

Low adherence to pneumococcal vaccination in lung cancer patients in a tertiary care university hospital in Southern Germany

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Abstract

Introduction

The aim of this study was to investigate the adherence to vaccinations, especially pneumococcal vaccinations, in lung cancer patients.

Methods

The study was performed at the University Hospital Regensburg, Germany. All patients with a regular appointment scheduled between December 1, 2020, and April 29, 2021, and who provided informed consent were included. Available medical records, vaccination certificates and a questionnaire were analyzed.

Results

136 lung cancer patients (NSCLC n = 113, 83.1%, SCLC n = 23, 16.9%) were included. A correct pneumococcal vaccination according to national recommendations was performed in 9.4% (12/127) of patients.

A correct vaccination was performed for tetanus in 50.4% (6/131), diphtheria in 34.4% (44/128), poliomyelitis in 25.8% (33/128), tick-borne encephalitis in 40.7% (24/59), hepatitis A in 45.5% (7/11), hepatitis B in 38.5% (5/13), shingles in 3.0% (3/101), measles in 50.0% (3/6), pertussis in 47.7% (62/130), influenza in 54.4% (74/136) and meningococcal meningitis in 0% (0/2).

Conclusion

Adherence to pneumococcal vaccinations, as well as other vaccinations, is rather low in lung cancer patients.

Introduction

Lung cancer is one of the most common cancers worldwide.(1, 2) Infectious diseases contribute to morbidity and mortality by delaying appropriate antineoplastic therapy.(1) Vaccinations are an important and effective preventive health care measurement, especially in patients with chronic diseases.(1)

Streptococcus pneumoniae (*S. pneumoniae*) is the leading pathogen in community- acquired pneumonia (CAP), and the main cause of lower respiratory infection morbidity globally.(3) Two different vaccines are available for adults: PCV13, a pneumococcal conjugate vaccine containing 13 different capsular types, and PPSV23, a pneumococcal polysaccharide vaccine containing 23 different polysaccharides.

To prevent pneumococcal infections in these patients, vaccinations are almost universally recommended. (1, 4) In Germany, the Standing Committee on Vaccination (STIKO) develops national recommendations for the use of vaccines. For patients with lung cancer sequential pneumococcal vaccination with PCV13,

followed by PPSV23 6–12 months later, is recommended; furthermore, a booster dose with PPSV23 should be given after six years. The US Center for Disease Control and Prevention recommends sequential pneumococcal vaccination and a booster dose with PPSV23 (with different intervals). (5)

Besides pneumococcal vaccinations, an annual influenza vaccination, as well as currently vaccination against SARS-CoV-2, are also very important in preventing morbidity and mortality in patients with lung cancer. (1, 6)

The aim of this study was to analyze whether vaccinations in patients with lung cancer are in line with STIKO recommendations. Pneumococcal vaccinations were analyzed in detail.

Methods

Study design

The current report is a prospective, single center study at the University Hospital Regensburg, Germany.

Adherence to vaccination recommendations in lung cancer patients was analyzed in detail by evaluating vaccination certificates, patient medical reports and a questionnaire.(4) All patients between December 1, 2020, and April 29, 2021, with a scheduled admission to a thoracic-oncological ward or to an oncological outpatient clinic were asked to show their vaccination certificates for review. Patients who possessed no vaccination certificate at all were rated as not vaccinated, patients that failed to present their vaccination certificates were excluded from the study, and in those patients who provided only parts of their existing vaccination certificates, only complete vaccinations were considered for the analysis.

STIKO recommendations (standard indication that are recommended for all patients, indication vaccination that are recommended for all patients with increased risk, and professional / occupational vaccination for patients with increased risk due to their profession) were analyzed. The study was approved by the Ethics Committee of the University of Regensburg, Germany (reference number 19-1467-2-101).

Patients

Eligibility criteria were applied as follows: histologically proven non-small cell lung cancer (NCSLC) or small cell lung cancer (SCLC), 18 years of age or older, written informed consent, no cognitive impairment, and ability to understand and complete the questionnaire.

Statistics

Statistics of continuous variables are presented as mean \pm standard deviation. Chi square test and Fisher's exact test was used for categorical variables. All significance tests were two tailed. A p-value $<$ 0.05 was considered as the threshold for statistical significance. Analyses were performed using Microsoft Excel (version 2016, Redmond, WA, USA) and IBM SPSS (version 24.0, IBM, Armonk, NY, USA).

Results

Baseline characteristics

A total of 136 patients (48.5% female) were enrolled (Table 1). Median age was 67.5 years. Non-small cell lung cancer was the predominant histological type (SCLC n = 23, 16.9% vs. NSCLC n = 113, 83.1%). The majority of patients had metastatic disease (NSCLC stage IV n = 90, 66.1%). 98.5% of the patients presented in a good or slightly reduced performance status (ECOG 0–2). The main therapeutic approach was palliative (n = 90, 66.1%). 34 (25.0 %) patients had pulmonary comorbidities (e.g. COPD, Asthma bronchiale, interstitial lung disease).

Table 1
Baseline characteristics (n = 136)

Age (median)	67.5 years	
ECOG status		
ECOG 0	88	64.7%
ECOG 1	34	25.0%
ECOG 2	12	8.8%
ECOG 3	2	1.5%
ECOG 4	0	
Cancer type		
SCLC	23	16.9%
NSCLC	113	83.1%
Therapeutic approach		
curative	46	33.9%
palliative	90	66.1%
ECOG: Eastern Co-operative Oncology Group		
SCLC: small cell lung cancer		
NSCLC: non-small cell lung cancer		

Vaccination status

110 patients (80.9%) brought all existing vaccination certificates and 17 patients (12.5%) reported not having a vaccination certificate at all. Table 2 shows the adherence to the STIKO vaccination guidelines. The total number of patients is the number at risk according to STIKO recommendations. Following the

diagnosis of lung cancer, vaccination status of 44 patients (32.8%) was reviewed by the general practitioner, and vaccination status of 4 patients (2.9%) was assessed by a chest physician.

Table 2
Pneumococcal vaccination status of the study population

PCV13	PPSV23	Number
vaccinated in line with STIKO recommendations		
yes	yes, < 72 months vaccination prior to presentation	3.1% (4/127)
yes, vaccination prior to diagnosis and < 12 months between vaccination and presentation	no	0% (0/127)
yes, vaccination after diagnosis and < 12 months between vaccination and presentation	yes, > 72 months vaccination prior to presentation	0.8% (1/127)
no	yes, prior diagnosis and < 12 months vaccination prior presentation	1.6% (2/127)
yes, vaccination after diagnosis and < 12 months between vaccination and presentation	no	3.9% (5/127)
		9.4% (12/127)
not vaccinated in line with STIKO recommendations		
yes	yes, > 72 months vaccination prior to presentation	2.4 % (3/127)
yes, vaccination prior to diagnosis and > 12 months between vaccination and presentation	no	1.6% (2/127)
no	yes, prior to diagnosis and > 72 months vaccination prior presentation	3.9% (5/127)
no	yes, prior to diagnosis and > 12 months vaccination prior presentation	8.7% (11/127)
yes, vaccination after diagnosis and > 12 months between vaccination and presentation	no	0.8% (1/127)
no	yes, after diagnosis	11.0% (14/127)
		28.3% (36/127)
not vaccinated at all		
no	no	62.2% (79/127)

A recommended pneumococcal vaccination (in line with STIKO guidelines, considering the time after initial cancer diagnosis and prior vaccinations) was performed in 9.4% (12/127, Table 2). Most patients (62.2%, i.e., 79/127) were not vaccinated with any pneumococcal vaccine, and some received a pneumococcal vaccination not in line with STIKO recommendations. The likelihood of correct vaccination increased significantly ($p = 0.001$) if vaccination status was reviewed by a medical doctor following the diagnosis of lung cancer.

A complete vaccination was performed for tetanus in 50.4% (66/131), diphtheria in 34.4% (44/128), poliomyelitis in 25.8% (33/128), tick-borne encephalitis in 40.7% (24/59), hepatitis A in 45.5% (7/11), hepatitis B in 38.5% (5/13), shingles in 3.0% (3/101), measles in 50.0% (3/6), pertussis in 47.7% (62/130), influenza in 54.4% (74/136) and meningococcal meningitis in 0% (0/2, Table 3).

Table 3
Results from the vaccination certificates

Vaccination	Standard Vaccination (S) - for universal application	Indication Vaccination (I) - for increased risk (rather than professional)	Occupational Vaccination (O) - for increased occupational risk	Any indication	Vaccination without current risk profile / vaccination in infancy / travel vaccination
Diphtheria	34.3% (44/128)			34.4% (44/128)	
Haemophilus influenza type b		0 patients		0 patients	0% (0/127)
Hepatitis A		37.5% (3/8)	66.7% (2/3)	45.5% (5/11)	15.4% (18/117)
Hepatitis B		25.0% (2/8)	60.0% (3/5)	38.5% (5/13)	15.7% (18/115)
Human papilloma virus				0 patients	0.0% (0/127)
Influenza	58.5% (55/94)	54.4% (74/136)	45.0% (9/20)	54.4% (74/136)	0 patients
Measles	50.0% (3/6)	0 patients	0 patients	50.0% (3/6)	4.1% (5/123)
Meningococcal		0.0% (0/2)	0 patients	0.0% (0/2)	ACWY: 0.8% (1/125) MenB: 0.0% (0/125)
Mumps			0 patients	0 patients	1.6% (2/128)
Pertussis	47.7% (62/130)	60.0% (3/5)	57.1% (8/14)	47.7% (62/130)	
Pneumococcal	41.8% (38/91)	9.4% (12/127)	0.0% (0/3)	9.4% (12/127)	0 patients
Poliomyelitis	25.8% (33/128)	0 patients	0.0% (0/2)	25.8% (33/128)	
Rabies			0 patients	0 patients	0.8% (1/127)
Rubella		0 patients	0 patients	0 patients	3.9% (5/129)

Vaccination	Standard Vaccination (S) - for universal application	Indication Vaccination (I) - for increased risk (rather than professional)	Occupational Vaccination (O) - for increased occupational risk	Any indication	Vaccination without current risk profile / vaccination in infancy / travel vaccination
Shingles	3.4% (3/88)	3.9% (2/51)		3.0% (3/101)	0.0% (0/26)
Tetanus	50.4% (66/131)			50.4% (66/131)	
Tick-borne encephalitis		40.7% (24/59)	0 patients	40.7% (24/59)	19.4% (14/72)
Varicella		0 patients	0 patients	0 patients	0.8% (1/128)
Yellow fever			0 patients	0 patients	n.a.

Patients' self-reports

83 patients (61%) were convinced that they had received all recommended vaccinations. 104 participants (76.4%) were willing to get vaccinated according to STIKO recommendations, and even more patients (113; 83.1%) reported they would like to be vaccinated against SARS-CoV2. Side effects after previous vaccinations were reported by 34 patients (25%), although the reported side effects were mild.

Discussion

To our knowledge, this is the first study analyzing vaccination status of lung cancer patients in Southern Germany.

Estimated pneumococcal vaccination rate in our cohort is low (9.4 % (12/127)). One possible explanation could be nescience of physicians. This conclusion is facilitated by the fact that only 32.8% of patients had their vaccination status verified following lung cancer diagnosis, which is by far lower than the annual influenza vaccination rate. If in fact insufficient attention of the treating physicians is related to the inadequate pneumococcal vaccination rate in lung cancer patients, greater effort should be put into an appropriate doctors' information campaign.

There is also an ongoing debate on the correct strategy of pneumococcal vaccination in patients without neoplasia, which might additionally contribute to uncertainty and a lower vaccination rate.(7) Furthermore, the fear of interference with the antineoplastic treatment may impact the adherence to vaccination guidelines.

Overall, 61% of the patients (n = 83) believed that their vaccination status was complete, and 76.4% of the study participants (n = 104) were willing to receive all vaccinations as recommended. Computer-aided reminder functions might result in a higher adherence to vaccination guidelines. Additionally, a more targeted approach might prove beneficial if oncologists were to supervise and control the vaccination status of their patients. Financial incentives may also be of further help in improving vaccination compliance.(8)

A recently published article by our study group demonstrated low adherence to pneumococcal and influenza vaccination also for patients with chronic pulmonary disease. (9) Insufficient adherence to recommended vaccinations has also been reported in other studies as well. For example, in an Italian survey among patients on dialysis only 57.5% of the participants received the seasonal influenza vaccination.(10) In our cohort, the vaccination rate for influenza was also low (54.4%), despite the fact that influenza increases hospitalization and mortality rates in patients with solid tumors.(11) Additionally, many patients with cancer are older and thus already have an indication for influenza vaccination due to their age.(1)

In summary, adherence to pneumococcal vaccination, as well as to all other recommended vaccinations, is very low in this study population.

Limitations

The study is subject to certain limitations. First of all, it is a single center study, and secondly, the cohort contains only a limited number of patients. Data on vaccination coverage was collected exclusively by assessing the vaccination certificate entries; non-documented vaccinations may thus have been missed. Also, patients that did not show the vaccination certificate (but possess a vaccination certificate) were excluded. This might have led to an overestimation of the real adherence rate to vaccinations.

Declarations

Funding: No funding was received for conducting this study.

Conflicts of interest/Competing interests:

A. Mohr: travel grants from Gilead Sciences.

B. Salzberger: personal fees from GSK, Sanofi, Roche and Falk-Foundation.

F. Hitzenbichler: travel grants from Gilead Sciences.

M. Pfeifer: grants from Gilead Sciences, Boehringer, Novartis, Glaxo SKB, AstraZeneca.

M. Kloos, C. Schulz, S. Bauernfeind, A. Plentz and M. Koch have no relevant financial or non-financial interests to disclose.

Availability of data and material:

Authors will respond to data sharing requests under the premise that an adequate research question is formulated. Original anonymized data will be made available up to one year after the publication of the paper.

Code availability: (software application or custom code)

Not applicable.

Authors' contributions:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all Mia Kloos, Arno Mohr and Myriam Koch. The first draft of the manuscript was written by Arno Mohr and Myriam Koch and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval: (include appropriate approvals or waivers)

The study was approved by the Ethics Committee of the University of Regensburg, Germany (reference number 19-1467-2-101).

The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to participate: (include appropriate statements)

Informed consent was obtained from all individual participants included in the study.

Consent for publication: (appropriate statements regarding publishing an individual's data or image)

Patients signed informed consent regarding publishing their data.

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Appendix

Questionnaire

1) Did you bring your vaccination certificate to the hospital today?

Yes

No

I do not have a vaccination certificate at all

Yes, but I have another one / older vaccination certificate that I did not bring with me.

2) Do you think that you received all vaccinations recommended for people of your age and your health status?

Yes

No

I do not know

3) Are you sceptical about vaccinations in general?

Yes

No

I do not know

If yes, why?

I am afraid of side effects

I am confused about the information about vaccinations in the media

I would need more information

Vaccinations are only used by pharmaceutical companies, and doctors only perform vaccinations to make money

I don't feel threatened by the diseases which are prevented by vaccinations

My immune system can handle the pathogens on its own

Other: _____

4) Have you ever felt any side effects after vaccination?

Yes

No

If yes, what kind of side effects?

fever

headache and limb pain

muscle pain

nausea

tiredness

redness, swelling or pain on the injection point

Other: _____

5) Would you get vaccinated if we recommend it to you in the discharge letter?

Yes

No

I do not know

6) Did somebody check your vaccination status after receiving the diagnosis lung cancer but before therapy started?

Yes

No

I do not know

I received no chemotherapy at all

If yes, which physician checked your vaccination status?

General practitioner

Specialist for pulmonary care

Cardiologist

Endocrinologist

Nephrologist

- Angiologist
- Rheumatologist
- Neurologist
- Oncologist
- Gynaecologist
- Gastroenterologist
- Other: _____

7) Have you visited your general practitioner since the diagnosis lung cancer and has he or she checked your vaccination certificate?

- Yes, I visited my general practitioner and he or she checked the vaccination certificate.
- Yes, I visited my general practitioner but he or she did not check the vaccination certificate.
- Yes, I visited my general practitioner and he or she asked for my vaccination certificate, but I left it at home.
- No, I have not been to my general practitioner since the diagnosis lung cancer.

8) Have you visited a specialist of pulmonary care since the diagnosis lung cancer and has he or she checked your vaccination certificate?

- Yes, I was at a specialist of pulmonary care and he checked the vaccination certificate.
- Yes, I was at a specialist of pulmonary care but he did not check the vaccination certificate.
- Yes, I was at a specialist of pulmonary care and he or she asked for my vaccination certificate but I left it at home.
- No, I have not been at a specialist of pulmonary care since the diagnosis lung cancer.

9) Has any other medical specialist checked your vaccination certificate since the diagnosis lung cancer?

- Yes
- No
- Yes, but I left my vaccination certificate at home

10) Did you visit your general practitioner in the last 12 months and has he or she checked your vaccination certificate?

- Yes, I visited my general practitioner and he or she checked the vaccination certificate.
- Yes, I visited my general practitioner but he or she did not check the vaccination certificate.
- Yes, I visited my general practitioner and he or she asked for my vaccination certificate but I left it at home.
- No, I have not been to my general practitioner in the last 12 months.

11) Did you visit your general practitioner in the last 36 months (=3 years) and has he or she checked your vaccination certificate?

- Yes, I visited my general practitioner and he or she checked the vaccination certificate.
- Yes, I visited my general practitioner but he or she did not check the vaccination certificate.
- Yes, I visited my general practitioner and he or she asked for my vaccination certificate but I left it at home.
- No, I have not been to my general practitioner in the last 36 months (=3 years).

12) Are you still working?

- Yes
- No

If no, since when?

- Before the diagnosis lung cancer
- Since the diagnosis lung cancer
- Since therapy has started or later

Which profession do you have? _____

Are you working as a professional first-aider?

- Yes
- No
- I do not know

Are you working

in an institution with many other people (e.g. sales person, office work with a lot of customer contact, etc.)?

as a day nanny, baby sitter of a newborn (<4 weeks old)?

in a function using welding and isolating metals?

13) Have you had chickenpox (in your childhood)?

Yes

No

I do not know

14) Have you had measles (in your childhood)?

Yes

No

I do not know

15) Have you had mumps (in your childhood)?

Yes

No

I do not know

16) There are vaccination recommendations for special risk groups. Do you belong to any of them?

Animals and nature

direct contact to poultry or wild birds

contact to bats

contact to ticks (e.g. in leisure time outdoors, garden work, etc.)

farmer

hunter

Resident in special facilities

- resident in an accommodation of asylum seekers or refugees
- resident in a nursing home
- resident in a psychiatric facility
- resident in an accommodation for people with abnormal behavior or cerebral palsy

Contact to pregnant women, children and newborns

- planned pregnancy of the partner/daughter/close contact person
- pregnancy of a close contact person with delivery in the next 4 weeks
- planned activity as day nanny / baby sitter of a newborn
- contact to newborns (<4 weeks old)
- contact to children (<1 year old)

Risk contact in private setting

- contact to immunosuppressed persons
- persons with dialysis in your own household
- close contact to a person with chronic hepatitis B
- close contact to a person who has not had chickenpox and was not vaccinated against it, with a severe neurodermatitis, planned immunosuppression or planned organ transplantation

Sexual preferences

- Men who have sex with men
- Sex with often changing partners

Other:

- active drug consumption (Intravenous)
- prison inhabitation since diagnosis lung cancer
- other: _____

Are you working voluntarily?

- Yes

in health care, including associated jobs (including laboratories, cleaning person)

in a shelter or home for people seeking asylum

in a health care kitchen

in day care or children's home or something similar

in a training facility for young adults

in a prison / penal system

Other: _____

No

17) Have you been vaccinated against seasonal influenza?

Yes

I would like to get vaccinated, but there is no vaccine left.

No, but I would like to get vaccinated

No, I do not want to get vaccinated this year

18) Are you willing to get vaccinated against SARS Cov2?

Yes, I have already been vaccinated

Yes, of course

Yes, if it is recommended

No, I would like to wait

No

If No, why?

I don't feel threatened by coronavirus

I am afraid of side effects

The vaccine has not been sufficiently tested

19) Any comments?

Thank you!