Outcomes of fundoplication in oesophageal atresia associated gastrooesophageal reflux disease

Antti I. Koivusalo*, Risto J. Rintala, Mikko P. Pakarinen

Children’s Hospital, Section of Paediatric Surgery, University of Helsinki, Helsinki, Finland

Abstract

Aim of the study: Conservative management of gastrooesophageal reflux (GORD) in oesophageal atresia (OA) is sometimes inefficient, and fundoplication is required. We assessed the outcomes of fundoplication among OA patients from 1980 to 2016.

Methods: After ethical consent, hospital records of 290 patients, including 22 referred patients, were reviewed. Included were 262 patients with end-to-end repair. Excluded were patients who underwent oesophageal reconstruction (n = 23) or no repair (n = 5). Primary outcome measures included survival, retaining the native oesophagus, resolution of GORD symptoms, failure of fundoplication, and long-term endoscopic results.

Main results: Gross types of OA in 262 patients were A (n = 12), B (n = 2), C (n = 217), D (n = 10), E (n = 19), and F (n = 2). Eighty-six (33%) patients, type A (n = 12, 100%), B (n = 2, 100%), C (n = 69, 31%), D (n = 3, 30%), and F (n = 1, 50%), underwent fundoplication at the median age of 5.4 (IQR 3.1–16) months. Main indications included recalcitrant anastomotic stenosis (RAS) in 41 (48%), respiratory symptoms in 16 (19%), and acute life threatening events (ALTE) in 15 (17%) of patients. Associated tracheomalacia in 25 (29%) patients were treated with aortopexy. Median follow-up was 7.5 (IQR 1.8–15) years. RAS resolved in 30 (73%) patients, whereas 11 (27%) with unresolved RAS underwent oesophageal resection (n = 8) or replacement (n = 3). Six (7%) patients died of heart failure (n = 4), bolus impaction (n = 1), and ALTE (n = 1). Fundoplication failed in 27 (31%) patients, and 13 (15%) underwent redo fundoplication. Fundoplication failure was predicted by long-gap OA RR = 3.8 (95%CI = 1.1–13), P = 0.04. In total GORD associated symptoms persisted in 7 (8%) patients, including one with permanent feeding jejunostomy. Latest endoscopy showed moderate or severe oesophagitis in 7% of fundoplicated and in 3% nonfundoplicated patients and intestinal metaplasia in 3% and 1% (p = 0.29).

Conclusion: Fundoplication provided a safe and relatively effective control of OA associated symptomatic GORD and oesophagitis. The failure rate of fundoplication was high in those with long-gap OA.

Type of study: Treatment study.

Level of evidence: IV
Main outcome measures were survival and degree of oral intake. Surgical complications were also recorded and assessed. Statistical calculations were made with StatView® 512 computer programme (Brain Power, Calabasas CA, USA). Data are presented as frequencies or medians with interquartile range (IQR). Categorical variables were compared with Fisher’s Exact Test, Risk Ratios with Logistic Regression Analysis. P values <0.05 were considered statistically significant. Data are quoted as median (interquartile range) unless otherwise indicated.

2. Results

During the study period 1980 to 2016 we treated 290 successive children with OA; twenty-two were referred from elsewhere. Five infants with Gross C-type OA and trisomy of chromosome 13 (n = 2), extreme prematurity (n = 1) died without undergoing definite repair and 23 (type A n = 11, B n = 4 and C n = 5) underwent oesophageal reconstruction without attempt of end-to-end repair. Included were 262 with native oesophagus at the time of fundoplication (A n = 12, B n = 2), C (n = 217), D (n = 10), E (n = 19) and F (n = 2). A total of 86 of 262 (33%) underwent fundoplication at the median age of 5.4 (IQR 3.1–16) months. Fundoplications by atresia type and associated anomalies are outlined in Table 1.

2.1. Indications and techniques

Main indications for fundoplication included recalcitrant anastomotic stenosis (RAS) in 41 (48%) (type A n = 7, B n = 1, C n = 29, D n = 3, F n = 1) acute life threatening events (ALTE) in 15 (17%) (type C n = 14, D n = 1) respiratory symptoms in 16 (19%) (type A n = 2, C n = 14, D n = 1) persistent oesophagitis in 11 (13%) (type C n = 11) and persistent vomiting in 3 (3%) (A n = 1, B n = 1, C n = 1) patients. Seventy-nine (92%) patients underwent an open operation (Nissen n = 49, Boix–Ochoa n = 23, Toupet n = 7) and seven (8%) had a laparoscopic Nissen fundoplication. Median age at open operation was 5.4 (IQR 3–17) months and at laparoscopic operation 8.5 (5.1–49) months (P = 0.28).

3. Results of fundoplication

3.1. Anastomotic stenosis

Median age of at fundoplication was 4.2 (IQR 2.7–6.3) months. Of 41 patients with recurrent anastomotic stenosis 30 (73%) eventually responded to postfundoplication endoscopic dilatations. Nine patients (types A n = 2, C n = 5, F n = 1) underwent rethoracotomy, resection of the stenosed anastomosis and end to end resection and eventually responded to continued dilatations. In addition, three patients with C-
type OA had recalcitrant anastomotic stenosis and they underwent oesophageal reconstruction because of a long stenotic area (from 4 to 5 cm) and associated recurrent fistula in two patients. Reconstructions included jejunum interposition (n = 1), gastric pull-up (n = 1) and reversed gastric tube (n = 1).

3.2. Acute life threatening events (ALTE)

Median age at fundoplication was 2.9 (IQR 2.2–4.6) months. Of fifteen patients with ALTE 9 (36%) underwent aortopexy for tracheomalacia. Fundoplication with or without aortopexy controlled ALTE in 10 (66%). In three children with congenital heart disease (Fallot’s tetralogy) ALTE stopped only after heart surgery. In two patients who underwent fundoplication with aortopexy for tracheomalacia ALTE persisted for two and three months but eventually attenuated and ceased.

3.3. Respiratory symptoms

Median age at fundoplication was 17 (IQR 11–29) months. Of seventeen children who underwent fundoplication for respiratory GER symptoms three had undergone a previous aortopexy for tracheomalacia. Five (29%) children had an associated syndrome (CHARGE n = 2, Di George n = 1, Down’s syndrome (n = 2). In all seventeen patients fundoplication attenuated respiratory symptoms, but none had total cessation of respiratory symptoms.

3.4. Persistent oesophagitis

Median age at fundoplication was 110 (IQR45–180) months. Eleven patients had GORD symptoms with endoscopically verified moderate or severe mucosal inflammation consistent with reflex oesophagitis. Before fundoplication all patients were administered proton pump inhibitors (1–2 mg/kg once daily) or ranitidine (5–10 mg/kg twice daily) for several months and the healing surveyed with repeated endoscopic biopsies. After a median of 115 (IQR 56–165) months of endoscopic follow-up eight (73%) children had no oesophagitis, two (18%) had mild oesophagitis, and one (9%) severe oesophagitis. In two with mild (n = 1) and severe (n = 1) oesophagitis biopsies showed also columnar (gastric) metaplasia.

3.5. Vomiting

Median age at fundoplication was 15 (IQR 9–26) months. Three children underwent fundoplication for persistent copious vomiting that was detrimental to enteral nutrition. One patient with A-type OA had a severe dumping syndrome. In all three vomiting was controlled by fundoplication and enteral nutrition was successfully continued.

3.6. Mortality, preservation of native oesophagus and long term endoscopic follow-up

Mortality in OA with fundoplication was 6/86 (7%) and in nonfundoplicated OA 17 /187 (9%) (P = 0.81). Of six children who died after fundoplication, four died of sequelae of heart surgery; one of the four had also severe associated tracheomalacia. One patient with isolated C-type OA with postrepair ALTE underwent fundoplication with aortopexy for moderate tracheomalacia and repair of minor laryngeal cleft by otolaryngologist. After four months and after a six-week remission of ALTE the child, however, succumbed to ALTE during his first probationary discharge. In addition, one child died of suffocation by a food bolus obstruction three months after fundoplication.

Three (3%) of 86 underwent oesophageal reconstruction (see anastomotic stenosis).

Endoscopic follow-up covered 244 (86%) of the 290 patients. Of the missing 46 patients 20 died before joining the follow-up program and 26 patients (OA type E n = 10, type C n = 16) were lost to follow-up. Patients included in the follow-up underwent a median of 3 (IQR 2–4) endoscopies during the follow-up. Results from the last endoscopy are outlined in Table 2. Children who underwent fundoplication had higher incidence of gastric metaplasia than nonfundoplicated patients. No cases with dysplasia or cancer were found. (See Table 3.)

3.7. Failed fundoplication

Endoscopic follow-up after the first fundoplication was found to be intact in 59 (69%) of children after a median of 7.8 (IQR 2.0–15) years. In 27 (31%) children, fundoplication failed after a median of 17 (IQR 8–183) months of follow-up. Failure rate in type A OA was 7/10 (70%), B 0/2 (0%), C 20/69 (29%), D 0/4(0%) and F 0/1 (0%). Logistic regression analysis of fundoplication failure showed that long gap OA (type A or B) was the only statistically significant predisposing factor, RR = 3.8 (95%CI = 1.1–13); P = 0.04.

Of 27 children with failed fundoplication two underwent oesophageal reconstruction because of recalcitrant anastomotic stenosis and recurrent tracheooesophageal fistula. Thirteen (54%) patients (OA type A n = 4, type C n = 9) underwent redo fundoplication because of recurrent significant symptoms of GORD a median of 17(IQR 5.6–37) months after the first fundoplication. Indications for redo fundoplication (RAS) n = 2, respiratory symptoms n = 5, vomiting n = 5, dysphagia n = 1) differed from the indications from the original fundoplication (RAS n = 11, ALTE n = 1, respiratory symptoms n = 1). Among 13 children with redo fundoplications four (31%) had a new failure and nine remain with a patent fundoplication.

Among the remaining 12 children with failed fundoplication (type A OA n = 3, type C n = 9) (original indications RAS n = 6, ALTE n = 4, respiratory symptoms n = 1, oesophagitis n = 2, vomiting n = 1) GORD associated symptoms attenuated or were successfully managed nonoperatively in nine. Seven with failed first or redo fundoplication remained with significant GORD symptoms. Of these seven, three

<p>| Table 2 | Indication for fundoplication in patients with oesophageal atresia (RAS = recalcitrant anastomotic stenosis, ALTE = acute life threatening events, Respiratory = respiratory symptoms) |
|---------|--------------------------------------------------|---------------------------------|---------------------------------|---------------------------------|--------|</p>
<table>
<thead>
<tr>
<th>RAS</th>
<th>ALTE</th>
<th>Respiratory</th>
<th>Oesophagitis</th>
<th>Vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n = 10)</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>B (n = 2)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C (n = 68)</td>
<td>29</td>
<td>14</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>D (n = 4)</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F (n = 1)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

| Table 3 | Endoscopic follow-up from birth to latest follow-up endoscopy, all OA patients from 1980- to 2016 (n = 290) included. |
|---------|--------------------------------------------------|--------------|--------|
| Follow-up | Results available in 165 (81%) | Results available in 81 (92%) |
| (median, yrs) | (IQR 3.0–16) | (IQR 5.5–17) | P |
| Oesophagitis | | | |
| • no | 127 (77%) | 54 (69%) | 0.16 |
| • mild | 33 (20%) | 19 (24%) | 0.50 |
| • moderate | 5 (3%) | 5 (6%) | 0.30 |
| • severe | 0 (0%) | 1 (1%) | 0.32 |
| • lost to follow-up | 39 | 7 | 0.02 |
| Metaplasia | | | |
| • No | 156 (94%) | 65 (82%) | 0.04 |
| • Gastric | 8 (5%) | 12 (15%) | 0.01 |
| • Intestinal | 1 (1%) | 2 (3%) | 0.24 |
have died and four children were unfit for further antireflux surgery and are managed with feeding jejunostomy (n = 2) or gastrostomy (n = 2).

4. Discussion

About 1/3 of our present series of children born with OA are coming to fundoplication. We feel that our main findings are a relatively low mortality (7%) caused by OA associated diseases rather than the fundoplication itself. Fundoplication aided materially in the management of GORD related symptoms although complete control of symptoms was not achieved. This is mainly because of the etiology of ALTE and respiratory symptoms in patients with OA is multifactorial including GORD, tracheomalacia, heart disease and reactivity of the respiratory tract and the decision to fundoplication is often based on clinical findings. Management of GORD with fundoplication had positive effect on the resolution of recurring stenosis of the oesophageal anastomosis by endoscopic dilatation. However, in approximately one fourth of the patients with anastomotic stenosis fundoplication did not result in resolution of the stenosis by continued dilatations, and surgery was required. Failure rate of fundoplication was relatively high, 31%, but compared with contemporary literature not exceptionally high in patients with OA [18,19]. Lastly endoscopic follow-up showed that those who have undergone fundoplication, i.e. those with the severest form of OA associated GORD, have a similar rate of oesophagitis and intestinal metaplasia as other patients with OA.

The weakness of our study is its retrospective design. Excluding anastomotic stenosis that can be diagnosed with an endoscope with reasonable objectivity, detailed assessment or grading of GORD symptoms such as heartburn and respiratory symptoms and their attenuation after fundoplication by retrospective review of hospital records is difficult. We could not show in a statistical analysis how much fundoplication managed the management of recalcitrant anastomotic stenosis, that is, whether lasting anastomotic patency was achieved with less endoscopic dilatations that would have been the case without fundoplication, because we had no control group of patients with recalcitrant anastomotic stenosis without fundoplication. Endoscopic follow-up, while being imposed on the majority of the patients, was not comparable of the modern diagnostic standards of Barrett's oesophagus.

GORD in those with OA is often persistent and it is known that the incidence of premalignant oesophageal mucosal changes such as Barrett's oesophagus with intestinal metaplasia increases when the patients reach young adult age [9,10]. In the present series the incidences of oesophagitis and intestinal metaplasia were relatively low in patients both with and without fundoplication. Compared with the rest of the series the patients who underwent fundoplication had higher rate of gastric metaplasia. While gastric metaplasia may be a result of an oesophageal biopsy taken too distally in relation to the oesophagogastric junction, an error easily made in a fundoplicated patient, the presence of gastric metaplasia in the distal oesophageal mucosa may be a true finding and signal the coexistence of intestinal metaplasia [20]. Whether fundoplication offers any protection against Barrett's oesophagus cannot be confirmed by our results.

We found that failure of fundoplication was common in patients with OA, and those with long-gap OA are at the highest risk of failure. GORD could be managed conservatively after the failure of the fundoplication in less than half of our cohort. We observed that several patients who as infants underwent fundoplication and had successful treatment of RAS or ALTE suffered failure of the fundoplication but the remaining GORD symptoms could be managed conservatively. In the majority of patients, however, failure of fundoplication resulted in recurrence of symptoms of GORD, although often in other forms than RAS or ALTE. After failure of first fundoplication, a trial of conservative management may, however, be worth trying because we found a not insignificant failure rate also in redo fundoplications.

References