Pediatric gastroesophageal reflux and upper gastrointestinal tract motility: the use of multichannel intraluminal impedance and high resolution manometry
van Wijk, M.P.
Evaluation of gastroesophageal function and mechanisms underlying gastroesophageal reflux in infants and adults born with esophageal atresia

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Submitted for publication
ABSTRACT

Objective: To evaluate the mechanisms underlying gastroesophageal reflux (GER) in patients following esophageal atresia (EA) repair, and to perform a comprehensive study of the gastroesophageal function both in infants and adults.

Design: 10 consecutive newborn infants with EA and 10 randomly selected adult EA patients from a large cohort were studied. In each subject a $^{13}$C-octanoate breath test and a combined esophageal pH-impedance-manometry study were performed. The latter test was used to detect mechanisms underlying GER episodes (3hr) as well as to perform esophageal function tests (EFT), following 10 liquid and 10 viscous bolus swallows.

Results: Transient lower esophageal sphincter relaxation (TLESR) was the most common mechanism underlying GER episodes, both in infants and adults (66% and 62% respectively). In 66% of all GER episodes, no clearing mechanism was initiated. On EFT, normal motility patterns were seen in 6 patients (4 infants, 2 adults). One of these adults had normal motility overall (>80% of swallows). Most swallows (78.8%) were accompanied by abnormal motility patterns. Despite this observation, impedance showed normal bolus transit in 108 out of 264 (40.9%) swallows. When normal motility was present, this number increased to 85.5%. Gastric emptying was delayed (>90th percentile for age and sex matched controls) in 57.1% of infants and in 22.2% of adults.

Conclusions: TLESR is the main mechanism underlying GER events in patients with EA. Most infants and adults have impaired motility, delayed bolus clearance and delayed gastric emptying. However, normal motility patterns were seen in a minority of patients. Future studies are needed to unravel the relation between the results found in this study and endoscopic findings and subsequently determine the most optimal follow up strategy for these patients.
INTRODUCTION

Congenital anomalies of the esophagus are relatively common with an incidence of about 1 in 3000-4500 newborn infants. Among those anomalies esophageal atresia (EA) and tracheoesophageal fistulas (TEF) are the most important. In 93% of the cases EA is accompanied by a form of TEF. EA is divided into five anatomical subtypes based on the location and type of anastomosis between trachea and esophagus. Type C, where a distal TEF is present, is by far the most common accounting for more than 85% of all forms of EA. Patients born with EA suffer significantly more often than healthy controls from gastroesophageal reflux (GER) disease and its long term complications, such as dysphagia, esophageal strictures, esophagitis, esophageal metaplasia and even esophageal carcinoma. In addition, Tovar et al found abnormally high esophageal acid exposure, suggestive of GER disease in fifteen out of twenty-two (68.1%) patients that considered themselves healthy. GER disease is considered a motility disorder, with transient lower esophageal sphincter relaxations (TLESR) being the most common mechanism underlying GER episodes in adults and infants with GER disease not associated with hiatal hernia. Currently, the degree to which this or other mechanisms are responsible for GER episodes in patients post EA-repair is unclear.

Most manometric studies that were performed, showed uncoordinated esophageal peristalsis in combination with relatively normal LOS pressures. However, low LOS pressure, is also described. Recent multichannel intraluminal impedance data in children born with EA showed that approximately half of the GER episodes in these patients are not detected by conventional pH-monitoring and that patients rarely report symptoms. In post EA repair children, delayed gastric emptying was found in patients with and without GER symptoms. It is unclear if, and to what extent, such abnormalities exist immediately after EA repair and how they develop over time.

The aim of our study, therefore, was to evaluate the mechanisms underlying GER episodes in patients following EA repair, and to perform a comprehensive study of the gastroesophageal function using combined multichannel intraluminal impedance, esophageal manometry and a non invasive $^{13}$C-octanoate gastric emptying test, both in infants and adults.

METHODS

Patients

Patients, born with EA type C without other congenital malformations and primary end to end anastomosis were eligible for this study. Adults were randomly selected from a previously described cohort born between January 1975 and January 1990, contacted by telephone and asked to participate after they had received written information about
the study. In our hospital, it is routine practice to give proton pump inhibitor therapy for at least three months after reconstructive surgery. All infants then receive a 24 hour pH-study within the first year of life (depending on practical factors and complaints), after which the therapy is sometimes ceased. The parents of infants, who visited the hospital for such a routine 24 hour pH-study, were contacted by phone well in advance of their appointment, were sent written study information and asked for their participation. Recruitment continued until ten adults and ten infants were included in the study. Patients with known structural abnormalities of the gastrointestinal tract, other than EA, and those with previous gastrointestinal tract or diaphragmatic surgery, other than during their initial EA repair were excluded.

All adults and all parents of the infants gave written informed consent. The study was approved by the medical ethical committee of the Academic Medical Center, Amsterdam, The Netherlands.

**Protocol**

*Infants (figure 1, top)*

In each subject a combined esophageal pH-impedance-manometry study and $^{13}$C-octanoate breath test were performed. The manometry catheter was zeroed at the level of the stomach of the patient when supine. The bed was leveled such that the patient

![Image of protocol](image)

*Figure 1. Study protocol for infants (on top of timeline) and adults (below timeline).* Note that the study for infants lasted 4 hours, while an adult study lasted 6 hours. GER: gastroesophageal reflux; EFT: esophageal function test; EBM: expressed breast milk.
could also take a sitting position (on parents lap in infants) with the proximal stomach at the same absolute height as when supine. The two catheters used were simultaneously positioned as shown in figure 2. After intubation, infants received their normal feed and MII/pH/manometry recordings were made during a 3-hour period. Infants were supine during these 3-hours, while adults were sitting upright. Afterwards, esophageal function was evaluated by giving five liquid (saline) and five viscous (thickened formula) boluses in both the supine and upright position. If infants were unwilling to swallow these boluses, they were infused into the proximal esophagus through an infusion port of the manometry catheter (figure 2). After completion of this esophageal function test, the

Figure 2. Catheter configuration for infants (left panel) and adults (right panel).
MII / pH: combined intraluminal impedance and pH catheter; LES: lower esophageal sphincter; Z1-6: segments over which electrical impedance (Ohms) was measured.
manometry catheter was removed. The MII/pH catheter remained in place to complete the 24 hour test the infants were initially referred for. Breath samples were taken for four hours, starting at the beginning of the first feed. The same instructions as for a routine 24 hour pH-study were given to prepare the infant for the study: parents were asked to stop any acid-suppressive or prokinetic medication at least 3 days before the study and all infants were fasted for at least 4 hours prior to the test.

**Adults (figure 1, bottom)**

The protocol for adults was identical to that in infants apart from the details outlined here. Instead of a liquid meal, adults received a pancake with 100 mg $^{13}$C-Na-octanoate. The breath test in adults lasted 6 hours. Patients were given the option to perform the last two hours of this test at home. No proximal infusion port was available in the adult catheter. MII/pH recordings were only extended to 24 hours when the attending physician ordered such a test. All patients stopped any acid suppressive and prokinetic medication 3 days before the test and were fasted for at least 6 hours prior to the commencement of the study.

**Catheters design**

Custom made manometry catheters and a combined multichannel intraluminal impedance and isfet pH catheters (K6011-E1-0634 (infants) and K6011-E1-0632(adults), MMS international, Enschede, The Netherlands) were used (figure 2). The esophageal side holes and the sleeve of the catheters were perfused with degassed distilled water by a low-compliance pneumohydraulic perfusion pump (Dentsleeve, Wayville, South Australia, Australia) at a rate of 0.04 mL/min and 0.15mL/min per channel in infants and adults respectively. The pharyngeal side hole was perfused with air at a rate of 2.6 mL/min in infants and with degassed distilled water at a rate of 0.15mL/min in adults using the same pump. Electrode rings positioned proximal to the midpoint of the sleeve allowed for the recording of 6 segments of intraluminal impedance throughout the esophagus as shown in figure 2 (Z1-Z6). A pH sensor was located 3 and 5 cm proximal to the lower esophageal sphincter (LES) midpoint in infants and adults respectively. Pressure and impedance signals were acquired at a frequency of 25 and 50 Hz respectively and pH-signals with a frequency of 0,25 Hz using a computerized acquisition system (MMS, Enschede, The Netherlands).

$^{13}$C-octanoate gastric emptying breath test

This test is described in detail elsewhere. In short, $^{13}$C-labeled Na-octanoate was added to the child’s feed, and breath samples were taken before, during and after the feed. Exhaled breath was collected through a nasal prong in infants and adults were asked to blow through a straw into a tube. Infants were given their normal amount of expressed
breast milk or formula containing 50 mg of sodium-\(^{13}\)C-octanoate. Breath samples were collected at 5 minute intervals for the first 30 minutes after the start of the feed and at 15 minute intervals for the remaining 210 minutes thereafter.

Adults received a \(^{13}\)C-octanoate labeled pancake made of 70 g standard pancake mix, 100 mL water and 100 mg Sodium-\(^{13}\)C-octanoate. Breath was collected at 15 minute intervals for the first two hours after finishing the pancake and then at 30 minutes intervals for the remaining 240 minutes.

**Data analysis**

All pH-impedance-manometry tracings were visually analyzed by two investigators. In case of inconsistency of the analysis, both investigators discussed the event and reached an agreement. All manometric pressures were calculated relative to gastric pressure.

**Gastro-esophageal reflux detection**

MII detection of GER events

Impedance tracings were analyzed for liquid, gas and mixed reflux episodes using established criteria.\(^{28,29}\) Reflux events were classified according to their acidity (acid GER (pH<4), weakly acidic GER (4 ≤ pH < 7) and weakly alkaline GER (pH ≥ 7))\(^{30}\) and proximal extent. A GER event was defined as a proximal reflux event, when the most proximal MII segment within the esophagus was reached by the bolus.

Manometry during reflux detection

In the post prandial period, manometric data were analyzed for mechanisms known to underlie GER episodes (TLESR, swallow related LES relaxations and multiple swallow related LES relaxations), and the presence and characterization of a clearing motor event, if present. The manometric tracings were analyzed without the MII tracing being visible. TLESRs were defined as per previously described criteria.\(^{31}\) If swallowing occurred within 4 s before and 2 s after the onset of LES relaxation it was defined as a swallow related relaxation. Multiple swallow related LES relaxations were defined as two or more swallows scored which sustained low LES pressure.\(^{32}\) Next, MII and manometric analyses were combined and GER events where no underlying mechanisms was scored were reviewed for other possible mechanisms, such as low LES baseline pressure, straining and cough induced GER. If no such evidence was present, the GER event was scored to be of unclear origin. For clearing mechanisms, primary peristalsis was described as a swallow related propagated pressure wave following a GER episode, while secondary peristalsis was defined as a propagated pressure wave which wasn’t preceded by a swallow.
Esophageal function testing

At the time of each indicated bolus swallow, total bolus transit time (TBTT) was calculated as defined by Nguyen et al. The first swallow after each bolus was classified as reaching complete or incomplete bolus bolus clearance. Bolus clearance was complete if bolus exit points were recorded in all measuring segments.

Incomplete bolus clearance for 30% and 40% or more of liquid and viscous swallows respectively was defined as overall abnormal clearance.

Manometric tracings were analyzed for esophageal contractions and LES relaxations during bolus clearance. Contractions were measured by the following parameters: peak pressure, duration of the contraction, contraction velocity and intrabolus pressure. In addition, peristalsis was classified in propagated and non-propagated. Peak pressures of at least 10 mmHg in all channels were defined as propagated pressures and if peak pressure was less than 10 mmHg in at least one channel, these pressures were called non-propagated.

Propagating contractions were further divided in normal, hypotensive (<20 mmHg) or hypertensive (>120 mmHg). Non-propagating pressures were further classified as focal failure (<10 mmHg in ≤ 2 channels), generalized failure (<10 mmHg in >3 channels) or synchronous when contraction velocity is > 60 mmHg/sec over 3 channels.

LES relaxations were classified using baseline pressure, nadir pressure and the duration of the relaxation. The time the LES pressure was < 3 mmHg was used to describe the period of complete LES relaxation.

Gastric emptying

The breath samples were analyzed for $^{13}$CO$_2$ content using an isotope ratio mass spectrometer. The $^{13}$CO$_2$ concentration in the breath samples was used to calculate the following GE variables: GE$_{1/2}$, GE$_{lag}$, GE$_{max}$, and the GE-coefficient. The $^{13}$CO$_2$ excretion curve was categorized as a single- or double peak curve. A double peak curve exists whenever more than two points deviate significantly from the excretion curve.

Gastric emptying times were compared to 75th and 90th percentile of age appropriate normal values.

Statistics

Normally distributed data are presented as a mean ± standard deviation and were compared using T-tests, while nonparametric data are presented as median (range) and were compared using Mann-Whitney-U test. Fisher’s exact (for 2x2 contingency tables) or Chi square test (all other instances) was used for proportional data. Spearman’s rho correlation analysis was used to explore the existence of correlations. A p-value < 0.05 was considered statistically significant.
RESULTS

Patient characteristics

We randomly selected 21 adult patients with esophageal atresia type C out of 161 who met inclusion criteria, ten of whom were unwilling to participate. One of the remaining volunteers dropped out due to problems with catheter placement. During the study period (Jan 2006 – Dec 2008), 14 infants with EA type C were born in our hospital and had a routine 24 hour pH-study scheduled. Three parents refused participation and 1 infant was excluded due to the impossibility to be intubated. Patient characteristics are given in table 1. In three ‘infants’ the routine pH-study was not scheduled before the age of 1. These children are nevertheless included in the infant group.

<table>
<thead>
<tr>
<th></th>
<th>Infants</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>0.67 (0.23 – 3.42)</td>
<td>24.5 (18.1 – 31.3)</td>
</tr>
<tr>
<td>Number male</td>
<td>5 (50%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>2900 (1350-3940)</td>
<td>2470 (1480-3880)*</td>
</tr>
<tr>
<td>Gestational age (wks)</td>
<td>38.5 (31-40)</td>
<td>39 (30-41)*</td>
</tr>
<tr>
<td>Proton pump inhibitor use</td>
<td>10 (100%)#</td>
<td>4 (40%)</td>
</tr>
</tbody>
</table>

Table 1. Baseline characteristics. *n=9, birthweight and gestational age of 1 volunteer could not be retrieved. #All infants are prescribed a proton pump inhibitor (PPI) until they have had their routine 24 hour pH study, which was at the time of study. Consequently all infants were using PPI.

Gastro-esophageal reflux detection

MII detection of GER events

In total, 3529 minutes of impedance tracings were analyzed during the reflux detection periods (figure 1). During this time 306 retrograde bolus movements were detected of which 181 (59.2%) liquid, 77 (25.2%) mixed and 48 (15.7%) pure gas episodes. Ninety-seven of the 306 (31.7%) reflux episodes were acidic, 192 (62.7%) weakly acidic and 17 (5.6%) weakly alkaline. The median number of GER episodes per patient was not significantly different between infants and adults (14 (9-33) vs 9.5 (4-44), p=0.23) Classification of GER events according to proximal extent and acidity are shown for both age groups in figure 3.

Manometry during reflux detection

A total number of 228 TLESR’s were identified, 31 of which were not accompanied by a GER episode as seen on MII. Of all 306 GER events, 197 (64.4%) occurred during a TLESR. The remaining GER episodes were caused by swallow related LES relaxations (n=28 (9.2%)), straining (n=27 (8.8%)), multiple swallow related LES relaxations (n=13, (4.2%)), low LES baseline (n=7 (2.3%)). For 34 GER events (11.1%) no underlying mechanism could be identified. There was a statistically significant difference between the distribution of GER events in infants and adults (figure 4).
Of all 306 MII detected GER episodes, 34 (11.1%) were followed by primary peristalsis and 71 (23.2%) by secondary peristalsis. In all other GER events (n=201 (65.7%) there was no clearing mechanism directly following the GER episode.

Esophageal function testing

Motility patterns
A median number of 17 (5-22) boluses per patient could be analyzed (total n=324). Missing data were primarily caused by movement artifacts in the infants. Sixty-four boluses were excluded for manometric analysis because the boluses were infused in the proximal esophagus, rather than swallowed. Analysis of the remaining 260 analyzable swallows showed 55 (21.2%) with normal peristalsis. These normal peristaltic waves were

Figure 3. Characterisation of MII detected bolus GER episodes. Absolute numbers are shown in left panel, relative numbers (%) in the right. GER: gastroesophageal reflux. Proximal GER is a GER episode which reaches the most proximal MII segment within the esophagus. * Statistically different distribution, p<0.01, Chi square test. # Statistically different distribution, p<0.01, Fisher’s exact test.

Of all 306 MII detected GER episodes, 34 (11.1%) were followed by primary peristalsis and 71 (23.2%) by secondary peristalsis. In all other GER events (n=201 (65.7%) there was no clearing mechanism directly following the GER episode.
found in 6 patients (4 infants, 2 adults). Of these 6 patients, one adult showed normal motility in 80% of swallows, while in the others more than 50% of all swallows had abnormal motility patterns. No normal peristalsis was seen in the remaining 14 patients. In 120 out of the 205 swallows that did not fulfill criteria for a normal peristaltic wave, normal peristalsis was observed in the proximal part of the esophagus, but did not propagate distally (58.5% of swallows with abnormal peristalsis; 46.2% of all analyzable bolus-swallows). Other abnormal peristaltic swallows were further identified as focal failure in 41 (15.8%), generalized failure in 27 (10.4%) and synchronous contractions in 17 (6.5%) of all analyzable bolus-swallows.

Mean LES resting pressure preceding a swallow was 13.1±10.1 mmHg and LES relaxation was complete in 271 (83.6%) swallows. Of the normally propagated contractions, 28 (50.9%) were normotensive, 21 (38.2%) were hypotensive and the remaining 6 (10.9%) hypertensive. Data were similar for infants and adults (data not shown).

Figure 4. Mechanisms underlying all MII detected GER episodes (left) and the type of GER episodes that were triggered by a TLESR (right). Data for infants are shown on top, for adults on the bottom. There was a statistically significant difference between infants and adults (Chi-squared test, p<0.05). TLESR: transient lower esophageal sphincter relaxation; SLESR: swallow related lower esophageal sphincter relaxation; MLESR: multiple swallow related lower esophageal sphincter relaxation.
## Motility and bolus clearance

In 264 boluses (median: 15 (3-20) boluses per patient) both impedance and manometry tracings were analyzable. Extremely low impedance baselines in the distal segments were the main reason that impedance tracings could not be analyzed. In 8 of 10 infants, one or more (median: 5 (1-20), total number: 64) boluses were given by infusion in the proximal esophagus. These infusions were taken into consideration for complete transit calculations, but not for other parameters. Impedance analysis showed complete bolus clearance in 108 out of 264 (40.9%) swallows. This figure did not change significantly when the infused boluses were not included (79 out of 200, 39.5%, p=0.83). All clearance results and TBTT’s are shown in table 2. Overall, no significant differences were found between liquid and viscous boluses (p=0.15), upright and supine position (p=0.54) or infants and adults (p=0.85). Normal motility caused significantly more normal clearance (47 of 55 (85.5%) boluses) compared to abnormal motility (61 of 205 (29.7%) boluses, p<0.0001).

## Gastric emptying

Gastric emptying data are available for 7 infants and 9 adults. Two infants vomited after their feed and one drank less than 50% of his normal feed. In one adult, breath samples could not be analyzed due to technical difficulties. Data are shown in table 3. No association was found between GE and esophageal motility (Spearman’s rho -0.48, p = 0.32). or between GE and bolus clearance (Spearman’s rho -0.56, p = 0.23).

### Table 2. Bolus clearance as detected by multichannel intraluminal impedance.

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<th>Infants</th>
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<th>Adults</th>
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<tbody>
<tr>
<td></td>
<td>Liquid</td>
<td>Viscous</td>
<td>Liquid</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>Upright</td>
<td>Supine</td>
</tr>
<tr>
<td>Normal clearance</td>
<td>13(46%)</td>
<td>11(55%)</td>
<td>9(33%)</td>
</tr>
<tr>
<td>TBTT</td>
<td>14 (6-141)</td>
<td>13 (3-86)</td>
<td>18(12-224)</td>
</tr>
</tbody>
</table>

### Table 3. Gastric emptying results.

<table>
<thead>
<tr>
<th></th>
<th>Infants (liquid meal, n=7)</th>
<th>Adults (solid meal, n=9)</th>
</tr>
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<tbody>
<tr>
<td>$T_{1/2}$</td>
<td>107.8 (54.0-173.7) min</td>
<td>98.0 (45.4-120.7) min</td>
</tr>
<tr>
<td>Delayed (&gt;75th percentile)</td>
<td>5(71.4%)</td>
<td>5(55.5%)</td>
</tr>
<tr>
<td>Delayed (&gt;90th percentile)</td>
<td>4(57.1%)</td>
<td>2(22.2%)</td>
</tr>
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</table>

No association was found between $T_{1/2}$ and esophageal motility (Spearman’s rho -0.48, p = 0.32). or between GE and bolus clearance (Spearman’s rho -0.56, p = 0.23).
DISCUSSION

This is the first study combining MII, manometry and gastric emptying data to evaluate mechanisms underlying GER events and gastroesophageal function in EA type C patients. As in healthy premature infants, infants with GER disease, healthy adult volunteers and adult GER disease patients,\textsuperscript{14,15,40-42} we have shown that TLESR is the main mechanism underlying GER episodes in EA type C patients, both shortly after a primary anastomosis, as well as in adulthood. No difference was found in the absolute number of GER episodes, but adults show more acid GER events and less GER events that reach into the proximal esophagus (\textit{figure 2}). It was recently shown that in adults, an acid pocket (the presence of unbuffered, highly acidic gastric juice in the proximal stomach) plays an important role in the pathophysiology of GER disease.\textsuperscript{43-45} Since adults were upright during the entire post prandial period, while infants were supine, in which position an acid pocket is less likely to play a role, this could explain the difference between infants and adults. Of course, other factors could play a role, such as the relative large volume of a meal in infants with more buffering capacity as a consequence and potentially more acid secretion in adults. The difference in proximal extent could in part be explained by the position of the patient; gravity will play a more important role in upright patients. However, probably more important, is the relatively small capacity of an infant esophagus in which a comparable volume would reach higher up into the esophagus.

Although TLESR are the main mechanism in infants and adults with EA, it seems that other mechanisms (especially straining in infants and (multiple) swallow related LES relaxations in adults) are more important than in infants and adults without EA. A control group with volunteers without EA could have clarified this in more detail, but was ethically unacceptable. It could be hypothesized that infants might strain more often as a result of the delayed bolus clearance and subsequent symptoms seen in this study.

Both in adults and infants, delayed gastric emptying as seen in a majority of patients in this study, might increase the probability of GER occurring during any form of LES relaxation. However, it should be noted that no clear relationship between gastric emptying and GER episodes has been shown to date.\textsuperscript{46}

Our study confirmed the presence of esophageal dysmotility in nearly all children with EA. This is in concordance with previous investigations that demonstrated the incidence of abnormal esophageal motility in postoperative EA patients to be almost universal.\textsuperscript{8,13,19} Several studies have attempted to find the origin of disturbed motility. Some suggested the disorder to be congenital (an inborn abnormal innervation)\textsuperscript{47-49}, while others reported an acquired origin due to inevitable damage by surgical dissection and mobilization of the esophagus and its nerve supply during reconstruction.\textsuperscript{50-52} The most commonly observed motor abnormality in our study, a normal initiation of a peristaltic wave, which does not propagate through to the distal esophagus, does not differentiate between the two theories.
Abnormal motility should affect esophageal clearance, resulting in abnormal bolus clearance and diminished clearance of reﬂuxed materials. The abnormal clearance of both swallowed boluses and reﬂuxed materials may have serious consequences for patients’ health. Several complaints, like dysphagia, are caused by abnormal clearance of swallowed boluses. In addition, abnormal clearance of reﬂuxed materials may result in severe mucosal damage and esophagitis and possibly esophageal carcinoma. The observation in our study that normal clearance can be achieved with abnormal motility patterns, raises the question as to what exact factors cause clearance to be normal/abnormal in these patients. More insight in this issue could possibly aid in preventing the long term complications as mentioned above.

The majority of infants and adults in our study has a delayed GE. Previous reports have shown GE to be delayed in some patients, but not as many as in our study. The etiology of disturbed gastric motility in children after surgical correction of EA has not been clarified. The origin has been suggested to be iatrogenic (vagal nerve injury due to dissection of an esophageal segment or infection due to an anastomotic leak), or a disturbed intrinsic innervation as part of to the congenital defect. Another possibility would be that genetic defects causing EA are also responsible for a more generalized motility disorder in the proximal gastrointestinal tract. However, we were unable to show a correlation between gastric emptying and the severity of esophageal motor abnormalities.

In conclusion, TLESR is the main mechanism underlying GER episodes in infants and adults with EA, but other mechanisms appear to be more important than in infants and adults without EA. Although some patients have effective clearance with abnormal motility, the majority of swallows have abnormal esophageal motility resulting in prolonged bolus transit times and bolus residues. Ideally, a large cohort should be followed and tested longitudinally, not only to get a better understanding of pathophysiology in these patients, but also to establish an ideal monitoring regime both in infants and adults. Moreover, further studies are needed to unravel the relationship between the abnormalities found in this study and endoscopy ﬁndings. Until such data are available, the abnormalities found in this study warrant at least some form of monitoring during childhood and probably beyond.
REFERENCES


Evaluation of gastroesophageal function and reflux in patients with esophageal atresia


