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A two-center comparative study of gastric pull-up and jejunal interposition for long gap esophageal atresia[☆]

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ABSTRACT

Purpose: When restoration of the anatomical continuity in case of long gap esophageal atresia (LGEA) is not feasible, esophageal replacement surgery becomes mandatory. The aim of this paper is to critically compare the experience of two tertiary referral centers in The Netherlands performing either gastric pull-up (GPU) or jejunal interposition (JI).

Methods: Retrospective chart review of all the patients with LGEA who underwent GPU in the University Medical Center Groningen and JI in the University Medical Center Utrecht. Main endpoints were short term morbidity, mortality and long term functional outcome (digestive functioning and growth). Descriptive analyses conducted using Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables.

Results: Nine children underwent GPU and 15 JI. Median age (years) at last follow up was fourteen (GPU) and eight (JI). One patient died, 10 years after JI. No grafts were lost. Perioperative anastomotic complications were reported more often after JI (73% vs. 22%, $p = 0.03$). However reintervention rate was the same in both groups (33%). Among long term outcomes, functional obstruction was not registered after GPU, while it was recorded in 46% after JI ($p = 0.02$). No other significant differences were found apart from some tendencies concerning full oral nutrition and gastroesophageal reflux (GPU > JI).

Conclusion: Comparative data from this study reveal no mortality but significant morbidity in both groups. No graft was lost. Although not statistically different as a result of small patient numbers, clinically important differences regarding gastrointestinal system were noted. Growth should be monitored closely in both groups.

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There is still debate on the optimal management of long gap esophageal atresia (LGEA). When restoration of anatomical continuity is not feasible, esophageal replacement surgery becomes mandatory. To this end, replacement with jejunum [1–3], colon [4], or stomach [5] has all been advocated. However, there are little comparative data.

The aim of this paper is to report the experience of two tertiary referral centers in the Netherlands performing two different procedures for LGEA.

1. Patients and methods

A retrospective chart review of all patients who underwent gastric pull-up (GPU) for LGEA at the University Medical Centre Groningen between 1985 and 2006 was performed. Medical records of all children who underwent jejunal interposition (JI) for LGEA in the

University Medical Centre Utrecht between 1988 and 2007 were reviewed for comparison. LGEA was defined as the impossibility to perform an immediate primary end-to-end anastomosis owing to the distance between the proximal and distal esophageal remnant.

1.1. Surgical procedures

All operations were performed by or under close supervision of one experienced pediatric surgeon in each center.

1.1.1. GPU

The technique as popularized by Spitz et al. [5–10] was used. In short: through a transverse laparotomy, the stomach is mobilized. The right gastric artery is preserved while the left gastric artery is divided close to the stomach. The distal esophagus is dissected. Mobilization of the duodenum is followed by a pyloromyotomy. The cervical esophagus is then mobilized through a neck incision. A transhiatal posterior mediastinal tunnel is created. The stomach is brought up into the neck through the esophageal hiatus and finally the esophagogastric anastomosis is performed at the apex of the stomach.

[☆] Conflict of interest: None.

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1.1.2. JI

The technique as popularized by Bax et al. [1–3] was used. In short: the diagnosis of long gap esophageal atresia is verified by thoracotomy or in the last patient by thoracoscopy. Next a median laparotomy is performed. The fundus is detached from the diaphragm and the upper short gastric vessels are severed. The left crus is mobilized and the posterior hiatus is opened. Then the pedicle graft is created: the first mesenteric vessels are divided close to the main mesenteric route. The jejunum is transected close to Treitz ligament and severed again opposite the level of the third mesenteric branch. The jejunum is then skeletonized upwards leaving the uppermost part in place for interposition. Bowel continuity is restored and the graft with vascular pedicle is passed through the posterior hiatus into the right chest. Finally anastomoses are made between the upper and lower esophagus and the graft.

All patients were admitted postoperatively to the intensive care unit and were mechanically ventilated.

1.2. Endpoints

Main outcome measures were perioperative morbidity and mortality, long term gastrointestinal function and growth. Most of the patients who received orthotopic jejunal pedicle graft interposition have already been described by Bax and Van der Zee [1–3]. Unlike the previous reports, the present series is a two-center study, has a longer follow up and focuses more on the long term outcome.

Under the term *perioperative complications* all the complications reported between the day of surgery and discharge from hospital were included.

Anastomotic complications comprise both leakage and stenosis.

Anastomotic leakage was defined as extravasation of water-soluble contrast medium with or without clinical symptoms of leakage.

Anastomotic stenosis was considered as anastomotic narrowing on contrast enema with clinical symptoms of stricture/passage problems necessitating dilatation.

Pneumothorax was defined as a pneumothorax requiring a thoracic drainage.

Other thoracic complications are listed in Table 3.

In the section *Long term outcome* we include mortality, gastrointestinal function, interventions and growth.

Interventions included all the reoperations after discharge from hospital, not including endoscopic procedures such as dilatation.

Under *gastrointestinal function* we report on the achievement of full oral nutrition, dysphagia, anastomotic stenosis, gastroesophageal reflux symptoms, and on the use of antacid medication and prokinetics. Symptoms of difficulty in swallowing solids without presence of reflux and graft obstruction were described under the term *dysphagia*. Graft *functional obstruction* was defined as delayed graft passage on contrast enema with associated symptoms of dysphagia but no endoscopic findings of anastomotic stenosis.

Standard deviation scores [SDSs] for height/weight were calculated using growth charts for Dutch children (corrected for Down's disease when needed), with a deviation of >-2 SD of the mean for age considered as pathological.

Statistics were computed by IBM SPSS Statistic 20 (SPSS, Chicago, IL). Descriptive analyses were conducted using Mann–Whitney U test for testing of continuous variables given a not normal distribution and Fisher's exact test for categorical variables, with a P value <0.05 considered as significant (two-tailed test).

2. Results

2.1. Patients

Nine children underwent GPU with pyloromyotomy (eight boys, one girl) for LGEA.

Table 1

Patients' characteristics.

	GPU (n = 9)	JI (n = 15)	P value
Median gestational age (weeks)	34 (29–39)	35 (32–41)	0.36
Median birth weight (g)	1680 (1030–3040)	2220 (1115–3755)	0.57
Median age at surgery (days)	128 (1–323)	63 (23–149)	0.04
Type atresia			
No fistula	5	8	1.0
Proximal fistula	3	6	1.0
Distal fistula	1	1	0.51
Trisomy 21	0% (-)	13% (2)	0.51
Congenital anomalies			
Vertebral	55% (5)	13% (2)	0.06
Anorectal	11% (1)	13% (2)	1.00
Cardiac *	33% (3)	20% (3)	0.63
Renal **	44% (4)	6% (1)	0.04
Limbs	0% (-)	13% (2)	0.41
Duodenal atresia	11% (1)	6% (1)	1.00
Pre replacement surgery			
Gastrostomy	88% (8)	100% (15)	0.37
Cervical esophagostomy	44% (4)	0% (-)	0.01
Previous attempt at anastomosis	0% (-)	13% (2)	0.51

GPU: gastric pull-up.

JI: jejunal interposition.

* Atrial septal defect, patent ductus arteriosus, dextrocardia.

** Renal agenesis, duplex collecting system.

Orthotopic JI was performed in fifteen patients (nine boys, six girls) with LGEA.

Table 1 depicts patient characteristics. In the GPU group seven patients (77%) were prematurely born (gestational age <37 weeks); in the JI group eleven children (73%) were premature. All the GPU patients presented at least with one associated congenital anomaly, 7/15 JI children (46%) presented without any other anomaly but the LGEA. Renal malformations were seen statistically more often in the GPU group.

In both groups gastrostomy was performed in every child in order to provide adequate feeding before definitive surgical correction, except in one patient who underwent GPU one day after birth. Cervical esophagostomy was performed in 4/9 GPU patients (44%) and in none of the JI patients ($p = 0.01$). No patients of the GPU group had an attempt at direct anastomosis before esophageal replacement. In the JI group 2 patients had esophageal replacement as a rescue procedure: one patient developed a long esophageal stricture after repair of an esophageal atresia with distal fistula; the second patient had two unsuccessful attempts of an open Foker technique elsewhere.

There was a significant difference ($p = 0.04$) between the two groups regarding age at surgery: replacement surgery was performed earlier in the JI group (median of 63 days) than in the GPU group (median of 128 days).

One child underwent GPU at first day of life: immediate primary anastomosis in this patient was not feasible owing to an unexpected extremely short proximal esophageal segment identified perioperatively, therefore it was decided to perform directly the esophageal replacement procedure. There were no significant differences regarding hospital stay (Table 2).

Table 2

Early postoperative outcomes of 9 patients undergoing GPU and 15 patients undergoing JI for LGEA.

	GPU (n = 9)	JI (n = 15)	P value
Intensive care period	13 (3–39)	15 (4–45)	0.67
Intubation period	8 (3–36)	7.5 (1–25)*	0.92
Postoperative admission	24 (15–233)	32 (13–189)	0.18

Values expressed as days: median (range).

* Assessed in 14 patients owing to lack of data in one patient.

Table 3

Perioperative complications.

	GPU (n = 9)	Jl (n = 15)	P value
Any anastomotic complication	22% (2)	73% (11)	0.03
Anastomotic leak	22% (2)	60% (9)	0.10
Anastomotic stenosis	11% (1)	40% (6)	0.19
Pneumothorax	22% (2)	40% (6)	0.65
Other thoracic complications *	33% (3)	20% (3)	0.63
Abdominal dehiscence	11% (1)	6% (1)	1.00
Total reintervention rate	33% (3)	33% (5)	1.00

* ARDS, capillary leak syndrome, mediastinitis, episodic aspiration pneumonia, temporary unilateral phrenic nerve paralysis.

2.2. Perioperative mortality and morbidity

There was no perioperative mortality and none of the grafts were lost in either group.

Perioperative complications are summarized in Table 3.

2.2.1. GPU

All nine patients (100%) reported a perioperative complication. There were two anastomotic leaks, of which one required surgery. Further surgery was necessary once for abdominal wound dehiscence and once for iatrogenic perforation of the graft during endoscopy. Stenosis was only reported once.

2.2.2. Jl

14/15 children (93%) registered at least one complication. Patients in this group suffered statistically significant more from anastomotic complications than patients after GPU. Although statistically not significant, anastomotic leaks occurred more frequently after Jl and could involve either the proximal or the distal anastomosis. The majority of these leaks could be treated conservatively, but three (33%) required surgery.

Again although not statistically significant, there were more stenoses in the Jl group. Most could be treated by dilatation but one required surgery.

One patient was reoperated for dehiscence of the laparotomy wound.

3. Long term outcome

3.1. Age

Median age at last follow up in the GPU group was 14 years (6–19 years), in the Jl group 8 years (1–19 years). Notably in the Jl group one patient was only one year old at last follow-up. This could be considered as a midterm rather than a long term follow up. Median age of the patients at present is 15 years in the GPU group and 16 years for the Jl group.

3.2. Mortality

There was no mortality in the GPU group at follow up. In the Jl group, one patient died. This boy with trisomy 21 died at the age of 10 years in an institution most likely as a result of massive aspiration.

3.3. Long term outcome

Tables 4a and 4b describe long term functional outcomes.

Functional obstruction was not registered after GPU, while it was present in 46% of the patients who underwent Jl ($p = 0.02$), mainly responding to propulsitoria. No other significant differences were noted between groups regarding long term gastro-intestinal and respiratory outcomes. However a few tendencies require attention.

3.3.1. GPU

Three out of nine (33%) children still needed extra feeding via jejunostomy at last follow up to gain adequate daily intake. In addition, one of them required home parenteral nutrition. None of these three patients received esophagostomy at birth.

Reflux symptoms were noted in 44% of the patients. Delayed gastric emptying was reported in one patient (11%).

3.3.2. Jl

All but one (93%) patients had full oral diet at last follow up. Reflux was reported in 2 (13%) of the patients.

One patient who manifested asthma-like symptoms died at the age of ten most likely because of massive aspiration.

3.4. Interventions during follow up

3.4.1. GPU

Three patients (33%) were reoperated: one for delayed gastric emptying, one for duodenal perforation during radiological placement of a feeding tube, and one for a missed proximal tracheoesophageal fistula.

3.4.2. Jl

Three patients (19%) underwent reintervention: one patient for iatrogenic perforation of the jejunum during an endoscopic dilatation procedure, one patient for functional obstruction of the distal anastomosis despite multiple dilatations and failed widening plasty of the distal anastomosis (the distal esophagus was resected and an anastomosis made between the jejunum and the stomach; however this resulted in severe gastroesophageal reflux and pulmonary problems); and a last one patient, affected by Down syndrome, for functional short bowel syndrome, requiring feeding by ostomy.

3.5. Growth

Data are given in Table 4b and Fig. 1.

In the GPU group an SDS below -2 for weight/age was registered in 44% of the children vs 26% in the Jl group.

4. Discussion

This paper is the first to systematically compare the results of GPU with Jl for LGEA.

There was no perioperative mortality but one patient in the Jl group died at follow up. None of the grafts were lost. While the pulled up stomach has abundant blood supply, this is less generous in jejunal grafts. The stomach can therefore be brought up high into the neck without problems but this is more challenging when using jejunum. Long pedicle grafts can be constructed but such grafts have tendency to curl. Moreover long pedicle grafts are constructed at the expense of the remaining jejunum. In the present series no thoracotomy was

Table 4a

Long term digestive outcome (follow up).

	GPU (n = 9)	Jl (n = 15)	P value
Patients who reported gastrointestinal problems during follow up	77% (7)	86% (13)	0.61
Full oral feeding rate	66% (6)	93% (14)	0.13
Dysphagia	11% (1)	6% (1)	1.0
Anastomotic stenosis	55% (5)	40% (6)	0.67
Median number of endoscopic dilatation per patient	3 (2–4)	4 (1–10)	
Functional obstruction	0% (-)	46% (7)	0.02
Delayed gastric emptying	11% (1)	0% (-)	0.37
Reflux symptoms	44% (4)	13% (2)	0.15
PPI's/H2-antagonists/prokinetics	66% (6)	33% (5)	0.20
Graft ulcer	- (-)	13% (2)	0.51

Table 4b

Long term anthropometric outcomes at last follow up.

	GPU (n = 9)	Jl (n = 15)	P value
Height/age < -2 SD	22% (2)	30% (5)	0.66
Weight/age < -2 SD	44% (4)	26% (4)	0.41
Weight/height < -2 SD	11% (1)	20% (3)	1.00
Median BMI	15 (14–19)	15 (12–18)	0.82

performed but a mediastinal tunnel was created, which is certainly less invasive than Jl. Gastric pull-up using minimal access principles has been described [11,12].

Jl had a significantly higher perioperative total anastomotic complication rate than GPU. When these complications were broken down into leakage and stenosis, the differences were not significant anymore but still the percentages were higher in Jl. Notably, in contrast to GPU in Jl two anastomoses have to be made. Leakage and stenosis rate in GPU in the present study were respectively 22% and 11%. Only one leak needed surgery. Spitz et al. [9] reported in his GPU series a comparable 12% leakage rate and a 19% stenosis rate. Only one leak required surgery, which is undoubtedly related to the fact that the esophagogastric anastomosis in GPU is made in the neck.

The 60% anastomotic leakage rate after Jl in the present study is high. Three of the six leaks needed surgery. In this series of Jl, anastomoses were made in the thorax.

The early stenosis rate in Jl in the present series was twice as high than in GPU but the late stenosis rate was similar. Two stenosis in the Jl group needed surgery versus none in the GPU group. When the distal esophagus is left in place in Jl, functional obstruction invariably occurs at the distal anastomosis, despite the retained peristaltic activity of jejunal grafts [2,3,13]. On contrast studies, it is obvious that the distal esophagus does not open up when the bolus arrives. Obstruction at the distal anastomosis with the esophagus can also be based on retained foregut remnants in the distal esophagus but this did not seem the case in the present series. Functional obstruction at the distal anastomosis has to be carefully watched as widening of the graft should be avoided. Once the graft becomes severely widened, resection of the distal anastomosis will lead to massive reflux as what happened in one case. The best treatment of functional obstruction is dilatation which was performed fairly regularly in Jl patients.

As preventive measures, the creation of a wider oblique opening of the distal esophagus in order to shorten the gastroesophageal sphincter may cause less functional obstruction. Alternatively the distal esophagus could be removed and a direct anastomosis between the jejunal graft and the cardia could be made. When performing this operation in two patients with long peptic stenosis not responding to therapy, both patients did not present with functional obstruction. These patients are not included in the present series.

Although not significantly different, 33% of the GPU patients were not on full oral nutrition at last follow up against only 6% in the Jl group. This may be related to the significant difference in median age at replacement which is, twice as high in the GPU group. Moreover only one patient in each group complained from dysphagia which is 11% in the GPU group versus 6% in the Jl group. Spitz et al. reported significant swallowing problems in 30% after GPU postoperatively of which half persisted [9].

Motility of the transposed stomach remains controversial [14]. There is evidence of swallow-related motor activity in the stomach after GPU, although a propagated antegrade propulsive peristalsis does not seem to be present [15]. Rather than a reservoir, the transposed stomach seems to act like a conduit with an extremely irregular biphasic emptying pattern. This consists of an initial rapid clearance of the majority of the intragastric contents into the small bowel, followed by a more leisurely emptying [16]. Alteration of this fragile system might be responsible for functional passage problems. In the present series one patient (11%) seemed to suffer from severe delay in gastric emptying. Spitz et al. [9] reported severe delay in gastric emptying in 8.7% of the patients. Jejunum, even free grafts, retains peristaltic activity [17]. Peristaltic waves however do not lead to relaxation of the lower esophageal sphincter.

Although it might contribute to functional obstruction, one of the rationales for preserving the distal esophagus and its sphincteric mechanism in Jl is to prevent back-flow of gastric contents. Though statistically not significant, 44% of children with GPU versus 13% of the children with Jl reported higher prevalence of reflux symptoms. Gastroesophageal reflux has been reported in 20–67% of adult patients with GPU [18]. Reflux after GPU might be related to the mobilization of the stomach in the mediastinum with alteration of the shape owing to stretching and displacement of the gastroesophageal junction through an unnaturally wide hiatus and consequent loss of the angle of His. Furthermore, reflux is promoted by the negative intrathoracic pressure and the positive intraluminal pressure in the transposed stomach. It might also be induced by stasis of the gastric content owing to delayed stomach emptying despite pyloromyotomy. Persistent impaired vagal innervation after GPU might correlate with decreased total acid production and reduced parasympathetic activity with consequent delayed gastric clearance. Gastroesophageal reflux is no major problem after Jl. It happened in two patients (13%), in one of them after resection of the distal esophagus for ongoing functional obstruction with dilatation of the graft. Saeki et al. [13] reported no reflux after Jl in children. Even after initial resection of the distal esophagus reflux is not very prevalent.

However, gastroesophageal reflux might be present subclinically and it might lead potentially to (micro) aspiration with consequent respiratory deterioration. Unfortunately not a congruous number of patients included in the present study underwent pH-metry in order to provide reliable data, so comparative data couldn't be provided here.

Growth in children with GPU or Jl deserves attention. At last follow-up height and weight for age were above 0 SDS in one patient only; weight for height was above 0 SDS in five patients. These results are static and do not reflect the growth curves. For a correct interpretation of growth it is important to identify any amelioration or worsening over time on curves.

The main limitations of the present paper are the retrospective nature of the study and the small number of patients. Because of the

Fig. 1. Growth at last follow up.

small numbers, comparison is difficult and statistically not-significant differences may be clinically important.

Another limitation is that procedures were carried out in two different centers; but this reflects the daily practice in the Netherlands, where different centers prefer different surgical procedures.

Moreover respiratory function after esophageal replacement is important, especially in the light of GERD and repeated (micro) aspiration. However, a formal assessment of pulmonary function goes beyond the scope of the present paper.

The patients were operated in period covering respectively 19 and 21 years. This means less than one case per center per year. In 2011 Spitz wrote that the importance of three general aphorisms needs to be considered [19]:

1. There is a well-defined and clear relationship between volume (of cases), management outcome, and research output.
2. Most medical and surgical procedures have better outcome when performed in hospitals that do a lot of the procedure in question.
3. Increased hospital specialisation is associated with improved patient outcomes.

The total incidence of esophageal atresia is between 2.5 and 3 per 10,000 births [20]. Esophageal atresia without fistula accounts for about 7% of the total incidence. For the Netherlands with an actual annual birth rate of 172,000 [21], 3–4 cases can be expected per year. Centralization of all these patients in one center in the Netherlands or even in a broader European context would seem appropriate. If in all cases an attempt is made at delayed primary anastomosis by using e.g. esophageal elongation technique, less cases would come to esophageal replacement making the number of children requiring an interposition even smaller.

5. Conclusions

GPU and JI are two optional procedures for esophageal replacement in case of LGEA. Comparative data from the present study demonstrate no mortality but significant morbidity after both procedures; patients undergoing JI suffer more frequently of early anastomotic complications and functional obstruction. There seems to be a tendency toward more reflux symptoms in the GPU group and better oral feeding ability after JI which is reflected in growth. Growth

should be monitored closely in both groups. Patients with LGEA should be centralised.

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