**Background**

To determine if birth-weight (BW) influences primary surgical management of newborns undergoing operation for esophageal atresia and tracheo-esophageal fistula (EA-TEF).

**Methods**

Newborns undergoing repair of esophageal atresia at a single specialist centre between 1999 - 2017 were categorised into three groups based on BW ; Group A < 1.5kg, Group B <2.5kg and Group C >2.5kg. Outcome data analysed were ( i ) technical ability of the surgeon to perform primary esophageal anastomosis, ( ii ) anastomotic leak, ( iii ) anastomotic stricture,

( iv ) esophageal replacement, ( v ) need for other procedures notably fundoplication, aortopexy, tracheostomy and ( vi ) mortality. Statistical analysis was performed using a two-tailed Fisher’s exact test and logistic regression.

**Results**

198 patients underwent surgery for EA-TEF during the study period, Group A (n = 13), Group B (n = 73) and Group C (n = 112). Inability to perform a primary anastomosis was significantly higher in Group A vs Group B (p = 0.003) and Group C (p = 0.004). Birthweight was a significant variable in the ability to perform a primary esophageal anastomosis (OR 1.009, p = 0.004). Mortality rate was significantly higher in Group A vs Group C (P = 0.0158).

**Conclusions**

Very low birth weight infants are less likely to achieve a definitive primary anastomosis during emergent repair of esophageal atresia, and have a higher mortality.

**Keywords**

Esophageal atresia, tracheo-esophageal fistula, primary anastomosis, clinical outcomes, mortality, birth weight.

**Level of evidence**

III

**Introduction**

It has been previously suggested that very low birth weight infants (VLBW) undergoing operation for esophageal atresia are a ‘high risk’ peri-operative group[1]. Spitz and colleagues havereported a marked decline in survival from 98% to 82% for newborns having a birthweight > 1500g compared to those with birthweight < 1500g[1]. VLBW has also been proposed as an independent risk factor for mortality for patients with esophageal atresia in several studies recently[2,3].

A recent report by Schmidt et al 2017 stated that in extremely low birthweight and very low-birth weight (VLBW) newborns with esophageal atresia, surgical outcome after primary EA-TEF repair did not differ significantly compared to those infants with a birth weight > 1500g[4].

Against this background of ongoing debate, this study analyzed a large cohort of newborns undergoing operation for EA-TEF at a ‘high volume’ UK specialist center to determine whether or not birth weight does impact on the surgical outcomes.

**Material and Methods**

Newborns undergoing surgery for EA-TEF during the era 1999 - 2017 at a single specialist UK paediatric surgical center were categorised into three ‘at risk’ groups based on birth weight: Group A (< 1.5kg), Group B (< 1.5 - 2.5kg) and Group C (> 2.5kg) [Figure 1].

Data collected on index cases included: ( i ) birth weight, ( ii ) date of primary surgery, ( iii) associated co-morbidities, ( iv ) Gross classification EA-TEF, ( v ) whether or not a primary esophageal anastomosis was safely feasible , ( vi) intra-operative complications including anastomotic leak, esophageal stricture rate(s), ( vii ) additional surgical operations notably fundoplication, aortopexy, tracheostomy, need for esophageal replacement, and ( viii ) mortality [Table 1].

Surgery was undertaken by a team of consultant surgeons with a sub-specialist interest in EA-TEF with the support of residents in pediatric surgery of varying training grade(s).

Only patients with Gross classification types A, B, C and D were included in the study.

Statistical analysis was performed using a two-tailed Fisher’s exact test to determine if there were significant difference(s) between the three groups in terms of the outcome measures. A p value < 0.05 was statistically significant. Logistic regression was also used to assess the effect of birthweight on the ability to perform a primary esophageal anastomosis.

**Results**

A total of 198 newborns underwent surgery for EA-TEF during the era 1999 - 2017 respectively . Thirteen babies had very low birth weight < 1.5kg ( Group A - VLBW ), 73 cases had low birth weight < 2.5kg ( Group B - LBW ) and 112 had ‘normal’ birth weight > 2.5kg ( Group C – NBW ). Gross classification - Type A n = 15, Type B n = 3, Type C n = 174 and Type D n = 6 ( Figure 1 ).

All patients following operations were followed up at a dedicated specialist multidisciplinary EA -TEF clinic until 18 years of age and then transitioned to adult services for ongoing aftercare.

With the exception of Group A having a higher proportion of index cases with genitourinary (GU) anomalies (duplex kidney, VUR, horseshoe kidney, hypospadias, renal agenesis, multicystic dysplastic kidney) vs Group C p = 0.043 all 3 groups did not differ in terms of other recorded co-morbidities as outlined in Table 2. The presence of genitourinary anomalies within Group A did not influence survival (3/5 patients with GU anomalies survived vs 6/8 without GU anomalies surviving p = 0.6084).

Inability to perform a primary esophageal anastomosis was significantly higher in Group A vs Group B ( 7/13 vs 10/73, p = 0.003 ) and Group C (7/13 vs 11/112, p = 0.004). This outcome measure did not differ significantly between Groups B and C ( 10/73 vs 11/112, p = 0.646). Logistic regression analysis showed birthweight was a significant variable in the ability to perform a primary esophageal anastomosis (OR 1.009, p = 0.004). Using the logistic regression model the probability of performing a primary esophageal anastomosis decreasesd sequentially from 91% for infants with a birthweight of 3000g to 61% and 50% for infants with a birthweight of 1000g and 500g respectively [Table 4].

No significant differences were observed in the three patient groups in terms of anastomotic leak rates - Group A (1/13) vs Group B (7/73) p = 1.000, Group A (1/13) vs Group C (6/112) p = 0.545, Group B (7/73) vs Group C (6/112) p = 0.378.

Esophageal stricture rates were significantly lower in Group A vs Group C ( 2/13 vs 61/112 p = 0.0086). Stricture rate did not differ between Group A vs Group B (2/13 vs 32/73, p = 0.0661) or between Group B vs Group C (32/73 vs 61/112, p = 0.1774).

No significant differences were found between the three groups in terms of the proportion of infants subsequently requiring major esophageal replacement ( Group A 3/13 vs Group B 8/73 p = 0.3603, Group A 3/13 vs Group C 9/112 p = 0.1114, Group B 8/73 vs Group C 9/112 p = 0.6043).

The requirement for additional major operative procedures other than esophageal replacement notably fundoplication, aortopexy and tracheostomy did not differ significantly between the three groups with the exception of a higher proportion of patients in Group A 3/13 requiring tracheostomy compared to patients in Group C 3/112, p = 0.0149 [Table 3].

Mortality rate was significantly higher in Group A vs Group C ( 4/13 vs 7/112, P = 0.0158 ), though did not differ between Group A vs Group B ( 4/13 vs 7/73, p 0.0577 ) or between Group B vs Group C ( 7/73 vs 7/112 p = 0.4093).

**Discussion**

Outcomes after operation for esophageal atresia can vary significantly and may be determined often by factors unrelated to surgery itself [5]. Infant birth weight and presence of a significant structural cardiac abnormality, independently and in combination with EA-TEF , are recognized as robust prognostic factors ( Spitz Classification 1994 ) affecting overall survival [1, 6-9].

A recent noteworthy publication by Schmidt et al 2017 claiming that surgical outcomes in very-low-birth weight (VLBW) EA-TEF newborns were entirely equivalent and comparable to those achieved in babies with a birth weight > 1.5kg challenges many previously held convictions by pediatric surgeons that outcomes are often notably considered poorer in VLBW groups [4-9].

In this study we have shown that birthweight is a significant variable in determining the surgeon’s ability to perform a primary esophageal anastomosis. The inability to safely undertake a primary esophageal anastomosis was significantly higher in VLBW (54%) infants compared to LBW (14%) and NBW (10%) infants. The decreasing probability of performing a primary esophageal anastomosis with each 100g fall in birthweight was thereafter calculated using a logistic regression modelling tool and is outlined in Table 4. Of interest these 3 groups of index EA-TEF newborn cases did not differ significantly in terms of their Gross classification which is considered to influence rates of primary esophageal anastomosis[9,10]. Taken together these findings indicate that the disparity in varied clinical outcomes observed can be attributed to ‘other factors’ not only infant birth weight. We propose that VLBW infants have significantly fragile delicate tissue anatomy such that even the most experienced EA-TEF surgeon cannot undertake safe mobilization of the ‘primitive esophageal upper pouch’ in these ‘ high risk ‘ cases making primary repair at initial thoracotomy far from safe or possible. The physiological instability of many VLBW infants with their immature lung development at the time of emergent surgery also prohibits lengthy operating times making TEF fistula ligation alone by the pediatric surgeon the key ‘life saving’ priority. We would therefore counsel in these VLBW cases that delayed esophageal anastomosis should be scheduled at a later time allowing the infant to gain weight ( > 3.5Kg ) in the setting of a staged elective operative procedure.

The high mortality rate we observed in VLBW (31%) babies versus NBW (6%) in this study has been shown before by some authors in a number of studies[1,7,11]. Factors to consider here include the vulnerability of the VLBW newborn to overwhelming sepsis, high grade intra-ventricular haemorrhage, presence of lethal chromosomal anomalies and poor prognosis structural cardiac malformations[12]. In this study the three groups did not differ in terms of their co-morbidities at baseline, with the exception of VLBW infants having a higher proportion of genitourinary anomalies compared to NBW cases (Table 2). Interestingly Hartley et al [13] showed that survival for babies with esophageal atresia may be dependent on renal malformations in addition to cardiac anomalies. However in this study although VLBW infants had a significantly higher proportion of GU anomalies, the presence of a GU malformation did not statistically influence patient survival.

The low stricture rate observed in the VLBW (15%) cohort compared to NBW cases (54%) may be due to several confounding factors most notable of which is that our surgical unit adopts a policy of vigilant ‘after care’ through provision of a specialist multidisciplinary EA-TEF clinic at Alder Hey where we practice a policy of prophylactic balloon dilatation in all patients manifesting any symptom to suggest a feeding difficulty. It is acknowledged in these cases we may often encounter ‘mild’ esophageal anastomotic narrowing at endoscopy and / or associated dysmotility but we prefer to undertake elective surveillance to offset the distress patients and families can experience with ‘out of hours’ emergency hospital presentation [14]. We speculate that anastomotic wound healing in VLBW premature infants may also result in ‘ less scarring ‘ perhaps analogous to ‘fetal scarless healing’ hence yielding lower stricture rates [15].

The observation that VLBW infants were more likely to require a tracheostomy than NBW infants may be largely due to this group category having a high number of premature infants requiring a prolonged period of ventilatory support and were consequently more likely to develop complications such as subglottic stenosis, tracheomalacia and tracheal stenosis [16, 17].

In closing this study offers compelling data that usefully shows that whilst medical care has undoubtedly improved significantly for many VLBW infants born with EA-TEF in the modern era of care many challenges are worth reflecting notably ( i ) inability to perform a successful primary esophageal anastomosis at the 1st emergent operation and ( ii ) higher mortality rate for these fragile babies.