Research Article

Investigating the Role of Open Lung Biopsy in Diagnosing the Type of Chronic Lung Disease in Children

Ashjaei Bahar1,2*, Modaresi Mohammadreza1,2, Amir Shakiba1,2, Najdi Fatemeh1,2, Movahedi Jadid Merisa1,2, Aghabarari Mojtaba1,2 and Ghavami Adel Maryam1,2

1Department of Pediatric Surgery, Children’s Medical Center (Pediatric Center of Excellence), Tehran University of Medical Sciences, Iran
2Department of Pediatric Pulmonary Disease and Sleep Medicine Research, Children’s Medical Center (Pediatric Center of Excellence), Tehran University of Medical Sciences, Iran

Abstract

Objective: This study was conducted for the practical use of biopsy in the diagnosis of chronic lung disease and the guidance of risks and benefits.

Design of Study: We studied 64 children with chronic lung disease who underwent open lung biopsy in 5 years at the Children's Medical Center.

Results: Biopsy results were diagnostic in 57 cases (89.1%) and non-diagnostic in 7 cases (10.9%). The biopsy determined the type of mass in all cases where a possible diagnosis of lung mass or thoracic wall was made. In 37 cases (57.8%) the diagnosis was changed and the exact diagnosis was determined. The main side effects (including pneumothorax, hemothorax, pyothorax, and pleural effusion) were 50% (32 cases), the most common of which were pneumothorax and pleural effusion, with a total of more than 87% of these major complications. 22 patients (34.4%) required intubation. 24 patients (37.5%) were admitted to the ICU after surgery. The death occurred in only one case, who was a 3-month-old boy with a disorder of INR and suffering from acute respiratory distress syndrome. There was no mortality that could be directly related to surgery.

Conclusion: Open lung biopsy is a gold standard for the histological diagnosis of chronic pulmonary disease in children and plays an important role in the treatment of children with chronic pulmonary diseases. However, serious and common side effects of this method should be considered.

© 2020 Ashjaei Bahar. Hosting by Science Repository. All rights reserved.

Introduction

Pediatric interstitial lung disease includes a wide range of rare respiratory disorders associated with high morbidity and mortality. The diagnostic approach is based on a combination of assessment, clinical examination, imaging, pulmonary function test, genetic test, Bronchial lavage lavage (BAL), and in most cases lung biopsy. Patients who had a previously known pathology, but the pulmonary symptoms cannot be justified by underlying disease are candidates for screening for pediatric interstitial pulmonary disease [1]. A definitive diagnosis of adult interstitial pulmonary disease is made by CT scan [2, 3]. However, in children, CT scans are usually non-specific and pulmonary biopsies are often required [4, 5]. When non-invasive tests are not enough to diagnose lung disease, lung biopsy is the gold standard for diagnosing the disease in children with persistent symptoms or worsening clinical condition. Lung biopsy is part of the diagnostic workup for multiple diseases [6], and it is performed for conditions with a high mortality rate. The procedure yields a definitive diagnosis in the majority of cases but infrequently changes therapy [7]. Pediatric surgeons are commonly asked to carry out lung biopsies in children to obtain tissue for definitive histological or microbiological diagnoses [8].

There are several ways to perform a lung biopsy. These include Transbronchial lung biopsy (TBLB), Trans thoracic lung biopsy (TTLB), Video-assisted thoracoscopic surgery (VATS), and finally open lung biopsy (OLB). Each has its own advantages and disadvantages. Open lung biopsy can help differentiate between reversible and irreversible
Investigating the Role of Open Lung Biopsy in Diagnosing the Type of Chronic Lung Disease in Children

Lung diseases and may guide therapy. Histological findings following an open lung biopsy may help clarify the underlying disease and deciding between continuation and withdrawal of ECMO or help in changing other aspects of the treatment [9]. It represents the final necessary step in diagnosis; however, a definitive diagnosis may still remain elusive and medical therapies may not be changed following biopsy [10]. Proceeding with OLB in vulnerable children who already have significant respiratory compromise can often carry significant risk, which needs to be considered when assessing the need for definitive diagnosis [11]. Therefore, careful patient selection is recommended to maximize diagnostic yield [8].

Open lung biopsy is an uncommon procedure in children. Previous reports on the diagnostic use of open lung biopsy have focused on two main groups: Children with undiagnosed lung parenchymal disease who have failed other diagnostic procedures and children with congenital heart disease and pulmonary vascular microanatomy which can provide valuable additional information for cardiac catheterization data [12-15]. The use of open lung biopsy in modern medicine cannot be judged well for several reasons using the available information. Many previous studies have been published more than a decade ago and have been reported before the introduction of current treatment strategies and diagnostic techniques, and the expected mortality spectrum (0% to 62%) and the diagnostic range (9% to 100%), previously reported, is very helpful in selecting criteria for patients who may benefit from this procedure [13, 16]. In addition, in the last decade, the pediatric intensive care unit and the number of immunocompromised children has increased. The diagnostic efficacy of open lung biopsy (57%) and VATS (54%) has been similar, but the morbidity resulting from VATS is clearly lower in terms of surgical duration, pulmonary embolism, and hospital stay [17].

The use of needle biopsy through the skin in combination with HRCT, with a diagnostic efficiency of between 58 and 100% and with low side effects, has been suggested as an alternative to open lung biopsy [5, 18]. But as much as open biopsy, the lungs do not provide stable results [19]. Although trans bronchial biopsy or trans thoracic biopsy has been used successfully in some cases, open lung biopsy (OLB) or video-assisted thoracoscopic surgery (VATS), are the gold standard for providing sufficient tissue for diagnosis. Complications of all types of biopsies include pneumothorax, hemothorax, empyema, atelectasis, pneumonia, etc. Depending on the type and extent of the invasive method, the incidence of each of these complications can be more or less.

Careful consideration should therefore be given to who would benefit most from lung biopsy [6]. Research on the role of OLB in middle and low-income countries is required to guide treatment of children with life-threatening DLD (diffuse lung disease) that does not respond to treatment [20]. Finally, due to the lack of complete knowledge of the subject and the risks of biopsy, as well as the need to perform it in cases where a diagnosis cannot be made for the patient, we decided to examine the role of lung biopsy in the diagnosis of chronic lung disease in children at the Children's Medical Center and by analyzing and reporting the data from our study to describe the role of lung biopsy in diagnosing the type of disease in chronic lung patients.

Methods

This study was a retrospective section and the population we studied on, was all children with chronic pulmonary disease who were referred to the Children's Medical Center Hospital (Children's Scientific Center) in last 5 years and underwent lung biopsy surgery. The criterion for patients to enter the study also included all children with chronic lung disease who were not given a definitive diagnoses of their various disease conditions and were in the age range of 2 months to 16 years, both boys and girls. Also, patients with underlying disease were excluded from the study. Related variables in this study include biopsy complications, post-biopsy mortality and post-biopsy diagnosis, and independent variables including age, sex, coagulation profile, pre-biopsy respiration rate, patient intubation requirement, ICU length of stay, and potential diagnosis Before biopsy, abnormal CXR before biopsy and the type of lung disease.

Each patient's information includes demographic information, information about the disease, the results of tests requested for the patient, therapies performed for the patient, pathology report, complications of pulmonary biopsy that are identified during periodic examinations in patients, and in the patient's clinic file. Other necessary information was entered in the data collection sheets designed to perform this study, according to the data collection sheet.

At the end, the collected information was entered into SPSS v.20 statistical software and analysed. Multivariate linear regression was used to investigate the effect of variables affecting postoperative complications such as age, sex, etc. We also used multivariate linear regression to identify the factors that cause postoperative mortality in children with chronic lung disease.

Results

A total of 64 children with lung disease who needed lung biopsy were included in the study. Patients ranged in age from 2 months to 16 years and averaged 3.5 ± 4.0 years. In terms of gender, 31 boys (47.7%) with an average age of 3.8 ± 4.1 years and 33 girls (50.8%) with an average age of 3.3 ± 4.0 years formed our patients. There was no statistically significant age difference between the sex groups (p = 0.91). Among the study subjects, 17 cases (26.6%) did not have Tachypnea, but 47 cases (73.4%) had a high respiratory rate. In terms of coagulation profile, 8 cases (12.5%) had impaired INR (above 1.5) and 10 cases (15.6%) had impaired PTT (above 45 seconds). Major complications (including Pneumothorax, hemothorax, pyothorax, and pleural effusion) occurred in half of the patients (32 individuals) after open lung biopsy. 22 patients (34.4%) required intubation. 24 patients (37.5%) were admitted to the ICU after surgery. the death occurred in only one case, who was a 3-month-old boy with a disorder of INR and suffering from acute respiratory distress syndrome. This patient died after 3 days of hospitalization in the ICU following surgery.

The most common complications in our patients were pneumothorax and pleural effusion, which accounted for more than 87% of major complications. The prevalence of major complications was 41.9% in boys and 57.8% in girls. Fisher's exact test showed no significant statistical dependency between sex and the occurrence of major complications of pulmonary biopsy.
complications (p = 0.317). Fisher's exact test did not show a statistically significant dependency between PTT and INR status with the occurrence of major complications after open lung biopsy (p = 0.634 and p = 354, respectively). The highest prevalence of major complications was observed in children under 1 year of age (57.9%) and the lowest prevalence of major complications was observed in children aged 3 to 6 years (29.4%). Table 1 shows the frequency distribution of all possible preoperative diagnoses. The most common possible diagnosis before lung biopsy was pneumonia. Table 2 shows the frequency distribution of radiographic findings in the studied patients.

Table 1: Frequency distribution of possible pre-biopsy diagnosis.

| Condition          | Frequency | Percentage |
|--------------------|-----------|------------|
| Mass               | 5         | 7.8        |
| Cavity damage      | 6         | 9.4        |
| Pulmonary HTN      | 2         | 3.1        |
| Pneumonia          | 27        | 42.2       |
| External object    | 2         | 3.1        |
| No diagnosis       | 14        | 21.9       |
| Other              | 8         | 12.5       |
| Total              | 64        | 100.0      |

Table 2: Frequency distribution of radiographic findings in the studied patients.

| Condition                      | Frequency | Percentage |
|--------------------------------|-----------|------------|
| Not reported                   | 20        | 31.3       |
| Mass                           | 9         | 14.1       |
| Cyst                           | 3         | 4.7        |
| Emphysema                      | 3         | 4.7        |
| Consolidation                  | 16        | 25.0       |
| Effusion                       | 6         | 9.4        |
| Pneumothorax                   | 5         | 7.8        |
| Other                          | 2         | 3.1        |
| Total                          | 64        | 100.0      |

Biopsy results were diagnostic in 57 cases (89.1%) and non-diagnostic in 7 cases (10.9%). In 13 cases which the probable diagnosis was unclear, 11 cases were confirmed after biopsy, but in 2 of these 13 cases was undiagnosed. Biopsy determined the type of mass in all cases, which a possible diagnosis of lung mass or thoracic wall was made. In 37 cases (57.8%) the diagnosis was changed and the exact diagnosis was made. Table 3 shows all the diagnoses before and after lung biopsy in our study.

Table 3: Diagnosis before and after open lung biopsy.

| Row | Preoperative diagnosis | Postoperative diagnosis | Postoperative diagnosis |
|-----|------------------------|-------------------------|-------------------------|
| 33  | Pneumonia              | Neuroblastoma           | Wilms metastatic mass   |
| 34  | Pneumonia              | Inflammatory pulmonary necrosis | Thoracic wall mass | Capillary hemangiomas |
| 35  | Unknown                | Inflammatory pulmonary necrosis | Simple lung cyst | Hydatid cyst |
| 36  | Pneumonia              | Inflammatory pulmonary necrosis | Pulmonary hypertension | Bronchiolitis Obliterans |
| 37  | Pneumonia              | Pulmonary tuberculosis | 5 | Pneumonia | Fibroconnective tissue & congestion |
| 38  | Swallowing an external object | External object | 6 | Pneumonia | Necrosis due to pneumonia |
| 39  | ALL with respiratory distress | Normal | 7 | Unknown | Lobar emphysema |
| 40  | AML & H1N1             | Metastasis of leukemic | 8 | Cystic adenomatous malformation | Cystic adenomatous malformation |
| 41  | Hemophagocytosis syndrome | Hemophagocytosis syndrome | 9 | Hydatid cyst | Hydatid cyst |
| 42  | DIC syndrome           | Hemophagocytosis syndrome | 10 | Emphysema | Atelactasis and emphysema |
| 43  | Pulmonary hypertension | Normal | 11 | Pneumonia | ILD |
| 44  | Pneumonia              | ILD                     | 12 | Pneumonia | Granulation tissue |
| 45  | Reserve disease        | Normal | 13 | Pneumonia | Inflammatory pulmonary necrosis |
| 46  | Hepatic encephalopathy | Reserve disease         | 14 | Pneumonia | Cystic adenomatous malformation |
| 47  | Gastroenteritis        | ILD                     | 15 | Chronic pneumonia | ARDS |
| 48  | Metabolic disease      | ILD                     | 16 | Pneumonia | ILD |
| 49  | Pneumonia              | Pulmonary tuberculosis | 17 | Pneumonia | ILD |
Discussion

The necessity for tissue biopsy should be critical to establishing a diagnosis, however, its indications and diagnostic utility remain unclear [10]. We reported the results of the 5-year experience of surgeons at the Pediatric Medical Center, with open lung biopsies. Our primary goal was to determine the diagnostic efficacy of open lung biopsy and to determine its complications. Open lung biopsy was diagnostic in 89.1% and non-diagnostic in 10.9%. Also, out of 13 cases without initial diagnosis, the histological sample obtained from open lung biopsy was diagnostic in 11 cases. The diagnosis was altered in 57.8% of cases, or a more accurate diagnosis was made, and treatment changed somewhat. The collections, which the results of them have been reported by Davies et al., Coren et al., and Greenhalgh et al., are the most comparable studies performed prior to this study in terms of size, study population, and surgical procedure used in our study [21-23]. These 4 studies are also similar in terms of diagnostic diversity (although in Davies et al.'s study, the prevalence of immunodeficiency and infections was higher).

Table 4 compares the findings of our study in terms of diagnostic efficiency, treatment change, complication rate and mortality rate with the other 6 studies conducted before our study. The mortality in our study was similar to the results of studies by Neuhaus et al., Coren et al. and Chan et al., but the complication in our study was similar to that of Davies et al., which the complication occurred in half of the cases [22-25]. This complication is one of the highest among similar studies. The diagnostic efficiency of our study (89.1%) and the change in treatment in our study (57.8%) was close to the results of previous studies. Among the similar studies listed in (Table 4), our study had the largest sample size after the study of Neuhaus et al. performed on 121 patients [24].

Table 4: Comparison of data from previous studies with the present study.

| Year | Number of patients | Change in treatment (%) | Histological diagnosis (%) | Mortality rate (%) | Complications (%) | Number of patients | Year |
|------|--------------------|-------------------------|---------------------------|-------------------|------------------|-------------------|------|
| 1997 | 47                 | -                       | 64                        | 24                | 51               | 1997              |
| 1998 | 26                 | -                       | 95                        | 5                 | 28               | 1998              |
| 1999 | 12                 | 69                      | 96                        | 38                | 8                | 1999              |
| 2003 | 12                 | 83                      | 100                       | 0                 | 25               | 2003              |
| 2013 | 33                 | 48                      | 79                        | 12                | 24               | 2013              |
| 2015 | 64                 | 57                      | 89                        | 1/5               | 50               | 2015              |

Table 5: Comparison of data from the present study with other studies.

| The authors | Date | Number of patients | Complications rate (%) | Mortality rate (%) | Histological diagnosis (%) | Change in treatment (%) |
|-------------|------|--------------------|------------------------|-------------------|----------------------------|-------------------------|
| Current study | 2015 | 64                 | 50                     | 1/5               | 89                        | 57                      |
| Lamoshi et al. [7] | 2015 | 99                 | -                      | 25                | 71                        | 16                      |
| Houmes et al. [9] | 2016 | 25                 | 0                      | 0                 | 88                        | 48                      |
| Gie et al. [20] | 2017 | 51                 | 12                     | 0                 | 86                        | 33                      |
| Sobrino et al. [6] | 2018 | 37                 | 16                     | 10                | 62                        | 43                      |
| Hafezi et al. [10] | 2019 | 19                 | 0                      | -                 | 63                        | 63                      |
| Chan et al. [8] | 2019 | 39                 | 2.5                    | 0                 | 64                        | 38                      |
| Sinha et al. [11] | 2019 | 42                 | 24                     | 0                 | 79                        | 52                      |
Table 5 also compares the results of our study with seven other studies. The diagnostic efficiency of our study is similar to that of Homs et al. and Gay et al. Also, in terms of changing the treatment, it is similar to the studies performed by Hafezi et al and Sina et al. The mortality rate in our study was similar to that studied by Chan et al., Sinha et al., Gie et al., Hounes et al., but in terms of the rate of complication, our study was not comparable to these studies and had the highest rate of complication.

It should be noted that the authors who reported a higher diagnostic percentage were from non-regional respiratory centers with higher experience and expertise in histological services. Although there have been changes in treatment in about half of the cases, this should not be construed to mean that half of the biopsies were unnecessary. Confirmation of the diagnosis can be as beneficial as a change in diagnosis, as it builds confidence in continuing the course of treatment, which is associated with serious side effects and also allows families to explain the process of possible progression and prognosis of the disease. Despite such benefits, a biopsy should not be used to confirm diagnoses that have previously been diagnosed with reasonable certainty. The results of our study showed that this complication after open lung biopsy is associated with the need for postoperative intubation as well as hospitalization in the ICU. As a result, efforts to reduce the complications of biopsy appear to lead to shorter hospitalization in hospital and intensive care units and reduce health care costs for these patients. Histological diagnosis is essential in determining the treatment of this group of children. Lung biopsy is useful in many cases, and by providing a sample of tissue, it helps to definitively diagnose the disease, which in many cases can manage and change the patient’s diagnostic and treatment program.

Open lung biopsy under general anaesthesia plays an important role in the treatment of children with chronic pulmonary disease. However, serious and common side effects of this method should be considered. The Complications occurred in half of our study subjects and mortality occurred in one case of total patients (1.5% mortality) in our study. There was no mortality that could be directly related to surgery. According to the report of the most serious complications after biopsy in the present study compared to previous studies, it seems that review of techniques used during open lung biopsy and postoperative care is required. It is important to minimize the risk of failure in clear diagnosis to avoid multiple procedures under general anaesthesia. Open lung biopsy is still the gold standard for histological diagnosis of unknown chronic pulmonary disease in children.

REFERENCES

1. Gail H Deutsch, Lisa R Young, Robin R Deterding, Leland L Fan, Sharon D Dell et al. (2007) Diffuse lung disease in young children: application of a novel classification scheme. Am J Respir Crit Care Med 176: 1120-1128. [Crossref]
2. J R Mathieson, J R Mayo, C A Staples, N L Müller (1989) Chronic diffuse infiltrative lung disease: comparison of diagnostic accuracy of CT and chest radiography. Radiology 171: 111-116. [Crossref]
3. K Nishimura, T Izumi, M Kitaichi, S Nagai, H Itoh (1993) The diagnostic accuracy of high-resolution computed tomography in diffuse infiltrative lung diseases. Chest 104: 1149-1155. [Crossref]
4. Fan LL, Mullen AL, Brugman SM, Inscore SC, Parks DP, White CW (1992) Clinical spectrum of chronic interstitial lung disease in children. J Pediatr 121: 867-872. [Crossref]
5. D A Spencer, H M Alton, F Raafat, P H Weller (1996) Combined percutaneous lung biopsy and high-resolution computed tomography in the diagnosis and management of lung disease in children. Pediatr Pulmonol 22: 111-116. [Crossref]
6. Justin A Sobrino, Nhatrang Le, Joseph A Sujka, Leo Andrew Benedict, Rebecca M Rentea et al. (2019) Therapeutic Direction Versus Adverse Outcomes in Children Undergoing Lung Biopsy. J Surg Res 236: 106-109. [Crossref]
7. Abdulraouf Y Lamoshi, Don K Nakayama (2015) Usefulness of lung biopsy in pulmonary pediatric conditions. Am Surg 81: 31-33. [Crossref]
8. Corey David Chan, Anindya Niyogi, Bruce Jaffray, Malcolm Brodlie, Hany Gabra (2020) Lung biopsy in children: when is it useful? Arch Dis Child archdischild-2019-318443. [Crossref]
9. Robert Jan Hounes, Chantal A Ten Kate, Enno D Wildschut, Rob M Verdijk, René M H Wijnen et al. (2017) Risk and relevance of open lung biopsy in pediatric ECMO patients: the Dutch experience. J Pediatr Surg 52: 405-409. [Crossref]
10. Niloufar Hafezi, Mark A Heimberger, Kyle A Lewellen, Thomas Maatman, Gregory S Montgomery et al. (2020) Lung biopsy in children's interstitial and diffuse lung disease: Does it alter management? Pediatr Pulmonol 55: 1050-1060. [Crossref]
11. Aditi Sinha, Edmund Cheesman, Oarendra Narayan (2019) Utility of open surgical lung biopsy in children. Palm Pharmacol Ther 58: 101816. [Crossref]
12. R Dinwidde, N Sharief, O Crawford (2002) Idiopathic interstitial pneumonitis in children: a national survey in the United Kingdom and Ireland. Pediatr Pulmonol 34: 23-29. [Crossref]
13. W M Toyama, C N Reyes, B R Lawton, R D Sautter (1971) Open lung biopsy in infants and children. Arch Surg 103: 195-198. [Crossref]
14. N J Wilson, M D Seear, G P Taylor, J G LeBlanc, G G Sandor (1990) The clinical value and risks of lung biopsy in children with congenital heart disease. J Thorac Cardiovasc Surg 99: 460-468. [Crossref]
15. E A Braunlin, J H Moller, C Patton, R V Lucas Jr, C W Lillehei et al. (1986) Predictive value of lung biopsy in ventricular septal defect: long-term follow-up. J Am Coll Cardiol 8: 1113-1118. [Crossref]
16. N A Shorter, A J Ross 3rd, C August, L Schnaufer, M Zeigler et al. (1988) The usefulness of open-lung biopsy in the pediatric bone marrow transplant population. J Pediatr Surg 23: 533-537. [Crossref]
17. L L Fan, C A Kozinetz, H A Wojtczak, B A Chatfield, A H Cohen et al. (1997) Diagnostic value of transbronchial, thoracoscopic, and open lung biopsy in immunocompetent children with chronic interstitial lung disease. J Pediatr 131: 565-569. [Crossref]
18. R L Smyth, H Carty, H Thomas, D van Velzen, D Heaf (1994) Diagnosis of interstitial lung disease by a percutaneous lung biopsy sample. Arch Dis Child 70: 143-144. [Crossref]
19. A G Nicholson, A Bush (2001) Methodology for assessing patterns of interstitial pneumonia in children. Arch Dis Child 85: 172. [Crossref]
20. A G Gie, J Morrison, R P Gie, P Schubert, J Jansen et al. (2017) Diagnosing diffuse lung disease in children in a middle-income
country: the role of open lung biopsy. *Int J Tuberc Lung Dis* 21: 869-874. [Crossref]

21. Robert M Greenhalgh, Iain E Yardley, Fran Child, James Bruce, Gill M Humphrey (2014) Lung biopsy for chronic pulmonary disease in children. *J Pediatr Surg* 49: 1075-1077. [Crossref]

22. L Davies, S Dolgin, M Kattan (1997) Morbidity and mortality of open lung biopsy in children. *Pediatrics* 99: 660-664. [Crossref]

23. M E Coren, A G Nicholson, P Goldstraw, M Rosenthal, A Bush (1999) Open lung biopsy for diffuse interstitial lung disease in children. *Eur Respir J* 14: 817-821. [Crossref]

24. S J Neuhaus, K S Matar (1997) The efficacy of open lung biopsy. *Aust N Z J Surg* 67: 181-184. [Crossref]

25. P W Chan, T M Ramanujam, A Y Goh, L C Lum, J A Debruyne et al. (2003) Open lung biopsy for diffuse parenchymal lung disease in children. *Med J Malaysia* 58: 636-640. [Crossref]

26. R Steinberg, E Freud, J Ben Ari, T Schonfeld, D Golinsky et al. (1998) Open lung biopsy–successful diagnostic tool with therapeutic implication in the critically ill paediatric population. *Acta Paediatr* 87: 945-948. [Crossref]