

# Relative Factors Analysis of the Occurrence and Location of Intratracheal Granuloma Following Tracheotomy

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**Aim:** Tracheotomy has become more prevalent in clinical settings, and effectively managing postoperative complications plays a crucial role in determining patient outcomes. However, there is a scarcity of clinical research focusing on the development of intratracheal granuloma after tracheotomy, and there is insufficient theoretical support for early detection in clinical settings. This study investigates the relationship between clinical factors and the occurrence and location of intratracheal granuloma.

**Methods:** Clinical parameters from 872 patients who underwent tracheotomy between January 1, 2010, and December 30, 2018, were collected from the Hospital Information System. A retrospective analysis was conducted, focusing on factors such as age, gender, smoking history, comorbidities, primary lesion location, benign versus malignant primary disease, pulmonary infection, duration of tracheal intubation prior to tracheotomy, surgical method and other factors.

**Results:** Intratracheal granuloma was observed in 50 (5.73%) cases of all tracheotomy patients. Factors such as smoking history, primary lesion location, and pulmonary infection were associated with the occurrence of intratracheal granuloma. Additionally, multivariate logistic regression identified smoking, pulmonary disease and pulmonary infection as independent risk factors for the development of intratracheal granuloma following tracheotomy. Regarding the location of the granuloma, 42 cases (84%) were found in the proximal trachea, while the remaining cases were located in the distal trachea. Univariate analysis indicated that age, gender, smoking history, and primary lesion location were related to the location of intratracheal granuloma. The median interval between the detection of intratracheal granuloma and tracheotomy was 52 days.

**Conclusion:** Considering the occurrence and location of intratracheal granulomas following tracheotomy, along with the associated risk factors outlined above, it is imperative that clinicians give these issues due attention in practice. Furthermore, approximately 50% of intratracheal granulomas develop within 52 days post-tracheotomy, offering valuable insights for clinicians in formulating effective follow-up strategies.

**Keywords:** tracheotomy, intratracheal granuloma, pulmonary infection

## Introduction

Tracheotomy is a widely employed surgical procedure that involves making an incision in the trachea in the neck, inserting a tracheostomy tube, and establishing a direct airway to alleviate breathing difficulties caused by various conditions. As early as 1909, Chevalier Jackson<sup>1</sup> provided a detailed description of the Standard Tracheostomy (ST), while Ciaglia<sup>2</sup> introduced the Percutaneous Dilatational Tracheotomy (PDT) technique in 1985. Building upon these foundational methods, numerous tracheotomy techniques have been developed through ongoing exploration and refinement. PDT is frequently utilized for patients with respiratory diseases and can be performed at the bedside by professionals in intensive care units (ICU), respiratory physicians, or otolaryngologists.<sup>3</sup> In contrast, ST is typically reserved for more complex cases. Although it is

generally performed in an operating room, it can also be executed at the bedside in emergency situations and is often conducted in conjunction with other surgical procedures.<sup>4</sup>

The primary indications for tracheotomy include situations where the airway above the tracheotomy is obstructed and the underlying cause cannot be resolved promptly; instances where sputum and secretions cannot be expelled from the airway due to respiratory tract burns, neurological disorders, or other factors; cases of neck injuries, to prevent contamination of the wound by respiratory secretions; and during surgeries involving the maxillofacial region, upper respiratory tract, and neck, to minimize the risk of flushing fluids entering the lungs and obstructing the airway. Additionally, for patients requiring prolonged mechanical ventilation, tracheotomy may be performed expediently to mitigate complications associated with endotracheal intubation.<sup>5</sup> Notably, tracheotomy has no absolute contraindications, except in cases of active cellulitis of the anterior cervical skin. Furthermore, it can enhance patient comfort, restore speech and swallowing functions, facilitate sputum suction and cannula replacement, and decrease the need for sedatives.<sup>6</sup> Complications following tracheotomy can be categorized into early and late stages, with intratracheal granuloma being a prevalent factor contributing to late complications.<sup>7,8</sup> Literature indicates that the incidence of intratracheal granuloma post-tracheotomy is approximately 7%.<sup>9</sup> A study involving pediatric patients who underwent tracheotomy due to vocal cord paralysis found that the most frequent complication associated with the procedure was the formation of tracheal and oral granulomas, with a combined incidence of 77.1%.<sup>10</sup>

The primary cause of intratracheal granuloma formation related to tracheotomy is the friction between the tracheal catheter and the cannula at the contact site, which results in injury to the inner wall of the trachea.<sup>11</sup> Furthermore, the inflammatory response elicited by the interaction of infectious factors also promotes cell proliferation. Overall, various cell types are involved in the development of intratracheal granuloma; these cells produce cytokines, recruit inflammatory cells and tissue repair cells to the site of injury, induce a monocyte inflammatory response, and stimulate neovascularization. This cascade of events ultimately leads to fibroblast proliferation, chemotactic migration, and the synthesis of extracellular matrix.<sup>12,13</sup>

Astrachan et al<sup>14</sup> observed 52 patients who underwent tracheotomy following prolonged tracheal intubation. They found that the mortality rate associated with complications from tracheotomy ranged from approximately 0.17% to 1%, with intratracheal granuloma identified as a significant cause of death.<sup>4</sup> When intratracheal granuloma obstructs the airway to a certain extent, it can result in difficulty with expectoration, potentially leading to obstructive pneumonia. Furthermore, granulomas are highly vascularized and have a fragile texture, making them prone to bleeding. If a patient experiences significant bleeding and does not receive prompt and professional medical intervention, airway obstruction may occur, which can be fatal. In cases where the granuloma is excessively large, it can directly result in respiratory failure and death.<sup>15</sup> For small granulomas, timely endoscopic treatment is advisable, as the associated adverse effects are relatively minimal. In contrast, larger granulomas can lead to significant airway obstruction, necessitating surgical intervention.<sup>16</sup> However, patients often present with underlying primary diseases and poor physical conditions, which can substantially elevate the surgical risks.<sup>17–20</sup> Additionally, some studies indicate that the incidence of postoperative complications—such as restenosis, suture granuloma, infection, bleeding, and pneumothorax—can reach as high as 14%.<sup>21</sup> Moreover, the likelihood of recurrence increases with granuloma size, and some patients may require multiple surgeries to address both the primary disease and related complications. Thus, early detection and treatment of intratracheal granulomas are of paramount importance. Currently, however, clinical research on the formation of intratracheal granulomas following tracheotomy remains limited. In clinical practice, small granulomas are often discovered incidentally during sputum aspiration via fiberoptic bronchoscopy or through imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) of the lung and neck. It is important to note that CT and MRI have certain limitations in differentiating between intratracheal granulomas, tracheal folds, and endotracheal secretions. The ability to detect intratracheal granulomas is contingent upon the procedural and diagnostic skills of the physicians involved. If other examinations suggest the presence of an intratracheal granuloma, fiberoptic bronchoscopy is warranted for definitive diagnosis. In cases where fiberoptic bronchoscopy fails to clarify the nature of the granuloma, corresponding specimens should be obtained for pathological examination to confirm the diagnosis. Larger granulomas are often identified through increased resistance during sputum suction tube insertion and extubation, heightened mechanical ventilation resistance and peak pressure, as well as signs of granuloma bleeding.<sup>7</sup> In severe cases, granulomas may

obstruct the airway, leading to dyspnea or even respiratory failure.<sup>7,22,23</sup> Detecting and addressing intratracheal granuloma at an earlier stage is an urgent issue that requires resolution.

Previous studies have established that gastroesophageal reflux is a significant factor contributing to the development of intratracheal granuloma and tracheal stenosis.<sup>24</sup> Various factors including age, gender, smoking history, diabetes history, duration of endotracheal intubation prior to tracheotomy, underlying diseases, pulmonary infections, scar constitution, duration of mechanical ventilation, repeated tracheotomies, long-term intubation, and the materials and types of endotracheal tubes or cannulas can influence the repair process of tracheal injuries, thereby affecting the formation of intratracheal granuloma.<sup>17,20,25–28</sup> However, most studies tend to focus solely on granulomas located at specific sites, neglecting the clinically relevant factors that may influence the location of intratracheal granulomas following tracheotomy. This study reviewed data from several hundred patients who underwent tracheotomy, documenting the incidence of intratracheal granuloma post-procedure while also recording the locations of these granulomas. Subsequently, a retrospective subgroup analysis was conducted to explore the relationship between clinical factors and the occurrence and location of intratracheal granulomas.

## Methods

### Study Design

This retrospective cohort study evaluated 872 hospitalized patients who underwent tracheotomy at Wuhan Pulmonary Hospital and Tongji Hospital, both affiliated with Tongji Medical College of Huazhong University of Science and Technology, between January 1, 2010, and December 30, 2018. The study received approval from the medical ethics committee of Wuhan Pulmonary Hospital (approval number: WHPH-2022-015). The committee exempted informed consent due to the retrospective nature of the study and the anonymity of all data.

### Participants and Data Collection

Data were collected from the Hospital Information System (HIS) of Wuhan Pulmonary Hospital and Tongji Hospital, which are affiliated with Tongji Medical College of Huazhong University of Science and Technology. This dataset included general information on all hospitalized patients who underwent surgical tracheostomy (ST) or percutaneous dilatational tracheostomy (PDT) either before or after admission. The collected data encompassed age, gender, smoking history, comorbidities, primary lesion location, the nature of primary disease (benign or malignant), pulmonary infection status, and the duration of tracheal intubation prior to tracheotomy.

Inclusion criteria for the study were as follows: (1) hospitalized patients with complete medical records; (2) patients who underwent ST or PDT before or after admission.

Exclusion criteria included patients with: (1) tracheal trauma; (2) tracheoesophageal fistula prior to tracheotomy; (3) primary tracheal tumors; (4) tracheal metastases; (5) foreign bodies in the trachea; (6) tracheal burn injuries; and (7) incomplete tracheal mucosa due to other causes before tracheotomy.

Intratracheal granuloma: color ultrasound, CT, nuclear magnetic resonance imaging (MRI), bronchoscopy or pathological examination was performed after tracheotomy, and the examination results showed intratracheal granuloma.

The location of the intratracheal granuloma was divided using the opening of the tracheal cannula as the boundary. Proximal trachea: the part of the trachea below the larynx and above the opening of the tracheal tube. The distal end of the trachea: the part of the trachea below the opening of the tracheal cannula and above the tracheal carina.

### Statistical Analysis

The SPSS statistical software package was utilized for data analysis. The Chi-square test was employed to assess differences between two or more rates or constituent ratios. In cases where the Chi-square test was not applicable, Fisher's exact test or the continuity corrected Chi-square test was used for analysis. Multivariate analysis was conducted using binary logistic regression. A P value of less than 0.05 was established as the threshold for indicating statistically significant differences.

## Results

### Correlation Between Different Clinical Factors and the Occurrence of Intratracheal Granuloma

According to the established grouping method, the general distribution of the subjects is presented in Table 1. It is important to note that, due to insufficient data, the specific timing of tracheal intubation prior to tracheotomy was not available for 19 (2.18%) cases.

There were no significant differences in the incidence of intratracheal granuloma among different age groups ( $P=0.463$ ), gender ( $P=0.973$ ), and comorbidities ( $P>0.05$ ) following tracheotomy. Conversely, the incidence was notably higher in patients with a history of smoking compared to those without such a history ( $P< 0.001$ ).

**Table 1** Correlation Between Different Clinical Factors and the Occurrence of Intratracheal Granuloma

| Variables  | Total<br>(N = 872) | Occurrence<br>(N =50) | Non occurrence<br>(N =822) | $\chi^2$ Value | P value             |
|--|--------------------|-----------------------|----------------------------|----------------|---------------------|
| Age (yr)   |                    |                       |                            |                |                     |
| (0, 20], n (%)   | 37 (4.24)          | 3 (6.00)              | 34 (4.14)                  | –              | 0.463               |
| (20, 40], n (%)  | 140 (16.06)        | 9 (18.00)             | 131 (15.94)                |                |                     |
| (40, 60], n (%)  | 414 (47.48)        | 19 (38.00)            | 395 (48.05)                |                |                     |
| (60, 100], n (%)   | 281 (32.22)        | 19 (38.00)            | 262 (31.87)                |                |                     |
| Gender, n (%)  |                    |                       |                            |                |                     |
| Male   | 661 (75.80)        | 38 (76.00)            | 623 (75.79)                | 0.001          | 0.973               |
| Female   | 211 (24.20)        | 12 (24.00)            | 199 (24.21)                |                |                     |
| Smoking history, n (%)                                   |                    |                       |                            |                |                     |
| Yes  | 247 (28.33)        | 27 (54.00)            | 220 (26.76)                | 17.221         | <b>&lt; 0.001**</b> |
| No   | 625 (71.67)        | 23 (46.00)            | 602 (73.24)                |                |                     |
| Comorbidities, n (%)                                     |                    |                       |                            |                |                     |
| Hypertension   | 150 (17.20)        | 11 (22.00)            | 139 (16.91)                | 0.857          | 0.354               |
| Diabetes   | 55 (6.31)          | 2 (4.00)              | 53 (6.45)                  | 0.153          | 0.695               |
| Uremia   | 4 (0.46)           | 0                     | 4 (0.49)                   | –              | 1.000               |
| Cirrhosis  | 5 (0.57)           | 0                     | 5 (0.61)                   | –              | 1.000               |
| COPD   | 39 (4.47)          | 1 (2.00)              | 38 (4.62)                  | 0.269          | 0.604               |
| Stroke   | 195 (22.36)        | 15 (30.00)            | 180 (21.90)                | 1.782          | 0.182               |
| Coronary heart disease                                   | 31 (3.56)          | 1 (2.00)              | 30 (3.65)                  | 0.048          | 0.827               |
| Primary lesion location, n (%)                           |                    |                       |                            |                |                     |
| Pulmonary  | 171 (19.61)        | 5 (10.00)             | 166 (20.19)                | 4.261          | <b>0.039*</b>       |
| Extrapulmonary   | 701 (80.39)        | 45 (90.00)            | 656 (79.81)                |                |                     |
| Benign or malignant primary disease, n (%)               |                    |                       |                            |                |                     |
| Benign   | 681 (78.10)        | 40 (80.00)            | 641 (77.98)                | –              | 0.737               |
| Malignant  | 191 (21.90)        | 10 (20.00)            | 181 (22.02)                |                |                     |
| Pulmonary infection, n (%)                               |                    |                       |                            |                |                     |
| Yes  | 318 (36.47)        | 29 (58.00)            | 289 (35.16)                | 10.614         | <b>0.001**</b>      |
| No   | 554 (63.53)        | 21 (42.00)            | 533 (64.84)                |                |                     |
| Duration of tracheal intubation prior to tracheotomy (d) |                    |                       |                            |                |                     |
| ≤ 7, n (%)   | 738 (84.63)        | 45 (90.00)            | 693 (84.31)                | 1.261          | 0.262               |
| >7, n (%)  | 115 (13.19)        | 4 (8.00)              | 111 (13.50)                |                |                     |
| Unidentified   | 19 (2.18)          | 1 (2.00)              | 18 (2.19)                  |                |                     |
| Surgical method, n (%)                                   |                    |                       |                            |                |                     |
| ST   | 287 (32.91)        | 19 (38.00)            | 268 (32.60)                | 0.622          | 0.430               |
| PDT  | 585 (67.09)        | 31 (62.00)            | 554 (67.40)                |                |                     |

**Notes:** The number in bold represented significant difference. \* $p < 0.05$ ; \*\* $p < 0.01$ .

**Abbreviations:** COPD, coronary heart disease; ST, surgical tracheostomy; PDT, percutaneous dilatational tracheostomy.

Additionally, the incidence in patients with extrapulmonary disease was greater than that in patients with pulmonary disease ( $P=0.039$ ); however, this was not associated with benign or malignant primary disease ( $P=0.737$ ). Furthermore, the incidence in patients with pulmonary infection was significantly higher than in those without pulmonary infection ( $P=0.001$ ). In this study, it is noteworthy that the incidence rate was not associated with either the surgical method employed ( $P=0.430$ ) or the duration of tracheal intubation prior to tracheotomy in this study ( $P=0.262$ ).

## The Multivariate Analysis Examined the Correlation Between Various Clinical Factors and the Occurrence of Intratracheal Granuloma

As indicated in Table 2, the regression model included age, gender, smoking history, comorbidities, primary lesion location, the nature of primary disease, pulmonary infection, surgical method and the duration of tracheal intubation prior to tracheotomy. The binary logistic regression analysis revealed that smoking history (OR: 4.076, 95% CI: 2.073–8.014,  $P<0.001$ ), primary lesion location (extrapulmonary disease) (OR: 3.368, 95% CI: 1.148–9.881,  $P=0.027$ ), and pulmonary infection (OR: 2.415, 95% CI: 1.316–4.430,  $P=0.004$ ) were identified as independent risk factors for the development of intratracheal granuloma following tracheotomy.

## The Distribution Characteristics of Intratracheal Granuloma Within the Population

A total of 50 patients presented with intratracheal granuloma, with the distribution across various subgroups detailed in Table 3. In one (2.00%) case, the specific timing of tracheal intubation prior to tracheotomy was not documented due to insufficient data.

## Correlation Between Different Clinical Factors and the Location of Intratracheal Granuloma

As shown in Table 3, age was associated with the location of intratracheal granuloma. The proportions of intratracheal granuloma occurring in the proximal trachea for the age groups (0, 20], (20, 40], and (40, 60] were higher than those observed in the (60, 100] age group. Conversely, intratracheal granuloma was more likely to occur in the distal trachea in the (60, 100] age group compared to the other three age groups ( $P=0.002$ ). Subgroup analysis by sex indicated that, following tracheotomy, the proportion of intratracheal granuloma in the proximal trachea was higher in male patients than in female patients ( $P=0.001$ ). Additionally, the occurrence of intratracheal granuloma in the proximal trachea was greater among patients with a history of smoking than in those without such a history ( $P=0.003$ ). Notably, comorbidities did not influence the location of intratracheal granuloma ( $P>0.5$ ).

In patients with pulmonary diseases, intratracheal granulomas were more likely to occur in the distal trachea. Conversely, in patients with extrapulmonary diseases, these granulomas were more frequently found in the proximal trachea ( $P=0.001$ ). The nature of the primary disease, whether benign or malignant, was not associated with the location of intratracheal granulomas ( $P=0.067$ ). Furthermore, the duration of tracheal intubation prior to tracheotomy ( $P=0.552$ ) and the presence of pulmonary infection during the course of the disease ( $P=0.146$ ) did not correlate with the location of intratracheal granulomas. Furthermore, the surgical method did not influence the location of the intratracheal granuloma ( $P=0.715$ ).

**Table 2** Multivariate Analysis of the Correlation Between Various Clinical Factors and the Occurrence of Intratracheal Granuloma

| Variables               | Assignment         | $\beta$ | SEM   | Wald   | P value        | OR    | 95% CI      |
|-------------------------|--------------------|---------|-------|--------|----------------|-------|-------------|
| Smoking history         | Yes = 1            | 1.405   | 0.345 | 16.598 | <b>0.000**</b> | 4.076 | 2.073–8.014 |
|                         | No = 0             |         |       |        |                |       |             |
| Primary lesion location | Pulmonary = 0      | 1.214   | 0.549 | 4.891  | <b>0.027*</b>  | 3.368 | 1.148–9.881 |
|                         | Extrapulmonary = 1 |         |       |        |                |       |             |
| Pulmonary infection     | Yes = 1            | 0.882   | 0.310 | 8.104  | <b>0.004**</b> | 2.415 | 1.316–4.430 |
|                         | No = 0             |         |       |        |                |       |             |

**Notes:** The number in bold represented significant difference. \* $p < 0.05$ ; \*\* $p < 0.01$ .

**Table 3** Correlation Between Different Clinical Factors and the Location of Intratracheal Granuloma

| Variables  | Total<br>(N=50) | Proximal<br>(N=42) | Distal<br>(N=8) | $\chi^2$<br>Value | P value        |
|--|-----------------|--------------------|-----------------|-------------------|----------------|
| Age (yr)   |                 |                    |                 |                   |                |
| (0, 20], n (%)   | 3 (6.00)        | 3 (7.14)           | 0               | –                 | <b>0.002**</b> |
| (20, 40], n (%)  | 9 (18.00)       | 9 (21.43)          | 0               |                   |                |
| (40, 60], n (%)  | 19 (38.00)      | 19 (45.24)         | 0               |                   |                |
| (60, 100], n (%)   | 19 (38.00)      | 11 (26.19)         | 8 (100.00)      |                   |                |
| Gender, n (%)  |                 |                    |                 |                   |                |
| Male   | 38 (76.00)      | 36 (85.71)         | 2 (25.00)       | 10.456            | <b>0.001**</b> |
| Female   | 12 (24.00)      | 6 (14.29)          | 6 (75.00)       |                   |                |
| Smoking history, n (%)                                   |                 |                    |                 |                   |                |
| Yes  | 27 (54.00)      | 27 (64.29)         | 0               | 8.742             | <b>0.003**</b> |
| No   | 23 (46.00)      | 15 (35.71)         | 8 (100.00)      |                   |                |
| Comorbidities, n (%)                                     |                 |                    |                 |                   |                |
| Hypertension   | 11 (22.00)      | 9 (21.43)          | 2 (25.00)       | 0                 | 1.000          |
| Diabetes   | 2 (4.00)        | 2 (4.76)           | 0               | –                 | 1.000          |
| Uremia   | 0               | 0                  | 0               | –                 | –              |
| Cirrhosis  | 0               | 0                  | 0               | –                 | –              |
| COPD   | 1 (2.00)        | 0                  | 1 (12.5)        | –                 | 0.160          |
| Stroke   | 15 (30.00)      | 12 (28.57)         | 3 (37.5)        | 0.007             | 0.933          |
| Coronary heart disease                                   | 1 (2.00)        | 1 (2.38)           | 0               | –                 | 1.000          |
| Primary lesion location, n (%)                           |                 |                    |                 |                   |                |
| Pulmonary  | 5 (10.00)       | 1 (20.00)          | 4 (50.00)       | –                 | <b>0.001**</b> |
| Extrapulmonary   | 45 (90.00)      | 41 (91.11)         | 4 (50.00)       |                   |                |
| Benign or malignant primary disease, n (%)               |                 |                    |                 |                   |                |
| Benign   | 40 (80.00)      | 36 (85.71)         | 4 (50.00)       | 3.358             | 0.067          |
| Malignant  | 10 (20.00)      | 6 (14.29)          | 4 (50.00)       |                   |                |
| Pulmonary infection, n (%)                               |                 |                    |                 |                   |                |
| Yes  | 29 (58.00)      | 22 (52.38)         | 7 (87.50)       | 2.113             | 0.146          |
| No   | 21 (42.00)      | 20 (47.62)         | 1 (12.50)       |                   |                |
| Duration of tracheal intubation prior to tracheotomy (d) |                 |                    |                 |                   |                |
| ≤ 7, n (%)   |                 | 38 (90.48)         | 7 (87.50)       | –                 | 0.522          |
| >7, n (%)  | 4 (8.00)        | 3 (7.14)           | 1 (12.50)       |                   |                |
| Unidentified   | 1 (2.00)        | 1 (2.38)           | 0               |                   |                |
| Surgical method, n (%)                                   |                 |                    |                 |                   |                |
| ST   | 19 (38.00)      | 15 (35.71)         | 4 (50.00)       | 0.134             | 0.715          |
| PDT  | 31 (62.00)      | 27 (64.29)         | 4 (50.00)       |                   |                |

**Notes:** The number in bold represented significant difference. \*\* $p < 0.01$ .

**Abbreviations:** COPD, coronary heart disease; ST, surgical tracheostomy; PDT, percutaneous dilatational tracheostomy.

For patients with intratracheal granuloma following tracheotomy, the interval between the identification of the granuloma and the tracheotomy procedure ranged from 3 to 7969 days. An analysis of the clinical medical records indicated that instances with an interval exceeding 2 years were likely attributable to the lack of granuloma-related examinations conducted in the early stages following the occurrence of the granuloma. After excluding this subset of data, the results revealed that the median interval between the discovery of intratracheal granuloma and tracheotomy was 52 days.

## Discussion

In this study, of the 872 patients who underwent tracheotomy, 50 developed intratracheal granuloma, resulting in an incidence rate of 5.73%, which is consistent with findings reported in other literature.<sup>29</sup> Although the results indicate that

the occurrence of intratracheal granuloma is not associated with age, it is noteworthy that several studies suggest elderly patients are at a higher risk for this complication. This increased risk is primarily attributed to their diminished immune function, a decrease in the ability of tracheal glands to secrete various immunoglobulins, and a reduction in airway, swallowing, and cough reflex functions.<sup>30</sup> Consequently, the efficiency of tracheal cilia is compromised, facilitating the migration of upper respiratory tract pathogens to the lower respiratory tract. Additionally, this complication is also prevalent among pediatric tracheotomy patients. Literature indicates that the incidence of laryngeal and intratracheal granuloma in pediatric patients with bilateral vocal cord paralysis can reach as high as 77.1%.<sup>10</sup> In a separate study, infants under 2 years old were monitored for 12 months post-tracheotomy and underwent examination via fiberoptic bronchoscopy, revealing that 38% developed intratracheal granuloma.<sup>31</sup> The relatively small number of cases involving children and elderly patients in this study may introduce confounding factors, potentially leading to results that differ from those of other studies, thus necessitating further research to expand the sample size. Regarding the location of intratracheal granuloma, findings from this study indicate that elderly patients over 60 years are more likely to experience this condition in the distal trachea. This observation may be linked to the compromised airway clearance function in elderly patients, making the distal trachea more susceptible to pathogens.<sup>30</sup> Reducing mechanical stimulation of the proximal trachea is beneficial in decreasing the incidence of granuloma in patients aged 60 and younger. For patients over 60 years old, in addition to the aforementioned measures, it is advisable to implement airway humidification, physical expectoration, and other treatments to facilitate sputum excretion and further reduce the occurrence of granuloma.

The level of estrogen in female patients is higher than that in males. Estrogen is known to promote the formation of granulation tissue during the skin scar repair process. In this study, no correlation was observed between gender and the formation of intratracheal granuloma.<sup>32,33</sup> Currently, there is a paucity of research investigating the effect of estrogen on the repair process of tracheal mucosa, indicating a need for further exploration. Nevertheless, univariate analysis revealed that intratracheal granuloma was more likely to occur in the proximal trachea of male patients following tracheotomy. This observation is speculated to be related to the higher prevalence of smoking among male patients compared to their female counterparts.

Univariate analysis and binary logistic regression analysis indicated that a history of smoking is associated with the formation of intratracheal granuloma following tracheotomy. Harmful substances in cigarette smoke can induce oxidative stress in the body, leading to inflammation of the mucous membranes in the lungs and respiratory tract.<sup>34</sup> Consequently, stimulation of epithelial cells results in increased cell permeability and mucus secretion, while the mucus clearance function of cilia is impaired, ultimately heightening the risk of intratracheal granuloma in smokers post-operation.<sup>30</sup> Furthermore, we observed that all instances of intratracheal granuloma occurred in the proximal trachea among patients with a smoking history after tracheotomy. This may be attributed to the higher concentration of harmful smoke in the proximal airway, which exerts a more pronounced stimulating effect on this region. Research has demonstrated that smokers are susceptible to developing pharyngitis at an early stage and are more likely to experience oropharyngeal inflammatory diseases.<sup>35–37</sup> Importantly, airway inflammation is reversible after cessation of smoking; therefore, patients undergoing elective tracheotomy should be encouraged to quit smoking as soon as possible to reduce the incidence of granuloma. For patients with a smoking history, regular follow-up by healthcare providers is essential for the early detection of intratracheal granuloma. Additionally, minimizing stimulation of the proximal trachea, maintaining oral hygiene, and actively managing upper respiratory tract infections may further decrease the occurrence of granuloma.

Patients with extrapulmonary primary diseases, such as giant goiter, thyroid carcinoma, laryngeal tumors, vocal cord paralysis, and severe craniocerebral trauma, may require prolonged intubation to maintain an unobstructed respiratory tract. However, extended intubation duration increases the risk of tracheal mucosal injury, which can subsequently lead to the formation of intratracheal granulomas.<sup>38</sup> In the present study, both univariate and binary logistic regression analyses indicated that patients with extrapulmonary diseases are more likely to develop tracheal granulomas compared to those with intrapulmonary diseases, highlighting a significant concern. Interestingly, the benign or malignant nature of the primary disease did not appear to influence the formation of endotracheal granulomas. Previous studies have suggested that certain chemotherapeutic agents, such as paclitaxel and mitomycin, may inhibit cell proliferation, reduce fibroblast activity, and limit scar formation.<sup>29,39–42</sup> Therefore, we hypothesize that the observed results could be attributed to the administration of these chemotherapeutic drugs, although this requires validation through further research. In cases where the primary disease is

predominantly infectious or neoplastic pulmonary disease, tumor patients may experience obstructive pneumonia due to airway blockage. Post-surgery, patients with malignant tumors may struggle to expel lower respiratory secretions due to wound pain, necessitating increased sputum suction compared to patients with extrapulmonary diseases, which may contribute to granuloma formation in the distal trachea. Conversely, in patients with extrapulmonary diseases, lung conditions are generally better, resulting in less need for sputum suction tubes and fiberoptic bronchoscopy, thereby reducing stimulation to the distal trachea and making granuloma formation less likely. Therefore, when the primary disease is a pulmonary condition, patients should be encouraged to independently cough and expel sputum. Additionally, we should minimize the use of the sputum suction device on the distal trachea to reduce the occurrence of granulomas. Furthermore, no correlation was found between benign and malignant primary diseases and the location of intratracheal granulomas, suggesting that a larger sample size may be necessary for further exploration.

Most sputum and secretions containing bacteria are excreted through the trachea. The use of sputum suction tubes and fiberoptic bronchoscopes may facilitate the attachment and migration of these bacteria. Consequently, in patients with pulmonary infections, the concentration of pathogenic bacteria in the trachea may be higher than in those without such infections, increasing the likelihood of local infections and the formation of intratracheal granulomas. Our research findings support this assertion. It is recommended that clinical practice include proactive measures for the prevention and control of pulmonary infections following tracheotomy, as this may effectively reduce the incidence of intratracheal granulomas. Additionally, in patients with pulmonary infections, closer monitoring of intratracheal granulomas should be prioritized. Generally, both J-shaped and T-shaped tracheal cannulas are employed post-tracheotomy in clinical settings. For patients with pulmonary infections using J-shaped cannulas, the physical barrier created by the tracheal cannula and air bag makes it difficult for pulmonary secretions to reach the proximal trachea, while the distal trachea, being directly connected to the lungs, may be more susceptible to pulmonary infections, potentially resulting in granulomas at the distal end. In contrast, for patients with T-shaped cannulas, both the proximal and distal trachea connect to the deeper parts of the airway, making them equally vulnerable to pulmonary infections, which may lead to similar rates of granuloma formation in both regions. In this study, the specific type of tracheal cannula was not documented in detail; therefore, the influence of this variable on the relationship between pulmonary infections and the location of granulomas warrants further investigation.

The results of this study indicated that prolonged tracheal intubation (greater than 7 days) prior to tracheotomy did not influence the incidence of intratracheal granuloma. Nevertheless, some studies have suggested that extended intubation before tracheotomy can damage the tracheal wall, leading to mucosal defects, necrosis, proliferation, and ultimately the formation of intratracheal granuloma.<sup>38</sup> Due to varying clinical needs, different types of tracheal cannulas are utilized; patients requiring mechanical ventilation predominantly use plastic cannulas with air bags. These materials and structures are comparable to those of tracheal intubation, and they are more likely to cause tracheal injury than metal or silicone cannulas. In our study, certain patients with severe craniocerebral trauma, coma, or myasthenia gravis underwent early tracheotomy due to their need for long-term intubation and ventilator support. Although these patients experienced a brief intubation period prior to tracheotomy, they subsequently used plastic cannulas with air bags for extended mechanical ventilation, which poses a higher risk of developing intratracheal granuloma. Therefore, future studies should consider the total duration of catheter or cannula use to investigate its impact on the occurrence of intratracheal granuloma. Furthermore, we found no correlation between the duration of tracheal intubation before tracheotomy and the location of intratracheal granuloma post-tracheotomy; however, due to the limitations of sample size, further investigation is warranted.

The analysis results of this study indicate that the type of tracheotomy does not influence the formation of intratracheal granuloma following the procedure. Additionally, the type of tracheotomy is unrelated to the location of intratracheal granuloma post-tracheotomy. Standard Tracheostomy (ST) refers to the placement of a tracheostomy cannula under direct vision after dissecting the pretracheal tissue and incising the tracheal wall. In contrast, Percutaneous Dilatational Tracheostomy (PDT) involves blunt dissection of the pretracheal tissue, followed by the insertion of a guidewire, dilation of the trachea using a dilator, and the final placement of a tracheal cannula.<sup>1</sup> Some studies have reported that wound infections associated with PDT are lower than those related to ST, which many attribute to the smaller incisions made during PDT.<sup>43,44</sup> However, it is important to note that wound infection rates are also influenced by factors such as aseptic technique during surgery, postoperative care, the nutritional status of the patient, and

the patient's immune response. This may explain why the choice of tracheotomy method appears to have no correlation with the formation of granuloma.

## Conclusions

Given the occurrence and location of intratracheal granuloma following tracheotomy, as well as the associated risk factors discussed, it is essential to prioritize these aspects in clinical practice and to implement proactive prevention and treatment strategies. Notably, approximately 50% of intratracheal granulomas arise within 52 days post-tracheotomy, which serves as a valuable reference for clinicians in developing follow-up protocols.

The subjects in this study consist of inpatients, which may introduce selection bias and limit the generalizability of the findings regarding the epidemiological characteristics of intratracheal granuloma in tracheotomy patients. Additionally, patients may opt for treatment at other hospitals after their tracheotomy, resulting in a lack of access to relevant data from those facilities and potentially decreasing the overall number of intratracheal granuloma cases included in this study. The small sample size further complicates the situation, as it may lead to the influence of confounding factors, which could diverge from conclusions drawn from larger, multicenter studies. Therefore, it is imperative to expand the sample size in future research, enhance the follow-up data, and conduct more comprehensive investigations.

## Ethics Statement

Our study adhered to the Declaration of Helsinki and received approval from the medical ethics committee of Wuhan Pulmonary Hospital (approval number: WPHH-2022-015). Patient consent was waived due to the retrospective nature of the study. The authors did not have access to any information that could identify individual participants during or after the data collection process.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

This work was supported by the Wuhan Pulmonary Hospital Research Fund (Grant No. YNZZ202217 and YNZZ202216) and Hubei Provincial Natural Science Foundation of China (Grant No. 2022CFB176).

## Disclosure

The authors have no conflicts of interest to declare.

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