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ORIGINAL ARTICLE

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Long-term evaluation of esophageal function in patients treated at birth for esophageal atresia

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Abstract Dysphagia, gastroesophageal reflux (GER) and esophageal metaplasia are reported with various incidence in the long term follow-up of patients treated at birth for esophageal atresia (EA). To evaluate the long term outcomes 26 patients treated at birth for EA with Tracheo Esophageal Fistula (TEF) were examined 8–28 (mean 15.8) years later by clinical evaluation, including barium meal, fiberoptic upper GI endoscopy, 24 hour ambulatory two-channel pH-monitoring and stationary esophageal manometry. 50% of patients complained of dysphagia. Mild esophagitis was found in 20% of patients but GER was detected in only 16.7% of the cases. By morphological X-ray, esophageal anomalies were detected in 31% of cases without significant functional relevance. Hundred percent of patients had a disorganized peristaltic esophageal activity and a low amplitude of the esophageal contractions was observed in 58% of them. In our series, esophageal dismotilty seems to be the main consequence of EA without any relevant disturbance of normal nutritional habit.

Keywords Dysphagia · Gastroesophageal reflux · Esophageal atresia · Tracheo esophageal fistula

Introduction

The great majority of babies born with Gross's C type esophageal atresia (EA) are operated on with success in the neonatal period. Even though a good re-establishment of the continuity of the esophagus can be acheived by primary end-to-end anastomosis, other problems related to EA may interfere with normal life in this group of patients. Dysphagia, gastroesophageal reflux(GER) and esophageal metaplasia are present at various levels in all series reported [1, 8, 10]. All these sequelae cause serious impairment to the quality of daily nutritional habits. This study was designed to evaluate the long term impact of EA in a group of patients treated at birth in our hospital by primary correction of EA with Tracheo-Esophageal fistula (TEF).

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Patients and methods

Twenty-six patients (were recurited for this study) from among 79 successful primary esophageal anastomosis performed at birth on babies affected by EA with TEF in the Department of Pediatric Surgery of Niguarda Cà Granda Hospital. Age at control was between 7–28 years (mean 15.8 years). We selected patients old enough to cope with the quite invasive set of procedures. The following set of tests was performed on all patients:

1. **Clinical evaluation** focused on esophago-gastric functions with particular attention to detection of the symptoms of GER and to checking the patient's eating and swallowing behavior.
2. **Upper GI X-ray** evaluation in order to detect anatomical features of the repaired esophagus and at the same time to study the esophago-gastric junction.
3. **Fiberoptic esophagogastroduodenoscopy** performed under ambulatory sedation. Particular attention was paid to the site of anastomosis, and also to the detection and sampling of any mucosal abnormality. Careful study of the lower esophagus and the cardia was attempted. The severity of esophagitis was graded endoscopically (0–4) according to the modification of the original Savary and Miller classification [6].
4. **Esophageal manometry** was carried out with a 8-lumen standard manometric catheter (type AMC8-A, Synetics Medical, USA), with four radial openings at 90° from each other, and the remaining four spaced 5 cm apart. The lumina were perfused with bubble-free distilled water at a constant rate of 0.6 ml/min by a low-compliance pneumohydraulic system (Arndorfer Medical Specialities, USA), and in turn connected through physiological pressure transducers to a multichannel polygraph recorder (paper speed: 1 mm/sec). At the above perfusion rate, the system yields a pressure rise to distal occlusion of more than 300 mmHg/sec. After an overnight fast, the lubricated catheter was inserted within the stomach, and then slowly retracted in 0.5–1 cm increments to

measure LES (Lower Esophageal Sphincter) pressure and length with the four radial openings. This was repeated 3 times to obtain the average of 12 measurements, in order to compensate for the radial asymmetry of the sphincter [13]. Thereafter, the catheter was positioned with one of the radial recording points within the LES (respiratory inversion point) and the four proximal 5 cm-spaced orifices at 3, 8, 13, and 18 cm above the LES, to measure esophageal body motor activity. For this purpose, 10 or more 5 ml water boluses were administered with a syringe at 30 sec intervals.

5. **Ambulatory 24-hour** esophageal p-monitoring was carried out according to a previously reported technique [3], with the use of a glass electrode (model 440 M3, Ingold GmbH & Co., KG, Switzerland). The pH catheter was calibrated in standard buffer solution at pH 7 and 1, before and after the study. Only recordings with an electrode drift of less than 0.2 pH units during the 24-hour monitoring period were considered. The electrode was placed 5 cm above the upper border of the manometrically determined LES and then connected to a portable digital datalogger (Digitrapper Mark III, Syneticts Medical, Sweden). PH values of the distal esophagus were continuously recorded, at 6-seconds intervals, for 24 hours. The patients were asked to remain in the upright or sitting position until they went to bed, to maintain a night supine position for at least 8 hours, and to follow a diet restricted to 3 meals. These meals were comprised of solids and liquids with a pH between 5 and 7. Between meals, only water was allowed. A diary of food and liquid intake was kept. Symptoms experienced during the monitored period, the time the supine position was assumed in preparation for sleep, and the time of rising in the morning were monitored. All medications known to interfere with foregut motor or gastric secretory function were suspended at least 48 hours before the study, with the exception of proton pump inhibitors, which were stopped at least 10 days before the study.

Variables

In addition to the age, sex, symptoms, and upper GI X-ray results, the presence or absence of esophagitis was recorded. The following pH-metric variables were analysed: (a) percent of total time below pH 4 in the esophagus, (b) percent of supine time below pH 4 in the esophagus, (c) percent of upright time below pH 4 in the esophagus, (d) total number of episodes below pH 4 in the esophagus, (e) duration of the longest episode, and (f) numbers of episodes lasting more than 5 minutes. The normal values for these variables were those from former studies on pH-metering [2, 7]. Patients were considered "non-refluxers" if their total time below pH 4 was $< 4\%$.

Patients with total time percentage below pH 4 $>$ %5 were considered refluxers.

Three manometric parameters of the LES were taken into consideration: sphincter pressure (the difference between the gastric baseline and the pressure at the respiratory inversion point during the middle of the respiratory cycle), abdominal length (the distance between the respiratory inversion point and the distal border of the sphincter), and overall length (the distance between the gastric baseline and the upper border of the sphincter). The end respiratory gastric baseline was used as zero reference for pressure measurement. Esophageal body motor variables were analysed according to previously described criteria [3]. Six esophageal body motor variables were taken into consideration: distal esopahgeal body wave amplitude (mmHg), proximal esophageal body wave amplitude (mmHg), peristaltic coordination (%), dropped sequences (%) (contraction in the upper esophagus not propagated into the distal esophagus), interrupted sequences (%) (initial contraction followed by no detectable contraction) or simultaneous sequences (%).

Results

All the 26 patients completed the clinical evaluation with symptoms summarized in Table 1. High prevalence of dysphagia (50%) was observed. Heartburn and regurgitation were less frequent, present in 14% and 7% of cases. No one reported chest pain. Dyspeptic symptoms were observed in the following prevalence: nausea (27%), epigastric burning (21%), postprandial fullness (14%), and epigastricpain (7%), Aspiration pneumonia (14%), chronic cough (7%), chronic pharyngitis (7%), hoarseness (7%), chronic laryngitis (7%), chronic bronchitis (7%) were some of the respiratory symptoms observed. None of the patients reported asthma.

X-ray studies were also performed on all the 26 patients. In 8 cases (31%) the upper esophagus above the anastomosis looked enlarged, in 4 cases (15%) a pseudodiverticulum near the site of anastomosis was observed during the barium swallowing. It must be pointed out that none of the patients showing pathological morphological features by x-ray had functional disturbances. In one case (3.8%) the barium meal revealed a severe GER according to the subjective clinical data previously recorded.

Only 15 patients underwent endoscopy (Table 2) and the others refused it. Only 3 cases (20%) of mild

Table 1 Prevalence (%) of symptoms in twenty-six patients

Typical symptoms of Gastro-oesophageal Reflux		
Regurgitation	1	(7%)
Dysphagia	13	(50%)
Heartburn	2	(14%)
Chest pain	0	(0%)
Dyspeptic symptoms		
Epigastric burning	3	(21%)
Epigastric pain	1	(7%)
Nausea	4	(27%)
Postprandial fullness	2	(14%)
Early satiety	2	(14%)
Eructation	2	(14%)
Respiratory symptoms		
Chronic cough	1	(7%)
Chronic pharyngitis	1	(7%)
Hoarseness	1	(7%)
Chronic laryngitis	1	(7%)
Chronic bronchitis	1	(7%)
Aspiration pneumonia	2	(14%)
Asthma	0	(0%)

Table 2 Endoscopic esophagitis in 15 patients

Patient No.	Sex	Age (yr)	Endoscopic esophagitis (degree 0–4)
1	F	25	0
2	M	10	1
3	F	16	0
4	F	9	0
5	M	18	0
6	F	15	0
7	F	15	1
8	M	7	0
9	F	17	0
10	F	19	0
11	F	21	0
12	F	18	0
13	M	18	0
14	F	15	0
15	M	16	1

esophagitis were found whereas all the remaning cases had a normal appearance of the esophageal and gastric mucosa. In some cases the site of anastomosis was not recognized. In one case (7%) substenotic anastomosis was detected without the need of dilation. In none was hiatus hernia found.

Twelve patients underwent motility esophageal tests (stationary manometry and 24-hour pH monitoring). Abnormal reflux was found in 2 cases (16.7%) (Table 3).

Hypotonic LES was found in 2 cases (16.7%) (Table 4). Short abdominal length of the LES was observed in 2 cases (16.7%). In no case was short overall length of the LES found. Abnormal percentage of relaxation of the LES was found in 1 case (50%). Two patients with hypotonic LES also experienced abnormal reflux and endoscopic esophagitis. Hypotonic distal esophageal amplitude (< 30 mmHg) was measured in 7 cases (58.3%) (Table 5). Low esophageal amplitude was found in all patients (proximal esophagus: mean = 18.58.0 SD; distal esophagus: 26.616.8 SD). Normal esophagus wave duration was found in all patients. Abnormal peristaltic coordination was found in 100% of our patients. Simultaneous sequences (30%) were observed in 9 cases (75%), interrupted waves (30%) in 4 cases (33.3%), and dropped sequences (30%) in 1 case (8.3%).

Discussion

Since it is reported by many authors that GER is common (40% to 80%) in survivors of EA [1, 10], we focused our late follow-up study on the detection of this disturbance in our population. In other studies, emphasis has been placed on the detection of mucosal metaplasia and Barret's esophagus in EA survivors [8].

When patients operated on at birth for EA reach school age they tend to consider themselves "normal" even though they have passed through a troublesome early postoperative period. It was, in fact, quite difficult to persuade our 26 patients and their parents to come back to hospital to evaluate the sequelae of EA.

It has been reported that in this particular group of patients the first years of life are the most dramatic in terms of the nutritional and respiratory complications which are the causes of frequent hospitalisation for these children [4]. Afterward they start to grow up in a way comparable to their peers [4, 5]. This was the case for our group. Many of our patients had reached an acceptable way of eating and they considered the symptoms reported in the clinical evaluation as minor problems. For the above reasons not all our patients gave us the consent for endoscopy and for esophageal motility tests.

Table 3 Ambulatory 24-hour pH esophageal monitoring in 12 patients

Patient No.	Sex	Age (yr)	Total time pH < 4 (%)	Upright time pH < 4 (%)	Supine time pH < 4 (%)	No. of Episodes	No. of Episodes > 5 min	Longest episode (min)
1	F	25	0.3	0.3	0	0	1	2
2	M	10	10.9	1.3	25.3	9	37	152
3	F	16	0	0	0	0	0	0
4	F	9	2.4	1.5	3.8	3	12	11
5	M	18	1.6	2.3	0.7	0	8	4
6	F	15	0.7	1	0	1	6	5
7	F	15	13.5	0.8	31.4	5	19	93
8	M	7	3.3	5.1	0	3	15	9
9	F	17	0	0	0	0	0	0
10	F	19	0.1	0.1	0	0	0	0
11	F	21	0	0	0	0	0	0
12	F	18	0	0	0	0	0	0

Table 4 Lower esophageal sphincter manometry in 12 patients

Patient No.	Sex	Age (yr)	Pressure (mmHg)	Abdominal length (mm)	Overall length (mm)	Relaxation (%)
1	F	25	13	15	45	100
2	M	10	4	15	55	100
3	F	16	32	15	55	100
4	F	9	20	5	20	100
5	M	18	23	10	30	100
6	F	15	12	10	40	100
7	F	15	8	10	30	50
8	M	7	25	27	30	100
9	F	17	14	25	50	100
10	F	19	43	35	50	100
11	F	21	18	25	35	100
12	F	18	15	7	37	100
Mean, SD*			18.9 ± 10.74	16.5 ± 9.30	39.7 ± 11.31	

*SD: Standard Deviation

Table 5 Body esophageal manometry in 12 patients

Patient No.	Sex	Age (yr)	Proximal Esophageal Amplitude (mmHg)	Waves Duration Proximal Esophagus (sec)	Distal Esophageal Amplitude (mmHg)	Waves Duration Distal Esophagus (sec)	Peristaltic Coordination (%)	Simultaneous Sequences (%)
1	F	25	20	2.6	41	2.6	40	30
2	M	10	15	2.5	24	2.5	0	0
3	F	16	34	4.0	40	3.0	0	10
4	F	9	29	2.5	33	3.5	60	40
5	M	18	22	2.0	65	4.0	0	90
6	F	15	10	2.0	10	2.0	0	10
7	F	15	10	6.0	11	6.0	0	20
8	M	7	10	4.0	12	3.0	0	0
9	F	17	10	4.0	10	4.0	0	70
10	F	19	18	7.0	36	4.0	50	50
11	F	21	16	5.7	20	5.0	20	80
12	F	18	25	2.0	20	3.0	0	10
Mean, SD*			18.5 ± 8.0	3.31 ± 0.07	26.8 ± 16.8	3.26 ± 0.05		

*SD: Standard Deviation

It is surprising that GER was found in a much lower proportion of our cases than has been reported in other studies [1, 10, 13] whereas all the data regarding esophageal dysmotility are comparable with the literature [12]. It is much more surprising in light of the fact that GER in EA survivors seems to depend upon the lack of esophageal acid clearance [12] which was expected to be low in our cases. In fact in 100% of cases, esophageal peristalsis was uncoordinated and, in 58%, accompanied by weak contractions of the distal esophagus.

It must be pointed out that the two ''refluxers'' we found in our study both had hypotonic low esophageal sphincter and esophagitis, one of them had already had the Nissen procedure performed on her twice.

Whether esophageal dysmotility in EA depends upon intrinsic factors such as incomplete and abnormal development of the neuro- muscular structures (related to the malformation itself); or is a consequence of surgical manipulations with partial damage to the vagus nerve; or a combination of both is still a matter of debate [11]. Results of recent experimental work [9] give appealing evidence about the role of intrathoracic traction of the low esophageal sphincter in the genesis of GER. In conclusion, even though our sample is small, we can speculate that in our cases, the component traction upward into the thorax of the esophagus was low which may explain why poorly motile esophaguses may not be refluxers.

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