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ORIGINAL ARTICLE

Transbronchial lung cryobiopsy: Associated complications

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Abstract
Introduction: Transbronchial lung cryobiopsy (TBC) has emerged as a diagnostic alternative to surgical lung biopsy in interstitial lung disease (ILD). Despite its less invasive nature, some associated complications have been described.
Objective: To evaluate complications of TBC and associated factors.
Methods: Prospective evaluation of all patients with ILD submitted to TBC in our centre. Clinicodemographic variables and factors associated to TBC complications were analyzed. The effect of the variables on the complication risk was evaluated by a logistic regression model.
Results: Ninety patients were included (mean age 60 ± 13 years; 58.9% male). Twenty-two patients presented pneumothorax, 18 (81.8%) of which were treated with chest tube drainage [median air leak time: 1 day (IQR = 2)]. Grade 2 and 3 bleeding was observed in 13 (14.4%) cases. Presence of visceral pleura in the sample accounted for almost more than 10 times the odds of pneumothorax (OR = 9.59, 95% CI 2.95–31.17, $p < 0.001$). Increased body mass index (BMI) was associated with bleeding (16% additional odds for each BMI unit increase (OR = 1.16, 95% CI 1.01–1.34, $p = 0.049$).
Conclusion: The most frequent complication of TBC was pneumothorax, although rapidly reversible. There was a positive association between pneumothorax and the presence of pleura in the biopsy samples as well as between bleeding and increased BMI. More studies about TBC complications are needed to improve the selection of the candidates for this procedure.

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Introduction

Interstitial lung disease (ILD) represents a heterogeneous group of diseases with different prognostic and therapeutic implications. The evaluation of patients with ILD is best achieved by a multidisciplinary approach combining clinical, radiologic, and pathologic features. In many circumstances a histological confirmation is required to establish the exact diagnosis.[1–5] Several techniques have evolved over the years and are employed in many centres. Conventional transbronchial lung biopsy (TLB) is not currently recommended in fibrotic lung disorders due to its low diagnostic yield[6]; besides, the procedure presents risks.[7]

Surgical lung biopsy (SLB) provides adequate lung specimens for histopathological analysis and is recommended as reference standard by current guidelines in ILD when a non-invasive diagnosis cannot confidently be made.[6,8] However, it requires hospitalization and chest tube drainage and may be associated with significant morbidity (2–20%), including prolonged air leak and acute exacerbation as well as mortality (2–17%).[9–12] Moreover, many subjects are excluded because of increased risks of perioperative morbidity and mortality by a combination of advanced age, comorbidity, severe respiratory failure, and pulmonary hypertension.

Cryotherapy has been used in bronchoscopy since the sixties, mainly in the management of endobronchial lesions in patients with bronchial obstruction.[13] More recently, transbronchial cryobiopsy (TBC) has been used for the assessment of ILD. The major advantage of TBC is that large pieces of tissue can be extracted with a higher percentage of alveolar tissue,[14–18] fewer crush artefacts and less atelectasis.[16–18] The greater volume of alveolar tissue correlates with a better diagnostic yield.[15–19] Despite its less invasive nature, some associated complications have been described. The potential for bleeding and the pneumothorax rates up to 33%, often requiring inpatient admission and chest tube drainage, are the most commonly described.[19–23]

We here investigate the safety of TBC in subjects with ILD and possible factors associated with its complications, in order to improve candidate selection for this procedure.

Methods

Study design

We conducted a prospective study of all patients with ILD undergoing TBC from May 2014 to December 2016 at the Bronchoscopy Unit of the Pulmonology Department of Vila Nova de Gaia/Espinho Hospital Centre. Medical records were analyzed and demographic data, chest high resolution computed tomographic (HRCT) scans, procedure and complications details and pathology were recorded. The indication for TBC was diffuse pulmonary infiltrates of unclear aetiology. The request for TBC was made by the pulmonologist dedicated to ILD. According to the standard of care protocol in our institution, patients were required to have a pO_2 of at least 60 mmHg under oxygen delivery up to 2liters/min, and normal blood count, electrolytes, markers of renal function and coagulation parameters. All anticoagulants were discontinued before the procedure as per guidelines.[24] Before the procedure, risks and possible complications were explained to each patient and informed consent was obtained.

The procedure

All procedures were performed under general anaesthesia and by a pulmonologist experienced in interventional bronchoscopy. After intubation with a rigid tracheoscope (Storz 12mm®), a videobronchoscope was advanced to the desired segment (previously identified in the HRCT) and a flexible cryoprobe (2.4 mm, model 20416-032, Erbokryo® CA, Erbe, Germany) was passed through the videobronchoscope into the bronchial segment under fluoroscopic guidance. After confirming correct positioning (defined as having the tip of the probe perpendicular and about to 10 mm from the chest wall), a freezing time of 5 s was applied, time after which the bronchoscope and cryoprobe were removed as a single unit and a bronchial blocker balloon (Olympus® B5-2c), previously placed in the segment was inflated, in order to prevent haemorrhage. The frozen specimen was thawed in saline and fixed in formalin. Each patient had at least one biopsy using this technique. Only one lung was biopsied per patient and the number of biopsies taken depended upon the researcher.

In patients who had not previous had bronchoalveolar lavage, it was performed before cryobiopsy, usually in the most affected pulmonary lobe.

Complications

Severity of bleeding was classified as: grade 0 – no bleeding; grade 1 – estimated volume of aspirated blood <50 ml; grade 2 – estimated volume of aspirated blood of between 50 and 100 ml and requiring endoscopic procedures as instillation of topical adrenaline and/or ice-cold saline; grade 3 – estimated volume of aspirated blood >100 ml and requiring endoscopic procedures as instillation of topical adrenaline and/or ice-cold saline and/or haemostatic tamponade therapy; grade 4 – any life-threatening bleeding requiring transfusion or escalation of care such as admission to the intensive care unit or surgery consultation. To rule out pneumothorax, a chest X-ray was obtained within at least 2 h of the procedure.

Statistical analysis

Descriptive statistics were used to analyze patient characteristics. The categorical variables were reported in frequencies (n) and percentages (%). Continuous data were described as means and standard deviations (SD) when variables had symmetric distributions and as median and interquartile range (IQR) when variables had no symmetric distribution. Inferences were tested by the chi-squared test (qualitative variables), the t-test (normally distributed quantitative variables) or the Mann–Whitney U-test (nonnormally distributed quantitative variables). The effect of the significant variables that emerged from the previous analysis on bleeding and pneumothorax risk was evaluated by a multivariate logistic regression model. A p value of <0.05

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