Review Article

Risk factors of wound infection after lung transplantation: a narrative review

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Background and Objective: The incidence of incision infection after lung transplantation is prominently high which affect the prognosis. Summarizing the risk factors related to incision infection after lung transplantation contribute to the control of incision infection by pre-controlling the risk factors. The objective is to summarize risk factors related to wound infection after lung transplantation.

Methods: PubMed was used to research the literature relating to the risk factors to incision infection after lung transplantation through 1990 to 2022. The retrieval strategy were Medical Subject Heading (MeSH) terms combined entry terms. Two researchers conducted the literature retrieval independently. Two researchers independently evaluate the quality of the literature and summarize the indicators.

Key Content and Findings: A total of 98 researches were collected from PubMed and 8 articles described the related risk factors of incision infection after lung transplantation. All of the 8 articles were retrospective studies, of which 4 articles were grouped by the delayed chest closure (DCC) execution and the other 4 articles were grouped by the surgical site infection (SSI) occurred. Two articles performed multivariate regression analysis to determine the independent risk factors of SSI after lung transplantation and the other 6 articles compared the SSI rate in different patients population. The integrated results showed that bronchoalveolar lavages (BALs), smoking status, body mass index (BMI), diabetes, operation duration, thoracic drainage tube placement time and DCC were related to the SSI after lung transplantation.

Conclusions: BALs, smoking status, BMI, diabetes, operation duration, thoracic drainage tube placement time and DCC were related to the SSI after lung transplantation.

Keywords: Lung transplantation; wound infection; risk factors

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Introduction

As an internationally recognized method for the treatment of end-stage benign lung diseases, lung transplantation has good clinical application effect for end-stage chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, primary pulmonary hypertension, bronchiectasis, and other diseases. The success rate of lung transplantation has improved significantly with advances in surgical techniques, newer immunosuppressants, and newer concepts of perioperative care, and the procedure can significantly prolong survival times and improve patients' quality of life (1). However, about 20% of lung transplant patients still

Table 1 The data retrieval strategy

Items	Specification
Date of search	10th March, 2022
Databases and other sources searched	PubMed
Search terms used (including MeSH and free text search terms and filters)	MeSH and free text search (Table S1)
Timeframe	2006 to 2022
Inclusion and exclusion criteria	Comparative clinical study; referred to the risk factors of wound infections after lung transplantation
Selection process	Literature retrieval and literature quality evaluation were carried out by two members respectively. When the evaluation criteria of the two members are inconsistent, it is necessary to discuss among the research members and determine whether the literature is included or not.

MeSH, Medical Subject Heading.

die in the first year after surgery (2), which may be closely related to transplant failure, acute rejection, infection, and other complications.

As an organ directly identical to the outside world, the lung has a higher risk of infection than others, and one study showed that surgical site infection (SSI) increased the risk of death in lung transplant subjects by about 35% (3). Infection of the incision site may also lead to other adverse consequences, such as prolonged hospitalization and an increased re-hospitalization rate, which negatively affect the prognosis of patients. One study showed about 15.7% of lung transplant patients developed surgical incision-related infections after surgery (4).

Related studies in thoracic surgery have made it clear that surgical incision infection is closely related to recipient factors including diabetes, hypertension and obesity, in addition to surgical factors (3,4). However, due to a certain degree of difference between lung transplantation and general thoracic surgery, the risk factors causing incision infection after lung transplantation also differ (5). This study intends to integrate the results of various others, and ultimately screen the risk factors of incision infection after lung transplantation through literature induction to further guide its clinical diagnosis and treatment.

However, due to the limited number of related studies on incisional infection after lung transplantation, the grouping conditions of the subjects are also different. Therefore, it is unreasonable to make a quantitative analysis of the current research. Therefore, this study uses a narrative review to summarize the current research results on incision infection after lung transplantation, so as to guide the clinical work (Table S1). We present the following article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-543/rc).

Methods

Retrieval strategy and data collection

Literature search

This study was identified via an electronic search of PubMed database (updated to March 2022) by two authors. The languages were limited to English. Medical Subject Heading (MeSH) database was used as a terminological search filter in combination with methodological search filters. The literature search was extended by "hand searching" in the "related citations" links of all included articles in PubMed (first 40 articles per included article, after sorting according to the relevance), and the references of all included articles. The specific retrieval strategy was shown in *Table 1*.

Results

Definition and epidemiology of lung transplantation incision infection

According to international standards proposed by the Center for Diseases Control and Prevention (CDC), incision infection can be classified as superficial surgical incision infection, deep surgical incision infection, and organ/space surgical incision infection (6). Incision infection is defined as: (I) the patient's body temperature continued to

rise, greater than 38 ℃; (II) there were noticeable purulent secretions at the incision site; (III) redness, swelling, pain, itching, and other symptoms are present the site, purulent secretions appear locally, and bacterial infection is confirmed after microscopic examination of the secretions; (IV) the occurrence of wound infection is determined based on the clinician's judgment (7). The incidence of incision infection after lung transplantation is between 5% and 15%, and its occurrence and development depend on many factors, including those of the organ donor and organ recipient, and the operation method (8,9). Due to immunosuppressants in lung transplantation patients, most symptoms and signs are not obvious. However, incision infection after lung transplantation is closely related to postoperative survival (10), and it is imperative to clarify it risk factors.

Research results

From literature search, a total of 8 studies (11-18) were collected into the narrative review, the specific information of the collected articles were shown in Table S2. Of which 4 articles (11,13,14,17) were grouped by the delayed chest closure (DCC) execution and the other 4 articles (12,15,16,18) were grouped by the SSI occurred. Two articles performed multivariate regression analysis (12,13) to determine the independent risk factors of SSI after lung transplantation and the other 6 articles compared the SSI rate in different patients population.

Influence of organ donor factors on wound infection after lung transplantation

The positive reaction of bronchoalveolar lavages (BALs) from the organ donor

Positive BALs in donor organs indicate the presence of pathogenic bacteria. In organ transplantation, pathogenic bacteria existing in the donor body can be transferred to the organ recipient, which is known as a donor-derived infection (DDI) (11). Previous bacterial cultures of BALs from clinical lung donors have shown that about 8% of donor BALs can be cultured with multidrug-resistant, pan-drug-resistant Gram-negative bacteria. While an epidemiological survey showed the incidence of DDI after lung transplantation was only about 1%, its occurrence was closely related to prognosis (12,13). The mortality of DDI patients and the incidence of pulmonary infection increases significantly after lung transplantation. In another study of lung transplant patients, patients with donor BALs with pathogens before surgery had a 29% higher risk of infection than patients with donor BALs without pathogens (14). Results of a retrospective study of lung transplantation site infection showed the proportion of donor BALs in patients with SSI was significantly higher than that in patients without SSI (63.1% *vs.* 6.9%, P<0.001) (15). Therefore, donor organs should be tested for BALs before clinical lung transplantation, and for donors with positive BALs, changes in the surgical incision should be paid close attention, and antibiotics should be applied to reduce the incidence of incision infection.

Smoking status of organ donors

Tobacco contains a variety of harmful substances, and the lung tissue of long-term smoking donors will induce pathological changes in the trachea and bronchus (16), including increased viscous secretions and reduced sewing ability of cilia. These pathological changes significantly reduce the clearance ability of donor lungs to pathogenic bacteria (17) and as a result, most smokers have some degree of chronic inflammation in their lungs. When donor lungs are transplanted into the body of a recipient patient, chronic inflammation genes do not expand after the body is stimulated by surgery-related factors, and severe pulmonary infectious disease develops (18). At the same time, due to the particularity of lung transplantation, there are many surgical incisions, including deep and shallow, and infection in one location of lung tissue can easily migrate to the surgical incision site, creating a secondary infection. Previous study has shown that incision site infection is higher in donor patients with a history of smoking than in those who did not smoke (21% *vs.* 5.9%, P<0.05) (19). Lung organ donor smoking also significantly increased the recurrence rate and mortality after lung transplantation (20). Therefore, strict screening criteria should be adopted in the selection of organ transplant donors to avoid the inclusion of donors with a long history of smoking to improve the prognosis of lung transplant patients. However, considering the shortage of organs, the criteria for lung organ donation can be relaxed when diseases threaten patients' lives.

Influence of organ recipient's factors on wound infection after lung transplantation

Body mass index (BMI) of the organ recipient

Study has shown that the BMI of organ recipients is

a risk factor for surgical incision infection after lung transplantation, and the BMI of patients with infection is significantly higher than those without (21). The median BMI of lung transplant patients with surgical incision site infection was greater than 24 kg/m^2 (22). As a systemic metabolic disease, obesity has become a serious global problem threatening human health (23). BMI >24 kg/m^2 will produce different degrees of symptoms of respiratory tract stenosis due to the increase of fat in the inner wall of the respiratory tract, and as a large operation, lung transplantation will cause a stress response in the body, aggravate a local inflammatory response, and increase the probability of incision infection (24). At the same time, because obese patients have more subcutaneous fat accumulation, and the sutures of lung transplantation are relatively tight, this will further increase the accumulation of subcutaneous fat at the surgical site, increasing the probability of fat liquefaction (25). Surgical incision site exudation will result in poor wound healing by providing a microenvironment for pathogenic bacteria to grow quickly (26). In hyperlipidemic patients, the proportion of fatty acid and phospholipid acid inside the airframe is unbalanced, affecting the function of lymphocytes, compromising the immune resistance of the patient (27). For these reasons, dietary control before surgery is essential in minimizing the likelihood of surgical incision infection.

Diabetes

Diabetes is a risk factor for incision infection after esophagectomy and orthopedic surgery. It also plays a significant role in causing incision infection in lung transplantation patients after surgery (28-30). The incidence of type 2 diabetes was significantly higher in lung transplant patients with SSI than in patients without SSI, according to a retrospective study (47.3% *vs.* 0.9%) (31). In diabetic patients (especially those with poor blood glucose control), the function of fibroblasts is reduced, and the rate of granulation tissue is slowed down, leading to delayed incision healing in lung transplantation patients (32). Immune function in patients with diabetes and insulin resistance is also lower than that of healthy people, and in an environment of high sugar, high permeability can increase local exudation and promote engraftment, further growth, and reproduction of local bacteria, and can even cause cracking of the incision (33).

Systemic microvascular lesions also result from high blood sugar, which further reduces immune function and weakens the chemotaxis ability of white blood cells, increasing the risk of bacteria and other microorganisms invading the surgical incision site (34). As a traumatic procedure, lung transplantation can also promote systemic stress response in the body, aggravating the degree of insulin resistance and further increasing the risk of incision infection (35). Insulin resistance will suppress the secretion of pancreatic islet beta-cells, promoting protein decomposition, reducing protein synthesis, delaying fibroblasts, reducing the synthesis of fiber, and slowing down the generation of new capillaries and maturation of granulation tissue, delaying healing and increasing the probability of infection (36). Therefore, for lung transplantation patients with type 2 diabetes, blood glucose fluctuation should be strictly controlled during the perioperative period.

Influence of surgical factors on postoperative incision infection after lung transplantation

Operation duration

Duration of the operation is closely related to postoperative incision site infection in lung transplantation patients. One study showed that the duration of operation time in patients with surgical site incision infection was significantly longer than those without surgical site incision infection (9.3 *vs.* 8.7 hours, P=0.043) (37). Therefore, the longer the operation time, the greater the corresponding risk of postoperative incision infection. As a large operation, lung transplantation has high requirements for the surgical environment and the surgeon's surgical techniques. Study in the operating room has shown that bacteria suspended in the air in the operating room are likely to fall to the field of vision during surgery, and statistical analysis showed that more than 30,000 colonies of bacteria were floating around the surgical field every hour (38). Therefore, the longer the operation time, the larger the surgical incision, the more bacteria contained in the air in the operating room fall in the surgical field, and the more significant impact the incision site. Study has also shown that patients with more than 3 hours of surgery are at increased risk of incision infection after surgery (39). At the same time, the extension of the operation time will further increase the pulling and squeezing of the incision during the operation, aggravating the degree of injury at the incision site, and further increasing the probability of incision infection (40). On this basis of these results, it is necessary to refine the operation

steps, shorten the operation time, and reduce the incision as much as possible.

Thoracic drainage tube placement time

Study has shown that the duration of chest drainage tube indwelling after lung transplantation is also closely related to postoperative incision infection (41). The duration of chest drainage tube placement was significantly longer in patients with infexction than those without (18.0 *vs.* 14.0 hours, P=0.009) (42). As a particular type of nosocomial infection, drainage tube-related infection can increase the incidence of incision site infection in patients after general surgery and thoracic surgery. The leading causes of its occurrence are improper placement of drainage tubes, untimely nursing, and a long duration of placement (43). The drainage tube itself is a sterile device and theoretically does not increase the probability of local infection. However, its location is relatively connected with the outside world, which will further promote the transplantation of pathogenic bacteria at the incision site and enter the drainage tube tip, causing the colonization and growth of pathogenic bacteria (44). The longer the drainage tube is placed, the greater the probability of pathogenic bacteria retrograding from the drainage tube mouth and the greater the probability of infection (45). Therefore, in lung transplantation patients, the number of drainage tube placements should be simplified as much as possible, and the time of drainage tube placement should be shortened as much as possible to reduce the probability of infection.

DCC

Delayed thoracic closure is commonly used in cardiac surgery when a single thoracic closure cannot be performed due to coagulopathy or hemodynamic impairment. In lung transplantation, other indications are hypoxia and hypercapnia due to pulmonary edema. In a series of published studies, the need for DCC after lung transplantation has been as high as 29%, although this practice may vary depending on the number of patients, practice variability and surgeon experience. While some studies report similar short-term outcomes in patients with delayed and primary thoracic closure, less is known about the long-term outcomes of rejection, infection, and lung function (11-14). From the narrative review, 4 articles focused on the efficacy of DCC on the occurrence of incisional infection after lung transplantation. Of which 2 articles showed that DCC was not correlated to incisional infection. Two other studies showed that postoperative wound infection in the DCC group was significantly higher than that in the PCC group. The indication for DCC depends on the choice of the intraoperative surgeon. In oversized lung allograft (OLA), there are size mismatches that require intraoperative management. In such cases, the surgeon has two options: lung allograft resection and/or expansion of the thoracic volume (removal of excess intrathoracic adipose tissue and diaphragm plication). However, surgical removal of lung volume should always be the last resort. Instead, DCC operation may be a more reasonable solution to allow spontaneous lung contraction. As a result, allografts can reach their normal size and can be treated with smaller procedures. Whether DCC increases the risk of infection is controversial. Of 232 patients who underwent lung transplantation between 2010 and 2014 by Aguilar *et al.* (13), 67 (29%) received DCC. In 22 (9%) transplanted patients, infection occurred at the surgical site. Among them, there were 18 cases of wound infection, 8 cases of pleural infection, and 4 cases of combined wound pleural infection. Infection was significantly more frequent in patients with gallbladder cancer than in those without (19% *vs.* 5%, P=0.001). In multivariate analysis, DCC is an independent risk factor for SSI. However, Force *et al.* (11) and Rafiroiu *et al.* (14) reported in their published case series that DCC did not increase the risk of infection. Therefore, the effect of DCC on wound infection after lung transplantation requires further study.

Summary and outlook

Lung transplantation is an effective treatment method for advanced lung benign disease and can effectively improve the survival cycle of patients and improve their prognosis. However, incision site infection seriously affects the outcome of surgery. Current studies have shown the detection results of alveolar lavage fluid of organ donors, donor smoking history, the recipients diabetes mellitus status and BMI, operation duration and chest drainage tube placement time are closely correlated with SSI. Prevention and intervention in the perioperative period to minimize the impact of these factors and to reduce the probability of postoperative incision site infection is crucial. However, the research on postoperative incision infection in lung transplantation patients is still in its infancy, and further and more in-depth research is required.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-543/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-543/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 The MeSH and entry terms of this study

ID	MeSH and entry terms
1#	"infection wound"[Title/Abstract] OR "infections wound"[Title/Abstract] OR "wound infections"[Title/Abstract] OR "wound infection"[Title/Abstract]
2#	((((((Grafting, Lung[Title/Abstract]) OR (Graftings, Lung[Title/Abstract])) OR (Lung Grafting[Title/Abstract])) OR (Lung Graftings[Title/Abstract])) OR (Transplantation, Lung[Title/Abstract])) OR (Lung Transplantations[Title/Abstract])) OR (Transplantations, Lung[Title/Abstract])

MeSH, Medical Subject Heading.

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Table S2 The characteristic of the included studies

Study ID	Type of research	Patients characteristics	Surgery type	Findings summary
Force SD, 2006 (11)	Retrospective cohort study	28 patients (7 patients suffered DCC)	Bilateral lung transplantation	There were no wound infections in either group
Shields RK, 2013 (12)	Epidemiological study	586 patients (31 patients suffered SSI)	Lung transplantation	Forty-one pathogens were recovered from 31 patients
				Univariate analysis showed previous thoracic surgery (non-transplant), diabetes mellitus and obesity (P=0.0008, 0.005 and 0.048, respectively)
				Multivariate logistic regression showed that prior thoracic surgery and diabetes were identified as independent risk factors (P=0.001 and 0.009, respectively; 4.15- and 3.03-fold increased odds of SSI)
Aguilar PR, 2017 (13)	Retrospective cohort study	232 patients (22 patients suffered SSI)	Lung transplantation (67 patients suffered DCC)	One hundred and sixty-five recipients (71%) underwent PCC, and 67 recipients (29%) underwent DCC
				A SSI developed in 22 recipients (9%). Among the 67 who underwent DCC, 13 recipients (19%) experienced a SSI compared with 9 of the 165 recipients (5%) who underwent primary closure
				LAS at the time of transplantation and DCC were important risk factors for surgical site
Rafiroiu S, 2020 (14)	Retrospective cohort study	769 patients	Lung transplantation (47 patients suffered DCC)	Composite late infections (1–6 months) of Clostridium difficile, empyema or DSWIs at 1 and 6 months were 14% and 23% in the delayed group, and 11% and 18% in the PCC group (P=0.6), respectively
Pellenc Q, 2020 (15)	Retrospective cohort study	154 patients	Lung transplantation	The rates of groin healing delay and groin wound infection were significantly lower in the PFA group (0.9% and 0%, respectively) than in the non-PFA group (20.8% and 18.9%, P<0.001 for both comparisons
Gatti G, 2020 (16)	Retrospective cohort study	843 patients	Lung transplantation	The DSWI occurred in 64 (5.7%) cases overall—in 4.3% (n=25) of BITA patients and in 7.3% (n=39) of SITA patients
Yeginsu A, 2021 (17)	Retrospective cohort study	60 patients	Bilateral lung transplantation	In the DCC group, postoperative wound infection was significantly higher than in the PCC group (18.6% *vs.* 0%, P=0.19)
Moraes JLS, 2020 (18)	Retrospective cohort study	121 patients (19 patients suffered SSI)	Lung transplantation	The incidence of primary SSIs was 15.7% (n=19). Of the 19 SSI cases, the most prominent topography was superficial incisional SSI (n=11; 57.8%), 1 (5.2%) case was deep incisional SSI, and 7 (36.8%) cases were organ/space SSI
				The median BMI was higher among recipients who developed SSI in comparison to those who did not: 24.4 (IQR, 22.3–25.8) and 22.5 (IQR, 19.0–25.6) kg/m^2, respectively (P=0.041). The median surgical time was 9.3 (IQR, 7.9–11.2) hours in the SSI group as compared to 8.7 (IQR, 7.5–9.5) hours in the non-SSI group (P=0.043). Moreover, the median duration of chest drain placement was 18 (IQR, 15–24) days among patients who developed SSI compared to 14 days among those who did not (IQR, 5–17 days; P=0.009)

DCC, delayed chest closure; SSI, surgical site infection; PCC, primary chest closure; LAS, lung allocation score; PFA, preclosing of the femoral artery; DSWI, deep sternal wound infection; BITA, bilateral internal thoracic artery; SITA, single internal thoracic artery; BMI, body mass index; IQR, interquartile range.

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