

Peer Review File

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Review Comments A

Comment 1: Clarify the dose of the inhaled steroid that is said to be effective in the early stages of TO.

Reply 1: In Zhu's study, inhaled corticosteroids (budesonide power, 400 ug, bid) were administered to 8 patients, two of whom belong to Stage I and six to Stage II. In the current study, two subjects in stage III and two in stage II were administered inhaled corticosteroids involving Budesonide and Formoterol Fumarate for Inhalation (160 ug / 4.5 ug, bid) or Salmetero Xinafoate and Fluticasone propionate Powder for Inhalation (50 ug / 250 ug, bid).

Changes in the text: Additionally two subjects in stage III and two in stage II were administered inhaled corticosteroids involving Budesonide and Formoterol Fumarate for Inhalation (160 ug / 4.5 ug, bid) or Salmetero Xinafoate and Fluticasone propionate Powder for Inhalation (50 ug / 250 ug, bid).(see page 7, line 130-134)

Comment 2: It is necessary to clarify the treatment period of inhaled steroids as it is considered necessary information.

Reply 2: In Zhu's study, remarkable improvement of the lesions under endoscopy was observed in 2 patients treated with inhaled corticosteroids 1 year later. In the current study, patients were administered inhaled corticosteroids for 3 to 24 months. Improvement of cough, dyspnea, performance status and living quality were observed.

Inhaled corticosteroids may be given chronically and regularly in TO patients just as chronic obstructive pulmonary disease (COPD), especially in those lesions filling with inflammatory cells, because nodules in the airway could not be completely corrected, and airway obstruction could not be reversed. The course and dose of inhaled corticosteroids, the interval of bronchoscopic intervention are still unclear because the limitations of retrospective study with small sample size. Large multicenter prospective study needs to be done to provide new sights about TO.

Changes in the text: One subject in stage III with sever obstruction in the tracheal and four in stage II underwent repeated bronchoscopic intervention such as argon plasma coagulation regularly for 6 to 24 months, among which the patient in stage III also received balloon dilatation. Additionally two subjects in stage III and two in stage II were administered inhaled corticosteroids involving Budesonide and Formoterol Fumarate for Inhalation (160 ug / 4.5 ug, bid) or Salmetero Xinafoate and Fluticasone propionate Powder for Inhalation (50 ug / 250 ug, bid), with duration of treatment varying from 3 to 24 months. (see page 7, line 130-134)

.....Inhaled corticosteroids may be given chronically and regularly especially in those lesions filling with inflammatory cells, because lesions in the airway could not be completely corrected, and airway obstruction could not be reversed.....The course and dose of inhaled corticosteroids, the interval of bronchoscopic intervention are still unclear because the limitations of retrospective study with small sample size. Large multicenter prospective study needs to be done to provide new sights about TO. (see page 10-11,line 203-214)

Review Comments B

Comment 1: Please consider a language editing of your manuscript (e.g. crucial vs crucial - abstract conclusion)

Reply 1: I am very sorry about the mistaken spelling, and I had corrected it in the text.

Changes in the text: Not only multi-disciplinary cooperation of clinical, endoscopic and histological assessment, but also awareness are crucial to TO diagnosis, especially in early stage of TO, which was difficult to identify. (see Page 2 line 45)

Comment 2: Change the Figure 2 providing more detailed images consistent with your legend as to me B is mostly lung parenchyma and C-D don't see cartilaginous or bone, i see mucosa with squamous metaplasia and mild inflammatory infiltrate.

Reply 2: We had reevaluated the pathology slice of TO patients in our study, and picked out some images that are more representative.

Changes in the text:

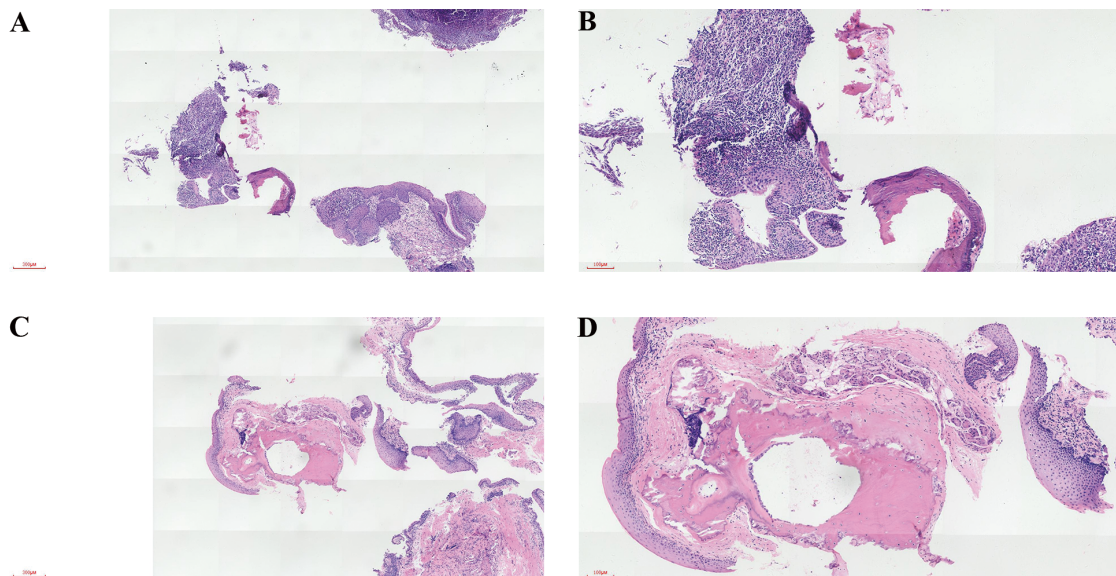


Figure 2 Histopathological findings of TO. Squamous metaplasia of the bronchial mucosa, infiltration of chronic inflammatory cells in the bronchial mucosa, cartilaginous and osseous deposition underneath the respiratory epithelium (bar in A and C 300um; bar in B and D 100um) .

