Effects of tobacco smoking on recurrent hospitalisation with pneumonia: A population-based cohort study

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Abstract

The incidence of, and risk factors for recurrent hospitalisation for pneumonia was investigated using data from Hospital Episode Statistics, linked to a UK primary care database. Within 90 days and 1 year of follow-up, 1,733 (3.1%) and 5,064 (9.0%) developed recurrent pneumonia respectively. Smoking status at the time of hospitalisation with index pneumonia was associated with the risk of readmission with recurrent pneumonia within a year of discharge; current vs never smokers: aOR 1.42,95% CI 1.32-1.53,p<0.001 and ex vs never smokers: aOR 1.24,95% CI 1.15-1.34,p<0.001. Other independent risk factors associated with recurrent pneumonia were age, gender, deprivation and underlying comorbidities.

Introduction

Preventing hospitalisation for pneumonia, especially during winter, is one of the priorities for respiratory disease in the NHS Long Term Plan, and for the British Thoracic Society. However, there are few studies related to recurrent hospitalisation for pneumonia and specifically no studies from the UK. Studies from the past two decades suggest recurrent hospitalisation for pneumonia occurs in 9-17.6% of adults during a follow-up of 1-3 years following index admission with pneumonia.[1–3] Non-modifiable factors associated with increased risk of recurrent pneumonia include increasing age, impaired functional status, comorbidities and medications.[4] Although there is a well-described dose-dependent association of tobacco smoking with the development of pneumonia, the evidence in recurrent pneumonia is mixed.[5–8]

The aims of this study were to determine the incidence of recurrent hospitalisation with pneumonia in England and the association of tobacco smoking, a potentially modifiable risk factor.

Methods

Hospitalisation data from Hospital Episode Statistics (HES, England), linked to the Clinical Practice Research Datalink (CPRD), and death registration data from Office for National Statistics (ONS), were used for this study. Ethical approval was provided by MHRA Independent Scientific Advisory Committee (ISAC) (study protocol number: 18_178A).

Adults aged ≥18 years with the first episode of hospitalisation for pneumonia (index date) recorded in HES between 1 July 2002 and 30 June 2017 were included. The Public Health England 'epidemiological year' definition of July- June was used as the unit of time to avoid the winter peak of pneumonia traversing two calendar years. Pneumonia was defined based on J12- J18 ICD-10 codes recorded as the primary code for the first episode of hospitalisation. Recurrent pneumonia was defined as at least one episode of hospitalisation for pneumonia more than 30 days after index pneumonia. Patients were excluded if they had less than a year of time registered to the practice before admission, hospital-acquired pneumonia (admission for at least a day in the 10 days preceding the index admission) or readmission within 30 days of discharge. Patients were followed up from day one after the date of hospital discharge to either the date of admission for recurrent pneumonia, end of data collection (30 June 2017), date of transfer out of practice, date of last data collection for the practice or date of death, whichever came first.

Read code lists for smoking status was developed using validated Read codes from previous research. The most recent documented smoking status (current, ex and never-smokers) in CPRD

before the index admission was used; 'never-smokers' with previous smoking history were recorded as 'ex-smoker'.

Descriptive statistics for the patient population were calculated. 'Time to first recurrence' was measured from day one after discharge from hospital to admission with recurrent pneumonia. The proportion of patients who developed recurrent pneumonia during a 5-year follow-up period was determined. Incidence rates (per 100 person-years) for recurrent pneumonia at different time intervals were determined; 90 days, 1 year and 5 years. Directed acyclic graph (DAG) was used to identify the minimum set of confounders to close the back-door paths, which included age, gender, deprivation, alcohol consumption and comorbidities (Supplementary File S1). Multiple imputation using chained equations was performed with 10 imputed datasets for smoking status (2.7% missing data) and alcohol consumption (15.0% missing data) (Supplementary File S2). Competing-risks regression analyses were conducted to determine the effect of tobacco smoking on hospitalisation for recurrent pneumonia with death as a competing event. Statistical analyses were performed using StataMP 15.

Results

The study cohort comprised 56,396 patients (**Figure 1**). Median age of the study cohort was 75 years (IQR 61-84 years) and 49.7% were male.

Figure 1: Flowchart of the study population

The median time to recurrence was 1.3 years (IQR 0.5-2.6 years). The incidence rates (per 100 person-years) for recurrent pneumonia at 90 days, 1 year and 5 years were 13.6 (95% CI 13.0-14.2), 11.1 (95% CI 10.8-11.4) and 7.10 (95% CI 6.97-7.23) correspondingly. Within 90 days and 1 year of follow-up, 1,733 (3.1%) and 5,064 (9.0%) developed recurrent pneumonia respectively, with 1,866 (36.9%) patients hospitalised for more than one recurrence during the 1-year follow-up period. The 30-day mortality for a recurrent pneumonia hospitalisation was 23.7% (n=3,011). Over the period 2002 to 2017, the proportion of recurrent pneumonia within one year of index admission increased from 5.6% to 11.4% (**Figure 2**).

Figure 2: Trend of recurrence of pneumonia within 31-90 days and 1 year of index pneumonia admission

Note: 1-year recurrence refers to recurrence between 31-365 days after discharge for index pneumonia. Patients readmitted to hospital within 30 days of discharge were considered to be readmissions for the index episode, hence excluded.

Current smoking at index admission was independently associated with a 42% increased risk of recurrent pneumonia compared to having never smoked at any point in time (**Table 1**). This risk was halved in ex-smokers. Other factors independently associated with recurrent pneumonia were age, gender, deprivation and Charlson Comorbidity Index score.

Table 1: Factors independently associated with recurrent pneumonia within a year of discharge: Competing-risks regression (CRR) analysis with death as competing event

	Total no of patients N	With recurrence n (%)	Multivariate CRR sHR (95% CI)	p value
Number of patients	56396	5064		
Smoking status				
Never	18179	1274 (7.0)	1.00 Reference	
Ex	14512	1517 (10.5)	1.24 (1.15-1.34)	<0.001
Current	23678	2273 (9.6)	1.42 (1.32-1.53)	<0.001
Age				
18-49	8208	247 (3.0)	1.00 Reference	
50-64	8830	556 (6.3)	1.76 (1.51-2.05)	<0.001
65-74	10499	986 (9.4)	2.37 (2.05-2.75)	<0.001
75-84	15317	1692 (11.0)	2.78 (2.41-3.22)	<0.001
≥85	13542	1583 (11.7)	3.17 (2.73-3.67)	<0.001
Gender				
Male	28002	2719 (9.7)	1.00 Reference	
Female	28394	2345 (8.3)	0.85 (0.80-0.90)	<0.001
Alcohol status				
Non-drinker	14780	1451 (9.8)	1.00 Reference	
Former drinker	3319	381 (11.5)	1.08 (0.96-1.22)	0.176
Occasional drinker	9047	854 (9.4)	0.95 (0.87-1.04)	0.237
Moderate drinker	21468	1772 (8.3)	0.88 (0.82-0.95)	0.001
Heavy drinker	7782	606 (7.8)	0.90 (0.81-1.01)	0.063
IMD (patient-level)				
1 (least deprived)	10596	875 (8.3)	1.00 Reference	
2	11407	1023 (9.0)	1.06 (0.97-1.16)	0.195
3	11909	1068 (9.0)	1.06 (0.97-1.16)	0.228
4	11263	977 (8.7)	1.02 (0.93-1.12)	0.689
5 (most deprived)	11171	1117 (10.0)	1.21 (1.10-1.32)	<0.001
Unknown	50	4 (8.0)	1.14 (0.45-2.89)	0.776
Charlson Index				
0	13636	608 (4.5)	1.00 Reference	
1	12290	955 (7.8)	1.43 (1.29-1.59)	<0.001
2	9912	986 (9.9)	1.65 (1.48-1.84)	<0.001
3	7777	867 (11.1)	1.76 (1.58-1.97)	<0.001
4	5096	634 (12.4)	1.90 (1.69-2.14)	<0.001
≥5	7685	1014 (13.2)	2.00 (1.79-2.23)	<0.001

Co-morbidities						
COPD	11798	1810	(15.3)	1.77	(1.65-1.89)	<0.001
Asthma	13347	1471	(11.0)	1.11	(1.03-1.18)	0.004
***Chronic lung disease**	896	106	(11.8)	1.56	(1.29-1.90)	<0.001
Congestive cardiac failure	5648	705	(12.5)	1.12	(1.02-1.23)	0.016
Myocardial infarction	5268	614	(11.7)	1.03	(0.94-1.13)	0.496
[#]Other cardiac diseases	23326	2344	(10.1)	1.05	(0.98-1.12)	0.149
Malignancy	12397	1402	(11.3)	1.17	(1.10-1.25)	<0.001
Chronic renal disease	10974	1343	(12.2)	1.16	(1.09-1.24)	<0.001
Cerebrovascular disease	6377	768	(12.0)	1.05	(0.97-1.12)	0.228
Diabetes mellitus	9390	996	(10.6)	1.14	(1.05-1.23)	0.001
Cognitive impairment	5834	660	(11.3)	1.11	(1.02-1.21)	0.017
Liver disease	531	53	(10.0)	1.24	(0.94-1.62)	0.128

The 2015 English Index of Multiple Deprivation (IMD) was used as composite measure of material deprivation at the patient level.

*Chronic lung disease excluding COPD and asthma

[#] Other cardiac diseases excluding CCF and MI (e.g. hypertension, arrhythmias, valvular heart disease, conduction disorder of the heart, pericarditis, myocarditis)

Two multivariate models were conducted: **Model 1:** all variables + Charlson Comorbidity Index (without individual comorbidities) and **Model 2:** all variables + individual comorbidities (without Charlson Comorbidity Index). Results are presented from Model 1, except for individual comorbidities from Model 2 as estimates for other variables in both models were similar.

See Supplementary File S3 for factors associated with death within a year of discharge.

Discussion

To our knowledge, this is the first UK study to investigate the incidence of, and risk factors for recurrent hospitalisation for pneumonia. Current tobacco smoking status at index hospitalisation for pneumonia was independently associated with a higher risk of recurrent pneumonia.

Studies from other countries having reported a range of incidences of recurrent pneumonia over different time-periods; 16.3% during a median follow-up of 475 days in Japan to 3.5% over an 11-year period in Sweden.[3,9] Marked differences in study methodology and healthcare system are likely to account for the variation, emphasising the importance of country-specific data. Our results are similar to data from Canada and Sweden; 2% recurrent pneumonia at 30 to 90 days from index admission, 17.6% recurrent pneumonia during a mean follow-up of under 3 years.[2,7] Of note, we observed a 23.7% 30-day mortality for recurrent pneumonia, twice as high as 30-day inpatient mortality for index pneumonia based on BTS National Audit data.[10] Similarly, Ishifuji *et al.* found that patients with recurrent pneumonia were almost three times more likely to have fatal outcomes during over a year's follow-up compared to those without (HR 2.81, p<0.001).[3] Our study also revealed a significant trend of increasing proportion of recurrent pneumonia between 2002- 2017.

Conversely, the BTS National Pneumonia Audit observed a decrease in mortality from index pneumonia over a ten-year period (2009 to 2019).[10] Whether these trends in survival are related to the trends in pneumonia recurrence requires further investigation.

Tobacco smoking is associated with an increased risk of developing community-acquired pneumonia.[5] We extend this observation to an association between tobacco smoking and recurrent pneumonia. In a case-control study, El Sohl *et al.* reported that current smokers were twice more likely to be admitted with recurrent pneumonia compared to never smokers (HR=2.04, 95% CI 1.48-2.82).[6] Conversely, two prospective cohort studies (Canada, n=2709 and Spain, n=1556) did not find any association between smoking and recurrent pneumonia.[7,8] These studies included younger patients (mean cohort ages 63 and 67 years).

A key strength of this study is the large sample size representative of the English population with long-term follow-up. We considered all key variables in our DAG; vaccination status, dysphagia, severity of index pneumonia, cardiac complications after index pneumonia, functional status, oropharyngeal hygiene and medications were not listed in the minimal sufficient adjustment set of confounders to close the back-door paths. A potential weakness is that we cannot exclude the possibility of information bias from miscategorisation of the study exposure, confounders and outcomes. Missing data in smoking status and alcohol consumption were handled using multiple imputation. Another limitation is that data regarding the type of tobacco smoked were only available in about half of the patients, with most consuming cigarettes and few consuming cigars (<5%).

In conclusion, our findings confirm a high and rising incidence of recurrent hospitalisation for pneumonia in England, and that current smoking status at index admission is associated with an increased risk of recurrent pneumonia. These findings support smoking cessation interventions as a key component of pneumonia management, in accordance with the NHS Long Term Plan.

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Not applicable

Competing interests

Professor Lim reports grants from National Institute for Health Research (NIHR) and Pfizer, outside the submitted work.

Statement of Contributorship

All included authors fulfil the criteria of authorship; VB, WSL and TM had substantial contributions to the study conception and design. VB had substantial contributions to the data acquisition and analysis. All authors contributed to the interpretation for the study. VB wrote the original draft. All authors revised the manuscript critically for important intellectual content, provided the final approval of the version to be published and agreed to be 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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Transparency Declaration

The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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