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Master Thesis

Minimally Invasive Surgery in Neurologically Impaired Children

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Declaration

I, hereby, declare that the following master thesis has been written only by the undersigned and without any assistance from third persons. Furthermore, I confirm that no sources have been used in the preparation of this other than those indicated in the thesis itself.

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Abstract

Introduction: Neurologically impaired children usually suffer from feeding difficulties, malnutrition and aspiration pneumonia, due to some anatomical and functioning health problems. Swallowing difficulties, dysphagia and severe gastroesophageal reflux (GER) are the most common causes of repeated hospitalizations from the very beginning of their lives, reducing their and their family's quality of life. A pediatric surgeon faces often the problems of these patients, which should be treated in the best way.
Methods: In this study we try to summarize the recent literature in using minimal invasive techniques (MIS) in neurologically impaired children, appling the up-to- date management protocols for these patients, recognizing the indications and contraindications for the different techniques and recommending the best surgical technique for each health problem of these children.
Results: Minimally invasive surgery gives a better life to these children and their family by firstly improving their quality of life, by a safer and easier way of feeding and redused hospitalizations. PEG and GJ tubes have been beneficial for neurologically impaired children, making their feeding easier. Secondly, having the advantage of choosing between different MIS techniques for treating the same problem or disease for each patient, every pediatric surgeon could choose the best technique with minimun complications for each of them. For example, MIS offers laparoscopic Nissen, Toupet, Thal fundoplication, GJ tubes and laparoscopic TOGD for the treatment of GERD, each one with special indications. Finally, offering less traumatic techniques with few complications, due to its technical advantages, MIS has a huge superiority compaired to open surgery.
Conclusions: In the future MIS procedures seem to be the gold standard in treating each health problem of neurologically impaired children. More effort should be given in the training of the young pediatric surgeons in order to have better results by using these techniques for neurologically impaired children.

Key words: Neurologically impaired children, GERD, gastrostomy, Nissen fundoplication, MIS techniques.

Abbeviations

CI : Confidence Interval

EEG : Electoencephalography

ESPGHAN : European Society for Pediatric Gastroenterology, Hepatology and Nutrition

FG : Fundoplication with Gastrostomy

GERD : Gastro-Oesophageal Reflux

GJ : Gastrojejunostomy

HRQoL : Health-related Quality of Life

LAG : Laparoscopy-Assisted Gastrostomy

LAPEG : Laparoscopic-Assisted Percutaneous Endoscopic Gastrostomy

LC: Learning Curve

MIS : Minimally Invasive Surgery

PEG : Percutaneous Endoscopic Gastrostomy

POD: Post- operative Day

RR : Risk Ratio

TODG : Total Esophago-gastic Dissociation

Introduction

Neurologically impaired children are characterised by a neurologic disorder. The term “neurologic disorder” applies to any condition that is caused by a disfuction in the brain or nervous system, affecting an idividual's speech, motor skills, vision, memory, muscle actions and learning abilities. Most importantly, it can affect the gastrointestinal system causing serious feeding problems due to oro-motor disfunction, failure to trive, hypotonia, dysmotility and severe gastro-oesophageal reflux **(**GERD) which can lead to malnutrition and growth failure. (**Romano et al 2017**)

The most common neurologic disorders in children are congenital, such as gene abnormalities, structural associated brain and spine malformations (myelomeningocele, spina bifida and hydrocephalus), mitochondrial diseases, muscular dystrophies and myopathies, related congenital heart diseases and metabolic syndroms. Some are developed after birth, with most common the cerebral palsy. Others are caused by infections (encephalitis, meningitis), perinatal asphyxia (hypoxic-ischemic injury), traumatic brain (intracranial hemorrhage) or spinal cord injuries and few are idiopathic or due to some autoimmune disorders.

Neurologically impaired children are a special group of patients. Because of their affected gastrointestinal system, most of them suffer from the very beginning of their lifes. Swallowing difficulties, dysphagia and severe GERD are the most common causes of repeated hospitalizations due to feeding difficulties, malnutrion and aspiration pneumonia. In a study from Sullivan et al (2000) in 271 parents of neurologically impaired children (aged 4 to 13 years), in which only 8% had a gastrostomy, showed that a lot of these children suffered from gastrointestinal problems and sickliness. 22% had significant problems with vomiting and 31% had suffered at least one chest infection the previous 6 months. Regarding feeding problems 89% needed help with feeding, 56% choked with food, whereas 20% of parents described feeding as stressful and unenjoyable. In addition, 38% of the parents considered their child to be underweight, whereas 64% of children had never had their feeding and nutrition assessed. Because of all these problems, regular nutritional assessment is not only essential but should also be a part of the child's care and rehabilitation. The aim is double: to advance weight and linear growth and to secure improved physiological and functional capacity. (**Sullivan et 2000**)

Nowadays the total percent of the hospitalizations of these children is incrising, due to their everyday problems or the surgeries they should undergone, as a treatment to their health problems. A study from USA of 25,747,016 hospitalizations of children through years 1997, 2000, 2003 and 2006 showed that in 2006 children with neurological impairment accounted for 5.3% of all hospitalizations, 13.9% of bed days and 21.6% (US $17.7 billion) of all hospital charges within all hospitals. There was also a decrease of 20.5 % in respiratory admissions for children with neurological impairment (48,334 in 1997 to 38,390 in 2006), thus there was a 27.1% increase in the number of gastrostomy/fundoplication procedures (7,579 in 1997 to 9,638 in 2006). (**Berry 2012**)

In order to maximise quality of life and reduce morbidity and mortality, each of these children should be carefully assessed and treated. Surgical therapy is always an option when enteral tube feeding and medical therapy fail. Nowdays minimally invasive surgery offers a less traumatic, cost-effective option with quicker recovery time and reduced postoperative pain for these patients. Despite the minor or majon disadvantages endoscopic, laparoscopic and robotic procedures may occur, they represent a critical component of improving outcomes in neurological impaired children's problems.

Purpuse of the study

Minimally invasive surgery tends nowadays to replase the open surgery in all surgical fiels. Many studies have been done reporting the advantages and disadantages of each kind of procedure in specific pathologies and patients. Until now a few studies have been done for neurologically impaired children and there is still a debate for using these techniques. We try to collect all the prospective or retrospective controlled studies, prospective or retrospective cohort studies, systematic reviews and meta-analyses that have been published during the last 20 years and to analyse for the first time the use of minimally invasive techniques in improving the gastrointestinal problems of neurologically impaired children, regarding feeding and malnutrition.

In this study we try to provide a critical appraisal of the recent literature in using minimal invasive techniques in neurologically impaired children, appling the up-to- date management protocols for these patients, recognizing the indications and contraindications for the different techniques and recommending the best surgical technique for each health problem of these children. More specifically, the first part of this thesis presents all the possible mininal invasive techniques in inserting feeding catheters, that are vital in feeding and restoring a normal nutritional status of neurologically impaired children. Whereas in the second part we analyse all the possible MIS techniques in the treatment of GERD, comparing with each other as with some open techniques. Finally, our discussion and conclusion includes some thoughts about training young pediatric surgeons in minimally invasive techniques improving the neurologically impaired children's and their family's life.

Methods

A systematic search of electronic databases was performed to identify all relevant studies refering to health problems in neurologically impaired children. All literature published from 2000 until September 2020 was searched using the PubMed and Cochrane database. Abbreviations and several synonyms were included both for different health problems of neurologically impaired children or children with neurological impairment, such feeding problems and malnutrition, GERD (Gastro-esophageal reflux disease) and different intervention techniques, including percutaneous endoscopic gastrostomy (PEG), laparoscopy-assisted gastrostomy (LAG), jejunostomy, gastrojejunostomy, surgical management of GERD, laparoscopic Nissen, Toupet and Thal fundoplication and pyloroplasty in children.

Inclusion criteria were prospective or retrospective controlled studies, prospective or retrospective cohort studies, systematic reviews and meta-analyses. If a study included data of pediatric population in general, regarding children with neurological impairment, was also included. Exclusion criteria included irrelevant publications (animal studies) and inappropriate patient populations (patients older than 18 years of age).

Results

A. MIS offering new options in improving malnutrition and feeding problems: Gastrostomy, Jejunostomy, Gastrojejunostomy in neurologically impaired children.

As it has been mentioned neurologically impaired children have a high incidence of feeding problems and malnutrition due to oropharyngeal dysfunction (dysfagia and swallowing problems), GERD and neurodevelopmental delay. The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommends the use of a gastrostomy or a jejunostomy for long-term nutritional support in children with neurological impairment. These tubes are well tolerated and provide improved quality of life compared to parenteral and nasogastric feeding for such patients, unable to feed adequately by mouth. **(Baker et al 2015), (Broekaert et al 2019)**

Nowadays, minimally invasive surgery techniques give the opportunity to the surgeons to choose between a lot of techniques and feeding catheters, the best option of each of neurologically impaired patients, depending on their problems. MIS techniques offer best results with reduced operative time, less post-operative pain, morbidity and mortality in these special group of patient. Without requiring special surgical skills and long operative learning curve every pediatric surgeon could help one neurologically impaired child to improve his/her family quality of life.

Gastrostomy tube

The main reason for eventually choosing a gastrostomy tube placement is an improvement of nutritional status and quality of life. The use of gastrostomy tube feeding has been shown to increase weight, improve overal health and decrease feeding times for children with neurological impairment. It has also demonstrated a significant, measurable improvement in the quality of life of carers. Thus, some studies have shown a lower Health-related quality of life (HRQoL) in neurological impaired children with gastrostomy compaired to a healthy pediatric population. But the effect of the gastrostomy placement in childrens' quality of life still remains unclear due to lack of studies before and after the placement of the tubes in such patients. **(Vermon-Roberts et al 2013), (Franken et al 2014)**

The placement of a gastrostomy for a long time ago consisted of open gastrostomy using the Stamm technique, introduced in 1894. After 100 years, Percutaneous Endoscopic Gastrostomy (PEG) was described in 1980 by Gauderer. Anderson et al. were the first in 1997 to describe the laparoscopy-assisted gastrostomy (LAG) tube placement method. During the last 30 years evolving technology gave rise to different minimal invasive procedures, which are currently used with different spectrum of outcomes, short- and longterm, minor or major complications, although the choice of the best technique in children remains controversial. **(Baker et al 2015)**

The Percutaneous Endoscopic Gastrostomy (PEG) technique is a technically easy and quick technique in experienced hands. It involves performing a gastroscopy to evaluate the anatomy of the stomach. The anterior stomach wall is identified and the light from the gastroscope is identified through the abdominal wall. A small needle is passed through the abdominal wall to the stomach, then a larger cannula and a soft quidewire is inserted through this and pulled out of the mouth. The gastrostomy tube is attached to the quidewire and pulled through the mouth, esophagus and stomac to the right possition. Then the gastrostomy is fixed to the skin.

Laparoscopically assisted gastrostomy (LAG) is an alternative to PEG. Children with previous abdominal surgeries may have adhesions requiring further dissection, having an increased incidence of conversion to open procedures. In LAG an incision is made in the umbilicus and a 5mm port is placed. Once pneumonoperitoneum is achived, a 5mm, 30-degree laparoscope is introduced in abdominal cavity. The premarked gastrostomy site is then incised and a locking grasper is placed under direct visualization. Alternatively a 5mm port is placed in this location and then a grasper through that port.The stomach is insufflated with air and an appropriate place on the stomach is selected as the gastrostomy tube site. The stomach is then grasped with the locking grasper in that previous selected location. Two securing sutures are placed. These will secure the stomach to the anterior abdominal wall. The gastrostomy tube will then be placed between these two sutures.

There is also a combination of those two minimally invasive techniques the laparoscopic-assisted percutaneous endoscopic gastrostomy (LAPEG), which is more often used in cases of failed PEG. The LAPEG technique requires a flexible endoscope, a stendard PEG kit, a 5mm, 30- degree laparoscope and a 5mm port. The 5mm port is placed through an infraumbilical incision using the Hasson technique. Once pneumonoperitoneum is achived, the laparoscope is introduced in abdominal cavity. The stomach is then identified and the assistant advances the endoscope into the stomach. The stomach is insufflated, and by using laparoscopy, an optimal placement of the gastrostomy catheter in the greater curve of the stomach is achieved. The PEG is then performed in the standard fashion. **(Yu et al 2005)**

Comparing minimally invasive procedures with open technique in making a gastrostomy in neurologically impaired children, they require a less invasive surgical approach, have proved beneficial in helping to minimize exposure to anesthesia and postoperative pain and are associated with rapid postoperative recovery time and reduced length of hospital stay. They also have an advantage in initiation of parenteral feedings and intravenous medication as the gastrostomy tube could be used within the first postoperative 24 hours. In addition, in many studies PEG appeared associated with a reduction in procedural time and potentially a reduction in direct costs. Studies reported on the success of these procedures, showing a completion rate of almost 100% after both PEG and LAG and a conversion rate of only 3-5%. **(Baker et al 2015), (Suksamanapun et al 2017)**

Comparing these minimal invasive techniques, LAG or LAPEG offer the hole visualization of the abdominal cavity, making these techniques safer and more accurate because of the anatomical deformity of neurological impaired children. It allows for immediate recognition of any possible inadvertent injury, such as unintended damage to abdominal organs and undiscovered bleeding, prior to completion of the procedure and operative correction can be undertaken with minimal overall patient morbidity. Because of the use of 30- degree laparoscope, frequently injuries of the gastrepiploic vessels and bleeding could be avoided. Comparing LAP to PEG gastrostomy insertion, the rate of visceral injury including colonic perforation was 1.72% (range 0-12.2%) in PEG, compared to 0.06% in LAP (range 0-0.96%). In addition, a frequently complication of PEG is the formation of a gastroenteric or a gastrocolocutaneous fistula with reported rate of 2% to 3,5%, due to the dilated bowel in neurological impaired children and the technical weakness of the method. **(Suksamanapun et al 2017)**

Laparoscopic techniques offer also the ability to choose the right possition of the gastrostomy tube and the stability of the stomach. The appropriate place for the gastrostomy is usually two thirds from the gastrointestinal junction to the pylorus. With the tube placement under direct visualization,

the ideal possition for gastrostomy for each patient could be choosen and pyloric obstruction could be prevented. An additional advantage of LAG is that it offers the opportunity to securely transfix the stomach to the anterior abdominal wall, preventing the need for operative management in case of accidental tube dislodgement. With LAG the surgeon could also primary place a low profile device, avoiding the need for a second operation under aneshesia, a very important matter for neurologically impaired children. **(Baker et al 2015), (Yu et al 2005)**

Regarding minor complications of minimally invasive techniques, most frequently reported were dislodgement of the tube, stomal complications such as granulation tissue, erosion, ulceration, non-healing skin and foreign body reaction, gastric content leakage to the skin. In a metanalysis of Suksamanapun et al in 2017, including five retrospective studies, comparing 550 PEG to 483 LAG placements in children, all articles reported on a number of reinterventions under general anesthesia. Patients who received a PEG had a relative risk of 2.79 (P=0.0008) due to most frequently tube dislodgements compared to patients who received a LAG (RR=2.79, P=0.0008). In patients who underwent LAG the most common cause were stomal complications. **(Suksamanapun et al 2017)**

Minor complications may play an important role in QoL of neurologically impaired children and their caretakers, because of a long-term indication for feeding throught gastrostomy. For example, hypergranulation can cause bleeding and leakage from the gastrostomy site and has a major influence in QoL of these children. They need an everyday meticulous care from their caretakers or nurses and a very offen visit into the hospital. However, no studies could be identified comparing the incidence of post-operative hypergranulation between PEG and LAG. Although, stomal infection and leakage of gastric contents to the skin were similar after PEG and LAG. **(Suksamanapun et al 2017)**

Regarding major complications, PEG seems to have the leading role. In 2015 a metanalysis from Baker et al, sumarizing 22 comparative studies, involving 5346 pediatric patients who have undergone gastrostomy placement, has revealed a significant increase in major complications with PEG. Thus, no differences in major complications were noted in studies comparing laparoscopic gastrostomy or PEG versus open approaches. 2018 a second metanalysis from Sandberg et al, including 1550 patients has also shown a higher risk for major complications 3.86 (95% C.I. 1.90-7.81, P<0.0002) in PEG than in LAG. The number needed to treat to reducce one major complication by performing LAG instead of PEG was 23. **(Baker et al 2015), (Sandberg et al 2018)**

Whether gastrostomy increases reflux and worsens reflux symptoms in neurologically impaired patients without pathologic gastroesophageal reflux has also been a subject of controversy. Hawahara et al suggest the increase of reflux in neurologically impaired children without pathologic GER after laparoscopical gastrostomy. Probably, the fixation of the stomach to the anterior abdominal wall and changes in the angle of His exerted a silence abverse effect on GER, although gastric emptying parameters did not change significantly. Razeghi et al recommended also in his study that avoiding placement of the gastrostomy tube in the andrum dicreases the possibility of GER. These two studies show the superiority of LAG over PEG in neurologically impaired children because of the ability of the surgeon to choose the best position of the gastrostomy, discreasing the possibility of GER. **(Kawahara et al 2014), (Razeghi et al 2002)**

Some other studies recommend pH monitoring in neurologically impaired children before and after gastrostomy. Hament et al and Samuel & Holmes used this technique in 96 and 44 respectively

neurologically impaired children and found no GER before and after PEG in 72% of the children, thus only 3% went under fundoplication, after the gastrostomy tube placement. Both of them came to the conclusion that a normal pH before PEG means a favorable prognosis. This statement has changed the strategy it was used until 80s for these children, when anti-reflux surgery was necessarily performed in compination with a gastrostomy, and increased the use of PEG for neurologically impaired children. **(Hament et al 2001), (Samuel et al 2002), (Capellano et al 2003)**

Gastrojejunostomy (GJ) tubes

Sometimes the enteral nutrition via a gastrostomy is totally impossible because of severe gastro-oesophageal reflux, delayed gastric emptying and antropyloric dysmotility. In such cases a jejunal or a gastrojejunal feeding (GJ) tube - transgastric jejunal feeding- is an alternative.

A gastrojejunal feeding tube may constitute a transitory alternative to antireflux surgery in infants and children whose symptoms may be temporary or who may be poor operative candidates. It has two separste lumens that provide access both to the stomach and to the duodenum. It requires the existance of a previous gastrostomy when is done endoscopically, could be obtained by direct jejunostomy and be also performed percutaneous with imaging guidance (primary gastrojejunostomy). It also permits rapid discharge of patients from hospital and the exchange of tubes without anesthesia is a viable option. However, the high frequency of minor or major complications and often tube replacement (median tube lifesplan 98 days – interquartile range 54-166 days) due to structural or mechanical problems (up to 43.1%) limits its use. **(Wilson et al 2020)**

Complications related to gastrojejunal tubes vary from minor such as peristomal irritation, wound infection, tube leakage and coiling with associated reflux, to major such as intussusception and bowel perforation. Reported complication rates for endoscopic or radiographic placement of gastrojejunal tubes are up to 87%. In Onwubiko C. et al study, which included the placement of 90 laparoscopic gastrojejunostomies in children, were two major procedural-related complications: one case of small bowel-small bowel intussuception and one case of jejunal perforation. Michaud L et al present 27 successfully plased gastojejunostomies in 29 children. Complications included 31 tube dislodgements, 16 obstructions, 7 leakages around the tube, 6 internal ballon ruptures and 1 intussusception. Another disadvantage that impacts in every day life of neurologically impaired children and their families is the duration of feeding required per day, which should be delivered at a slow rate. Neurologically impaired children may need to be connected to a feeding pump anywhere from 12 to 24 hours a day. **(Onwubiko et al 2017), (Michaud et al 2012), (Wales et al 2002)**

Despite the high rates of minor complications, the use of gastrojejunostomy seems to be safe in neurologically impaired children and a viable option to achieve their sustained growth. DeRaddo J.S et al studied a total of 44 developmentally disabled children who underwent successful conversion of a surgically plased gastrostomy to a gastrojejunostomy. This study has shown a significantly increased average change in weight-for-age z-scores ranging from +0.81 to +1.39 at each 6-month interval that continued past 25 months. Patients whose rate of minor complications were above the median rate of minor complications (0.20/100 device-days) did not show a significantly lower average change in weight-for-age z-scores (+0.60, 95% CI : -0.94 to 2.15, P=0.44) across the study period, compared with those below the median rate. **(DeRaddo JS et al 2019)**

Gastrojejunal tubes are also used in neurologically impaired children as an alternative in the GERD treatment. No guidelines currently exist that provide specific recommendation regarding the use of fundoplication with gastrostomy (FG) versus gastojejunostomy tubes (GJ). However, the use of GJ as an alternative in the GERD is one big achivement of minimally invasive surgery in neurologically impaired children. Gastrojejunostomy is a less invasive option, requiring less recovery time (less than 24hours hospital stay) and can be removed if symptoms of gastroesophageal reflux improve. On the other hand, FG requires general anesthesia, longer operative time and a minimum hospital stay of 3-5 days in an experienced center with higher complication rates in neurologically impaired children. Most researchers have attempted to explain the higher failure rate of antireflux surgery in neurological patients as a result of an alteration of the esophageal peristaltic waves, a permanently supine position, spasticity, lack of coordinated diaphragmatic movements and a delayed gastric emptying. **(Veeker et al 2008), (Esposito et al 2013)**

However, few studies have been done to compare these two options. In 2015 a Meta-analysis from Livingston M. et al including 556 children from three retrospective studies, has shown no differences in all- cause mortality in two different groups (13% in children who undergone fundoplication and gastrostomy (FG) versus 14% in children with gastrojejunal tube). The risk of pneumonia during the follow-up period was also similar: 17% for FG and 20% for GJ. Regarding the major complications there was an increased risk in children with FG 29%) compared to GJ (12%) (risk ratio = 1.70, 95% C.I 0.85-3.41, p=0.14). Minor complications were more common with GJ (70%) than FG (45%), a non statistically significant difference (risk ratio = 0.38, 0.05-3.07, p=0.36). Wales P.W et al in a retrospective review of 111 neurologically impaired children with GERD found that for children who underwent GJ were more likely to continue taking antireflux medication after the procedure ($p < 0.05$) and only 8.3% of patients went on to require a fundoplication for persistent problems. However, further studies are needed to characterize which patients are best served with a gastrojejunal tube (GJ) versus the gastrostomy tube and fundoplication combination (FG). **(Livingston et al 2015), (Wales et al 2002)**

Jejunostomy tube

As it has been mentioned a GJ feeding tube is a brilliand option in neurologically impaired patients with severe gastroesophageal reflux as an alternative to antireflux surgery or prolonged parenteral nutrition. The rate of recurrent GERD in those children after reflux procedure is 10 and 14% and a re-do fundoplication has a high failure rate of 20-30%. However, the high frequence of complications and tube replacament limits the GJ use. Hence, for a long term post-pyloric feeding in such children, a direct jejunostomy tube provides more stable and secure jejunal access. Jejunostomy allows these patients to achieve an excellent weight gain and reduces episodes of recurrent respiratory infections, reducing the severe GERD. Thus, the jejunostomy tube is limited used, as the ESPGHAN recommends its use in specific cases (gastric feeding failure in critically ill patients, pediatric intestinal pseudo-obstruction with gastrostomy failure, gastroparesis, severe GERD with aspiration risk). **(Belsha et al 2016), (Esposito et al 2013), (Broekaert et al 2019), (Egnell et al 2014)**

Jejunostomy is performed by a number of techniques: open or minimally invasive such percutaneous endoscopy and laparoscopy or laparoscopic assisted techniques. Unfortunately,there are no data that demonstrate superiority in effectiveness and safety of anyone. The choice depends on the surgeon's experience and his/her preferences. **(Broekaert et al 2019)**

The percutaneous endoscopic technique requires the use of a gastroscope or colonoscope placed into the proximal jejunum. Then, using the Seldinger technique, a needle is inserted into the jejunal lumen at the site of the maximal transillumination and snared tightly, fixing the small bowel against the abdominal wall. The plastic sheath with stylet should then be inserted adjacent to the needle and snared by a wire loop that has been removed from the needle. The wire is then passed through the plastic sheath and grasped with a snare or a grasp forcep. After that the gastroscope with the wire is pulled out through the duodenum, stomach, oesophagus and mouth. The wire is then secured to the loop at the end of the feeding tube with an internal jejunal bolster and the assembly is pulled through the mouth all the way to jejunum. The tube is pulled through the incision in the abdominal wall, sufficiently tight to compress the jejunal wall against the anterior abdominal wall. **(Broekaert et al 2019)**

Regarding the laparoscopic technique, after the port insertion the surgeon lift up the transverse mesocolon identifing the ligament of Treitz. About 40 cm distal to that, the jejunum is grasped. A proximal stay suture is placed, tacking the bowel to an optimal position on the abdominal wall to ensure minimal tension. The introducer needle is passed through the abdominal wall into the jejunum under direct camera vision and a wire introduced. The needle is retrieved and serial dilation is performed using a Seldinger technique. The catheter is then passed through the peel-away sheath distally into the jejunum.Verification of appropriate positioning of the tube is accomplished by injecting 20 cc of air and observation of distal bowel inflation. The balloon can then be injected with 1–2 cc of water, as not to cause any bowel obstruction. The jejunostomy insertion site can then be fashioned to the anterior abdominal wall in a stamm manner, and the tube pulled back so the balloon is only gently snug, as not to cause bowel wall necrosis. Some authors recommend the Witzel technique and prefer to tunnel the catheter proximally with several additional sutures. Finally, the tube is secured to the abdominal wall and skin using several sutures to prevent dislodgement and migration. (**Bakhos et al 2019**)

Minimally invasive surgery gives also an alternative combined method. Laparoscopic assisted jejunostomy is technically easier than the laparoscopic one and extremely simple, requiring the identification of the first jejunal loop laparoscopically and then exteriorizing it to the trocar orifice under visual guide. The jejunostomy is then created outside the abdominal cavity similar as in the open procedure. (**Esposito et al 2013**)

Regarding the complications that may occur, peristomal granulation, infection, leakage of bile acids and buried bumper syndrome, due to pressure-indused necrosis are common. Major complications, such as intestinal perforation and intussusception are rare. Diarrhoea is also very common regardless the insertion technique of the jejunostomy related to hyperosmolar feeds. Children on exclusive jejunal feeds may be also at a risk for iron deficiency due to feeds bypassing the duodenum, which is the primary site for iron absorption. It may also cause vitamin B12 deficiency, malabsorption of zinc, selenium and copper, developing secondary cytopenia. (**Broekaert et al 2019**)

B. MIS as a therapeutic procedure in Gastroesophageal Reflux Disease (GERD) in neurologically impaired children.

GER occurs when gastric contents flow back into the esophagus and produce symptoms.In neurological impaired children GERD has a high incidence. More than 77% of these patients suffer from GERD, as the central nervous system controls the enteric nervous system. In a study of 101 neurologically impaired children who received 24-hour esophageal pH monitoring the reflux index was higher in patients with abnormal electoencephalography (EEG) than in those with normal EEG results. Decreased lower esophageal sphincter tone, delayed gastric emptying, impaired esophageal motility, poor posture, recurrent seizures, respiratory symptoms, scoliosis and various medications are also though to contribute to GERD in these children. **(Kim et al 2017), (Lauriti et al 2018)**

Unfortunatly the diagnosis of GERD in neurological impaired children is difficult as the symptoms are not specific and these children most of the time could not express theirselves. Therefore, the diagnosis is often delayed until troublesome symptoms or complications occur, such as food refusal, vomiting, substernal/retrosternal pain, dysphagia, esophagitis or aspiration pneumonia, which can result in a poor clinical prognosis and impair health-related quality of life. This is why GERD is a very serious condition in neurologically impaired children and should be monitored and managed attentively. (**Kim et al 2017**), (**Esposito et al 2015**)

The primary aims of therapy are relieving the symptoms of GERD, promoting feeding and weight gain and preventing respiratory complications. Generaly in children the first-line therapy is lifestyle changes as feeding changes and positioning therapy. But in neurologically impaired children this is usually very difficult to be done, due to their anatomical and other neurological problems. In addition, there are a lot of pharmacologic agents for treatment of GERD, which act by neutralizing gastric acid and reduce esophageal acid exposure and symptoms. If medical therapy fails or patients are at risk for life-threatening complications of GERD, surgical therapies are reserved. Fundoplications are generally prefered, such the Nissen, the Thal and the Dor techniques, with the laparoscopic Nissen antireflux procedure (360o fundic wrap around the esophagus) the gold standard for the treatment of GERD in children. **(Esposito et al 2015), (Rothenberg et al 2013)**

I. Fundoplications: Nissen, Thal, Dor laparoscopic techniques

Nissen fundoplication (360o fundic wrap around the esophagus)

Nissen fumdoplication was first described by Nissen in 1956, thus the laparoscopic Nissen fundoplication was first performed in children in 1993. Since then it has beccome a promising treatment for GERD and the gold standard therapy in children. The procedure begins with the typical insertion of 5 trocars in the abdominal cavity. The gastrocolic ligament is then divided and the esophageal dissection begins by developing the plane between the esophagus and the right crus. The posterior vagus nerve should be identified and the pericardium should be gently separated from the esophagus. Once the esophagus is freed from the mediastinum the stomach is grasped just off the greater curve on its anterior surface 10-15 cm inferior to the angle of His and the short gastric vessels are divided close to the stomach. Fundic mobilization is completed with dividing the high retrogastric vessels and gastropancreatic attachments. The fundus is wrapped around the esophagus (“shoe shine” maneuver) and sutured. At least a 2.5cm of tension-free intra-abdominal esophagus should be measured for a successful subsequent fundoplication. At the end the esophageal hiatus and crural are clossed. (**Deschner et al 2017**)

Laparoscopic Nissen fundoplication has satisfactory results in neurologically impaired children with their parents expressing their satisfaction after surgery, although a few studies have been done. A study from Fuhakori et al in 13 neurologically impaired children, in whom laparoscopic Nissen was performed, showed the successfully treatment of GERD. Three of these patients fed orally without problems such as dysphagia, after the surgery. The 24 h pH monitoring that has been performed before and after the surgery showed that the mean numbers of total acid and nonacid reflux episodes after the operation were significantly lower than those before ($p < 0.01$) in those children. Also a study from Rothenberg including a 20-years follow up in laparoscopic Nissen fundoplications showed that the overal wrap failure rate for primary laparoscopic Nissen fundoplication in children was 4.6% and highest in neonates under 6-month age, whereas the failure rate in the redo group was 6.8%. (**Fukahori et al 2016**), (**Rothenberg et al 2013**)

On the other hand, there are studies that support that the open Nissen has lower persentange of recurence of GERD and is better or equal to laparoscopic one. A metanalysis from Lee et al showed that GERD recurrence was higher in children who underwent laparoscopic Nissen fundoplication than in those in open, with OR of laparoscopic Nissen versus open 2.98 (95% CI = 1.29-6.87), P = 0.13. A randomized controlled trial in 87 children, regarding 23 with neurological impairment, from Fyhn et al, showed that more patients even undergoing laparoscopic fundoplication by an experienced surgeon experienced recurrence of GERD (37%) compaired to those undergoing open (7%). The risk ratio for recurrence in the laparoscpic group was 5.5 (95% CI: 1.6-16.6), $p < 0.001$. Also an other study from Pacilli et al, including 39 children, 31 of whom with neurological impairment- 15 underwent an open procedure and 16 underwent a laparoscopic Nissen. Incidence of recurrent GER in a follow up of 4 years was 12.5% in open and 20% in the laparoscopic group. This study concluded to that both open and laparoscopic Nissen provide similar control of reflux. **(Lee et al 2017), (Fyhn et al 2015), (Pacilli et al 2014)**

However, all the studies show that there was no significant difference in mortality, reoperation and other postoperative complications, such as dysfagia and wound infection, between those who operated open versus the laparoscopic group. Technically laparoscopy seems to be more difficult in children with severe scoliosis, as the possibility of bleeding is higher than in non-scoliotic children. Regarding the duration of the surgery the laparoscopic procedure seems to be longer than the open whereas the results of length of postoperative hospital stay remaine inconformity. Considering the financial costs of the two procedures, the total charges do not differ significantly. Generaly, laparoscopic Nissen fundoplication has better cosmetic effect, less pain and wound problems, shorter hospital stay, lower morbidity and decreased time to initiation of feeding. (**Lei et al 2017**), (**Ismaru et al 2016**), (**Wakeman et al 2016**)

Thal fundoplication (270o anterior)

Thal fundoplication is an anterior, partial fundoplication, which was firstly described by Thal. The laparoscopic technique is nowadays performed by plicating the fundus of the stomach in 2 layers over 180 to 270 degrees against the distal anterior intra-abdominal part of the esophagus and the diaphragmatic crus. The first layer of the fundoplication is created by suturing the fundus to halfway the intra-abdominal esophagus, using non-absorbable sutures. In the second layer, the fundus is hitched up approximately 1 cm more distally on the fundus, depending on the age and size of the child, and sutured against both the esophagus at the highest intra-abdominal point and diaphragmatic ridge. As in Nissen technique, before the fundoplication the distal esophagus is fully mobilized, both vagal nerves are identified and closure of hiatus is performed. **(Mauritz et al 2014)**

Thal fundoplication seems to be benefecial for neurologically impaired children at the beginning but it has not such satisfactory results during the following years. A prospective 10- to 15-year follow up study by Mauritz et al showed that at 3 to 4 mounths, at 1 to 5 years and at 10 to 15 years after the procedure 81%, 80% and 73% of children where free of reflux symptoms. The percentages of patients completely free of symptoms were similar for both neurologically impaired children and non- neurologically impaired patients at 3 to 4 months after the surgery (80.2% versus 80.6%, respectively). After longer follow-up, neurologically impaired children seemed to have slightly less effective subjective reflux control, with 76.9% of them versus 82.1% of non- neurologically impaired patients being completely free of reflux symptoms at 1 to 5 years. At 10 to 15 years, 69.2% of neurologically impaired children versus 75% of non- neurologically impaired patients were completely free of reflux symptoms. These differences were not statistically significant. The disease-free survival also showed that fewer neurologically impaired children were symptom free at 10 to 15 years after laparoscopic Thal fundoplication than the non- neurologically impaired patients (49% vs 64.7%, $P = 0.182$). At 3 to 4 months after the surgery, the 24-hour pH monitoring was still pathological (13.8% of non- neurologically impaired patients vs 23.1% of neurologically impaired children), by this difference increased to 38.1% for non- neurologically impaired patients versus 57.1% for neurologically impaired children after 10 to 15 years. However, none of the results showed statistically significant differences between these two groups of patients. Thus, postoperative dysphagia was seen more frequently in non- neurologically impaired patients. In coclusion, more long follow up studies are needed evatuating the benefits of Thal foundoplication in the treatment of GERD in neurologically impaired children. (**Mauritz et al 2014**)

Toupet fundoplication (partial posterior 270o fundoplication)

In 1963 Andreas Toupet described his technique in which the fundus was wrapped around three quarters of the esophagus behind the cardia. Today, in adults with GERD, Toupet fundoplication is as equal as Nissen fundoplication. However, only a few surgeons are convinced of its advantages in children, as the majority of the studies criticized the use of a partial wrap in children as it has a higher long-term failure rate compared with a full wrap in Nissen fundoplication, especially in patients with severe GERD, as neurologically impaired children. (**Miyano et al 2015**)

Thus, a study from Miyano et al in 131 neurologically impaired children with GERD, who all underwent a laparoscopic Toupet fundoplication, supported that their overal recurrence rate was 2.3%, similar to long-term outcome of laparoscopic Nisssen fundoplication in children. The same authors claim that Toupet fundoplication would seem to suppress pressure build-up around the cardia which prevents suture dehiscence and slipping that could cause the recurrence of GERD. An other study from Montupet in 574 children, 17 neurological impaired, showed a recurence of laparoscopic Toupet only in 6 patients, including 1 neurologically impaired child. However, in a previous study of Steyart et al, the author claims that laparoscopic Toupet is more difficult to be done in the most effective way because it requires more sutures and is difficult to master. Unfortunately, there are a few long-follow up studies in children and still remains a debate in the literature if this technique is efficient for the neurologically impaired children. **(Miyano et al 2015), (Steyaert et al 2003), (Montupet et al 2002)**

Regarding the laparoscopic Toupet technique four trocars are used of 3mm, 5mm and 10mm, depending the size of each of the patients. During the procedure the short gastric vessels are dissected, the right and left cruva of the diaphraggm are identified and the hepatogestric ligament is prepared. The the abdominal part of the esophagus is well mobilized. Distal crurorraphy is

performed with nonabsorbable sutures between the anterior wall of the esophagus and each of the diaphragm. The anterior part of the fundus is passed behind the esophagus to the righ, wrapped around the esophagus anteriorly and fixed I three places on both sides in order to form a partial dorsl wrap covering 270o of the circumference of the esophagus. **(Miyano et al 2015)**

Comparing the outcomes of laparoscopic redo surgery for failed laparoscopic Nissen and Toupet foundoplication Miyano et al reported in their study 4 out of 134 laparoscopic Toupet and 6 out of 53 laparoscopic Nissen foundoplications. In this study they claimed that redo surgery will be more challenging after Nissen than Toupet foundoplication because of the adhesions and changed anatomic landmarks, although mean operative time and blood loss seemed to be similar in both surgical techniques. **(Miyano et al 2019)**

II. Other MIS techniques as GERD treatment

In neurologically impaired children, especially in those affected by seizures, the risk of recurrence of GER and mortality after a fundoplication is higher compared with patients with a normal neurological level. A review from Lauriti et al showed that the recurrence or persistence of GER symptoms after fundoplication was significantly higher in neurologically impaired children (14.2±8.3%, range 0–33.3%) than in non neurologically impaired ones (9.4±5.2%, range 0–21.0%), RR 1.55 (95% CI 1.24, 1.93)/ p=0.0001. A redo-foundoplication has always technical difficulties because of dense adhensions, distorted tissue planes and gross anatomy that necessitate advanced laparoscopic skills and an experienced surgeon. Pacilli et al reported a 42% failure rate in redo foundoplication. In other studies more serious complications such as esophageal perforation, visceral injury and gastric leak due to difficult dissection in redo surgeries have been described. **(Pacilli et al 2007), (Lauriti et al 2018)**

In addition, a nationwide study from the US found that the rate of neurologically impaired children undergoing fundoplication was redused from 1996 to 2006, suggesting that alternative techniques would have better results. Although, nowdays only a few studies support that there are not major differences in outcomes after Nissen foundoplication between non- and neurologically impaired children, as 90% of both had improved. However, MIS offers also other beneficial techniques for treating GERD and progressing feeding, like the gastrojejunal catheters, transluminal endoscopic fundoplication, combined foundoplication with vagotomy and pyloroplasty and the total oesophagogasstric dissociation (TOGD).. (**Lasser et al 2006**), (**Knatten et al 2016), (Lauriti et al 2018)**

Gastrojejunal (GJ) catheters

In neurologically impaired children gastrojejunal (GJ) feeding is increasingly regarded as a popular alternative to surgery in the treatment of GERD. Long-term GJ feeding has been proposed by some as an effective option to treat refux particularly in neurologically impaired patient, as it has been menshioned in the previous capital “MIS offering new options in improving malnutrition and feeding problems: Gastrostomy, Jejunostomy, Gastrojejunostomy”.

Fundoplication with vagotomy and pyloroplasty

The combination of fundoplication with vagotomy and pyloroplasty has been done in neurologically impaired children, as an alternative therapy in GERD treatment. Nissen fundoplication is performed and then the vagal trunks and any additional fibres are divided along the abdominal oesophagus and a Heineke-Mikulicz pyloroplasty is done with absorbable sutures and an overlaid omental patch to

protect against any leaks. Horwood et al presented a study of 244 children, from which 132 had known neurological impairment, compairing the simple fundoplication to comblined one. 54 neurologically impaired children underwent Nissen fundoplication and 78 had primary the combined technique. The revision rates of both techniques (failure rate after first procedure) were 18.5% for Nissen fundoplication and 3.9% for those who underwent the combination of fundoplication with vagotomy and pyloroplasty. Although the very satisfactory results of that study, there are still few studies in literature about the results of that method in neurologically impaired children. **(Horwood et al 2015)**

TOGD: Total oesophago-gastric dissociation

Recent years total oesophago-gastric dissociation (TOGD) has obtained a higher consensus in surgical treatment of GERD in neurologically impaired children. It is one of the biggest advantages of MIS in this field, changing a major benefficial surgical approach from an open to a laparoscopic one and even to a robotic-assisted with very good results especially for these children. The first described laparoscopic procedure was by Boubnova et al in 2009 in patients with severe neurological impairment, respiratory, and nutritional failure status. Then in 2017 Mattioli et al described the first robotic-assisted TODG cases. **(Mattioli et al 2020)**

The operation is performed following the technique described by Adrian Bianchi. In laparoscopic approach five trocars are used: one 12mm transubilical for a 30o laparoscopic camera, two 5mm trocars in the right and left hypochondrial regions and two further 5- or 3mm disposable accessory trocars for suction, traction and LigaSure device. The jejunum is marked at 40cm distal to Treitz ligament, exteriorized and divided at the marker suture. A tension-free vascularized isoperistltic Roux-en-Y jejunal loop is fashioned distally dividing the mesenteric vessels appropriately. Then an end-to-side jejunojejunostomy at 20 to 30cm from the proximal end of Roux-en-Y is established. Abdominal portion of oesophagous is identified preserving paraesophageal neurovascular structures and is fixated to the diaphragm to avoid oesophageal retraction into the mediastinum. Oesophagous is sectioned from the stomach, gastric fundus is closed and a oesophago-jejunal anastomosis is done. Then, usually a Stamm gastrostomy is performed. For the robotic approach, a Da Vinci SI system was used with only three arms and the whole technique was similar to the previous discribed one. **(Mattioli et al 2020)**

TODG is now considered as a valid option not only as a rascue intervention in patients with recurrence of GERD after fundoplication, but also as primary procedure with very good results in neurologically impaired patients. It has a high likelihood of permanently treating recurrent reflux and aspiration, improving the QOL of the patient and their caregiver by reducing respiratory healthcare, visits and readmissions, improving the feeding habits of neurologically impaired children. **(DeAntonio et al 2017), (Mattioli et al 2020).**

Comparing the open to laparoscopic technique seems to have similar results regarding the operative time, the hospital stay and the restart of feeding. Specifically, there were no differences in operative time since TODG is performed in all cases by an experienced surgeon. In DeAntonio et al study the operative time of laparoscopic operations ranged from 299 to 631 min (avg. = 462 min), whereas in Mattioli et al the median operative time was 170 min. On the other hand, a review from Lauriti et al shows a main operative time of 255 ± 90.0 min, MD − 113.34 (95% CI − 141.84, − 84.83), $p <$ 0.00001, with a relevant yet not significant heterogeneity between the studies ($I2$ = 58%, p = ns) in 71 open TODG from 4 different studies. Regarding median hospital stay in Mattioti et al study was

17 days and in DeAntonio 12 (5-20) days, thus in Battaglia et al study which included 30 open TODG, the hospital stay was 23 days (15–90) for primary dissociations and 22 days (16–97) for ‘‘rescue’’ dissociations with a median value for hospital stay of 22.5 days (15–97) that was not statistically significant ($p = 0.3$). In addition, the feeding restarted in 7th POD (range 5-11) in Mattioli's study, in 8.4 ± 9.0 days in Lauritti's review and in Battaglia's study enteral nutrition was established largely by the 8th day (6–17) for primary TOGD and by the seventh day (7–9) for the ‘‘rescue’’ subgroup, with a median time of 8 days. Although these results show that there is no difference between open and laparoscopic TODG comparing hospital stay and POD of refeeding, still there is no review study or metaanalyse in the literature to compare open and laparoscopic techniques. **(Battaglia et al 2020), (Mattioli et al 2020), (DeAntonio et al 2017), (Lauriti et al 2018)**

Comparing robotic and laparoscopic TODG, in the study by Mattioli et al including 10 neurologically impaired children, 5 laparoscopic and 5 robotic TODG, the benefits of minimally invasive approach were seen, with first mentioned the excellent visualization and the conservation of the vague nerves. Nevertheless, in laparoscopic approach the costs were lower and the operative time shorter, although the learning curve for both approaches was similar. Thus, more studies are needed in the future for both techniques which are performed from a few and experienced surgeons by the time.(**Mattioli et al 2020**)

Discussion

Neurologically impaired children are a special group of patients. Their nutritional assessment and management is the most difficult part of themselves and their family everyday care because of their neurological problems. Physiological abnormalities, as oro-motor dysfunction and associated incoordination of oropharyngeal reflexes, and anatomical problems such as scoliosis, seizures, spasticity of abdominal musculate and constipation worsen their physical condition. Due to their physical disabilities, they spend long periods in supine position increasing the risk of aspiration and lung infection. In addition, swallowing difficulties, dystonia, dysphagia and severe GERD are the most common causes of repeated hospitalizations due to feeding difficulties, malnutrition and aspiration pneumonia. Their behavioural problems and their inability to feed independently are also poor prognostic factors which lead to malnutrition and growth failure. (**Sullivan et al 2000**), (**Vernon-Roberts et al 2013**)

Eventhough, their nutritional care is very difficult due to severe serious health problems, every neurologically impaired child diserves the best treatment with the minimum disadvantages and complications. Minimally invasive surgery gives a better life to these children and their family, improving their quality of life, by a safer and easier way of feeding and redused hospitalizations. Specifically, PEG has radically changed the handling of neurologically impaired children who, before the introduction of this procedure, were force fed parenterally or enterally, by nasogastric tube, conventional surgical gastrostomy or central venous access. On the other hand, GJ tubes are more appropriate for neurologically impaired children with severe GERD and feeding problems, improving their nutritional status. That is the reason why nowadays these techniques are more commonly used in pediatric surgery and they have complitely improved neurologically impaired children's lives. (**Ceriati et al 2006**)

Endoscopic, laraposcopic, laparoscopic-assisted and robotic surgery are used, each for the treatment of the same problem in different ideal indications, with the best results. This is the second advansment that MIS gave to the surgeons: the ability to choose the best operative technique for

each patient with the equal health problem, bringing surgery one step more closer to the patient. For example, neurologically impaired children usually suffer from GERD. During the last decade the treatment was fixed for every child including the open Nissen foundoplication, with few to choose Thal or Toupet. But nowadays every surgeon could choose between the use of a GJ tube, the combination of gastrostomy and foundoplication, the laparoscopic or robotic Nissen, the laparoscopic Toupet or Thal, even though more advanced techniques such as TODG. Depending to the patient's health condition and nutritional status the surgeon has the ability to perform the most appropriate technique for each child, regarding operative time and exposure to anesthesia, postoperative pain, wound healing and postoperative feeding.

Finally, MIS generally has some technical advantages that are beneficial for neurologically impaired children. It offers less traumatic techniques than in open surgery. This is very important for neurologically impaired patients as they suffer from malnutrition, poor wound healing and elevated intra-abdominal pressure because of irritating cuffing. In such patients small wounds as in laparoscopic, laparoscopic-assisted and robotic techniques or even though no wounds as in endoscopic techniques, reduce the propability of serious postoperative complications regarding eviscaration and induce the wound healing time. Also, both the laparoscopic and laparoscopic-assisted techniques give more details in the operative field, offering the hole visualization of the abdominal cavity, making these techniques safer and more accurate. Due to anatomical anomalies neurologically impaired children have,MIS is safer and could be performed in a more detailed way.

However, these new techniques require an initial steep phase in which the ability of the surgeons to complite a procedure, “the learning curve (LC)”, incrises rapidly. The review studies of Dagash et al in 2003 and Macdonald et al in 2016 publish data on LC and proficiency skills in MIS techniques. In pediatric surgery, case volume and frequency of treating the health problems of neurologically impaired children are typically low. The adverse impacts of learning for a pediatric surgeon are more acutely felt, as a significantly greater time is required to reach a plateau of competence. LC is very important because it has always an impact on patients outcomes and hospital's costs. But unfortunately a standarized multioutcome approach reporting the impact on trainees involvement in those surgical approaches still not exists. Nowadays a number of techniques/models exist for improving technical skills before performing each of those surgical procedures in operative field. Thus, the prior experience of a learner, if relevant, can impact not only their starting point on the curve but also the rate at which they learn. More studies reporting the LC in different MIS approaches should be encouraged for a better evaluation of different techniques in neurologically impaired children, in order to recognize and standarize them. **(Dagash et al 2003), (Macdonald et al 2016)**

Conclusion

Nowadays MIS is running through a long experimental period in pediatric surgery. Its use in treating the health problems of neurologically impaired children seems to be beneficial improving their and their family's quality of life. Although these MIS procedures now require to be performed by experienced surgeons for better results, soon residents should be trained in order to perform them with equal results. Nevertheless, much more effort should be given during young surgeons's training especially for these difficult and special group of children. In the future MIS procedures seem to be the gold standard in treating each health problem of this special group of patients.

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