## JPGN Journal of Pediatric Gastroenterology and Nutrition Publish Ahead of Print

DOI: 10.1097/MPG.000000000000961

# Insufficient body weight of adults born with esophageal atresia

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Word count: 2623

Number of tables: 2

Number of figures: 0

## **Roles of each author:**

Dr Presse was responsible for conception of the work, data analyses, interpretation of data, and drafting of the manuscript.

Ms Taillefer was involved in conception of the work, data collection, and interpretation of data.

Dr Maynard was responsible for conception of the work, data collection, and interpretation of data.

Dr Bouin was responsible for conception of the work, interpretation of data, and critical revision of the manuscript.

All authors gave final approval of the manuscript.

Insufficient body weight of adults born with esophageal atresia

### ABSTRACT

**Objectives**: Impaired growth has been reported in children born with esophageal atresia (EA). Their nutritional fate at adulthood remains uncertain though. Our objectives were to determine the body mass index (BMI) of adult EA patients followed-up from 2009 to 2011 in the EA clinic of a university-affiliated hospital in Quebec (Canada); and investigate characteristics associated with underweight.

**Methods**: The 40 adult EA patients attending the clinic were invited to participate. Height and weight were measured and BMI calculated. Patients with BMI<18.5kg/m<sup>2</sup> were deemed underweight. Patients' characteristics were obtained, including digestive symptoms and compensatory eating behaviors. Non-parametric tests were used to compare the proportion of underweight among EA patients with that found in the Quebec population, and to compare the characteristics between EA patients deemed underweight and those with BMI  $\geq$ 18.5kg/m<sup>2</sup>. **Results**: The final sample included 16 women and 21 men, aged 18 to 44 years. Mean BMI was 21.3±4.9 kg/m<sup>2</sup> and 24.3% had BMI<18.5kg/m<sup>2</sup>, which is higher than in the Quebec adult population (2.5%; *P*<0.001). Compared to EA patients having BMI $\geq$ 18.5kg/m<sup>2</sup>, underweight patients had more often failure to thrive that persisted beyond 12 years old (55.6 vs 7.4%; *P*=0.006), severe postprandial fullness (62.5 vs 21.4%; *P*=0.040), the need to eat slowly (87.5 vs 46.4%; *P*=0.045), and severe difficulties to swallow dry solid foods (50.0 vs 14.3%; *P*=0.054). **Conclusions**: Insufficient body weight is prevalent in this sample of adult EA patients and could result from digestive symptoms. Follow-up with a gastroenterologist and nutritional counselling should be considered for adult EA patients.

Keywords: esophageal atresia, adults, body mass index, underweight.

## What is Known:

-EA is surgically corrected in neonates with survival rates now over 90%.

-EA patients present often esophageal morbidities and feeding difficulties.

-Growth retardation has been observed in children born with EA.

# What is New:

-There is a high prevalence of insufficient body weight in adults operated for EA in childhood.

- EA adults with insufficient body weight were more likely to have suffered from failure to thrive up to their adolescence.

-Virtually all EA adults reported gastro-intestinal symptoms and/or compensatory eating behaviors.

-Postprandial fullness, slow eating and dysphagia were associated with insufficient body weight in EA adults.

### INTRODUCTION

Esophageal atresia (EA) with or without tracheoesophageal fistula (TEF) is a rare congenital malformation occurring in 1.8 to 3.2 per 10,000 live births (1-3). EA is surgically corrected in neonates, with survival rates currently over 90% (2, 4-6). However, despite the surgical correction, EA patients often remain with esophageal morbidities and feeding difficulties (7). The most reported problems are dysphagia and gastroesophageal reflux disease (GERD), but other conditions such as food impaction, prolonged meal times, hiatal hernia, Barrett's esophagus, esophagitis, and epithelial metaplasia are relatively frequent (7, 8). Complications such as esophageal stricture and recurrent fistula can also arise, which would require subsequent surgical procedures. This can be further compounded by the presence of other congenital anomalies which are associated with approximately half of EA cases, notably cardiac and renal malformations, axial skeleton and limb reduction defects, anal atresia, and genital anomalies (3-5). Respiratory problems, such as bronchiolitis, respiratory infections and tracheomalacia, are also frequent in EA patients and often require further hospitalizations (5).

Feeding difficulties, in addition to the burden of morbidities and repeated surgical procedures, can impair the nutritional status and thus, lead to failure to thrive and malnutrition in children born with EA. In fact, growth retardation has been reported repeatedly, although most data suggesting a mild degree of severity (4, 5, 8-12). Recent data from the French National Esophageal Atresia Register also revealed a prevalence of malnutrition of 15% at 12 months of age (5). Data drawn on older individuals remain scarce though. Little *et al* reported low weight-to-age in 17% of 42 EA patients aged 10-26 years (8). Conversely, three studies based on samples of adult EA patients observed only a few cases of insufficient body weight (7, 13, 14). However, most individuals included in these studies are born before 1980 so that these data could be no longer representative.

As survival rates improved, the number of EA patients reaching adulthood has increased, and so as the need to gain further insights on lifelong morbidities associated with EA (15). In light of the limited updated data in regard to the nutritional status of adult EA patients, we undertook a study aiming to: 1) determine the height, weight, and body mass index (BMI) of adults born with EA and attending the EA clinic of a university-affiliated hospital between 2009 and 2011; and 2) investigate which characteristics differ significantly between adult EA patients who were underweight (BMI<18.5 kg/m<sup>2</sup>) and those with BMI≥18.5kg/m<sup>2</sup>. These characteristics included gender, age, and self-reported gastrointestinal problems and compensatory eating behaviors, in addition to the characteristics of the EA, the presence of associated anomalies, and prior history of failure to thrive during childhood and adolescence.

## **METHODS**

The study was conducted at the EA clinic of the gastroenterology service, Hôpital St-Luc, Centre Hospitalier de l'Université de Montréal (CHUM), Montréal, Canada. From 2009 to 2011, the 40 patients aged 18 years or older, followed at the EA clinic, have been invited to participate in the present study. Patients were also asked to authorize access to their medical records from the pediatric hospital where the surgery was performed. The study has been approved by the Research Ethics Committee of the CHUM. Data collection has been conducted by a physician and a research assistant.

# Data collection

Each EA patient has been interviewed once at the EA clinic. Gender, age (years), the type of EA according to Gross classification (16), the type of correction surgery of EA, and the presence of other congenital anomalies have been determined. Height (m) and weight (kg) of patients have been measured and BMI calculated as kg/m<sup>2</sup>. Z-score for height, according to

gender and age (up to 20 years), has been calculated based on CDC growth charts (17). Patients were deemed as being of 'short' or 'tall' stature when their Z-score was below or above 1.96, respectively. Weight for height has been evaluated using BMI, classification being as underweight (BMI<18.5 kg/m<sup>2</sup>), normal weight ( $\geq$ 18.5 and <25 kg/m<sup>2</sup>), overweight ( $\geq$ 25 and <30 kg/m<sup>2</sup>), and obese ( $\geq$ 30 kg/m<sup>2</sup>).

Adult EA patients were then questioned about their gastrointestinal problems and compensatory eating behaviors. Patients were first asked whether they suffered from heartburn, regurgitation, dysphagia, food blockage, odynophagia, epigastric burning, nausea, vomiting, postprandial epigastralgia, eructation, postprandial fullness, bloating, diarrhea, constipation, abdominal pain, and fecal incontinence. For those who reported suffering from dysphagia, they were further asked to specify which kind of foods poses swallowing difficulties: liquids, thick liquid foods, solids, dry solid foods, and soft solid foods. Patients were then asked whether they have compensatory eating behaviors including the need to drink while eating, the need to eat slowly, and the avoiding of some particular foods. For each gastrointestinal symptom or compensatory eating behavior reported, patients were asked to grade their severity on a scale from 1 to 4. Symptoms have been deemed 'severe' whenever a score of 3 or 4 were selected. Of note, none of EA patients included in this sample received tube feeding or parenteral nutrition at the time of data collection.

When possible, any data on height (cm) and weight (kg) up to 18 years old have been collected from the growth chart available in their medical records of the pediatric hospital where the surgery was performed. Failure to thrive has been defined as weight less than the 3<sup>rd</sup> percentile for age, according to the CDC growth charts (17). EA patients who had at least one record of 'failure to thrive' before the age of 18 have been identified. Among them, those who did not catch-up before the age of 12 years old were also identified.

#### Statistical analyses

Characteristics of EA patients at birth and adulthood have been summarized as means (±SD) or percentages, as appropriate. Median Z-score for height has been tested different from zero using Wilcoxon test; zero being the median z-score expected in the adult population (17). Similarly, one-sample binomial test was used to compare the proportion of 'short stature' in our sample of adult EA patients in comparison with that expected in the CDC grow charts (2.5%) (17). Wilcoxon test was used as well to compare median BMI of the study sample with that reported in a population survey conducted in 2009-2010 in the Province of Quebec, Canada (18). Similarly, one-sample binomial test was used to compare the proportion of 'underweigh' in our sample of adult EA patients in comparison with that expected in the Quebec population (2.5%) (18).

Among the sample of adult EA patients, median BMI was compared between sex using the Mann-Whitney test. Spearman correlations were used to assess the relationship between BMI and age and between BMI and Z-score for height. Finally, one-tailed Fisher exact tests were used to examine whether some patients' characteristics were significantly more frequent among underweight adult EA patients, in comparison with adult EA patients with a BMI  $\geq 18.5$ kg/m<sup>2</sup>. *P*<0.05 has been considered significant. All statistical analyses were performed using IBM SPSS Statistics 22 software (SPSS Inc, Chicago, IL).

## RESULTS

Sixteen women and 21 men, aged from 18 to 44 years at the time of the medical interview, agreed to participate in the present study. At birth, most had EA with distal TEF and two thirds had at least one associated congenital anomaly, mainly vertebral defects and congenital heart diseases (Table 1). For most patients, EA was surgically corrected by primary anastomosis.

### Height, weight, and body mass index

Review of medical records from childhood (n=36) revealed that 23 EA patients (63.9%) had history of failure to thrive during childhood in terms of weight-to-age. Most caught-up before the age of 12 years old but still, 7 patients (19.4%) had low weight-to-age during adolescence. Once they have reached adulthood, data revealed that mean Z-score for height was negative and significantly different from zero (P=0.002), indicating that adult EA patients in our sample were overall smaller than what would be expected in a sample of the adult population, according to the CDC grow charts (17) (Table 2). Consequently, the proportion of patients with 'short stature' was also higher than expected from the CDC grow charts (16.2% *vs* 2.5%; P<0.001). Of note, no patients were found with 'tall stature'.

Median BMI in our sample (20.9 kg/m<sup>2</sup>) was significantly lower than that found in a survey conducted in the Quebec adult population (25.2 kg/m<sup>2</sup>; P<0.001) (18). Nine adult EA patients (24.3%) had BMI<18.5 kg/m<sup>2</sup>, which is 10 times higher than what can be expected in adults of Quebec (2.5%; P<0.001). Only 2 of our patients were obese (BMI  $\geq$ 30 kg/m<sup>2</sup>).

Among adult EA patients included in this study, median BMI did not differ between sex (P=0.21), and BMI was not significantly correlated with age (Spearman rho=0.26; P=0.13) or with the Z-score for height (Spearman rho=0.08; P=0.65). Nonetheless, none of EA patients aged >30 years (n=8) were underweight. Also, underweight EA patients have more often suffered from failure to thrive that persisted beyond 12 years old (55.6 vs 7.4%; P=0.006), in comparison with adult EA patients with BMI ≥18.5 kg/m<sup>2</sup>. Conversely, no significant difference was found with the type of EA, the type of correction surgery performed, and failure to thrive at any time before adulthood.

#### Gastrointestinal problems and compensatory eating behaviors

Thirty-six of the 37 EA patients agreed to be questioned about their gastrointestinal problems and compensatory eating behaviors. Virtually all of them (89.2%) reported at least one gastrointestinal symptom and/or compensatory eating behavior (Table 2). The most common were 'the need to drink while eating', dysphagia, 'the need to eat slowly', and postprandial fullness. Dysphagia was most often associated with difficulties to swallow solid foods (58.3%), especially dry solid foods (36.1%). Severe problems were infrequent, except for dysphagia and postprandial fullness which were both deemed severe by 30.6% of patients. Results from the Fisher exact tests showed that underweight EA patients reported significantly more often to have severe postprandial fullness (62.5 vs 21.4%; P=0.040), and the need to eat slowly (87.5 vs 46.4%; P=0.045), than adult EA patients with BMI  $\ge$ 18.5 kg/m<sup>2</sup>. Severe difficulties to swallow dry foods also tended to be more frequent among underweight adult EA patients than others (50.0 vs 14.3%; P=0.054).

### DISCUSSION

The present study contributes significantly to the body of knowledge on nutritional status in adults operated for EA in childhood. Our findings showed a high prevalence of insufficient body weight among adult EA patients, especially in young adults who have suffered from failure to thrive up to their adolescence. Postprandial fullness, slow eating, and dysphagia can be important factors leading to underweight in adult EA patients.

To our knowledge, there is only one study reporting BMI data from adults operated for EA during childhood (7). Their results contrast with ours since none of their 101 EA patients, aged 21-57 years old and born between 1947 and 1985, had BMI<18.5 kg/m<sup>2</sup>. The fact that our findings contrast with those of Sistonen *et al* can stem from two biases, either a survival and/or a

sampling bias. A survival bias is likely in studies of EA adults as survival rate has increased over decades (2, 4, 5). In the present study, no patients aged over 30 years were found to be underweight. These findings can reflect the overall improvement in care over time, which allows for more severely ill and complex neonates with EA to survive and reach adulthood (19). In consequence, comparison with previous studies might be made with caution, bearing in mind that the EA cohort is becoming more severely ill over time. A sampling bias is also possible among our study participants as all of them have been referred to a gastroenterologist once they reached 18 years old. These patients could have more morbidities than those who were not referred and thus, be more likely to present poor nutritional status. In fact, while the sex ratio and the types of EA in our sample are typical (2-4), the proportion of patients with associated anomalies was slightly higher than that reported in a recent population-based cohort; 67.6% in our study *vs* 53% in France (2). Nonetheless, despite this contrast with the study by Sistonen *et al*, our findings raise concern regarding the nutritional fate of these patients over a lifetime.

Factors associated with underweight in adult EA patients have not been examined in previous reports. In a 60-year series of 269 surviving EA patients from The Netherlands, 7% were found with height and weight below the fifth percentile for age during the postoperative period (4). In this latter study, impaired growth were associated with GERD and low birth weight, while no association was found with the type of EA (4). History of GERD was also associated with low weight to height in a sample of 57 EA patients aged 9.5-18.5 years, but not dysphagia or the presence of associated anomalies (20). In the present study, failure to thrive beyond the age of 12 years old was the patients' characteristic most strongly associated with underweight at adulthood, suggesting that these patients had prior history of feeding difficulties and insufficient energy intake. Our findings also underlined that these patients were more likely to report severe postprandial fullness, slow eating, and severe difficulties to swallow dry solid

foods, three digestive symptoms which were common in our patients as well as in other samples of EA adolescents and adults (20-22). These digestive symptoms could be the result of poor esophageal emptying due to impaired esophageal motility. In fact, esophageal manometry in adult EA patients showed that 78-80% had non-propagating peristalsis and 85-95% low and ineffective distal wave amplitudes of the esophageal body (7, 23). High prevalence of impaired motility of the esophagus has been also reported in adolescent and young adult EA patients (24-28). This lack of effective propulsive contractions means that the esophageal of many EA patients basically empties by gravity, which implies slow eating, early fullness sensation, and increased risk of foods that get stuck in the esophagus such as dry solid foods. Symptoms of dysphagia have in fact been correlated with impaired esophageal motility in a previous study (27). Moreover, symptoms associated with slow esophageal emptying may be set to increase as EA patients age since esophageal transit time has been shown to be longer in EA adults compared with EA adolescents and children (28). Prospective research focusing on the relationships between esophageal motility, its associated digestive symptoms and its impacts on dietary intakes and the nutritional status should be conducted in adult EA patients.

Our findings have clinical implications. They foremost reinforced the fact that despite EA surgical correction, patients age with several esophageal morbidities that can impact their growth and lead to poor nutritional status at adulthood. This stresses the need for a lifelong follow-up by a gastroenterologist and when relevant, by a dietitian to ensure adequate energy intake despite the digestive symptoms. In a recent study conducted in France, it was shown that less than 10% of EA patients consulted with a gastroenterologist, and no further follow-up has been done after the age of 12 years old (9). Similarly, nutritional counseling does not seem integrated in care to EA patients. In fact, according to Gischler *et al*, only 13% of parents consulted with a dietitian during the child's first year, despite the nutritional morbidity following the EA surgery (12). In

the Netherlands, the multidisciplinary follow-up schedule of EA patients has been recently described by IJsselstijn *et al* and surprisingly, does not include follow-up by a dietitian at any time throughout the life course (29). As suggested in a previous report (15), our findings bring support for a lifetime follow-up by a gastroenterologist and when relevant, by a dietitian. Moreover, it seems advisable to recommend monitoring the weight of adult EA patients in order to ensure early nutritional management of underweight patients or of any unintentional weight loss.

Limitations of the present study include the cross-sectional design and the small sample size, although this number is appreciable given the low incidence of EA. As discussed above, generalizability of our data may also be limited by a potential selection bias. Finally, the use of non-parametric tests could have limited the power of statistical analyses but at the same time, has ensured the robustness of our findings.

In conclusion, the present study suggests that BMI<18.5kg/m<sup>2</sup> is not uncommon in this sample of adults who have been operated for EA during childhood. Digestive symptoms could be important risk factors of poor nutritional status, especially the early sensation of fullness at meals. Lifetime follow-up by a gastroenterologist, and nutritional counselling when needed, should be integrated in care of EA patients to prevent failure to thrive and avoid insufficient body weight at adulthood. Results from the present report also stress the need for further research focusing on the nutritional status of adults born with EA.

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followed at the EA clinic of a university-affiliated hospital.	
Characteristics	Values
Male, %	56.8
Male/Female ratio	1.31
Type of esophageal anomaly, % <sup>a</sup>	
EA without TEF, type A	16.2
EA with distal TEF, type C	83.8
Associated congenital anomalies, %	67.6
Vertebral defects	45.9
Congenital heart diseases	29.7
Renal abnormalities	18.9
Anorectal malformations	13.5
Central nervous system anomalies	13.5
Genital hypoplasia	10.8
Limb abnormalities	5.4
Others	32.4
Type of EA correction surgery, %	
Primary anastomosis	81.1
Gastric pull-up	10.8
Colonic transposition	8.1
EA esonhageal atresia: TEE tracheoesonhage	al fistula

**Table 1.** Neonate characteristics of 37 adult EA patients followed at the EA clinic of a university-affiliated hospital.

EA, esophageal atresia; TEF, tracheoesophageal fistula <sup>a</sup>According to Gross classification.

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Characteristics	Values
Age, y, mean±SD	25.3±6.9
Nutritional status	
Height, Z-score, mean±SD <sup>a</sup>	-0.87±1.64
Short stature (Z-score <-1.96), %	16.2
Body mass index, $kg/m^2$ , mean $\pm$ SD	21.3±4.9
Underweight (<18.5 kg/m <sup>2</sup> ), %	24.3
Overweight or obese ( $\geq 25.0 \text{ kg/m}^2$ ), %	16.2
astrointestinal problems, % <sup>b</sup>	
Dysphagia	63.9
Postprandial fullness	55.6
Regurgitation	52.8
Heartburn	44.4
Food blockage	44.4
Bloating	33.3
Epigastric burning	30.6
Diarrhea	27.8
Eructation	22.2
Postprandial epigastralgia	19.4
Nausea	19.4
Odynophagia	19.4
Constipation	19.4
Abdominal pain	16.7
Fecal incontinence	11.1
Vomiting	8.3
ompensatory eating behaviors, % <sup>b</sup>	
Need to drink while eating	69.4
Need to eat slowly	55.6
Avoiding some particular foods	13.9

**Table 2.** Characteristics of 37 adult EA patients from the EA clinic of a university-affiliated hospital.

<sup>a</sup>Z-scores were determined based on the CDC growth charts. <sup>b</sup>Percentages are based on n=36.