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Infections Related to Airway Stenting: A Systematic Review

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Key Words
Airway stent · Interventional pulmonary medicine · Infection · Complications

Abstract
Background: Airway stenting is nowadays an established method for the palliative and/or curative treatment of central airways obstruction. However, complications related to the use of airway stents have been reported. ***Objective:*** We endeavored to systematically evaluate the currently available evidence regarding the infections associated with airway stenting. ***Methods:*** We independently searched in PubMed for relevant reports. We considered articles which reported on clinical infections related to airway stenting. A case was identified as stent-associated respiratory tract infection (SARTI) according to the authors of the individual papers, based on clinical findings with or without radiological or microbiological confirmation. ***Results:*** Twenty-three articles (19 cohorts/case series and 4 case reports), involving 501 patients with airway stents, were included. The indication for airway stenting was malignancy and benign disease in 45 and 55% of the included patients, respectively. Ninety-three (19%) out of the 501 stented patients experienced SARTI. Pneumonia was the most common type of SARTI (47%), followed by bronchial infection (24%), cavitary pneumonia/lung abscess and intraluminal fungus ball. *Staphylococcus aureus* (39%) and *Pseudomonas aeruginosa* (28%) were the most commonly identified pathogens. Twenty-six (68%) out of the 38 patients with SARTI, for whom outcome data were available, died. ***Conclusion:*** The accumulated and evaluated evidence suggests that SARTI probably involves 1 in 5 patients with airway stent. Although the possibility of SARTI should not discourage the interventional pneumologists from inserting airway stents, the data seem to underline the urgent need for establishing a consensus definition and diagnostic criteria for SARTI.

Introduction

The insertion of metallic or polymeric materials into the trachea and the main bronchi for the treatment of various airway diseases dates back to 1952 [1]. Since then, airway stenting has become an important technique for the treatment of central airway obstruction, caused by either malignant or benign diseases. Airway stents are hollow prosthetic devices that come in different shapes, lengths and diameters and are constructed of metals, polymers or a combination of both [2]. New types of stents, such as bioabsorbable stents designed to overcome the disadvantages of the previous ones, are currently being introduced into modern practice.

Although the use of stents is nowadays an established method for the palliative and/or curative treatment of airway abnormalities that leads to a significant improvement in symptoms and quality of life of patients [3], complications related to airway stenting have also been mentioned [4]. The latter include stent fracture, migration,

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adjacent tissue erosion, granuloma formation, mucus impaction and infection [3, 5, 6]. In a recent prospective study, Noppen et al. [7] revealed a rate as high as 78% of stent colonization at a short period (3–4 weeks) following stent implantation.

Given that indications for airway stenting are expanding, involving not only patients with malignancies but also those with benign disorders with a considerable life expectancy [3], it is expected that stent complications commonly overlooked, such as infection, are bound to receive more attention by the practicing clinician. Thus, we endeavored to accumulate and evaluate the available evidence regarding the infections associated with airway stenting.

Methods

Search Strategy

The protocol of this systematic review was approved by the Ethics Committee of the Alfa Institute of Biomedical Sciences, Athens, Greece. Two reviewers (M.A. and I.I.S.) independently performed the literature search, study selection, and data extraction. Any disagreement between the two reviewers was resolved by consensus in meetings of all authors. We searched in PubMed (articles indexed up to December 2007) by using the following key words: '(laryngeal *OR* tracheal *OR* bronchial *OR* endobronchial *OR* endotracheal *OR* tracheobronchial *OR* laryngotracheal *OR* airway) *AND* stents *AND* (infection *OR* pneumonia *OR* bronchitis *OR* complications)'. We also hand-searched the bibliographies of the initially retrieved papers. No restriction was set regarding the time; papers in English and French were included. Abstracts presented in international conferences were not searched.

Study Selection and Data Extraction

A paper was considered eligible for inclusion in our systematic review if it reported at least 1 patient with clinical infection related to airway stenting or if it reported a zero rate of infectious complications following stent insertion. Studies reporting only on colonization were omitted. The following data were extracted from each study: first author, year of publication, number and demographics of patients with stents, cause of obstruction (benign or malignant) and comorbidity, site of stricture, and number and type of stents placed. We also recorded the number of stented patients with respiratory tract infection in each study, the time interval between stent implantation and infection, type of infection, implicated pathogens, treatment (interventional and/or antimicrobial) as well as outcome.

Definition

A case was identified as stent-associated respiratory tract infection (SARTI) according to the authors of the individual papers, based on clinical findings (fever, increased volume and purulence of the sputum) with or without radiological (suggesting pneumonia or lung abscess) or microbiological documentation. The definition also included the requirement of active intervention to treat SARTI.

Results

Characteristics of the Selected Articles

In figure 1, we present a flow diagram with the process we followed to locate relevant reports. Out of the 864 initially retrieved papers, 23 articles, involving 501 patients (range: 1–82 patients, median: 15) with airway stents, fulfilled our inclusion criteria. To be precise, we reviewed four case reports, four case series and fifteen cohorts [8–30]. Characteristics and outcome data of the eligible reports are depicted in detail in online supplementary tables 1 and 2 (www.karger.com/doi/10.1159/213244).

Out of the 23 reviewed papers [8–30], 3 papers [20, 22, 28] enrolled patients with malignant disease (primary or secondary), 12 papers [8–13, 15, 18, 19, 23, 25, 29] enrolled patients with benign disorder, while the remaining studies [14, 16, 17, 21, 24, 26, 27, 30] consisted of a mixed (malignant and benign) patient population. In total, the indication of airway stenting was malignancy and benign disease in 45% (224/501) and 55% (277/501) of included patients, respectively. Seventy-two (26%) of the 277 patients in the latter group underwent lung or heart-lung transplantation; in one study, the number of transplant patients was not specified [21].

All but two [17, 19] of the review studies reported on the number of stents employed; the total number was 598. On the other hand, based on data from 20 articles [8–16, 18, 20–25, 27–30] regarding the type of stents placed, 233 (48%) stents were polymeric, 178 (37%) were metallic and 75 (15%) were hybrid. In the remaining three studies [17, 19, 26], a combination of metallic and polymeric and hybrid and metallic stents was used, but the exact number of each subcategory was not specified.

Frequency of SARTI

Data on the number of patients with SARTI among those managed with airway stenting were provided by all studies included in the systematic review. Ninety-three (19%) out of the 501 stented patients experienced SARTI. This was also the case for the frequency of SARTI reported in each of the eligible cohorts/case series [8–30], as depicted in online supplementary table 1. Based on data from seven studies, the incidence of infections in stented patients with malignant disease approximates 16% [14, 16, 17, 20, 22, 24, 28]; similarly, the incidence of SARTI in either transplants [8, 9, 12, 15, 17, 19, 23–26] or patients with nontransplant benign disease [10, 11, 13, 14, 16, 18, 24, 29] is 19%. The incidence of SARTI in patients with metallic stents [8–10, 13, 15–17, 21, 23–25, 27] was approximately 21%, while the incidence of SARTI in pa-

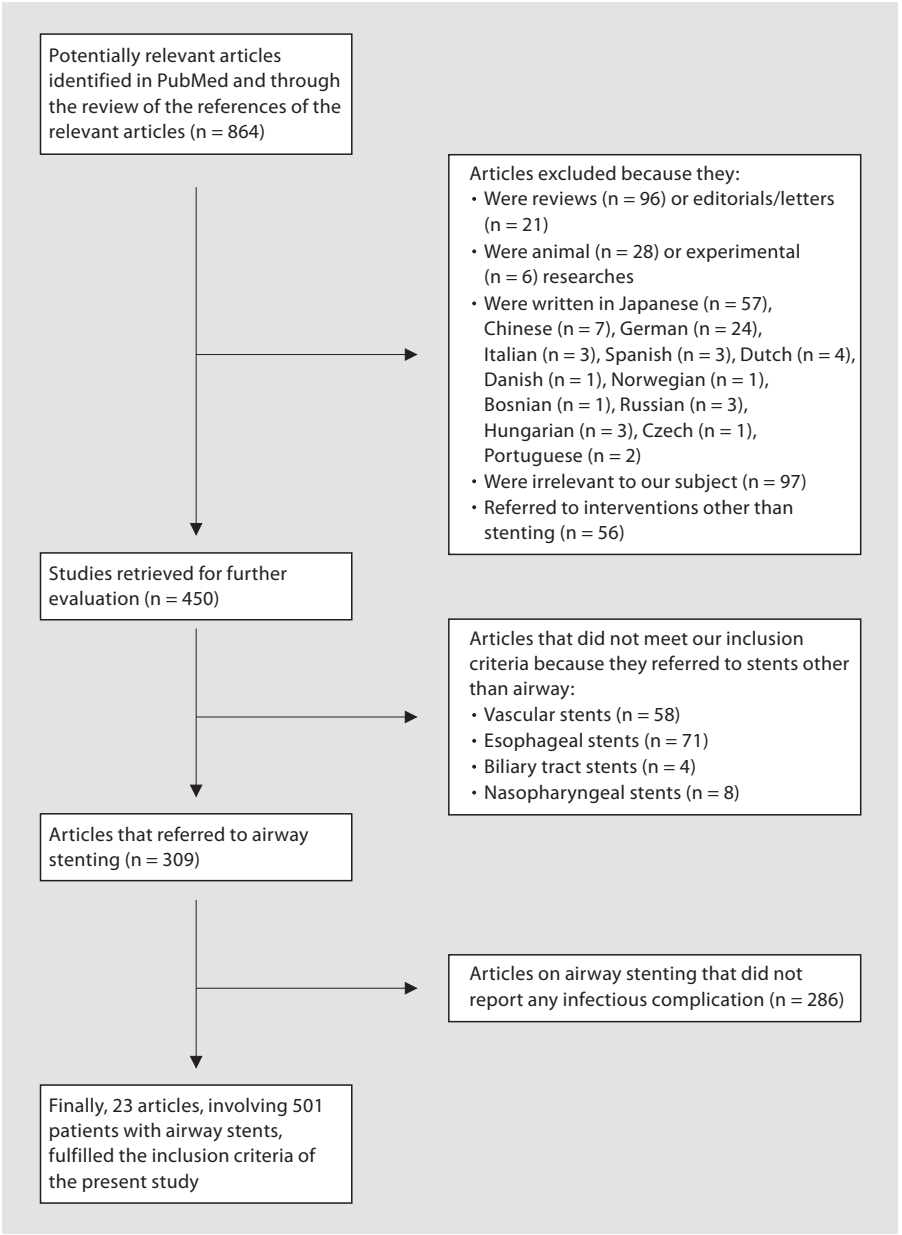

Fig. 1. Flow diagram of the reviewed articles.

tients with polymeric [12, 18, 20, 29, 30] and hybrid [14, 28] stents was 20 and 23%, respectively. We should note that in one study involving transplanted patients only episodes of infection that were related to patient death were reported [23]. Similarly, in another study, although it was reported that the incidence of respiratory tract infection decreased after stent placement in patients with benign airway disease, only 1 case requiring an antimicrobial immediately after stent placement was detailed [17].

With respect to the recurrences of SARTI, the studies by Mondain et al. [18] and Madden et al. [24] noted that 6 and 4 patients, respectively, suffered from multiple episodes of infection. Likewise, two other studies reported on recurrent SARTI [14, 20].

Type of SARTI and Implicated Pathogens

Out of the 23 selected papers [8–30], 19 provided specific information on the type of SARTI [8–11, 13, 14, 16–23, 25–28, 30]. Pneumonia was the most common complication (44/93, 47%), followed by bronchial infection (22/93, 24%), cavitary pneumonia/lung abscess (2/93, 2%) and intraluminal fungus ball (2/93, 2%), whereas the

type of infection was not specified in the remaining 23 patients with SARTI (25%).

Eleven [8–10, 14, 19–21, 23, 25, 26] of the eligible articles provided data on the pathogen isolated from a patient with SARTI. *Staphylococcus* spp. (7/18, 39%), *Pseudomonas aeruginosa* (5/18, 28%), fungi (4/18, 22%), *Proteus mirabilis* (1/18, 6%) and *Streptococcus viridans* (1/18, 6%) were the identified pathogens. Stents, bronchial secretions and bronchoalveolar lavage fluid were the specimens cultured for pathogen identification [8–10, 20].

Interventional Treatment

Data on interventional treatment of patients with SARTI were available for seven studies [10, 11, 20, 21, 25, 26, 29] included in the systematic review. Stent removal or replacement was required for the treatment of 6 patients with bronchial infection and of 1 patient with recurrent pneumonia associated with tumor overgrowth. In 2 of the above patients with bronchial infection necessitating stent removal, *Staphylococcus aureus* was the culprit pathogen. Stent removal or replacement was also employed to treat stent-related complications (including infection) in some patients in the article by Ernst et al. [29]. Similarly, in the report by Noppen et al. [11], a silicone stent was inserted inside a metallic expandable stent to treat postobstructive pneumonia.

Antimicrobial Treatment

Only 3 [9, 10, 26] out of the 21 eligible articles reported on the antimicrobial treatment of patients with SARTI. In detail, 1 patient with *P. aeruginosa* pneumonia related to stent placement after heart-lung transplantation received imipenem-cilastatin for 1 week [9]. Similarly, in the case report by Abbas et al. [10], a patient with relapsing polychondritis and airway symptoms managed with stent placement presented with lung abscess due to *P. aeruginosa* in the contralateral lung and was treated with ceftazidime and polymyxin for 3 months. In addition, a combination of amphotericin B and fluconazole for 8 weeks was successfully used for the treatment of 1 transplanted patient with intraluminal fungal stent infection in a study by Saad et al. [26].

Mortality

Data on mortality were available for sixteen of the included papers [8–14, 16, 17, 19–24, 28]. In the study by Belleguic et al. [22], 1 patient with SARTI died, while the outcome of the other patient with SARTI was not given. Similarly, in the study by Dasgupta et al. [21], outcome data are not available for 2 out of 3 patients with SARTI. In total, 26 (65%) out of the 38 patients with SARTI, for whom outcome data were available, died. Based on the available data from seven studies [14, 16, 17, 20, 22, 24, 28], the mortality for stented patients with malignant disease approximates 76%; similarly, the mortality rate for transplants [8, 9, 12, 17, 19, 23, 24] and patients with no nontransplant benign disease [10, 11, 13, 14, 16, 24] is 88 and 42%, respectively.

Discussion

By accumulating data from 501 patients with airway stents (polymeric, metallic or hybrid), the findings of the present systematic review suggest that the frequency of SARTI was as high as 19%. The most common type of airway stent-related infection was pneumonia, while the pathogens most frequently implicated were *S. aureus* and *P. aeruginosa*.

Although only an association rather than an etiopathogenic correlation between stent insertion and the respiratory tract infection could be confirmed from the available data, there is evidence providing the rationale why insertion of an airway stent may increase susceptibility to infections or complicate an existing infectious process. For instance, silicone stents may migrate or interfere with mucociliary clearance, bronchial toilet and cough effectiveness [3, 5, 6]. On the other hand, metallic stents are most commonly associated with adjacent tissue erosion, tumor ingrowth and granuloma formation [3, 5, 6, 31]. Other factors, such as stent misplacement [8], may also have a contributory role. Susceptibility to infections in stented patients can also be related to the severity of background disease (namely malignancy), presence of structural airway abnormalities and previous or concurrent interventional or pharmacological treatment. For similar reasons, mortality rate as a result of SARTI is high, even if, for patients with malignancy or those with low expectancy of life, other factors, such as end-of-life decisions, may also have played a role.

Our data suggest that SARTI may present in two different patterns. First, it may manifest as a postoperative complication in patients with or without previous respiratory tract infection. This category also includes patients in whom stenting complicated the clinical course of a respiratory tract infection that was active prior to stent placement and is potentially associated with clinical deterioration or death. Second, SARTI may present at various time intervals following stent implantation in patients with or without previous respiratory tract infections. Appreciation of the above patterns may have implications on prevention and management strategies.

Recurrent infections following stent implantation were frequently reported in the selected articles. Although none of the selected studies was designed to evaluate the incidence of respiratory tract infections before and after stent insertion, some limited information on that aspect is offered by two eligible reports. In detail, in the study by Herrera et al. [23], the incidence of respiratory tract infections increased at 3 and 6 months after stenting, but not later. Also, in the study by George et al. [17], the incidence or respiratory infections in patients with benign airway disease (including transplants) was reported to decrease following stent insertion. Similarly, in another study on transplant patients, infection distal to the site of obstruction resolves with antibiotic therapy after stenting [15]. Finally, a retrospective cohort study has shown that the infection rate decreased during a 12-month follow-up period in lung transplant patients following insertion of metallic stents to treat airway abnormalities [31]; this particular study was not eligible for inclusion in our review.

The present systematic review highlights the absence in the literature of a definition for SARTI and, moreover, underscores the need for establishing diagnostic criteria for airway stent-related infections. While seeking for the appropriate definition for SARTI, we should bear in mind that many stent candidates have a history of previous or recurring respiratory tract infections and, in some cases, stent insertion aims at improving the outcome of such an episode. In our opinion, the use of the term 'stent-associated respiratory tract infection' (SARTI) is mostly justified, when the following criteria are fulfilled: (1) the radiological and/or bronchoscopic findings involve predominately the stent, the stented airway or the anatomical region it drains; (2) the patient presents with symptoms attributable to infection (namely fever, increased sputum volume and purulence, fatigue) with or without deterioration in dyspnea scores or lung function tests, and (3) the condition necessitates antimicrobial treatment and/or stent replacement/removal. A positive culture of the stent or of a specimen obtained from the affected area (i.e. bronchial washing, brushing, bronchoalveolar lavage) may also be an additional criterion, although the increased rate of stent colonization should always be considered [7]. This definition may also include cases in which stent placement complicates a respiratory tract infection that started prior to stent placement by worsening symptoms or slowing down the healing process.

Our contribution is not without limitations. First, since in some cases definite diagnostic criteria or clinical data are lacking and due to the absence of a definition for SARTI, the distinction between 'clinical infection' and 'colonization' is not always possible. Also, available reports tend to focus on technique details and related complications. In addition, there are several differences between the studies included in the review regarding the provided poststent healthcare as well as the follow-up period. Also, the vast majority of the studies are retrospective and none of them was originally designed to evaluate the incidence and the mortality of airway stent-related infections. Furthermore, treatment with other pharmacological or interventional modalities before, during or after stent insertion might act as a confounding factor and influence outcome by affecting the clinical course of primary disease or by causing additional complications. End-of-life decisions in terminally ill patients may influence therapeutic choices and outcome. For the abovementioned factors we cannot exclude that the incidence and mortality of SARTI in this systemic review might be overestimated.

In addition, one might argue that some of the results might not be relevant to modern practice since some types of stents, such as the Gianturco, the Palmaz and the Wall stents, are now rarely used, while stents made of biodegradable materials have recently been introduced [2]. However, we attempted to carry out a comprehensive review on the issue by including all available airway stents. In addition, none of the included studies provided information on the potential preventive role of mucolytics against SARTI. Similarly, although it would be interesting to know if an association exists between persisting smoking habits and susceptibility to SARTI [33], the available data were not adequate to confirm or reject such an association. Last, since clinical details are occasionally lacking, an anatomopathologic correlation between the site of the stent and the location of the infectious complication attributed to it could not be established.

Conclusion

Despite the limitations present in the original studies, we believe that this systematic review is clinically valuable. The accumulated and evaluated evidence suggests that probably 1 in 5 patients with airway stent is affected by SARTI. Although the possibility of SARTI should not discourage the interventional pneumologists from inserting airway stents, the urgent need for establishing a consensus definition and diagnostic criteria for SARTI is underlined. Prospective studies seem to be warranted to identify risk factors for SARTI and to determine optimal prevention and management strategies.

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