Research Article

Non-cystic fibrosis bronchiectasis: Analysis of clinical profile and surgical outcome

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Abstract
Objective: To evaluate the clinical profile and surgical outcome in patients with non- cystic fibrosis (non-CF) bronchiectasis. **Patients and methods**: This retrospective study reviewed medical records of 30 patients who underwent surgery for non-CF bronchiectasis over a period of five years, between 2011 and 2016. The analysis included patient demographics, clinical features, severity of bronchiectasis, indication for surgery, type of surgical procedures, mortality, postoperative complications, and clinical symptomatic improvement. **Results:** The study included 9 (30%) male and 21 (70%) female patients, with mean age of 30.2±10.6 years (range: 9-52 years). The most frequent etiologic factor of non-CF bronchiectasis was post-infectious (40%), and the most frequent pattern of pulmonary function was normal (43.33%). The main presenting symptom was cough (80%). The most frequently isolated microorganism on sputum cultures was Pseudomonas aeruginosa (43.33%). The surgical procedures were: pneumonectomy (3.3%), lobectomy (76.6%), bilobectomy (10%), lobectomy plus segmentectomy (6.7%), and segmentectomy (3.3%). Complete lung resection was achieved in 73.3%. The mortality rate was 3.3%. Postoperative complications were reported in 23.3%. Patients with complete lung resection had lower incidence of postoperative complications than those with incomplete resection (9% versus 62.5%, P=0.002). During mean follow-up period of 29±15.7 months (range: 6-54 months), 70% of patients were symptom free and 20% had improved symptoms. **Conclusion:** Surgery is a safe and effective option for treatment of non-CF bronchiectasis, especially with proper patient selection and preparation and when complete resection can be achieved.
Keywords: Bronchiectasis, lung resection, outcome

Introduction
Bronchiectasis is a suppurative lung disease which was originally described in 1819[1]. It is found in a variety of pulmonary diseases, both genetically caused and acquired, such as severe pulmonary infections and cystic fibrosis (CF) [2]. Most of the cases of bronchiectasis are not due to CF, so-called non-CF bronchiectasis[3]. Pathologically, patients with non-CF bronchiectasis have a vicious circle of impaired clearance of mucus and bacterial infection resulting in persistent airway inflammation and irreversible bronchial dilation[2].
Clinically, patients presented with chronic cough, purulent sputum, recurrent exacerbations, and progressive airway destruction.

Despite, the advent of antibiotics and the decreased prevalence of non-CF bronchiectasis in developed countries, this problem remains significant in developing countries because of tuberculosis, pneumonia, pertussis, and serious rubella infections[4]. High resolution chest computed tomography (HRCT) is the main tool for diagnosis of bronchiectasis with specific criteria including larger internal diameter of the bronchus than that of its accompanying vessel, in addition to failure of the bronchus to taper in the periphery of the chest[5].
The aim of bronchiectasis management is to prevent progression of the disease and to reduce symptoms and exacerbations[4]. The surgical treatment is reserved for focal disease and when

medical treatment is no longer effective. The surgical resection for bronchiectasis should remove permanently damaged lung lobes or segments to prevent recurrent infections where antibiotic penetration is poor. Surgery for bronchiectasis currently still plays an important role in thoracic surgical practice[6]. However, the optimal treatment of bronchiectasis remains controversial[7]. Therefore, the aim of this study is to review and evaluate the clinical profile and the role of the surgical treatment in patients with non-CF bronchiectasis at our institution.

Patients and methods

This retrospective study included 30 patients underwent pulmonary resection for non-CF bronchiectasis, at unit of cardiothoracic surgery, Minia University, between 2011 and 2016. Data were collected from the medical records. The inclusion criteria were: available data, localized non-CF bronchiectasis proved by high-resolution computed tomography (HRCT) (Fig. 1), symptoms of bronchiectasis, perfusion studies, adequate cardiopulmonary reserve, and failure of medical treatment. Patients were referred to surgery due to failure of medical treatment in all patients, in addition to recurrent chest infection in 16 (53%) patients, recurrent hemoptysis in 11 (37%) patients, and destroyed lung in 3 (10%) patients.

All patients received preoperative nonsurgical measures including antibiotic therapy, physiotherapy, and bronchodilator treatment, to reduce purulent sputum and expectorations to less than 20mL/day during the last two weeks before surgery.

Preoperative evaluation included physical examination, chest radiography, HRCT, pulmonary function tests, arterial blood gases, sputum culture for pyogenic and tubercular bacilli, and bronchoscopy to rule out any intraluminal pathology or bronchial edema. The type of lung resection was determined according to the affected sides and cardio-pulmonary reserve.

All operations were performed under general anesthesia via a posterolateral thoracotomy. Adhesions were released by meticulous dissection and lung resections were performed using standard techniques. The bronchial stump was kept short, closed with interrupted sutures and covered by adjacent pleural flap or mediastinal tissue. At the end of surgery, two intercostal tubes were placed for drainage for at least 48 hours. The bronchial suture was bronchoscopically checked with removal of secretions from the airways. The resected specimens were sent to histopathological examination.

The collected data were patient demographics, clinical features, severity of bronchiectasis, indication for surgery, type of surgical procedures, mortality, postoperative compli-cations, and clinical symptomatic improvement. Complete resection was defined if all affected segments on preoperative HRCT were anato-mically resected. The clinical symptomatic improvement was categorized as previously described [8], as excellent if there is a complete absence of preoperative symptoms leading to surgery (symptom free patients); good if there is a marked reduction in preoperative symptoms (improved patients); or unchanged if there is no reduction in preoperative symptoms.

The statistical analysis was performed using Statistical Package for Social Sciences version 16.0 (SPSS, Inc., Chicago, IL, USA). Conti-nuous variable data were presented as mean and standard deviation, and categorical variable data were presented as percentages. The comparison of categorical variables was performed using Chi-square or Fisher's exact test, while continuous variables were compared with Student's unpaired t-tests. Differences were considered significant when the probability value (P-value) were < 0.05.

Results

The demographic and clinical findings in our 30 patients with non-cystic fibrosis bronchiectasis are shown in Table 1. The study included 9 (30%) male and 21 (70%) female patients, with mean age of 30.2±10.6 years (range: 9-52 years). The etiologic factors of non-CF bronchiectasis were post-infectious (40%), idiopathic (30%), history of past tuberculosis (10%), COPD (6.67%), bronchial asthma (3.33%), foreign body aspiration (3.33%), or unknown (6.67%). The most frequent pattern of pulmonary function was normal (43.33%), followed by obstructive pattern (36.67%).

Clinically, the main symptoms and signs were: cough (80%), expectorations (70%), dyspnea

(43%), hemoptysis (30%), and wheezing (16.67%). In accordance to BSI, bronchiectasis was mild in 23.33%, moderate in 70%, and severe in 6.67%. The isolated microorganisms on sputum cultures were: Pseudomonas aeruginosa (43.33%), Haemophilus influenza (20%), Staphylococcus aureus (10%), Streptococcus pneumoniae (6.67%), tuberculosis (3.33%), and no pathogen (16.67%). The surgical procedures in our cases with non-CF bronchiectasis (Fig. 2) were: pneumonectomy (1 patient; 3.3%), lobectomy (23 patients; 76.6%), bilobectomy (3 patient; 10%), lobectomy plus segmentectomy (2 patient; 6.7%), and segmentectomy (1 patient; 3.3%).

Table (1): Demographic and clinical findings in 30 cases with non-cystic fibrosis bronchiectasis

Variables	Patients (n=30)
Age, mean±sd (years)	30.2±10.6 (range: 9-52)
Sex: M/F	9(30%)/21(70%)
Etiologic factors:	
Post-infectious	12 (40%)
Idiopathic	9 (30%)
Past tuberculosis	3 (10%)
COPD	2 (6.67%)
Bronchial asthma	1 (3.33%)
Foreign body aspiration	1 (3.33%)
Unknown	2 (6.67%)
Pattern of PFTs:	
Normal	13 (43.33%)
Obstructive	11 (36.67%)
Restrictive	4 (13.33%)
Mixed	2 (6.67%)
Symptoms and signs:	
Cough	24 (80%)
Expectoration	21 (70%)
Dyspnea	13 (43%)
Hemoptysis	9 (30%)
Wheezing	5 (16.67%)
Severity of bronchiectasis:	
Mild	7 (23.33%)
Moderate	21 (70%)
Severe	2 (6.67%)
Isolated microorganisms:	
Pseudomonas aeruginosa	13 (43.33%)
Haemophilus influenzae	6 (20%)
Staphylococcus aureus	3 (10%)
Streptococcus pneumoniae	2 (6.67%)
Tuberculosis	1 (3.33%)
No pathogen	5 (16.67%)

COPD: Chronic obstructive pulmonary disease, PFTs: Pulmonary function tests

The mean follow-up period was 29±15.7 months (range: 6-54 months). The mortality rate was 3.3% (n=1) due to respiratory insufficiency. Postoperative outcome in relation to completeness of lung resection are presented in Table 2. Complete lung resection was achieved in 22 patients (73.3%) while incomplete resection was found in 8 patients

(26.6%). Postoperative complications were reported in 7 patients (23.3%) including: atelectasis (10%), persistent air leak > 2 weeks (6.67%), pneumonia (3.33%), and broncho-pleural fistula (3.33%). There was a significant decrease in the overall incidence of post-operative complications in patients who underwent complete lung resection versus those underwent incomplete resection (9% versus 62.5%, P=0.002). The clinical improvement after surgery was symptom free in 21 patients (70%), improved in 6 patients (20%), and unchanged in 3 patients (10%). Despite the higher frequency of symptom free patients when complete resection was achieved, the difference from patients with incomplete resection did not reach the significance level (77.27% versus 50%, P=0.14).

Table (2): Postoperative outcome in relation to completeness of lung resection

Variables	Total (n=30)	Complete resection (n=22)	Incomplete resection (n=8)	P-value
Postoperative complications:	7 (23.3%)	2 (9%)	5 (62.5%)	0.002*
Atelectasis	3 (10%)	1 (4.55%)	2 (25%)	0.09
Persistent air leak > 2 week	2 (6.67%)	1 (4.55%)	1 (12.5%)	0.43
Pneumonia	1 (3.33%)	0 (0%)	1 (12.5%)	0.09
Bronchopleural fistula	1 (3.33%)	0 (0%)	1 (12.5%)	0.09
Clinical improvement:				
Symptom free patients	21 (70%)	17 (77.27%)	4 (50%)	0.14
Improved patients	6 (20%)	4 (18.18%)	2 (25%)	0.67
Unchanged	3 (10%)	1 (4.55%)	2 (25%)	0.09

*Significant difference

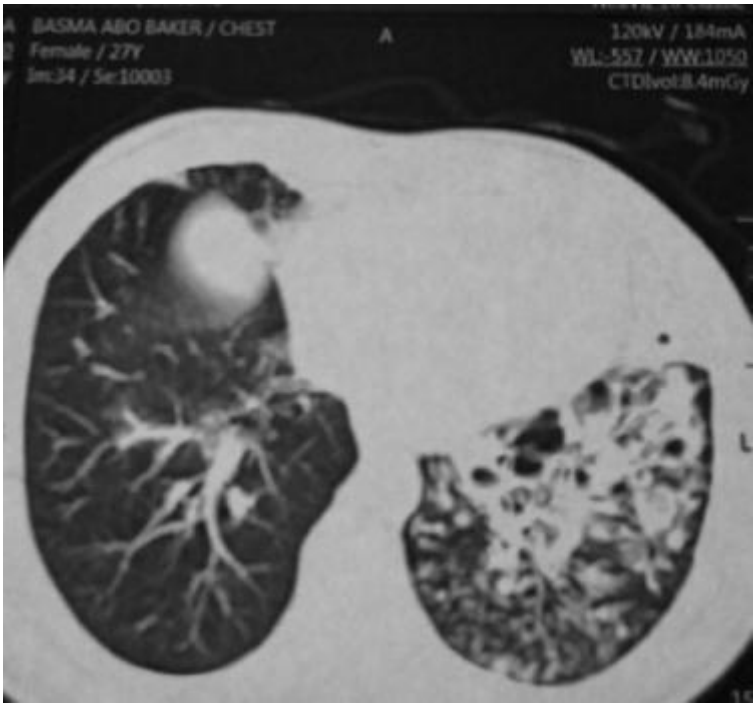

Fig. (1): Axial view of high resolution computed tomography showing bronchiectasis at the left lower lobe with bilateral consolidations in a 27-year old female patient

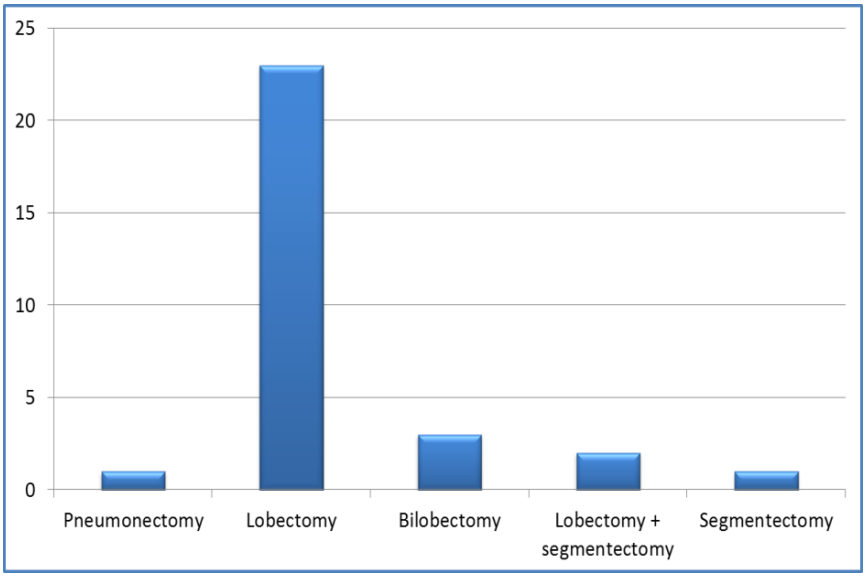

Fig. (2): Surgical procedures in 30 cases with non-cystic fibrosis bronchiectasis

Discussion

The prevalence of non-CF bronchiectasis has been increased in the past two decades, which may be attributed to increased use of high-resolution chest CT (HRCT) in diagnosis of respiratory diseases which helps increase recognition of previously undiagnosed cases [9], in addition to the increased incidence of antibiotic resistance and autoimmune diseases [10]. Our study included 9 (30%) male and 21 (70%) female patients with non-CF bronchiectasis. Gender differences in bronchiectasis were reported in literature[11]. The typical clinical profile of a patient with bronchiectasis is a middle-aged non-smoker woman. Females are more likely to have non-CF bronchiectasis of idiopathic causes or associated with asthma [12]. The reasons behind the gender differences in both CF and non-CF bronchiectasis include increased comorbidities, anatomical and physiological factors, chronic infection and inflammation, impairment of host defences and environmental influences [13].

The most common etiologic factor of non-CF bronchiectasis in our patients was post-infectious (40%). Post-infectious bronchiectasis is still the leading cause in developing countries because of poor access to healthcare and a high infection rate. Several respiratory infections can cause bronchiectasis, including measles, pertussis and tuberculosis, but also viruses (HIV, paramyxovirus, adenovirus and influenza), Gram-negative bacteria (*Pseudomonas aeruginosa*, *Haemophilus influenzae*) and other atypical mycobacteria[9]. This finding is correlated to our micro-biological results as the most frequently isolated microorganism on sputum cultures was *Pseudomonas aeruginosa* (43.33%) followed by *Haemophilus influenza* (20%). Beside post-infectious causes other possible etiologies as found in non-CF bronchiectasis phenotyping studies and clinical trials include COPD, bronchial .asthma, immunodeficiency, mechanical obstruction (tumor, foreign body, lymphadenopathy), sequelae of inhalation or aspiration, auto-inflammatory conditions, congenital conditions, and other uncommon etiologies[4].

The pathogenesis of non-CF is related to vicious cycle of infection. Regardless of the etiologic factor, when mucociliary clearance is impaired, mucous is retained in the airways. This in turn leads to microbial colonisation or infection with a subsequent development of an inflammatory response[14]. Gram-negative bacteria are the most frequently identified organisms in the sputum of patients with bronchiectasis including *Pseudomonas aeruginosa*, *and Haemophilus influenzae*. Gram-positive organisms are less common and include *Streptococcus pneumoniae* and *Staphylococcus aureus*[1]. Most of the isolated

microorganisms in bronchiectasis can form biofilms in the bronchial airways facilitating the persistence of the vicious cycle of bronchiectasis because the biofilms protect bacteria from clearance by the host immune system and reduce the effects of antibiotics further potentiating airway inflammation[15].

The main presenting clinical features in our patients were cough (80%) and expectorations (70%). The symptoms and signs of NCFB are variable. Although the symptoms and signs of non-CF bronchiectasis are variable, it should be suspected in any patient with chronic cough and sputum production or frequent respiratory infections[1]. Additional important clinical features include hemoptysis, chest pain, weight loss, bronchospasms, rhinosinusitis, fatigue, dyspnoea and decreased exercise tolerance[1, 8]. The most frequent pattern of pulmonary function in our series was normal (43.33%) followed by obstructive pattern (36.67%). Disturbed pulmonary function in the form of reduced forced expiratory volume in 1 s (FEV_1) has been reported in patients with non-CF bronchiectasis, particularly when there are severe exacerbations, colonisation with *Pseudomonas aeruginosa*, or systemic inflammation[16]. The treatment of symptomatic bronchiectasis is primarily medical, in order to reduce airway obstruction and eradicate bacteria from the lower respiratory tract[17]. Surgery is the only curative treatment in localized bronchiectasis that are refractory to clinical management, provided that underlying diseases that contribute to onset have been ruled out. Surgery with palliative intent is also indicated in cases of severe hemoptysis with ineffective embolization, or of abscessed areas that cannot be cured with antibiotic treatment [2]. The most common indication for surgery in our series was the persistence of symptoms after failure of medical treatment, in agreement with other studies[7,8,18,19]. Our surgical procedures include pneumonectomy (3.3%), lobectomy (76.6%), bilobectomy (10%), lobectomy plus segmentectomy (6.7%) and segmentectomy (3.3%). Similar high frequency of lobectomy for treatment of bronchiectasis has been reported in other studies[6-8].

In our patients, the mortality rate was 3.3%, and postoperative complications were reported in 23.3% of our cases. These acceptable rates are consistent with other studies where the incidences of postoperative complications and mortality after surgical treatment of bronchiectasis were 9.4%-24.6% and 0%- 8.3%, respectively[7,8,18-21]. Factors such as the existence of residual bronchiectasis, *Pseudomonas aeruginosa* or non-tuberculous mycobacteria infection and immunosuppression can still result in a poor clinical response after surgery[2]. Appropriate preoperative preparations may help reduction in the rates of postoperative morbidity and mortality. As previously recommended[9], the strategy of preoperative preparation at our institution was to reduce purulent sputum and expectorations to be <20mL/day, in addition to a bronchoscopic evidence of absent bronchial edema during the last two weeks before surgery.

During mean follow-up period of 29±15.7 months (range: 6-54 months), 70% of our patients were symptom free and 20% had improved symptoms, while the remaining 10% had unchanged symptoms. Our findings are in agreement with other studies in literature. In a meta-analysis of 35 studies consisting of more than 4000 patients who underwent surgical resection for the management of non-CF bronchiectasis, the pooled proportion was 66.5% for patients free of symptoms, 27.5% for patients who were improved, and 9.1% for patients who showed no clinical improvement.
Complete lung resection was achieved in 73.3% of our patients. Complete lung resection associated with lower incidence of postoperative complications than that with incomplete resection (9% versus 62.5%, P=0.002). The surgical treatment should aim to complete resection of the affected segments as well as preservation of maximum pulmonary function by sparing a minimum of two lobes or six pulmonary segments to ensure adequate pulmonary function[18]. Similar association between good results and complete resection has been reported by others[7,8,18,19], with a range of complete resection from 64.7%[18] to 90.7%[7].

The limitations of this study are retrospective nature, small cohort of patients undergoing surgery for treatment of non-CF bronchiectasis, and conduction of the study at a single institution. Therefore, to validate our findings

there is a need for further prospective large, multicenter studies evaluating long-term outcome.

In conclusion, lung resection of non-CF bronchiectasis is safe and effective with acceptable postoperative results and symptomatic improvement. The favorable outcome is related mainly to proper patient selection, appropriate preoperative preparation, and complete resection of the lesion.

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