days from cardiac surgery.

Results:
A total of 1013 consecutive children underwent cardiac surgery (age 1.9 ± 3.2 years), Seventy-three (7.2%) cases developed gastrointestinal complications (8.3 ± 7.9 postoperative days) leading to abdominal surgery in 4 (0.4%) cases. The postoperative C-reactive protein value was significantly higher in the abdominal surgery group (271.2 ± 114.1 vs. 126.6 ± 71.3 mg/l, $p<0.001$) and best predicted the need for abdominal surgery (odds-ratio 1.015, 95% confidence interval 1.007 – 1.024; $p=0.004$) with a 100% sensitivity and 74.8% specificity using the cut-off value of 159.6 mg/l (area under the curve of 0.903 ± 0.48; 95% confidence interval 0.809 - 0.996, $p=0.005$). The postoperative CRP cut-off value of ≥159.6 mg/l was reached in all 4 (100%) patients in the abdominal surgery group and in 253 (25.1%) patients in the non-abdominal surgery group ($p=0.004$). It's overall prevalence was 0.4%, the positive likelihood ratio was 1.6%, the negative likelihood ratio was 0%.

Conclusion:
The postoperative C-reactive protein value predicts the need for abdominal surgery following cardiac surgery for congenital heart disease in children.

Abdominal wall movement predicts intraabdominal pressure changes in rats: a novel non-invasive intraabdominal pressure detection method.
ID: 848

Deirdre Vincent*[1], Stefan Mietzsch[1], Magdalena Trochimiuk[1], Konrad Reinshagen[1], Michael Boettcher[2]
[1]*Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Kinderchirurgie, Hamburg, Deutschland*, [2]*Kinderchirurgische Klinik, Universitätsklinikum Mannheim, Mannheim, Deutschland*

Background:
Increases in intraabdominal pressure (IAP) in neonates are the result of either (1) tissue edema or (2) intraperitoneal fluid collection, with physiological decompensation beginning when IAP rises above 8-10 mmHg. Thus, IAP increases beyond 20 mmHg can cause irreversible tissue injuries. Currently, IAP within the neonatal population is assessed invasively using a urinary bladder pressure measurement, which is associated with an increased risk for complications, such as infection. As a result, the aim of this study was to establish a novel non-invasive and accurate method to detect IAP changes in the neonatal population, using an animal model.

Materials and methods:
IAP was measured in 19 rats (1) non-invasively, via a Graseby capsule applied to the abdominal skin of the upper abdomen and (2) invasively, via Codman intracranial pressure (ICP) probe placed in the lower left quadrant of the abdomen per mini laparotomy. IAP was increased up to 20mmHg, using air, which was administered and controlled by a syringe connected to a Heidelberg extension, placed in the lower right quadrant per mini laparotomy.

Results:
The results suggest a high correlational relationship between changes in abdominal wall distension, as measured by the Graseby capsule, and the Codman ICP probe (r=0.9264, CI 0.9249-0.9279).

Conclusion:
The study showed that small changes in abdominal wall distension were identified by the Graseby capsule, which in turn correlated highly with Codman ICP probe measures within the rat population. Thus, given the high correlation, IAP changes in rats can be detected non-invasively using a Graseby capsule. This is particularly advantageous in monitoring neonates at risk for developing NEC or midgut volvulus, as these diseases often present with increases in IAP, possibly rendering intravesical pressure measurements obsolete. However, further studies are necessary to assess whether a correlation between measurements in intravesical pressure and the Graseby capsule can be found within the neonatal population.

Social media in Pediatric Surgery
ID: 819

Andrea Schmedding*[1], Martin Hutter[1], Udo Rolle[1]
[1]*Universitätsklinikum Frankfurt, Klinik für Kinderchirurgie und Kinderurologie, Frankfurt am Main, Deutschland*

Background:
Social media has changed the use of the Internet in recent years including in medicine. They are used for personal communication as well as information. Parents of pediatric surgical patiens belong to an age group that is used to social media in every-day life. This should be optimal prerequisite for medical providers to use them to attract new patients. On the other hand pediatric surgeons, especially head of departments belong to an older age group, so they might not see the benefit of these media. This study analyzes the coverage of social media in German hospitals with pediatric surgery and the use of social media by pediatric surgeons.

Materials and methods:
All hospitals providing specialized pediatric surgery were registered at the homepage of the German society of pediatric surgery. These hospitals were analyzed regarding their presence in different social media. Facebook, YouTube, Instagram and Twitter were analyzed further. Data were taken for the year 2020. In 2021 a survey was sent to the members of the German society of Pediatric Surgery (DGKCH) about the use of social media in private live and the profession.

Results:
All units of pediatric surgery provide information on a homepage provided by their hospital: 81.2% of the hospitals had an account on Facebook, 35.3% on Twitter, 48.9% on Instagram, and 70.7% on YouTube. Three units had their own Facebook account. The #Kinderchirurgie (which means pediatric surgery in German) at Twitter addressed 19 units (14.3%); 14 units (13.5%) provided at least one film on YouTube. 77 persons answered the questionnaire. 56% were males, 44% females. 60% were under 50 years old. 82% work in a pediatric surgical department. In private life 87% use Youtube, 48% Facebook, 33% Instagram, 12% Twitter. In professional life 78% use Youtube, 55% Research Gate, 37% LinkedIn, 29% Facebook, 21% Xing, 17% Instagram, and 9% Twitter. 60% use social media for professional exchange and for research, 58% for training, 26% for interaction with patients, but only 5% to attract new patients.

Conclusion:
The use of social media is still low among the German pediatric surgery departments. Pediatric surgeons use social media in private and professional life, but use of social media for interaction with and attraction of patients is still sparse.