



Radiation exposure in infants with oesophageal atresia and tracheo-oesophageal fistula

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Abstract

Purpose Oesophageal atresia and tracheo-oesophageal atresia require surgical repair in early infancy. These children have significant disease-related morbidity requiring frequent radiological examinations resulting in an increased malignancy risk.

Methods A single-centre, retrospective review was performed of radiation exposure in children with OA/TOF born 2011–2015. Medical records were reviewed to determine the number and type of imaging studies involving ionising radiation exposure enabling the calculation of the estimated effective dose per child over the first year of life.

Results Forty-nine children were included. Each child underwent a median of 19 (IQR 11.5–35) imaging studies, which were primarily plain radiography (median = 14, IQR 7–26.5). The overall median estimated effective dose per patient was 4.7 (IQR 3.0–9.4) mSv, with the majority of radiation exposure resulting from fluoroscopic imaging (median 3.3 mSv, IQR 2.2–6.0). ‘Routine’ postoperative oesophagrams showed no leak in 35/36 (97%) with the remaining study showing an insignificant leak that did not alter management.

Conclusions Careful consideration should be given to the use of imaging in OA/TOF to minimise morbidity in these vulnerable infants. Oesophagrams in children without the symptoms of anastomotic leak or stricture should be discontinued. Standardisation of monitoring protocols with regard to radiation exposure should be considered.

Keywords Oesophageal atresia · Tracheo-oesophageal fistula · Radiation exposure · Fluoroscopy

Abbreviations

| | |
|--------|---|
| OA/TOF | Oesophageal atresia and tracheo-oesophageal fistula |
| GORD | Gastro-oesophageal reflux disease |
| IQR | Interquartile range |
| EED | Estimated effective dose |

Introduction

Oesophageal atresia and tracheo-oesophageal fistula (OA/TOF) are congenital conditions affecting approximately 1 in 4100 live births worldwide, with neonates typically

undergoing surgical repair within the first days of life [1, 2]. Although mortality has decreased with improving surgical technique and intensive-care children with OA/TOF still have ongoing morbidity and typically require frequent review and investigations [3, 4]. Many children experience significantly impaired health related quality of life due to persistent dysphagia, gastro-oesophageal reflux disease (GORD), and recurrent respiratory infections [5, 6].

Children with OA/TOF are frequently exposed to radiation through medical imaging for the purposes of diagnosis, monitoring, or therapeutic intervention. The consequences of exposure to high doses of ionising radiation have been documented in children treated for childhood cancers, particularly in the form of secondary malignancies [7]. Children are more vulnerable to the harmful and potentially carcinogenic effects of ionising radiation than adults, with the greatest risk occurring in those exposed early in life [7]. Furthermore, young children have a much longer life expectancy than adults and, therefore, a longer period during which to express these effects [8]. Little data is available regarding radiation exposure in complex neonatal surgical conditions; however, based on available data, infants with

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OA/TOF are exposed to higher levels of ionising radiation than other cohorts such as premature/low birth weight neonates and infants with necrotising enterocolitis [9, 10].

To date, two single-centre Canadian studies have measured radiation exposure in infants with OA/TOF. Zamiara et al. (2015) estimated radiation exposure over 0–3 years in 69 patients, but it was unclear as to when the exposure occurred and how these findings influenced management [11]. Yousef and Baird (2017) considered radiation exposure during the neonatal unit stay on 53 patients from another centre for the 9-year period 2005–2013 [12]. Neither study made specific recommendations on the impact of the studies on clinical management.

The aim of this study was to quantify the levels of radiation exposure in infants with OA/TOF within the Australian setting and to identify which imaging studies have the most significant contribution to this exposure. Secondly, our aim was to analyse the use of medical imaging, particularly fluoroscopy, in this cohort as to whether this resulted in a change in management. We hypothesise that this cohort of infants is exposed to significantly higher levels of ionising radiation than recommended due primarily to the use of fluoroscopy.

Methods

A retrospective review was performed of all patients admitted to the Children's Hospital at Westmead, Sydney, a large tertiary children's hospital, for management of OA/TOF between January 2011 and December 2015 with local ethics approval (HREC/15/SCHN/283). Patients with a coded diagnosis related to OA/TOF were identified. Patients who had their primary surgery at another institution were excluded.

The primary endpoints of the study were the number and type of medical imaging studies involving ionising radiation performed in the first year of life, as well as the overall radiation exposure during this period. Secondary outcomes included analysis of the use of fluoroscopy in this cohort and whether these studies affected management. The medical records and imaging studies of all patients were reviewed. Imaging studies not involving exposure to ionising radiation were not included. Estimated effective doses (EED) in mSv were calculated for each study based on historical published data from comparable institutions [11, 13, 14]. Based on these data an EED of 0.01 mSv per chest X-ray and 1.2 mSv per oesophagram (age 0–3 months) or 0.9 mSv (age 4–12 months) was used for calculation of overall radiation exposure [11]. Data analysis was performed using Prism 7 (GraphPad Software, Inc) with overall imaging and radiation exposure represented by the median and interquartile range. The use of oesophagrams was also analysed separately

including the indication for each study and the effect on management based on the medical records.

Results

General demographics

Fifty patients were identified who were treated at the Children's Hospital, Westmead for OA/TOF between 2011 and 2015. Forty-nine (98%) survived until discharge and were included for analysis. One preterm infant died on day 25 of life following the development of necrotising enterocolitis and was excluded.

27/49 (55%) were male with a mean birth weight of 2572 \pm 680 g. The mean gestational age was 37 \pm 3 weeks with 14 (29%) born less than 37 week gestation. 12/49 patients (24.5%) had at least two other features of VACTERL association in addition to OA/TOF. The distribution of type of OA/TOF was similar to the published literature, with the majority of patients (nearly 80%) type C OA/TOF (Gross classification) followed by 10% with isolated oesophageal atresia (type A), 6% with type B and 2% with type D and E (Table 1).

Method of repair

Overall, 37 of the 49 patients underwent repair of OA/TOF within the first 4 days of life. In 33/37 (89%), this was performed via a right thoracotomy. Four underwent thoracoscopic repair; however, one patient required conversion to thoracotomy due to failure to tolerate the induced pneumothorax.

Twelve patients (24%) required a delayed repair, due to long-gap oesophageal atresia. Six patients underwent a staged Foker procedure, and in two, a successful anastomosis

Table 1 General patient characteristics

| Patient characteristic | Number |
|------------------------------------|------------|
| Total number of OA / TOF patients | 50 |
| Number survived to discharge | 49 |
| Male:female | 27:22 |
| Mean birth weight (g) | 2572 |
| Mean gestational age (weeks) | 37 |
| VACTERL association | 12 (24.5%) |
| Type of OATOF | |
| A (isolated OA) | 5 (10.2%) |
| B (OA and proximal TOF) | 3 (6.1%) |
| C (OA and distal TOF) | 39 (79.6%) |
| D (OA and proximal and distal TOF) | 1 (2%) |
| E (isolated TOF) | 1 (2%) |

Table 2 Imaging studies by modality

| Imaging modality | Median number of studies (interquartile range) |
|---------------------|--|
| Total | 19 (11.5–35) |
| Plain radiography | 14 (7–26.5) |
| Fluoroscopy | 4 (3–8.5) |
| <i>Oesophagrams</i> | 2 (1–3.5) |
| CT | 0 (0–0) |
| Nuclear medicine | 0 (0–0) |
| Other | 0 (0–0) |

could not be achieved and the patients were discharged with an oesophagostomy in situ. Of the remaining six patients, one had a delayed diagnosis of H-type fistula without oesophageal atresia, and underwent a neck dissection and fistula ligation at 6 weeks of age. The other five patients initially had a gastrostomy formed followed by further delayed surgery. In two patients, oesophageal anastomosis was not feasible and an oesophagostomy was formed with the aim for a later repair. The remaining three patients underwent successful anastomosis.

Imaging by type

Within the first year of life, each patient underwent a median of 19 (interquartile range 11.5–35) medical imaging studies involving exposure to ionising radiation (Table 2). The greatest contribution to the overall number of studies was plain radiography with a median of 14 radiographs per patient (IQR 7–26.5). Fluoroscopic studies, both diagnostic and interventional, accounted for the second greatest number of imaging studies, with patients undergoing a median of four fluoroscopic studies overall (IQR 3–8.5) and two oesophagrams (IQR 1–3.5) during the first year of life (Fig. 1).

Radiation exposure

Overall, each patient was exposed to a median EED of 4.7 mSv (IQR 3.0–9.4) due to medical imaging within the first year of life (Table 3). Fluoroscopic imaging accounted for 70% of the total radiation dose with a median EED of 3.3 mSv (IQR 2.2–6.0) per patient. Oesophagrams were the study with the highest overall contribution to the EED with a median of 2.1 mSv per patient (IQR 1.2–3.8), making up 63.6% of the total fluoroscopic dose and 44.7% of the overall EED (Fig. 2).

Oesophagrams

Of the 45 patients who underwent an oesophageal anastomosis, only three (6.7%) did not undergo a routine postoperative

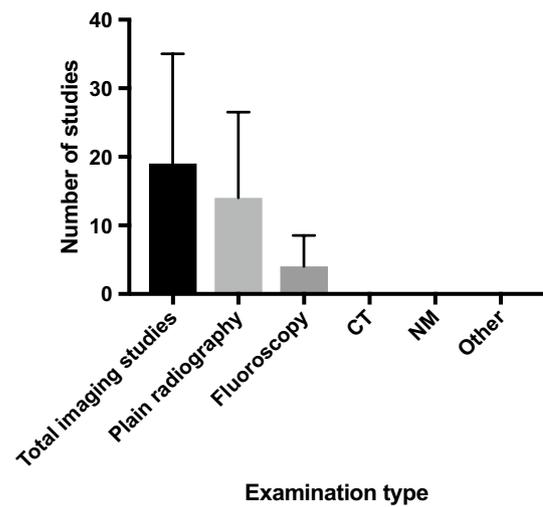


Fig. 1 Number of medical imaging studies (median + interquartile range)

Table 3 Median effective dose per patient

| Imaging modality | Median estimated effective dose in mSv (interquartile range) |
|--------------------|--|
| Total | 4.7 (3.0–9.4) |
| Plain radiography | 0.3 (0.2–0.4) |
| Fluoroscopy | 3.3 (2.2–6.0) |
| <i>Oesophagram</i> | 2.1 (1.2–3.8) |
| CT | 0 (0–0) |
| Nuclear medicine | 0 (0–0) |
| Other | 0 (0–0) |

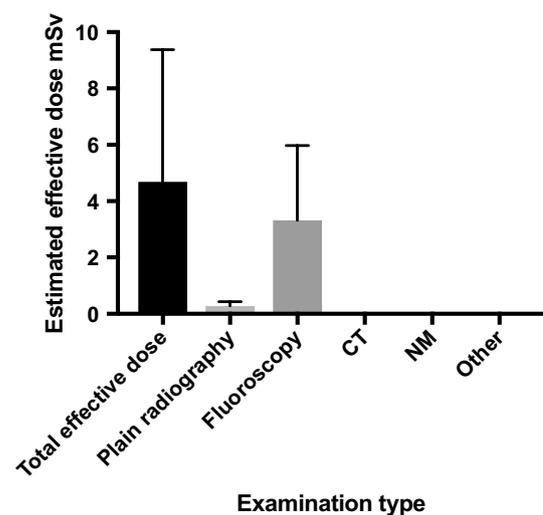


Fig. 2 EED per imaging type (median + interquartile range)

oesophagram. All three patients had uncomplicated recoveries and were discharged on oral feeds.

Of the remaining 42 patients, 6 patients (14%) had clinical suspicion of a leak, which was confirmed on contrast study in 3 patients. Out of the 36 patients who had 'routine' fluoroscopy with no clinical evidence of anastomotic leak, one patient had radiologic evidence of minor leak that was managed conservatively. There was no evidence of a persistent leak on a repeat contrast study performed 2 weeks later.

After the initial postoperative study, further oesophagrams were most frequently performed for investigation of a suspected stricture. In this cohort, 82.5% of patients who underwent contrast studies had clinical symptoms of a stricture as their indication for the contrast study (or, in the case of one patient, a known severe stenosis from an abnormal tracheobronchial remnant). Overall, 36.8% (21/57) of the oesophagrams resulted in a change in management (dilatation of stricture or in the case of the previously mentioned patient further surgery). In asymptomatic patients, however, oesophagrams only resulted in the change of management in 10% of cases, compared with 42.6% in patients with symptoms or other clinical suspicion of a stricture.

Discussion

Patients in our study were exposed to a median EED of 4.7 mSv during their first year of life, equating to approximately three times the average annual background radiation exposure in Australia of 1.5 mSv [15]. The exact risk of cancer development due to low-dose radiation from medical imaging (less than 10 mSv) is currently unknown but likely to be relatively insignificant compared to the overall lifetime risk of cancer in the general population [16]. There does, however, appear to be a linear relationship between cancer risk and radiation dose with no lower limit existing below which the associated risk is zero. Best practise, therefore, dictates limiting the number of radiological studies that patients undergo and ensuring that the radiation exposure per study is as low as is feasible [17]. This is of particular significance in children who are at higher risk due to their increased sensitivity to radiation and longer life expectancy in which to develop radiation-related side effects [16].

To date, little data have been published regarding radiation exposure in neonates and infants with surgical conditions despite the particular vulnerability of this cohort to the effects of ionising radiation. Various studies have demonstrated relatively low levels of radiation exposure in premature infants requiring intensive-care admissions, although this level increases with associated conditions such as chronic lung disease or requirement for central line placement [10, 18, 19]. Regarding surgical conditions specifically, infants with necrotising enterocolitis are exposed

to significantly higher levels of radiation than infants without surgical conditions [9, 10, 20]. The cumulative effective dose reported in infants with NEC is, however, significantly lower than in infants with OA/TOF based on the published literature.

The results of our study demonstrate comparable or lower radiation exposure in infants with OA/TOF to that reported by Zamiara et al. and Yousef and Baird. Zamiara et al. (2015) in their retrospective review of OA/TOF patients at the Hospital for Sick Children, Toronto, between 2001 and 2005 reported a mean effective dose of 17.4 mSv by age 3 years from a mean of 40 studies [11]. Fluoroscopy contributed the largest amount to radiation exposure (70% of total dose) with a mean of five studies per patient. Similarly, Yousef and Baird's 2017 review of 53 patients treated at the Montreal Children's Hospital over the period 2005–2013 demonstrated a median EED of 5.52 mSv per patient during the neonatal period, corresponding to a median 130-fold increased cumulative cancer mortality risk, primarily due to fluoroscopy (in particular oesophagrams) [12].

Given the differing time periods over which Zamiara et al. and Yousef and Baird conducted their reviews, it is difficult to directly compare the overall EED per child. Zamiara et al. reported an EED of 17.4 mSv over the first 3 years of life. This would correspond to a mean of 5.8 mSv per year, although it is likely that the radiation exposure during the first year of life would be significantly higher than in subsequent years. Similarly, Yousef and Baird's review only included data from the neonatal period where it would be expected that the highest number of imaging studies would be performed during the primary admission. Our results of a median 4.7 mSv over the first year of life, therefore, demonstrate lower radiation exposure than previously reported.

In our study, oesophagrams were the single investigation with the highest contribution to overall radiation exposure. Only five patients did not undergo an oesophagram at some point during their first year of life. Typically, patients who have undergone repair of oesophageal atresia undergo a routine postoperative contrast study prior to starting oral feeds. Further contrast studies may also be undertaken for the investigation of anastomotic leak or stricture, which remain significant complications following OA/TOF repair. In some centres, symptoms of anastomotic stricture such as dysphagia would be primarily investigated with endoscopy as opposed to fluoroscopy. Endoscopy provides certain benefits over fluoroscopy including the lack of radiation exposure, ability to assess and biopsy the oesophageal mucosa at the same time, as well as to perform a dilatation if required [21]. It is, however, associated with its own risks including those of undergoing anaesthesia.

Previous studies have questioned the necessity of routine oesophagrams in infants with OA/TOF. Yanchar et al. (2001) found that complications following OA/TOF repair (both

early and late) can often be predicted based on intraoperative findings and postoperative clinical signs and symptoms, and so suggested that contrast studies should be limited to symptomatic patients to confirm a diagnosis [22]. Patel et al., (2002) reported their experience with 40 patients with OA/TOF where contrast studies were not performed routinely but only when there was clinical suspicion of a leak or other complication. Only four patients required a contrast study during their admission; three due to symptom development (sepsis, lung consolidation, and tachypnea during feeds); one due to significant intraoperative dissection necessitating a prolonged period of postoperative paralysis and ventilation [23]. Similarly, Nambirajan et al., (1998) found that evidence of a radiological leak on contrast study without clinical evidence was not clinically significant and did not influence management or predict later stricture formation [24]. Golden et al. (2017) in their review of 3255 infants from 48 children’s hospitals in the United States reported that the use of oesophagrams in asymptomatic patients did not change the incidence of chest drain placement, re-operation, or dilatation within the initial postoperative period [25]. The authors, however, limited their analysis to oesophagrams performed within the first 15 days postoperatively and so were unable to comment on their use for the investigation of stricture and need for oesophageal dilatation beyond the initial postoperative period.

We demonstrated similar findings in our study. Postoperative oesophagrams in patients without a significant clinical suspicion of a leak were not found to change management. Beyond this initial study, we found that when used for investigation of anastomotic stricture in asymptomatic patients, contrast studies only resulted in a change in management in one out of ten cases. We would propose an algorithm for the management of patients with OA/TOF where oesophagrams are limited to patients with clinical symptoms of anastomotic leak or stricture (see Figs. 3, 4).

There are several limitations to our study. First, as direct estimates of radiation dose per study were not available from our institution, radiation dose was based on previously published historical data, primarily obtained from Zamir et al.’s 2015 study due to the comparable cohort and type of imaging studies undergone by the subjects [11]. Our results, therefore, reflect an estimate of the overall effective dose that, within the limitations of the data available from our institution, allows for the closest estimate of radiation dose and risk for each patient. We propose that to determine the actual radiation dose and risk for OA/TOF patients within the Australian context a prospective study would be of benefit using institute-specific radiation doses, particularly for fluoroscopy.

Second, our results are based only on medical imaging studies undertaken at our institute. As infants with OA/TOF require definitive management at a tertiary paediatric

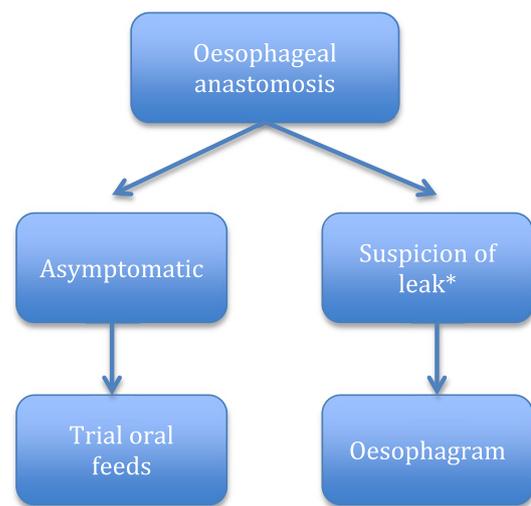


Fig. 3 Use of postoperative oesophagrams (*suspicion of leak on clinical findings such as increased drain output, respiratory infection/compromise, or persistent pneumothorax)

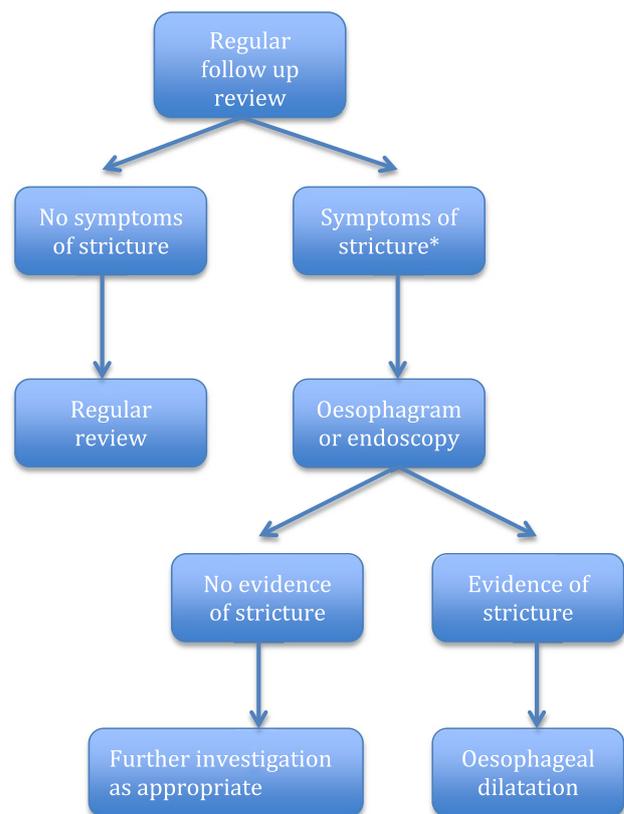


Fig. 4 Investigation of stricture (*symptoms of stricture including dysphagia, vomiting, choking, and feed intolerance)

centre, many patients in our study were transferred from other centres (both nationally and internationally). The actual number of imaging studies over the first year of life

is, therefore, likely to be higher than what is reported in our study as following discharge patients may have presented to and undergone investigations at their local hospital. It is difficult to estimate the overall contribution this may have had on the EED per patient; however, it is likely to have been low as studies such as fluoroscopy involving high radiation doses would typically be performed at a tertiary paediatric hospital.

Conclusions

Children with OA/TOF are exposed to significant levels of radiation throughout their first year of life. Our findings show that fluoroscopy and, in particular oesophagrams, contributed the greatest amount to the overall radiation exposure in these children. Routine postoperative oesophagrams prior to establishing oral feeds were non-contributory to management in those in whom there was no suspicion of anastomotic leak. Similarly, the use of oesophagrams in children without symptoms of stricture does not influence management. As children with OA/TOF may go on to have further complications and hospital admissions throughout childhood, it is likely that many will continue to be exposed to high levels of ionising radiation throughout childhood and in some cases into adulthood. Clinicians should be aware of the significant potential radiation exposure associated with fluoroscopy when requesting these investigations and limit these studies to symptomatic patients. A consensus approach to the role of fluoroscopy for OA/TOF infants would also be a useful clinical tool to develop.

Author contributions Dr Roberts conceptualised and designed the study, collected data and carried out data analysis, drafted the initial manuscript, and revised the manuscript. Associate Professor Karpelowsky, Professor Fitzgerald, and Dr Soundappan conceptualised and designed the study, supervised data collection and analysis, and reviewed and revised the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was approved by the Sydney Children's Hospital Network Human Research Ethics Committee. This study was performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Not applicable (requirement for informed consent waived by the institutional research committee as a retrospective, de-identified study).

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