Morbidity related to major lung thoracoscopic resections in children

Sara Ugolini,[1,2] Lorenzo Tofani,[3] Elisa Zolpi,[4] Louise Montalva,[5] Cosimo Lotti,[6] Antonino Morabito,[7] Fabio Chiarenza,[4] Arnaud Bonnard[5,8,9]

[1]Thoracic Surgery Department, Barts Thorax Centre, St Bartholomew's Hospital, Barts NHS Fuondation Trust, London, United Kingdom; [2]Ph.D. in Cardio-Nephro-Thoracic Sciences, Department of Medical and Surgical Sciences, Alma Mater Studiorum Università di Bologna, Italy; [3]Department of Statistics, Informatics, Applications, University of Florence, Italy; [4]Department of Pediatric Surgery, Pediatric Minimally Invasive Surgery and New Technologies, San Bortolo Hospital, Vicenza, Italy; [5]Department of Pediatric Surgery and Urology, Robert-Debré University Hospital, Paris, France; [6]Physiotherapy Department, Princess Royal University Hospital, King's College Hospital NHS Foundation Trust, London, United Kingdom; [7]Department of Pediatric Surgery, IRCCS – Azienda Ospedaliero Universitaria Meyer, University of Florence, Italy; [8]Paris University, Paris, France; [9]Université Paris Diderot-Sorbonne Paris Cité, Paris, France

Abstract

In pediatric thoracic surgery, reported predictors for increased risk are symptoms and active/previous infections (RAP). We investigated the adverse events related to Video-Assisted Thoracic Surgery (VATS) in pediatric patients when considering RAP predictors. A retrospective analysis of pediatric VATS major lung resections in 2008-2021 was conducted at three institutions. We employed the pediatric surgical risk calculator to define patients' preoperative predicted risk (PredR). Postoperative complications were classified according to the Thoracic Morbidity & Mortality (TM&M) system. The observed TM&M rate (ObsR) and the PredR were compared. A subgroup analysis by RAP predictors was conducted. 37 patients (54% female) were included. Mean age and weight were 5.8 years and 22.8 kg. 56.7% had respiratory symptoms, 38.9% active infection and 59.5% history of infections (RAP subpopulations). VATS procedures were lobectomy (n=32), segmentectomy (n=3), bilobectomy (n=1) and pneumonectomy (n=1). The conversion rate was 5.4%. The mean PredR was of 4.43% (±1.8) and the overall ObsR was 45.94% with a median severity of II (I-III). This difference was significant and a higher PredR was not associated with complications development. PredR does not show association among the RAP vs non-RAP group. ObsR showed positive association with RAP, even if it reached statistical significance only for "respiratory symptoms" risk factor. ObsR reflected the number of bronchiectasis patients in our series (n=9), aligning with the hypothesis of "earlier and safer surgery". The risk calculator underestimates VATS morbidity. Multicentre studies will clarify the correlation between inflammation and surgical adverse events.

Correspondence: Sara Ugolini, Ph.D. in Cardio-Nephro-Thoracic Sciences, Department of Medical and Surgical Sciences, Alma Mater Studiorum Università di Bologna, Italy.
E-mail: Sara.ugolini13@studio.unibo.it

Key words: lung; respiratory system abnormalities; video-assisted thoracic surgery; thoracoscopy; postoperative complications; clavien-dindo.

Conflict of interest: the authors declare no potential conflict of interest, and all authors confirm accuracy.

Ethics approval: This study is based on information routinely collected during normal clinical care, no additional data were collected for the purposes of the study, and no additional intervention/medication was given solely for the purposes of the study. All the patients, as declared, have signed the consent form for clinical data utilisation in reasearch, with the clear intent of retrospective analysis and no personal information showing. Therefore, institutional review board approval was waived.

Acknowledgments: the authors thank Roberto Armellini for the cooperation in data collection and George Whittaker for proofreading the article.

Received: 21 March 2024.
Accepted: 21 May 2024.

Licensee PAGEPress, Italy
La Pediatria Medica e Chirurgica 2024; 46:337
doi:10.4081/pmc.2024.337

Introduction

When compared to other pediatric subspecialties, thoracic surgery is the one that suffers most from a lack of gold standards on surgical indications and timings.[1-13] Whilst research at high levels is currently being carried out on natural history and cancer-related risk of pediatric thoracic surgical diseases,[14,15] reports on postoperative outcomes are scarce. According to the narrative literature, predictors commonly reported to relate to poor outcomes and higher risks are Respiratory symptoms, Active infections, and Previous infections (RAP predictors).[16] Slow surgical research progress could be explained by the fact that studies often mix thoracic/abdominal conditions with subsequent bias and little progress. Furthermore, while short-term surgical outcomes are regularly reported (such as operative time or length of hospital stay), the paucity of morbidity data could be explained by the absence of specific pediatric thoracic reporting systems. Among the multiple adverse events reporting systems available for adult thoracic surgery, the Thoracic Morbidity & Mortality (TM&M) is based on the Clavien-Dindo (CD) classifi-

cation which offers a grading I-V of severity proportionally to the intervention required to treat the complication.[17-23] The paucity of knowledge on risks associated with VATS (Video-Assisted Thoracic Surgery) major lung resections translates ultimately on quality of patient consenting, safety, and professional liability. One of the available tools meant to support the clinician is the American College of Surgeons National Surgical Quality Improvement Program® (ACS NSQIP®) pediatric surgical risk calculator which provides an individualized risk for surgery.[24-27]

We retrospectively investigated the adverse events (Observed Rate: ObsR) related to VATS major lung resections in a multicentre paediatric population. Moreover, a comparative analysis of ObsR and RAP predictors was conducted. As a secondary aim, we employed the ACS NSQIP® pediatric surgical risk calculator to retrospectively define patients' preoperative Predicted Risk (PredR). A comparison was made between ObsR and PredR to assess the reliability of the calculator for thoracic conditions and an analysis by RAP predictors was conducted to answer the question: "Are RAP predictors actually associated with poor postoperative outcomes?"

Materials and Methods

Data collection

A retrospective analysis was conducted on children undergone major pulmonary VATS resections in the period 2008-2021 at three institutions. Data recorded included: i) general demographics and biometrics; ii) clinical history (diagnosis, history of infections, history of respiratory symptoms); iii) perioperative data (type of surgery, conversion rates, intraoperative bleeding/non-bleeding complications, operative and anesthesia times); iv) postoperative outcomes (chest tube duration, postoperative length of hospital stay [pLOS], adverse events). The RAP subpopulations have been defined as those where "Respiratory symptoms", "Active infection", "Previous infection" were identified.

Surgical procedures

Thoracoscopy was established using standard triportal VATS in all cases except in three cases operated by means of uniportal VATS.[28] Uniportal VATS was carried out by single-lung ventilation either with a double-lumen endotracheal tube or, depending on patient size (below or above 25-27 kg), with a single-lumen and bronchial blocker. Non-selective intubation and low-volume CO2 inflation were established for the multiportal VATS cases. In cases of severe parenchymal inflammation, parietal adhesions or fissure obliteration, the dissection was carried out by the Ultracision Harmonic Scalpel™ device (Ethicon Endosurgery, Somerville, NJ) or LigaSure™ vessel sealer (Medtronic, Dublin, Ireland).

Definition of the preoperative adverse events PredR

The ACS NSQIP® pediatric surgical risk calculator is thought to help provide the patients with an individualized risk for surgery and it is based on 17 predictors and the Current Procedural Terminology (CPT®) code of the planned surgery (USA current system).[24-27] Predictors are age, neonatal status, sex, transfer status, elective/urgent, ASA, wound classification, inpatient/outpatient, sepsis before surgery, ventilator, oxygen or nutritional support, cognitive level, and neuromuscular, hematologic, cardiac, central nervous system disorders. The algorithm gives the percentage risk for a patient to experience any of the nine different outcomes within 30 days following surgery: "any complication", "pneumonia", "cardiac complications", "surgical site infection", "urinary tract infections", "venous thromboembolism", "renal failure", "unplanned reintubation" and "death". In our study, the ACS NSQPI surgical risk online calculator was employed to define the preoperative PredR: all the 17 required fields were filled in for each patient according to definitions. The CPT® procedural codes used were: "32663–Thoracoscopy, surgical; with lobectomy (single lobe)" for VATS lobectomy, "32669–Thoracoscopy, surgical; with the removal of a single lung segment (segmentectomy)" for VATS anatomical segmentectomy, and "32482–removal of lung, other than pneumonectomy; 2 lobes (bilobectomy)" for pneumonectomy (as pneumonectomy is not currently included in the calculator). The system allows the surgeon to manually increase the risk by 1 or 2 standard deviations, which was not performed in our study. The final PredR value given by the online platform ("overall risk of complications") was recorded for each patient.

Morbidity and mortality reporting system and definition of the adverse events ObsR

According to the CD classification developed in 1992, a complication is defined as any deviation from the expected recovery from surgery and the grade (a scale I to V) reflects the intervention required to treat it.[17] Grades I and II include minor complications requiring no therapy or pharmacologic intervention only. Grades III and IV are significant complications that require surgical intervention or life support. Grade V complications result in patient death. In 2010, the TM&M was developed by Seely and colleagues to be a thoracic-adapted version of the CD.[18-23] According to TM&M, an adverse event is defined by a system (*i.e.* cardiovascular, pleural, pulmonary, gastrointestinal), a type (*i.e.* pneumothorax, prolonged air leak, prolonged pleural drainage) and a grade (I-V). Adverse events in our population were classified accordingly to the TM&M system.[18]

Data analysis

Descriptive statistics were used to present the general population data. The TM&M postoperative ObsR of complications and the mean preoperative PredR given by the calculator have been reported. A comparison between ObsR and PredR and an analysis by the RAP predictors have been conducted. Continuous variables were presented by mean +- SD (or median and range according to distribution) and categorical variables by absolute and relative frequencies. Differences in continuous variables distribution among groups was analyzed by T-test, Satterthwaite's T-test and Mann-Whitney test, according to Shapiro-Wilk and Bartlett's test for normality and homoschedasticity. To compare ObsR and PredR, the one sample z-test for proportion was employed. A logistic regression model was used to assess the relationship between binary outcome and risk factors (including PredR when considered as a risk factor for complications). Odds ratio (OR) and the 95% confidence interval were reported. The significance level was set to 5% ($p<0.05$).

Results

Population and procedures

A total of 37 patients underwent a major pulmonary resection by VATS in the study period (Table 1). 54% (n=20) were females and the mean age was 5.9 years± 5.6 (IQR 0.9 – 10.6). Among them, 12 were below 10 kg, 16 were between 10 and 30 kg, and 9 above 30 kg; the mean overall weight was of 22.85 kg±18.13.

Upon investigation of RAP predictors, the vast majority of patients (56.76%) complained of respiratory symptoms, 38.89% had signs of or a known active infection, and 59.46% of patients had a

history of at least one episode of respiratory tract infection (RAP populations).

Diagnoses leading to surgical indication were: n=13 Congenital Pulmonary Airway Malformations (CPAMs), n=4 Congenital Lobar Emphysema (CLE), n=7 Bronchopulmonary Sequestration (BPS), n=9 bronchiectasis, and n=4 chronic atelectasis (Table 1). Among the bronchiectasis group: n=2 had a history of previous foreign body inhalation; n=1 had an underlying diagnosis of primary ciliary dyskinesia, n=1 of ICF syndrome and n=1 of cystic fibrosis; n=1 HIV-patient had an EBV-related lymphoproliferative disease with a previous pneumopathy due to EBV-CMV coinfection. In one case, bronchiectases were due to a previous tuberculosis infection and in one otherwise healthy patient an underlying CPAM could not be ruled out with histology. Ultimately, one post-infectious bronchiectasis was secondary to subglottic stenosis in a case with a history of prolonged intubation due to long-gap esophageal atresia. Among the patients operated on for chronic atelectasis: n=2 had an underlying diagnosis of cystic fibrosis (one of these patients, undergoing left pneumonectomy, had complete chronic atelectasis of the lung with pulmonary hypertension); n=1 was affected by a corticoid-dependent nephrotic syndrome and a pneumopathy characterized by chronic atelectasis, bronchiectasis and chronic pulmonary embolism; n=1 experienced chronic complete atelectasis of the left lower lobe after an obliterative bronchiolitis post-mycoplasma.

Among the procedures there were n=32 lobectomy, n=3 segmentectomy, n=1 bilobectomy and n=1 pneumonectomy (Table 1). 33 (89.1%) procedures were performed by multiportal VATS, 1 (2.7%) by biportal and 3 (8.1%) by uniportal approach. Mean operative time and total time under anesthesia were 178 minutes±78 and 249 minutes±90. In 2 out of 37 cases (5.4%) an open conversion was necessary; arterial bleeding occurred in a patient undergoing pneumonectomy and adhesions in a tuberculosis case required conversion due to safety concerns. In n=5 (13.5%) patients, intraoperative blood transfusion was performed. Intraoperative complications were observed in n=2 patients (5.4%): an inability to extubate was due to lavage fluid inhalation through a dilated bronchial stump (while suturing it); In another case, the aforementioned arterial bleeding occurred from the main pulmonary artery leading to open conversion. In one case, surgeons experienced significant issues related to a suboptimal selective intubation which was felt unsafe, impacted significantly on operative times and was managed by switching to conventional double lung ventilation. In 89.2% of cases (n=33), a chest tube was left postoperatively with a median duration of 3 days (min-max range 1-62). The postoperative rate of antibiotics usage was 83.8% (n=31) and the median pLOS was 5 days (min-max range 2–66).

Preoperative PredR

According to the ACS NSQIP® pediatric surgical risk calculator, the estimation of complications occurring within 30 days after surgery (PredR) was a mean and a median of 4.43% (± 1.82) and 3.8% (min-max range 2 – 11.2) respectively.

When considering RAP subpopulations (Table 2), the mean PredR does not show statistical significance among the RAP vs non-RAP group: 4.42±1.85 and 4.44±1.85 (p=.27) between symptomatic and asymptomatic patients (R predictor="respiratory symptoms"); 4.46±2.1 and 4.44±1.72 (p=.18) between patients who had signs of infection and those who had not (A predictor="active infection"); 4.46±2.25 and 4.38±0.97 (p=.19) among patients who had positive history and those who had not (P predictor="history of infections").

Postoperative morbidity and mortality

According to the TM&M system, the incidence of postoperative complications (ObsR) was 45.94% with a median severity value of

Table 1. Surgical outcome of patients operated by a thoracoscopic major lung resection in the period 2008-2021.

Diagnosis	CPAM	13
	CLE	4
	BPS	7
	Bronchiectasis	9
	Chronic Atelectasis	4
Procedures (n)	**37**	
	Lobectomy	32
	Segmentectomy	3
	Bilobectomy	1
	Pneumonectomy	1
Patients (n)	**37**	
	Patients 10 kg	12
	Patients 10-30 Kg	16
	Patients 30 kg	9
Mean weight (kg)	**22.85** (±18.13)	
Mean Age (years)	**5.88** (±5.56)	
Mean preoperative Predicted Risk (PredR) (%)	**4.43** (±1.82)	
Mean Time Under Anesthesia (min)	**249** (±90)	
Mean Operative Time (min)	**178** (±78)	
Conversion (n)	**2** (5.4%)	
Intraoperative Complication Rate (%)	**2** (5.4%)	
Postoperative Complication Rate (ObsR) (%)	**45.95**%	
Median Grade of the postop TMM System (I - V)	**II** (I – III)	
Median Chest Tube Duration (days)	**3** (1-62)	
Median pLOS (days)	**5** (2-66)	

CPAM, Congenital Pulmonary Airway Malformation; CLE, Congenital Lobar Emphysema; BPS, Bronchopulmonary Sequestration; pLOS, Postoperative Lengh of Hospital Stay; PredR, mean preoperative Predicted Risk.

II (range I–III). Two events of grade I were registered (apical pneumothorax treated conservatively). Among adverse events of grade II severity, we recorded: n=2 pneumothorax managed conservatively with prolonged pleural drainage, n=4 prolonged air leak, n=1 infection of the surgical site requiring systemic antibiotics, and n=1 central catheter thrombosis needing heparin at therapeutic dose. Among the grade III of severity, n=3 atelectasis requiring bronchoscopy (IIIa), n=1 pneumothorax requiring tube thoracostomy positioning under general anesthesia (IIIb), n=1 atelectasis of the middle lobe due to inadvertent bronchus stapling at the time of upper lobectomy (IIIb; this 5-year-old patient was affected by chronic atelectasis, bronchiectasis and chronic pulmonary embolism with a history of corticoid-dependent nephrotic syndrome). Moreover, n=1 bronchopleural fistula developed after a right inferior lobectomy for CLE requiring a thoracotomy at 2 and 5 weeks for bronchial repair (IIIb; in this otherwise healthy 11-year-old patient, the pLOS was of 66 days). No mortality was observed.

In Table 3, ObsR is analyzed with consideration to RAP predictors: the RAP populations ("symptomatic", "active infection", and "previous infections") showed a higher probability of complications development than the "non-RAP" asymptomatic population (respectively, OR 7.46 [IC 1.65 – 33.78], OR 2.23 [IC 0.57 – 8.75], and OR 2.27 [IC 0.59 – 8.82]). The findings could not reach statistical significance for the respiratory infection risk factors (p values=.2496 and=.2354), whereas the presence of "respiratory symptoms" risk factor is significantly associated to a higher probability of complications (p=.0092); Moreover, the "respiratory symptoms" risk factor shows a discrete predictive capability as shown by the area under the ROC curve of 0.74 (IC 0.59 – 0.88). Additionally, ObsR (45.94%) was statistically significantly higher (p<.0001) then calculated mean PredR (4.43%). Moreover, PredR was not associated with complications development OR 1.175 [CI 0.8 – 1.72], p=0.41).

Discussion

Outcomes of pediatric thoracic surgery is an unknown field characterized by heterogenous data on unshared definitions. Predictors commonly reported to relate to a higher morbidity are respiratory symptoms, active infection, and previous infections.[16] In the future, multicentre data and systematic reporting systems will allow to adequately face the increased number of congenital pulmonary malformations. As per the Eurocat prevalence table, the CPAMs rate has risen from 0.22 cases per 10,000 births in 1996 to 1.57 in 2019.[27] An agreed consensus exists for the treatment of symptomatic infants. For those asymptomatic however, there is lack of evidence, irrespective of the risk of developing acute symptoms or pneumothorax, infection-related complications, and cancer. The issue is of particular importance with regard to patient consenting: for the patient/parents to make an informed choice we need clear information on outcomes, risks and adverse events. To this aim, mortality must also be discussed, even if aiming to treat a benign disease. Nowadays, patient consenting is based on "pros & cons": surgery is intended to prevent lung infections, resolve respiratory symptoms (and maybe chronic disease) and abolish lung cancer risk, when performed radically. Moreover, early resection can take advantage of compensatory lung growth, lowers parental anxiety, and has a reduced lifelong radiological exposure when compared to the conservative approach. Nonetheless, the rate of adverse events is supposed to be lower for early surgery (before established symptoms). On the other hand, "cons" of surgery are related to procedural morbidity and mortality, and in some cases, especially with wheezing, it is unlikely to relieve symptoms.

In our study population we addressed the question of adverse events rate. The TM&M is a classification system based on the CD classification which defines complication as whatever deviates from the expected postoperative course. Because of the definition itself, the system overestimates the risk compared to other tools, such as the ESTS risk prediction tool.[21,29]

In the available literature, RAP predictors are the current rationale for operating on asymptomatic lesions such as CPAMs, along with the cancer risk.

In our series, 37 patients have been included. 56.76% complained about respiratory symptoms, 38.89% had signs or a known active infection, and 59.46% of patients had a positive history of infection (RAP populations). According to the TM&M, the postoperative overall complications rate (ObsR) was of 45.94% with a median value of severity of II (range I – III). This finding might align with the reported morbidity in adult thoracic surgery which is 15-60% depending on the classification system used [22,30,31].[22,30,31] On the other hand, it may be overestimated by the n=9 bronchiectasis patients who are expected to be with a higher degree of adhesions and bacterial contamination. This phenomenon might be in line with the hypothesis of "earlier and safer surgery".

When looking at RAP predictors ("respiratory symptoms", "active infection", "history of infections"), a higher probability of complications (ObsR) was found compared to the "non-RAP" population. The findings were statistically significant for the

Table 2. The mean preoperative Predicted Risk (PredR) is analyzed in relation to the RAP predictors ("Respiratory symptoms", "Active infection", "Previous infections"). As shown, PredR does not show association among the RAP vs non-RAP group.

	RAP +	RAP -	
Respiratory symptoms	4.42±1.85	4.44±1.85	P=.27
Active respiratory infection	4.46±2.1	4.44±1.72	P=.18
History of respiratory infections	4.46±2.25	4.38±0.97	P=.19

Table 3. "The association between the Observed complication Rate (ObsR) and presence of RAP predictors ("Respiratory symptoms", "Active infection", "Previous infections") is analysed. ObsR showed positive association with RAP, even if it reached statistical significance only for "respiratory symptoms" risk factor.

	RAP +			
Respiratory symptoms	**OR 7.46**	**IC**	**1.65-33.78**	**P=.0092**
Active respiratory infection	OR 2.23	IC	0.57-8.75	P=.2496
History of respiratory infections	OR 2.27	IC	0.59-8.82	P=.2354

"respiratory symptoms" risk factor (p=0.0092), which was also associated to a discrete capability of postoperative complications prediction.

The ACS NSQIP Pediatric risk calculator is meant to provide the surgeons with a patient-tailored percentage risk (PredR) to aid in both decision-making and informed consenting. As a secondary aim, in order to test its reliability in thoracic conditions, we included PredR in our analysis. The mean PredR was 4.43% (± 1.82) and, in average, it was not higher in the RAP group when compared to the non-RAP.

The comparison between mean PredR and ObsR showed that they are significantly different and a PredR was not associated with complications development in our study population (meaning that increasing PredR values did not relate to a higher chance of adverse events).

This study allowed us to evaluate the reliability of the risk calculator in thoracic surgery since underestimating the associated morbidity could potentially mislead clinicians and patents/parents at time of consenting.

The reasons might be due to the fact that the risk calculator does not take into account some specific thoracic surgery features that significantly add discomfort and harm to patients (e.g. atelectasis requiring bronchoscopy [which has to be under general anesthesia in pediatrics], air-leak or prolonged chest tube duration). Moreover, if we speculate RAP as associated with poor outcomes, there is no mention of them among the 17 parameters considered for the algorithm of the calculator, in which only two are about the respiratory system in general (O2 requirement and ventilatory support requirement).

We believe that understanding thoracic surgery morbidity is of primary importance for proper patient consenting, and multi□centre studies will clarify the actual relationship between inflammation and surgical adverse events.

The limitations of our study are primarily related to the retrospective nature of the project and the small sample population that could not allow further statistical analysis.

References:

1. Kantor N, Wayne C, Nasr A. Symptom development in originally asymptomatic CPAM diagnosed prenatally: a systematic review. Ped Sur Int 2018;34:613-620.
2. Wong KKY, Flake AW, Tibboel D, et al. Congenital pulmonary airway malformation: advances and controversies. Lancet Child Adolesc Health 2018;2:290-7.
3. Kunisaki SM, Saito JM, Fallat ME, et al. Development of a multi-institutional registry for children with operative congenital lung malformations. J Ped Sur 2020;55:1313-8.
4. Cook J, Chitty LS, De Coppi P, et al. The natural history of prenatally diagnosed congenital cystic lung lesions: long-term follow-up of 119 cases. Arch Dis Child 2017;102:798-803.
5. Downard CD, Calkins CM, Williams RF, et al. Treatment of congenital pulmonary airway malformations: a systematic review from the APSA outcomes and evidence based practice committee. Ped Surg Int 2017;33:939-53.
6. Hall NJ, Stanton MP. Long-term outcomes of congenital lung malformations. Semin Pediatr Surg 2017;26:311-6.
7. Kapralik J, Wayne C, Chan E, et al. Surgical versus conservative management of congenital pulmonary airway malformation in children: A systematic review and meta-analysis. J Pediatr Surg 2016;51:508-12.
8. Kunisaki SM. Narrative review of congenital lung lesions. Transl Pediatr 2021;10:1418-31.
9. Bonnard A. Thoracoscopic lobectomy for congenital pulmonary airway malformation: where are we in 2019? Eur J Pediatr Surg 2020;30:146-9.
10. Annunziata F, Bush A, Borgia F, et al. Congenital lung malformations: unresolved issues and unanswered questions. Front Pediatr 2019;7:239.
11. Jelin EB, O'Hare EM, Jancelewicz T, et al. Optimal timing for elective resection of asymptomatic congenital pulmonary airway malformations. J Pediatr Surg 2018;53:1001-5.
12. Ng C, Stanwell J, Burge DM, Stanton MP. Conservative management of antenatally diagnosed cystic lung malformations. Arch Dis Child 2014;99:432-7.
13. Naito Y, Beres A, Lapidus-Krol E, et al. Does earlier lobectomy result in better long-term pulmonary function in children with congenital lung anomalies? A prospective study. J Pediatr Surg 2012;47:852-6.
14. Patrizi S, Pederiva F, d'Adamo AP. Whole-Genome Methylation Study of Congenital Lung Malformations in Children. Front Oncol 2021;11:689833.
15. Casagrande A, Pederiva F. Association between congenital lung malformations and lung tumors in children and adults: a systematic review. J Thorac Oncol 2016;11:1837-45.
16. Clark RA, Perez EA, Chung DH, et al. Predictive factors and outcomes for successful thoracoscopic lung resection in pediatric patients. J Am Coll Surg 2021;232:551-8.
17. Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility in cholecystectomy. Surgery 1992;111:518-26.
18. Seely AJ, Ivanovic J, Threader J, et al. Systematic classification of morbidity and mortality after thoracic surgery. Ann Thorac Surg 2010;90:936-42; discussion 942.
19. Ivanovic J, Al-Hussaini A, Al-Shehab D, et al. Evaluating the reliability and reproducibility of the Ottawa Thoracic Morbidity and Mortality classification system. Ann Thorac Surg 2011;91:387-93.
20. Ivanovic J, Al-Hussaini A, Al-Shehab D, et al. Evaluating the reliability and reproducibility of the Ottawa Thoracic Morbidity and Mortality classification system. Ann Thorac Surg 2011;91:387-93.
21. Salati M, Refai M, Pompili C, et al. Major morbidity after lung resection: a comparison between the European Society of Thoracic Surgeons Database system and the Thoracic Morbidity and Mortality system. J Thorac Dis 2013;5:217-22.
22. Ivanovic J, Seely AJ, Anstee C, et al. Measuring surgical quality: comparison of postoperative adverse events with the american college of surgeons NSQIP and the Thoracic Morbidity and Mortality classification system. J Am Coll Surg 2014;218:1024-31.
23. Akbilgic O, Langham MR Jr, Walter AI, et al. A novel risk classification system for 30-day mortality in children undergoing surgery. PLoS One 2018;13:e0191176.
24. Bruny JL, Hall BL, Barnhart DC, et al. American College of Surgeons National Surgical Quality Improvement Program Pediatric: a beta phase report. J Pediatr Surg 2013;48:74-80.
25. Kraemer K, Cohen ME, Liu Y, et al. Development and Evaluation of the American College of Surgeons NSQIP Pediatric Surgical Risk Calculator. J Am Coll Surg 2016;223:685-93.
26. Stey AM, Kenney BD, Moss RL, et al. A risk calculator predicting postoperative adverse events in neonates undergoing major abdominal or thoracic surgery. J Pediatr Surg 2015;50:987-91.
27. EUROCAT. Prevalence tables. 1996-2019. Accessed: July 2022. Available from: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en

28. Ugolini S, Coletta R, Lo Piccolo R, et al. Uniportal video-assisted thoracic surgery in a pediatric hospital: early results and review of the literature. J Laparoendosc Adv Surg Tech A 2022;32:713-20.
29. ESTS. Database Annual Report 2020. Available from: https://www.ests.org/_userfiles/pages/files/Silver_Book2020_Part1_2_Short_300920OK.pdf
30. Sandri A, Papagiannopoulos K, Milton R, et al. Major morbidity after video-assisted thoracic surgery lung resections: a comparison between the European Society of Thoracic Surgeons definition and the Thoracic Morbidity and Mortality system. J Thorac Dis 2015;7:1174-80.
31. Andalib A, Ramana-Kumar AV, Bartlett G, et al. Influence of postoperative infectious complications on long-term survival of lung cancer patients: a population-based cohort study. J Thorac Oncol 2013;8:554-61.