Journal of Pediatric Surgery 53 (2018) 1365–1368

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Oncology

Prediction of respiratory collapse among pediatric patients with mediastinal tumors during induction of general anesthesia☆

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ARTICLE INFO

Article history:
Received 13 April 2017
Received in revised form 26 August 2017
Accepted 19 September 2017

Key words:
Mediastinal tumor
Child
General anesthesia
Dyspnea
Orthopnea

ABSTRACT

Purpose: Fatality resulting from respiratory collapse (RC) during general anesthesia (GA) induction in children with mediastinal tumors has been reported. We explored potentially useful parameters for predicting the risk of RC based on objective imaging results.
Methods: We retrospectively reviewed the records of 31 patients (median age: 4 years; range: 4 months–15 years) with mediastinal tumors treated between 2000 and 2015. Comparing those with RC under GA induction to those without (RC group vs. non-RC group), we analyzed a variety of factors that might predict respiratory obstruction during GA induction, including our new parameter, the standardized tumor volume (STV), which is adapted from the formula for the volume of an ellipsoid.
Results: All eight patients in the RC group had large tumors in the anterior mediastinum, including lymphoma, teratoma, and germ cell tumor. The mean STV value of the RC group was significantly larger than that of the non-RC group (3.6 ± 1.4 vs. 1.4 ± 1.0, $p = 0.006$). Using an STV cut-off value of 2.5, the sensitivity and specificity for predicting RC under GA induction were both 0.86, making STV more useful than previously reported risk factors.
Conclusion: Anterior mediastinal tumors in children can often cause airway obstruction under GA induction. Measuring STV can help predict the respiratory risk during GA among pediatric patients with anterior mediastinal tumors.
Level of Evidence: III.

Clinical features of pediatric mediastinal tumors vary depending on the age of the patient and on the size, location, and pathological traits of the tumor. While biopsy or extirpation is often indispensable for the precise diagnosis, fatalities resulting from respiratory problems during general anesthesia (GA) induction among children have been reported [1–3]. Several clinical parameters for the risk of respiratory collapse (RC) associated with GA, such as orthopnea and mediastinal mass ratios (MMR), have been suggested. However, there have been no articles reporting parameters based on detailed imaging findings [4–7].

Here, we retrospectively investigated the clinical features of mediastinal tumors in children at our medical facilities, analyzed various clinical factors potentially predictive of RC risk under GA induction, and compared the efficacy of our new parameter to previously reported indices [4–7].

1. Patients and methods

We reviewed records of 31 pediatric patients diagnosed with mediastinal tumors between 2000 and 2015 at Chiba University Hospital, Tokyo Women's Medical University Yachiyo Medical Center, and Matsudo City Hospital. We collected data on sex, age at diagnosis, primary symptoms, anatomical location of tumor, histopathological diagnosis, and perioperative management.

We defined the RC group as pediatric patients who, owing to airway compression by a large tumor, could not retain the minimum gas exchange to survive – via either mechanical or manual ventilation – during GA induction. We investigated potential risk factors by comparing clinical features between pediatric patients with and without RC. We also developed a new parameter, standardized tumor volume (STV), and evaluated its predictive utility among pediatric patients with anterior mediastinal tumors compared to previously reported risk factors (orthopnea, superior vena cava syndrome, hydrothorax, and MMR) [4–7]. The STV (in [cm^2]) is calculated using measurements obtained by CT, patient height, and an equation for approximating the volume of an ellipsoid as follows: STV = $4/3\pi \times$ (1/2 tumor height $\times$ 1/2

Abbreviations: AUC, area under the curve; GA, general anesthesia; MMR, mediastinal mass ratio; RC, respiratory collapse; ROC curve, receiver operating characteristic curve; STV, standardized tumor volume.

☆ Funding Sources: This research did not receive any specific grant money from funding agencies in the public, commercial, or not-for-profit sectors.

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https://doi.org/10.1016/j.jpedsurg.2017.09.013
0022-3468/

tumor width × 1/2 tumor depth) / body height (all measurements in cm). MMR was defined as the maximum width of the mediastinal mass divided by the maximum intrathoracic width, which was typically measured at the level of the diaphragm on an anterior–posterior radiograph [4].

For statistical analyses, we used Pearson's chi-squared test and Student's t-test. *P* values <0.05 were deemed statistically significant. We used the receiver operating characteristic curve (ROC) analysis (JMP®11 statistical analysis software, SAS Institute Inc., Cary, NC, USA) to set our cut-off STV as the value that maximized the area under the curve (AUC).

2. Results

Details of demographics and relevant medical histories are presented in Table 1. Seventeen (55%) of the patients in our study were male and 14 (45%) were female. The median age at diagnosis was four years, and ages ranged from four months to 15 years; eight patients (26%) were diagnosed prior to one year of age. Ten of the cases (32%) were asymptomatic, and were diagnosed during follow-up for incidental abnormal findings seen on X-ray images taken for school check-ups or screenings for other diseases. Among symptomatic patients, the most common complaint was mild respiratory symptoms (29%), such as cough or wheeze, followed by dyspnea (26%) and pleuritic pain (13%). The tumor was located in the anterior mediastinum in 16 patients (52%), the middle in 1 patient (3%), and the posterior in 14 patients (45%). Histologically, neuroblastoma (39%) and mature teratoma (32%) were the most common tumor types in our series, followed by lymphoma (13%), immature teratoma (6%), and ganglioneuroma (6%).

As presented in Fig. 1, in our study population, neuroblastoma was the most common tumor type in infants and toddlers: 75% of patients less than one year and 57% of those less than five years of age had neuroblastoma, while patients aged six to 15 years manifest a variety of tumors, including lymphoma, ganglioneuroma, and germ cell tumor.

The eight patients (median age: 10 years; range: 4 months — 11 years) who suffered RC during GA induction (RC group) all had large tumors in the anterior mediastinum. Histologically, four of these were teratomas (2 mature; 2 immature), three were malignant lymphomas, and one was germ cell tumor. No patients with middle or posterior mediastinal tumors had any difficulties in maintaining respiratory function during GA induction. Thus, large anterior mediastinal tumors appeared to dramatically increase the risk of respiratory obstruction during GA induction ($p < 0.001$).

Focusing on anterior mediastinal tumors, therefore, we explored potentially valuable parameters for predicting airway obstruction during GA induction by statistically comparing clinical factors between the RC and non-RC groups (Table 2). Among several previously reported risk factors, orthopnea was the most promising indicator ($p < 0.001$), with sensitivity at 1.00 and specificity at 0.86, followed by superior vena cava (SVC) syndrome ($p = 0.13$; sensitivity: 0.25; specificity: 1.00). The presence of hydrothorax was not significantly different between the two groups ($p = 0.30$), but MMR was, with 56.0 ± 8.5 cm^3 in the RC group, as compared to 37.0 ± 12.7 in non-RC group ($p = 0.03$). Setting the cut-off point of MMR at 44%, as suggested by King et al. [4], the sensitivity and specificity were 0.86 and 0.67, respectively. Our newly invented STV was 3.6 ± 1.4 cm^2 in the RC group and 1.4 ± 1.0 cm^2 in non-RC group, with a difference that was statistically significant ($p = 0.006$). With a cut-off STV value of 2.5, its sensitivity and specificity were 0.86 and 0.86, respectively, such that STV was nearly equivalent to the clinical sign of orthopnea and far superior to other parameters, including MMR, for predicting the risk of RC during GA induction among pediatric patients with anterior mediastinal masses.

Table 1
Demographic data.

Characteristics	$N = 31$
Sex	
Male	17 (55%)
Female	14 (45%)
Age at diagnosis	median: 4 years (range: 4 months–15 years)
Primary symptom	
Asymptomatic	10 (32%)
Slight respiratory symptoms (cough or wheezes)	9 (29%)
Dyspnea (desaturation, labored respiration)	8 (26%)
Pleuritic pain	4 (13%)
Location	
Anterior	16 (52%)
Middle	1 (3%)
Posterior	14 (45%)
Histopathological diagnosis	
Neuroblastoma	12 (39%)
Mature teratoma	10 (32%)
Lymphoma	4 (13%)
Immature teratoma	2 (6%)
Ganglioneuroma	2 (6%)
Germ cell tumor	1 (3%)

3. Discussion

Previous reports have suggested that pediatric mediastinal tumors occur across all age groups [8,9]. In this study, however, an exceptionally high proportion (26%) of patients were less than one year of age, leading to a fairly young median age at diagnosis of four years [9–12]. This high representation by infants might be because of the inclusion of neuroblastoma (6 cases), three cases of which were discovered during a mass screening conducted between 1985 and 2004 in Japan [13]. Another likely factor is that in our study, the proportion of lymphoma was relatively small (13%), whereas previously, it has been found to be the most common (18%–43%) mediastinal tumor in children [8–11]. This smaller proportion of lymphomas in our study also contributes to differences in our results, as compared to those of other papers, with regard to the locations of pediatric mediastinal tumors—especially the frequency of middle mediastinal tumors, which has previously been reported as 25%–52% [8,9,11] (as compared to 3% in our study).

Malignant tumors comprised 52% of all cases in our study, which is comparable to previous reports of 25%–82% [8–12,14] and emphasizes the importance of obtaining a pathologic diagnosis prior to initiating therapeutic protocols. It is true that obtaining adequate sample volume of tumor is ideal, but any procedures performed under GA can cause RC during GA induction among pediatric patients with mediastinal tumors [1–3]. Thus, open or (CT-guided) needle biopsy under local anesthesia or sedation might be an option for especially high-risk patients. However, deep sedation, technical difficulty, radiation exposure, and the high probability of collecting inadequate diagnostic material are also serious concerns among small children.

For cases with suspected lymphoma in the anterior mediastinum and with high risk of cardiorespiratory morbidity during GA, prebiopsy steroid treatment and/or radiation can be considered to reduce the size of the tumor [15], even though these options can lead to apoptosis and/or necrosis of the tumor cells and thus hinder definitive, accurate, and prompt diagnosis.

Risk factors associated with airway obstruction during GA induction in pediatric mediastinal tumors have been previously analyzed [4–6,16], and some authors have shown that orthopnea is a useful predictive indicator [4,6,17]. Clinically, orthopnea in the setting of an anterior mediastinal tumor is likely caused by gravity-dependent, front-to-back compression of the trachea by the tumor, such that it is exacerbated when a patient is supine and improved when sitting upright. Our study confirmed the predictive utility of orthopnea among patients