

# Sporadic Obliterative Bronchiolitis: Case Series and Systematic Review of the Literature

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## Abstract

**Objective:** To describe the clinical characteristics and outcomes of patients diagnosed with obliterative bronchiolitis (OB) not associated with transplantation or point-source exposures to inhaled toxins.

**Patients and Methods:** We compiled all confirmed diagnoses of OB at our institution and analyzed their demographic characteristics, treatments, and outcomes as defined by pulmonary function tests (PFTs) and transplant-free mortality. The study period ranged from July 2007 to August 2017. Histological diagnosis was confirmed by a pathologist, and high-resolution chest computed tomography (CT) scans were reviewed and scored by chest radiologists. We also performed a systematic literature review of sporadic OB series.

**Results:** We identified 19 confirmed cases at our institution and 9 publications in the literature containing 104 patients. In both our series and the literature, patients were disproportionately middle-aged Caucasian women. The disease was idiopathic in 42% and was associated with connective tissue diseases and inhalational exposures in 31% and 15%, respectively. Chest CT showed expiratory air trapping in all patients. Patients were treated with corticosteroids, steroid-sparing agents, and macrolides in 77%, 46%, and 22%, respectively. Over a median follow-up in our series of 1703 days (range, 11-3206 days), PFTs did not change significantly. In all series combined, mortality incidence from any cause was 82/1000 patient-years (95% CI, 65-102). Of 14 patients who died, 3 deaths were due to respiratory failure and 5 were potentially related to complications of immunosuppressive therapy.

**Conclusion:** Sporadic OB is a rare disease that is uniformly associated with air trapping on high-resolution chest CT. The diagnosis should be established with surgical biopsy if possible. The illness is not typically progressive.

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Obliterative bronchiolitis (OB) is an uncommon disease characterized by inflammation and fibrosis of conducting airways with a diameter less than 2 mm.<sup>1</sup> The disease is best described as a manifestation of chronic allograft dysfunction in lung transplant recipients, and graft-versus-host disease in bone marrow and stem cell transplant recipients.<sup>2</sup> It has also been characterized in outbreaks after well-defined point-source exposures to inhaled toxins.<sup>1</sup> In contrast, far less is understood about the natural history and outcomes of patients with OB outside these contexts: knowledge of such sporadic cases is limited to a few

case series, with considerable gaps in our understanding of pathogenesis, diagnosis, and treatment of these patients.

In this work, we sought to describe a cohort of patients who presented with sporadic OB, to summarize the literature, and to compile all the available data on this entity. We sought to describe treatment regimens and outcomes after diagnosis, primarily transplant-free mortality and pulmonary function test (PFT) change over time. In addition to compiling data systematically, we aimed to compare the results from our experience with 19 patients vs the sum of data acquired from the literature.

## PATIENTS AND METHODS

### Patients

After approval by our institutional review board, we queried the University of Virginia Clinical Data Repository with the search terms “obliterative,” “bronchiolitis,” “constrictive,” and *International Classification of Diseases, Ninth Revision* codes of 491.8, 466.19, and 506.4, and excluded patients with simultaneous diagnoses that included the search terms “transplant” or “transplantation.” The repository contains deidentified clinical information for approximately 1.5 million patients and 5 million encounters at the University of Virginia in the last 20 years. Of the resulting 35 patients, 11 were excluded: 6 duplicate accessions, 1 with insufficient clinical data, and 4 had alternative diagnoses (1 each of hypersensitivity pneumonitis, lymphocytic interstitial pneumonia, pulmonary Langerhans cell histiocytosis, and OB after stem cell transplantation). Samples from the remaining 24 were reviewed by a pathologist (M.H.S.), who was blinded to clinical data, to confirm the histologic diagnosis. This excluded 5 additional patients (2 respiratory bronchiolitis-associated interstitial lung disease, and 1 each of organizing pneumonia, usual interstitial pneumonia, and hypersensitivity pneumonitis), yielding 19 patients for analysis (see [Supplemental Figure](http://mcpiqjournal.org), available online at <http://mcpiqjournal.org>).

We retrospectively reviewed the medical records. The etiology of OB was assigned according to the treating pulmonologist. Gastroesophageal reflux disease (GERD) was classified on the basis of history or long-term therapy with acid-suppressing medications. Death was ascertained in the medical records or using the publicly available Social Security Death Index. Patients were censored at the date of last interaction with any provider in the medical records.

Chest high-resolution computed tomography (HRCT) scans were reviewed and scored independently by 2 thoracic radiologists (L.F. and M.H.), who were blinded to clinical data and each other's interpretations. Computed tomography (CT) abnormalities were quantified using a published scoring system previously used in lung transplantation-associated bronchiolitis obliterans syndrome<sup>3</sup> as detailed in the Supplemental Data (see

[Supplemental Table](http://mcpiqjournal.org), available online at <http://mcpiqjournal.org>). Mean scores were reported as a measure of extent of each radiographic abnormality.

### Review of the Literature

We searched the National Library of Medicine's PubMed, the Cochrane Central Register of Controlled Trials, MEDLINE, PubMed Central, and EMBASE databases with the search terms “constrictive bronchiolitis,” “obliterative bronchiolitis,” and “bronchiolitis obliterans,” excluding publications linked with “transplantation” and “organizing pneumonia.” The results were refined to English language series that reported 3 or more adults, and excluded point outbreaks. This generated 104 separate cases,<sup>4-12</sup> published between 1981 and 2014 (see [Supplemental Figure](http://mcpiqjournal.org)).

The date of the last study search was September 22, 2018. We used 3 separate search terms to account for the heterogeneity in the nomenclature of this disease. Exclusion criteria were selected to eliminate transplanted-related OB and series of organizing pneumonia, a separate entity with a similar name. Series were defined as those reporting 3 or more patients. Point outbreaks of OB were excluded because this entity is well described. Patient characteristics and clinical data were acquired through manual review of each study. Primary measures among both groups included associated demographic characteristics and comorbidities, as well as transplant-free survival and PFT decline.

### Statistical Analyses

Categorical variables were compared between series using Fisher exact or  $\chi^2$  test; continuous variables were compared using the Mann-Whitney test. Linear regressions were modeled for PFT progressions excluding 1% outliers and using 95% CIs. Survival times were calculated from the date of diagnosis to censoring or death, and were expressed as a Kaplan-Meier curve. Pulmonary function test variables were expressed as percent of predicted value according to the Third National Health and Nutrition Examination Survey database. Statistical analysis and data plotting were performed using Prism 7.0a (GraphPad Software).

TABLE 1. Characteristics of Patients With Sporadic Obliterative Bronchiolitis in the Current Series<sup>a</sup>

Age at diagnosis (y)	Sex	Risk factor	Basis for diagnosis	Follow-up (d)	Death
41	M	Idiopathic	Biopsy	2100	No
60	F	Idiopathic	Biopsy	1434	No
61	F	Inflammatory bowel disease	Biopsy	1176	No
39	F	Idiopathic	Biopsy	1703	No
68	F	Sjögren syndrome	Biopsy	591	Yes
57	F	Inhalational exposure <sup>b</sup>	Biopsy	2093	No
77	M	Connective tissue disease	Clinical	907	No
44	F	Connective tissue disease	Biopsy	912	No
52	M	Pemphigus vulgaris	Biopsy	183	Yes
67	F	Connective tissue disease	Biopsy	2533	No
57	F	Idiopathic	Biopsy	2353	No
62	F	Connective tissue disease	Biopsy	2747	Yes
28	F	Psoriatic arthritis and diffuse large B-cell lymphoma	Biopsy	2144	No
58	M	Idiopathic	Biopsy	3206	No
72	F	Polymyositis	Biopsy	1893	Yes
56	F	Idiopathic	Biopsy	194	Yes
54	M	Idiopathic	Biopsy	2561	No
27	M	Inhalational exposure <sup>c</sup>	Biopsy	755	No
52	F	Idiopathic	Biopsy	11	No

<sup>a</sup>F = female; M = male.

<sup>b</sup>Exposure to domestic birds and farming environments with serologic evidence of sensitization.

<sup>c</sup>Inhalational exposures during the 2003 Iraq war.

## RESULTS

### Demographic Characteristics and Associated Illnesses

The current series included 19 patients with OB who were seen between July 2007 and August 2017. The patients were predominantly women (68%) and Caucasian (89%), with median age at diagnosis of 57 years (Table 1). Obliterative bronchiolitis was deemed idiopathic in a plurality (42%); among the remainder, it was associated with connective tissue diseases in 32%, inhalational exposures in 2 patients, and inflammatory bowel disease, pemphigus, and psoriasis and lymphoma in 1 patient each. Two patients smoked at the time of diagnosis and 14 were never-smokers (74%); the remainder smoked a median of 20 pack-years. Most patients had GERD (84%).

In reviewing the previously published literature, we identified 104 patients with sporadic OB (Table 2), among whom the diagnosis was reached by surgical biopsy in 58 patients (56%). Most subjects were women and were

diagnosed in the fifth decade of life; among series that reported race,<sup>5,10</sup> 20 of 22 patients were Caucasian. Obliterative bronchiolitis was most commonly idiopathic, associated with connective tissue diseases or inhalational exposures. The illness rarely occurred after a reported history of respiratory infection or as a result of a suspected paraneoplastic etiology. Among series that reported on smoking,<sup>4,5,7-12</sup> 21% of patients had a history of smoking. The previous series did not report the incidence of GERD.

### Pulmonary Function Testing

Eighteen of the 19 patients in the present series underwent PFTs. These results did not show a consistent pattern: a third of patients had a normal result and, among the abnormal results, both restrictive and obstructive patterns were observed (Table 3). The extent of impairment in spirometry variables, diffusion capacity, and static lung volumes ranged from moderate impairment to normal. Ours is the only series in the literature to report

TABLE 2. Summary of Characteristics of Patients With Sporadic Obliterative Bronchiolitis in All Available Series<sup>a</sup>

Reference, year	Number of patients	Female (%)	Age (y) <sup>b</sup>	CTD (%)	Preceding infection (%)	Inhalational (%) <sup>c</sup>	Paraneoplastic (%)	Idiopathic (%)	Lung biopsy (%)
Turton et al, <sup>4</sup> 1981	10	9 (90)	48	5 (50)	3 (30)	0 (0)	0 (0)	2 (20)	0 (0)
Seggev et al, <sup>5</sup> 1983	3	1 (33)	48	0 (0)	1 (33)	2 (67)	0 (0)	0 (0)	3 (100)
Epler et al, <sup>6</sup> 1985	10	—	—	1 (10)	1 (10)	0 (0)	0 (0)	8 (80)	10 (100)
Kraft et al, <sup>7</sup> 1993	4	4 (100)	47	0 (0)	0 (0)	0 (0)	0 (0)	4 (100)	4 (100)
Hansell et al, <sup>8</sup> 1997	15	15 (100)	47	5 (33)	1 (7)	0 (0)	0 (0)	9 (60)	3 (20)
Myong et al, <sup>9</sup> 2001	3	3 (100)	47	0 (0)	0 (0)	0 (0)	1 (33)	2 (67)	3 (100)
Markopoulo et al, <sup>10</sup> 2002	19	14 (74)	45	4 (21)	2 (11)	3 (16)	0 (0)	10 (53)	19 (100)
Parambil et al, <sup>11</sup> 2009	29	20 (70)	54	13 (45)	1 (3)	3 (10)	3 (10)	9 (31)	9 (31)
Kawassaki et al, <sup>12</sup> 2014	11	8 (73)	49	3 (27)	0 (0)	8 (73)	0 (0)	0 (0)	7 (64)
All series including current	123	87 (77)	49	38 (31)	9 (7)	18 (15)	5 (4)	52 (42)	76 (62)

<sup>a</sup>CTD = connective tissue disease; — = data not reported.

<sup>b</sup>Age reported as median in Hansell et al<sup>8</sup> and Parambil et al<sup>11</sup> and mean in all other studies.

<sup>c</sup>Toxic fumes or agents associated with hypersensitivity pneumonitis.

6-minute walk distance in this population; we found notable reduction in this variable in most patients (Table 3).

Pulmonary function test reported in the previous literature showed most patients to have an obstructive ventilatory defect that was severe in a quarter and was associated with elevation of reserve volume, indicating air trapping. A third of patients had a restrictive, mixed, or normal pattern. Overall, median forced expiratory volume in 1 second and forced vital capacity values were moderately reduced, and median values of other PFT variables were within the normal range (Table 3).

### Chest HRCT

In the current series, 15 patients had chest HRCT available for review. The studies were obtained a median of 36 days before biopsy (interquartile range, -49 to 84 days in relation to biopsy). Air trapping was universally present in the 13 studies that included expiratory images; in addition, it was the most severe abnormality, affecting 25% to 50% of the lungs (Table 4). Bronchial wall thickening was similarly universally present and was moderate in extent. Mosaic ground-glass attenuation was present in most patients but was mild in extent; bronchial dilation was both uncommon and mild (Table 4).

Among the published literature, 5 series reported at least some CT findings on a total of 68 patients.<sup>8-12</sup> These studies are heterogeneous

with respect to the reported CT findings, because (a) not all reported on the presence of all CT abnormalities; (b) the presence of mosaic ground glass and air trapping were part of the inclusion criteria in 1 study<sup>11</sup>; and (c) previous series reported only on the presence, but not the extent, of each abnormality. These caveats notwithstanding, evidence of air trapping on expiratory images was a universal feature in patients with OB in the literature. In addition, most patients had evidence of mosaic perfusion and bronchial wall thickening, but only a minority had evidence of bronchiectasis or bronchioloectasis (Table 4).

### Treatments, Follow-up, and Outcomes

The present series provides the longest duration of follow-up for patients with sporadic OB, with a median follow-up duration of more than 5 years. During this time, 15 patients underwent serial PFT and 5 had serial 6-minute hall walk tests. We found no statistically significant change in forced vital capacity, forced expiratory volume in 1 second, gas transfer, or hall walk distance in the group over time (Figure A). The most commonly prescribed medication to the patients in our series were corticosteroids and long-term macrolides, each in more than half of the patients; a third were treated with other immunosuppressive drugs, and 4 received no therapy (Table 5). Over the follow-up period, 5 patients died (Figure B). The cause of death

**TABLE 3. Comparison of Presenting Pulmonary Function Tests in the Current Series and Published Literature<sup>a</sup>**

PFT interpretation	Number in current series (%)	All series including current (%) <sup>b</sup>
Obstructive	3 (17)	69 (71)
Restrictive	9 (50)	13 (13)
Combined	1 (6)	4 (4)
Normal spirometry	5 (28)	11 (11)

Variable <sup>c</sup>	Current series	All series including current (%) <sup>d</sup>
FVC	68 (46-90)	61 (46-78)
FEV <sub>1</sub>	68 (48-85)	51 (32-76)
FEF <sub>25-75</sub>	78 (55-98)	67 (32-93)
DL <sub>CO</sub>	70 (52-90)	85 (61-100)
TLC	80 (63-91)	96 (82-103)
RV	76 (66-105)	117 (77-194)
6-min walk distance (m)	275 (233-352)	—

<sup>a</sup>DL<sub>CO</sub> = diffusing capacity of the lung for carbon monoxide; FEF<sub>25-75</sub> = forced expiratory flow at 25%-75% of forced vital capacity; FEV<sub>1</sub> = forced vital capacity in 1 s; FVC = forced vital capacity; PFT = pulmonary function test; RV = residual volume; TLC = total lung capacity.

<sup>b</sup>Current series and references 4, 5, 7, and 9-12; denominators varied because of variable reporting of PFT values between studies.

<sup>c</sup>PFT variables are reported as median of percent-predicted values (interquartile range); half walk distance is reported as median distance (interquartile range).

<sup>d</sup>Current series and references 5, 7, 9, 10, and 12.

was unrelated to bronchiolitis obliterans in 2 patients (1 each septic shock and amyotrophic lateral dystrophy), was unknown in 2, and was progressive respiratory failure in 1.

The published series provided longitudinal follow-up data for a median of 2 years on a total

of 79 patients, but did not provide data on serial PFT or half walk distance. Most patients were treated with corticosteroids, less than half received other immunosuppressive drugs, and long-term macrolides were used uncommonly. Nine patients died and 4 underwent lung transplantation. The cause of death was respiratory failure in 2 and nonrespiratory in 5 (1 renal failure and 2 each of lymphoma and opportunistic infection) and unknown in 1.

### Comparison of the Present Series With the Previous Literature

The present series was similar to the previous literature with respect to demographic characteristics and causes of OB ( $P=.37$  for sex and  $.43$  for cause). The HRCT findings were similar between our series and the previous series, but the pattern of PFT differed significantly ( $P<.001$ ), with a pure obstructive pattern in 17% in our series and 84% in previous studies. Our series instituted immunosuppressive therapy less often than did the previous series ( $P=.003$ ) and used long-term macrolides more frequently ( $P=.01$ ), whereas the rate of nontreatment did not differ significantly ( $P=.10$ ). The rate of death or transplantation was not significantly different between our series and the previous literature ( $P=.51$ ), despite significantly longer follow-up in our series ( $P=.007$ ).

### DISCUSSION

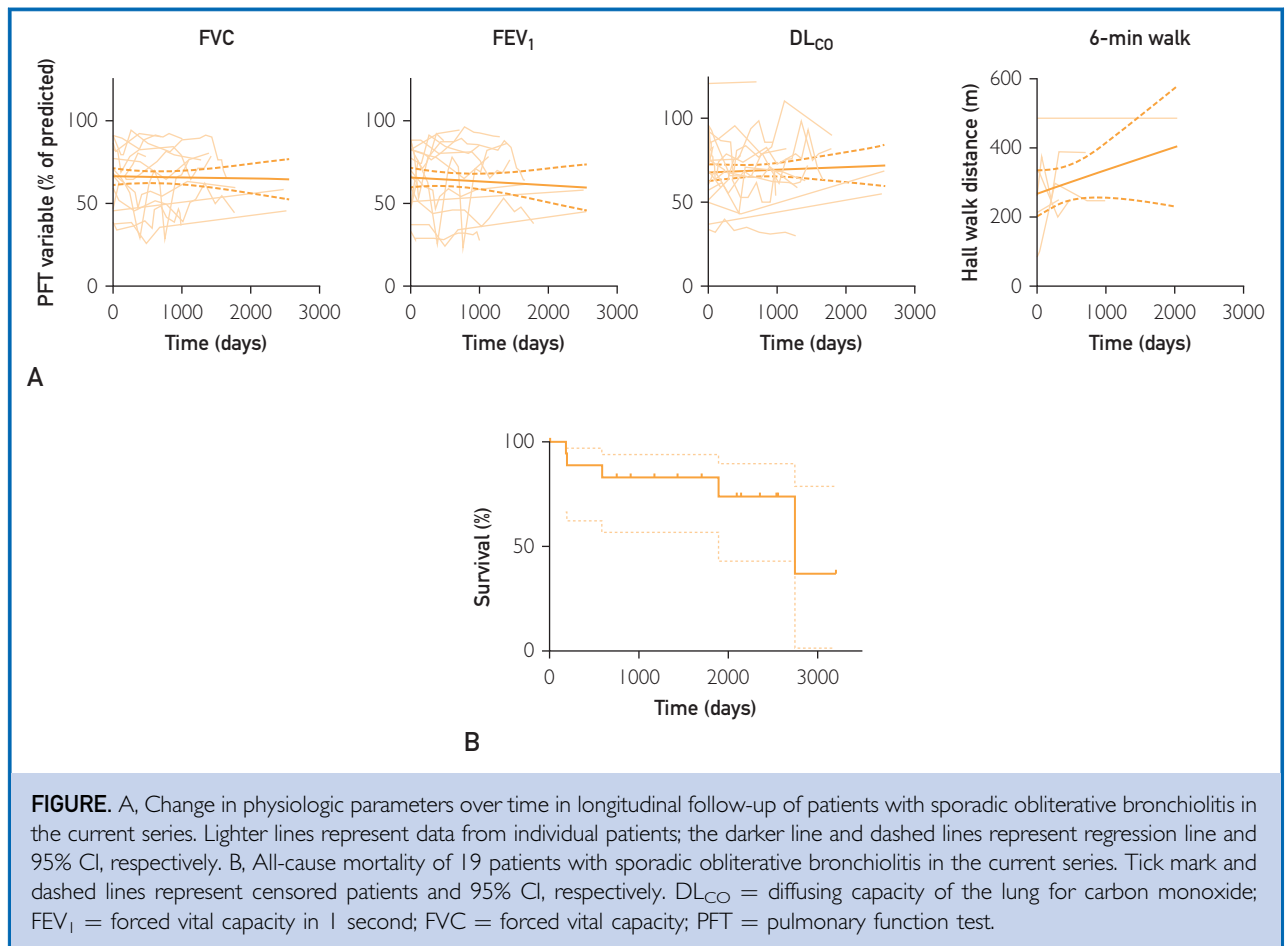
Obliterative bronchiolitis is best characterized as a complication of stem cell transplantation or lung transplantation, and as a consequence of point-source exposures. In contrast, the data regarding the natural history, management, and outcome of sporadic OB are limited to a few case series. We sought to add to this

**TABLE 4. Comparison of Chest CT Findings of Patients in the Current Series and Published Literature<sup>a</sup>**

HRCT findings	Current series		All series including current (%) <sup>b</sup>
	Number (%)	Mean severity score	Number (%)
Air trapping on expiratory CT	13 of 13 (100)	2.1 (scale 0-4)	65 of 65 (100)
Mosaic perfusion	12 of 15 (80)	1.3 (scale 0-4)	66 of 83 (80)
Bronchial wall thickening	15 of 15 (100)	1.4 (scale 0-2)	36 of 43 (84)
Bronchial dilation	4 of 15 (27)	0.25 (scale 0-2)	27 of 72 (38)

<sup>a</sup>CT = computed tomography; HRCT = high-resolution computed tomography.

<sup>b</sup>Current series and references 8-12; differing denominators are due to variable reporting between studies.



**FIGURE.** A, Change in physiologic parameters over time in longitudinal follow-up of patients with sporadic obliterative bronchiolitis in the current series. Lighter lines represent data from individual patients; the darker line and dashed lines represent regression line and 95% CI, respectively. B, All-cause mortality of 19 patients with sporadic obliterative bronchiolitis in the current series. Tick mark and dashed lines represent censored patients and 95% CI, respectively. DL<sub>CO</sub> = diffusing capacity of the lung for carbon monoxide; FEV<sub>1</sub> = forced vital capacity in 1 second; FVC = forced vital capacity; PFT = pulmonary function test.

literature by contributing our experience with this illness, and by consolidating the existing data.

The data indicate that sporadic OB disproportionately affects women in the fourth or fifth decade of life. The disease was most often idiopathic, and the most commonly identified causes were connective tissue diseases and inhalational exposures. Although smoking can cause another small airway disease, respiratory bronchiolitis,<sup>13</sup> smoking history was not associated with sporadic OB. In contrast, history of GERD was markedly overrepresented in our series. Previous series did not report the incidence of GERD in sporadic OB, but is highly associated with lung transplant-associated OB.<sup>14</sup> The high incidence of idiopathic OB suggests either an unrecognized mechanism, or the need for clinicians to probe further into risk factors, including a thorough exposure history and

workup to assess for the possibility of autoimmune diseases. The literature review indicated that 6% of patients reported that symptoms of respiratory tract infection preceded the diagnosis of OB, but we consider this as unconvincing evidence of a causal link for 3 reasons: first, symptoms of a respiratory tract infection may be difficult to distinguish from symptoms of OB; second, it is not clear that this rate is higher than in subjects without OB. Finally, this association is almost certainly tainted by recall bias.

The data indicate that PFTs were not diagnostically helpful, because they can demonstrate an obstructive, restrictive, or normal pattern. Evidence of air trapping on expiratory HRCT, however, was present in every patient with OB in the literature, suggesting a high sensitivity and usefulness of the test to rule out the diagnosis. There was a notable discrepancy in the use of surgical lung biopsy to reach the diagnosis

**TABLE 5. Treatments and Outcomes in Patients With Sporadic Obliterative Bronchiolitis in the Current Series and Published Literature<sup>a</sup>**

Treatments and outcomes	Current series	All series including current (%) <sup>b</sup>
Median follow-up duration (IQR) (mo)	63 (25-84)	24 (8-42)
Therapy, n (%)		
None	4 of 19 (21)	6 of 79 (8)
Corticosteroids	11 of 19 (58) <sup>c</sup>	61 of 79 (77)
Steroid-sparing agent	6 of 19 (32) <sup>d</sup>	36 of 79 (46) <sup>e</sup>
Any immunosuppressant	8 of 19 (42)	47 of 49 (96)
Macrolides	10 of 19 (53)	17 of 79 (22)
Death or lung transplantation	5 of 19 (26)	18 of 98 (18)

<sup>a</sup>IQR = interquartile range.

<sup>b</sup>Current series and references 4, 5, 7, 9, 11, and 12; differing denominators are due to variable reporting between studies.

<sup>c</sup>Arbitrarily defined as a minimum of 10 mg prednisone daily for 6 wk, or equivalent.

<sup>d</sup>Mycophenolate in 3, azathioprine in 2, and oral cyclophosphamide in 1 patient.

<sup>e</sup>Methotrexate in 9; azathioprine in 6; cyclophosphamide in 5; etanercept in 4; mycophenolate and sulfasalazine in 3 each; chloroquine and hydroxychloroquine in 2 each; and leflunomide and infliximab in 1 each.

of OB between our series and the rest of the literature. We caution against the diagnosis of OB without surgical biopsy, for 2 reasons: first, the symptoms, signs, and noninvasive testing results for OB are nonspecific. Second, OB, a rare entity, represents a minority of patients who have air trapping on chest HRCT.<sup>15,16</sup>

An unexpected difference between our series and the previous literature is the far lower incidence of a pure obstructive PFT pattern in our series. Although the explanation for this discrepancy is unclear, we note that all patients in both groups had air trapping on expiratory CT, but that the rate of histologic (and thus definitive) diagnosis of OB was 95% in our series and 56% in the previous series. This raises the possibility that, in patients without biopsy, other more common causes of air trapping on HRCT—namely, asthma, smoking-related lung disease such as respiratory bronchiolitis, and bronchiectasis<sup>15,17</sup>—may have been misclassified as OB.

Our series adds to the field by providing 5 years of follow-up with serial PFTs, hall walk distance, and mortality data. There was a cumulative all-cause mortality of 55 deaths per 1000 patient-years in our series and 82 per 1000 patient-years in other series, with only 21% of deaths caused by respiratory failure.

For context, this mortality rate is lower than that of chronic kidney disease in the United States.<sup>18</sup> Consistent with this, we found stability in PFT and 6-minute walk distance during the follow-up period in our series. Taken together, we conclude that sporadic OB is not typically a progressive disease.

Most patients (82%) received some form of immunosuppression, most often oral corticosteroids. The rationale for immunosuppressive therapy is strongest in autoimmune diseases, and in cases of OB with histologic evidence of inflammation rather than fibrosis.<sup>9,10</sup> However, 36% of deaths were due to infection or lymphoma, and thus could reasonably be linked to immunosuppressive therapy. Macrolide therapy is an established treatment for another small airway disease, diffuse panbronchiolitis,<sup>19,20</sup> and has been effective in OB associated with lung transplantation<sup>21,22</sup> but not stem cell transplantation.<sup>23,24</sup> Compared with the previous literature, our series used macrolides more frequently, and immunosuppressive therapy less frequently, with equivalent outcomes and no documented decline in lung function, despite a longer follow-up period. This observation lends tentative support to a less aggressive immunosuppressive therapy in sporadic OB.

The strengths of our series were that (a) it is relatively large compared with previous series; (b) the diagnosis of OB was ascertained on surgical biopsy on all but 1 patient, and was hence definitive; (c) it reports details of imaging and serial physiologic studies not reported elsewhere; and (d) it provides by far the longest follow-up data for this illness. The limitations of the entire literature on sporadic OB, including our series, include the confounding effect of referral bias. Identification of some presumptive etiologies, such as previous respiratory infection or inhalational exposures, is confounded by recall bias and thus overestimates the relevance of these exposures. Most of the published literature did not provide data on all the variables, resulting in an incomplete data set and thus a potential reporting bias. As noted above, the diagnosis of OB without histologic confirmation may have led to misclassification of more common diseases as OB in the literature. The numbers of patients in individual series are small, increasing the likelihood of false-negative

findings, that is, failing to find true associations due to low statistical power. Finally, the retrospective nature of these data precludes meaningful conclusions about the effectiveness of the therapies used.

In summary, sporadic OB is an often-idiopathic disease that disproportionately affects middle-aged Caucasian women. The diagnosis can be excluded in the absence of air trapping on expiratory chest HRCT, and should be established with surgical biopsy if at all possible. Workup for potential etiologies should focus on connective tissue diseases (commonly rheumatoid arthritis, Sjögren syndrome, and psoriatic arthritis) and inhalational exposures. The illness is not typically progressive and evidence for the use of immunosuppression is sparse.

#### SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <http://mcpiqjournal.org>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

**Abbreviations and Acronyms:** CTD = connective tissue disease; GERD = gastroesophageal reflux disease; HRCT = high-resolution computed tomography; OB = obliterative bronchiolitis; PFT = pulmonary function test

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