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TITLE PAGE

Features of post-obstructive pneumonia in advanced lung cancer patients, a large retrospective cohort

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ABSTRACT

Background: Post-obstructive pneumonia refers to an infection of the lung parenchyma distal to a bronchial obstruction. Previous experience-based studies reported a high prevalence of this infection among patients with a medical history of advanced lung neoplasia, up to 40-55%.

Objectives: The current study was designed to investigate the features of post-obstructive pneumonia in lung cancer, including its predictors and the discriminants for 30-day mortality.

Method: Data from medical records at the tertiary University centre, UZ Brussel, were collected retrospectively between January 2016 and January 2021. Patients affected by lung cancer stages III and IV were included. A multidisciplinary team, composed of a pulmonologist, an infectious disease specialist and a chest radiologist, identified patients affected by post-obstructive pneumonia.

Results: 408 patients were included, of which 46 (11%) were diagnosed with post-obstructive pneumonia. Multivariable logistic regression for predictors of disease onset found significant differences for squamous cell carcinoma (OR:2.46 p-value:0.014) and hilar location of the tumour (OR:2.72 p-value:0.021). However, no significant differences were identified with regards to age or comorbidities. Furthermore, 30-day mortality among post-obstructive pneumonia patients was 30%. Multivariable logistic regression for prediction of 30-day mortality found significant differences in CURB-65 score (OR:73.20 p-value:0.001) and smoking status (OR:0.009 p-value:0.015)

Conclusions: Within this cohort, the prevalence of post-obstructive pneumonia in advanced lung cancer patients was lower than previously reported. Squamous cell carcinoma and a hilar tumour location were two variables associated with disease development, independent of age and comorbidities. Furthermore, a higher CURB-65 score at post-obstructive pneumonia diagnosis was correlated with mortality.

TEXT

Introduction

The most common cause of central airway obstruction is the extension of a tumor into the airway. Bronchogenic carcinomas account for the vast majority, however, esophageal and thyroid cancers may also be implicated [1, 2]. Post-obstructive pneumonia (POP) may occur in patients with airway obstruction. It is defined as an infection of the lung parenchyma distal to a partial or complete bronchial obstruction [3-5]. However, a standardized definition of POP is lacking, and conflicting results are reported in the literature [4-6]. A two-year prospective monocentric study found an incidence of POP among patients diagnosed with community acquired pneumonia (CAP) of 5.4% [4]. The same study identified a substantial difference in disease presentation between patients affected by POP in comparison to CAP. Fever, sputum production and leukocytosis were less prominent features in patients affected by POP, in contrast to the higher rate of hemoptysis. Furthermore, POP was associated with significantly less favorable outcomes; 16% of patients with POP developed a cavitating lesion and a 30-day mortality up to 40% was reported [4]. In an expert-opinion review, Rolston *et al*. make a distinction between POP in patients with CAP and POP in patients with

advanced lung cancer. The prevalence of POP in the setting of advanced lung cancer may be as high as 40-55% with a more symptomatic clinical presentation [5].

Pathogen isolation in patients affected by POP is limited. The above-mentioned prospective study was able to identify in 10% and 17% of POP cases a responsible bacterial or viral pathogen, respectively [4]. The author concluded that retained epithelial secretion, rather than an infective process, may be primarily responsible for the post-obstructive pneumonia in a large proportion of patients with airway obstruction [4]. Another prospective study performed ultrasound-guided transthoracic needle aspiration of collections distal to the obstruction [7]. Through this invasive diagnostic approach, a bacterial pathogen was isolated in 35% of POP cases. A poly-microbial infection was most often identified with in particular gram-negative and anaerobic bacteria [7]. Due to the limited detection rates of an infectious pathogen, most of the previous studies suggest broad antibiotic treatment [3, 5, 8].

Finally, considering the limited literature on POP in advanced lung malignancy, which is based on case reports, expert opinion reviews and editorials, clinical studies are needed to shed more light on this topic.

Aim of the study

The current monocentric retrospective observational study has been designed to describe and investigate factors associated with the development of POP in a cohort of patients affected by stage III and IV lung cancer. Furthermore, discriminants for 30-day mortality in patients diagnosed with POP were analyzed.

Materials and methods

Patient population

Medical records of patients treated in our tertiary care hospital for anatomopathological confirmed lung cancer, between January 2016 up to January 2021, were included in the current study. The medical records of all the included patients were reviewed, and the patients with suspicion of POP were identified. Only hospitalized patients were included, due to insufficient available data for outpatient management. A multidisciplinary panel, composed of a pulmonologist, an infectious disease specialist and a chest radiologist, confirmed or rejected this diagnosis. The diagnostic criteria are expressed below, in the paragraph variables definition. After this step, patients retrospectively diagnosed with POP were selected for further analysis.

Variables definition

As a clear definition of POP is not available in the literature, the following diagnostic criteria were selected to ease the patient selection: acute respiratory symptoms (cough or pleural pain or fever, tympanic temperature > 38°C) together with airway compression (presence of an endobronchial tumour or an extrinsic compression to the main bronchus or lobar bronchus visualized by bronchoscopy or chest computed tomography (CCT)) and new-onset or modification of a pulmonary opacification on CCT. Patients affected by post-obstructive atelectasis were excluded, whenever signs of infection were clinically absent (hypothermia, tympanic temperature < 36°C or fever, tympanic temperature > 38°C and leucocytosis > 12000 white blood cell/mm^3 or leukopenia < 4000 white blood cell/mm^3). All the selected patients were reviewed by the above-mentioned multidisciplinary team and a final decision for each patient was made. Bacteria responsible for POP were classified as sensitive or multi-

drug resistant (MDR) based on the European Center of Disease and Control definition (ECDC) [9]. 30-day mortality was defined as, all-cause, crude death percentage up to 30 days from the POP diagnosis.

Patient data collection

Epidemiological, clinical, biological, and microbiological data were collected from the medical records of the included patients. Data at POP diagnosis was gathered for patients diagnosed with this type of pneumonia. Furthermore, comorbidities were classified using the Charlson comorbidity index (CCI), a validated tool to quantify the burden of comorbidities [10]. Two validated prognostic scores in CAP were computed for each patient diagnosed with POP at diagnosis to assess the disease severity and predict mortality [11, 12].

Statistical analysis

A positive outcome was defined as the development of POP in the first statistical analyses. Secondly, 30-day mortality from diagnosis of POP was chosen as the endpoint of the additional analysis.

Data are expressed as median and interquartile range for continuous variables, numbers, and proportions for categorical variables, as all the analyzed data was considered as non-normal distributed. Independent predictors of the development of POP were initially analysed through a bivariable analysis. The variable hilar cancer and SCC were retained as clinically and statistically significant. Furthermore, age and CCI were added to adjust for potential confounding factors. The four variables were fitted in a multivariable logistic regression analysis.

Additional analyses were performed only in the group of patients affected by POP to assess the discriminant for 30-day mortality. Conform to our first analysis, bivariable logistic regression was computed. The variable do-not-resuscitate (DNR) orders was statistically significant, but not clinically. Furthermore, the variables active smoking, CURB-65, and SMART-COP were clinically and statistically significant. Subsequently, a multivariate regression model was performed. The variable SMART-COP lost its significance and was excluded from the final model.

All the analyses were performed with IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp, released in 2011.

Results

Baseline characteristics of the study population

Baseline characteristics of the cohort are expressed in table 1.

Four hundred and eight patients were treated at the University Hospital UZ Brussel from January 2016 up to January 2021. The median age was 69 (IQR: 62-77) years and 62% were male (n=255). Most of the patients (72%, n=296) were affected by stage IV lung neoplasm and in particular adenocarcinoma (59%, n=218). The median CCI was 9 (7-10) and 36% were actively smoking (n=141). After initial selection, 55 patients were selected as possibly affected by POP. After retrospective multidisciplinary revision, the diagnosis of POP was rejected in nine patients. The main reason for rejection was the absence of clinical and radiological features of infection. These patients were classified as having post-obstructive

atelectasis without signs of infection. Furthermore, antibiotic therapy was not prescribed to these patients and their evolution was favorable. Therefore, after multidisciplinary review, 46 of the 55 patients initially selected as possibly affected by POP were retrospectively confirmed. The study flowchart is depicted in figure 1.

The median age of the patients affected by POP was 68 (IQR: 62-76) years where the median age in the group of patients not affected by POP was 69 (62-78) years. The same burden of comorbidities was found in both groups (median CCI 9, IQR: 7-10). Patients affected by POP had an anatomopathological diagnosis of adenocarcinoma in 45% of cases (n=20) and of squamous cell carcinoma (SCC) in 36% of cases (n=16). Furthermore, in 24% of patients (n=10) the tumor was located in the hilar zone of the lung. Patients not diagnosed with POP had an anatomopathological diagnosis of of adenocarcinoma in 60% of cases (n=198) and of SCC in 19% of cases (n=63) with a tumor located in the hilar zone in 9% of patients (n=29). Half of the patients (52% n=24) received a simultaneous diagnosis of lung cancer and POP. Nine patients developed POP within three months of lung cancer diagnosis and three patients developed POP after one year.

All the patients diagnosed with POP underwent a CCT. Fifteen patients were diagnosed with the combination of CCT and positron emission tomography (PET). These imaging tools found a progression towards lung abscess in six cases of POP (13%).

Patients in the POP group received chemotherapy in 60% of cases (n=27), with no patients receiving targeted therapy. Patients belonging to the other group received chemotherapy in 59% of cases (n=214) and 8% were treated with targeted therapy (n=30).

Microbiology and antibiotic treatment of the patients affected by POP

In the present study, 33 patients (72%) were microbiologically investigated with sputum, and/or deep respiratory samples. Sputum specimens were obtained in 25 patients (45 samples), 23 patients had a bronchial aspirate, and four patients had a broncho-alveolar lavage (BAL). All broncho-alveolar lavage specimens were cultured for anaerobic bacteria. A bacterial pathogen was isolated in fourteen of the patients affected by POP (30%) (Supplementary Materials Table 1). The analyzed specimens included: upper respiratory tract specimens for nine patients, BAL for four patients, and blood cultures for one patient. Nineteen bacteria were identified with six of the fourteen positive samples growing more than one bacterium. The most commonly identified bacterium was *Staphylococcus aureus* (21% n=4), followed by *Enterobacter cloacae* (16% n=3) and *Klebsiella species* (16% n=3, in particular twice *Klebsiella pneumoniae,* and once *Klebsiella oxytoca*). In one patient affected by POP (2%), in one of the two aerobic blood culture bottles obtained grew *Streptococcus pneumoniae*. Five of the nineteen identified bacteria (26%) were considered multi-drug resistant (MDR) based on the ECDC criteria. The most frequent MDR bacteria was *Enterobacter cloacae*, with all those isolated being MDR with one isolation fulfilling the criteria of extended-spectrum beta-lactamases. The other MDR pathogens were a methicillin-resistant *Staphylococcus aureus* and a *Citrobacter freundii*. One patient had negative BAL cultures for bacteria, but viral cultures performed on the same specimen showed the presence of cytomegalovirus. Supplementary Materials Table 2 illustrates specimens obtained for viral tests.

The preferred empirical first-line treatment was amoxicillin with clavulanic acid (70%, n=32), followed by moxifloxacin (15%, n=7) and piperacillin-tazobactam (13%, n=6) (Supplementary Materials Figure 1). Twenty-five patients were, in addition, treated with a

second antibiotic after the termination of the first course (Supplementary Materials Figure 2). The most used antimicrobial in second line was piperacillin-tazobactam (76%, n=19). Four patients were prescribed a chronic suppressive antibiotic. Two patients received amoxicillin with clavulanic acid while the other two received a fluoroquinolone-based regimen. The median duration of antibiotic treatment was 12 days. The patient affected by CMV pneumonia was treated with ganciclovir for 45 days.

30-day mortality analysis within the part of cohort affected by POP

Baseline characteristics of patients affected by POP for the outcome mortality are expressed in table 2.

There was a 30-day mortality of 30% (n=14) within the group of patients diagnosed with POP. The baseline characteristics for the outcome 30-day mortality are reported in table 2. Median age and median CCI were similar for both groups (deceased and alive) with a median age of 68 years and median CCI of 9. Half of the survivors were actively smoking (53%, n=17), while only one patient within the deceased group (7%) was actively smoking at POP diagnosis. 86% of the deceased patients (n=12) had a stage IV malignancy compared to 62% of the survivors (n=20). Furthermore, the median CURB-65 score at diagnosis of POP was 2 (IQR: 2-3) and 1 (IQR: 1-2), in the deceased group and the survivor group, respectively. The survivor group had a median SMART-COP score of 2 (IQR: 1-3), compared to a score of 4 (IQR: 3-5) in the deceased group. The diagnostic accuracy of the CURB-65 and SMART-COP scores for prediction of 30-day mortality is pictured in figures 2 and 3, respectively. The sensitivity of the CURB-65 score for the prediction of mortality was 93% with a negative predictive value of 96% whenever the CURB-65 score was greater than or equal to two at

diagnosis of POP. A SMART-COP score greater than or equal to three resulted in a specificity of 86% for the prediction of mortality and a negative predictive value 91%. Finally, the patients who died had do-not-resuscitate (DNR) orders in 93% of cases (n=13) compared to 56% of the survivors(n=18).

Factors associated with POP onset

Multivariable logistic regression was used to predict "POP development" with the independent variables: age, CCI, SCC, and hilar lung cancer (table 2). The probability to belong to the group of patients diagnosed with POP increases whenever an SCC or hilar lung cancer was observed in the medical history as shown by the above-mentioned logistic regression. However, increasing age and CCI were not associated with the development of POP.

Discriminants for 30-day mortality

Multivariable logistic regression was also used to predict "30-day mortality" with the independent variables active smoking and CURB-65 (table 3). Patients who actively smoked or with higher CURB-65 score at diagnosis of POP had a higher probability to belong to the group of patients who died within 30 days of the POP diagnosis.

Discussion

During a period of five years, 408 patients affected by advanced lung cancer were screened for POP and only 46 patients, 11% of the cohort, were retrospectively diagnosed with this type of pneumonia. Kenneth *et al.* reported, in their experience-based review, a higher

prevalence of this complication in patients affected by advanced lung cancer, as high as 40-50% [5]. In the current study a multidisciplinary team was involved to make this diagnosis retrospectively. We believe that extensive diagnostic procedures such as chest CT scan and bronchoscopy are essential to confirm this diagnosis. Therefore, patients with limited workup might not have been correctly diagnosed. Furthermore, only hospitalized patients were considered in this study. The prevalence of POP could therefore be underestimated. However, two previous retrospective studies on patients with lung cancer, found a prevalence of POP of less than 10% [6, 13]. This is in line with the current study results, suggesting that the prevalence of POP in advanced lung cancer patients might be lower than previously reported.

Previous studies have found that small cell lung carcinoma and squamous cell carcinoma (SCC) have mostly a hilar location. SCC is centrally located in 60% of the affected patients and is the most frequent lung neoplasm to give bronchial obstruction [14, 15]. Furthermore, a higher frequency of SCC was found in patients affected by POP in a previous retrospective study [13]. In the current cohort, squamous cell carcinoma (SCC) and hilar tumor location were factors associated with the development of POP. The development of POP was independent of the age and comorbidities.

The development of pneumonia may reveal the presence of an underlying lung cancer. In previous epidemiological studies, 2.5% up to 9.3% of patients hospitalized with pneumonia were affected by lung malignancy and this association was enhanced by cigarette smoking [16, 17]. In this study, 52% (n=24) of patients received the diagnosis of both POP and lung cancer during the same admission. Of these patients, 54% (n=13) were actively smoking. Only six percent (n=3) of patients in the POP group were affected by pneumonia more than a year after the diagnosis of lung malignancy.

Only in 30% (n=14) of the patients affected by POP, a pathogen could be isolated in the current study. Even though six cultures were polymicrobial, no anaerobe was grown as previously shown [7]. Respiratory samples such as sputum and BAL fluid were used to isolate pathogens instead of a bronchial biopsy, therefore anaerobes could have been underestimated in this cohort. The most isolated pathogens were typical nosocomial bacteria with 27% of the pathogens being MDR. Respectively, *Staphylococcus*, *Enterobacter,* and *Klebsiella* were the most frequent isolated genus. Only one patient was diagnosed with a viral pathogen. This is in contrast to a previous study where viruses were routinely searched with molecular methods and where more viral pathogens than bacteria were isolated [4]. According to microbiological stewardship principles, representative airway samples should be obtained for microbiological analysis before the start of empiric treatment. In patients with a suspicion of POP, sputum or endotracheal aspiration are non-invasive sampling technique which may yield the responsible pathogenic microbe. However, only qualitative samples (< 25 epithelial cells/low power field and > 10-25 leucocytes/low power field) with a sufficient quantitative bacterial growth ($>10^5$ colony forming unit (CFU)/mL) should be considered. BAL fluid examination may reduce the risk of contamination by the high airway flora and should be preferred to sputum. To date, no studies favour bronchial biopsy to other respiratory samples. The biopsy of respiratory tissue could be related to several complications and its diagnostic rate may be only slightly superior to less invasive sampling techniques [4, 7]. Moreover, viral pathogens should not be overlooked, for instance nucleic acid-based tests for respiratory viruses might be performed on BAL fluid. Finally, empirical treatment should be selected taking into consideration the local environment, targeting also anaerobic bacteria whenever lung collections are present [7]. Prompt de-escalation based on representative

cultures (for example, BAL fluid with <1% epithelial cells growing significant cultures (> 10^3 CFU/mL) should be applied.

In the current study, patients who were actively smoking were associated with lower 30-day mortality. This concept seems controversial. However, patients with longstanding and more advanced lung cancer might receive profound smoking counselling and the rate of active smokers in such a population may be lower. In this cohort, a higher rate of stage IV cancer patients was found within the group of deceased patients, but this difference was not statistically significant. Furthermore, previous studies on hospital-acquired pneumonia and Legionnaire's disease report similar results [18, 19].

Simple clinical scores used in the context of CAP may be suitable to estimate the prognosis of patients affected by POP. In the current study, CURB-65 at diagnosis of pneumonia was a discriminant of 30-day mortality. A score greater than or equal to two was associated with a high sensitivity and negative predictive value for 30-day mortality. Consistent with the findings of this study, higher negative predictive values for prediction of intensive care hospitalisation and early mortality were found in a meta-analysis [20].

The strength of the current study relies on the multidisciplinary approach to diagnosing the disease with several experts reviewing each patient suspected of POP to confirm or reject this diagnosis [21 - 23]. This method minimizes the possibility of false inclusion and increases the reproducibility of the study. Finally, the current study enforces evidence-based knowledge on the discriminants of POP onset and the possible clinical prognostic scores. However, some study limitations should be mentioned. Due to the retrospective design, some confounding factors could not have been excluded. Causal reasons for the higher mortality

in patients with greater CURB-65 at diagnosis could only be hypothesized based on the study's results. Furthermore, selection bias may have influenced study results as only patients with stage III and IV lung cancer were selected. Patients with metastases or metastatic lymphadenopathy from other types of neoplasms may also be affected by POP and therefore the actual number of affected patients might be underestimated.

Conclusion

In summary, the prevalence of POP in patients with lung cancer stages III and IV might be less than previously reported. In the current study, 11% of patients were affected by this type of pneumonia. Centrally located tumours and particularly SCC were associated with the development of POP, independent of age and comorbidities. POP should be considered in patients with hilar malignancy presenting with pneumonia and an extensive diagnostic work-up with CCT and bronchoscopy should be considered. Furthermore, the CURB-65 score at diagnosis of pneumonia was a discriminant for 30-day mortality. A value of two or greater had an excellent negative predictive value in this cohort, and its clinical application might be reasonable as it is easy to perform. Finally, a multidisciplinary approach to the disease, involving a respiratory physician, oncologist, infectious disease specialist, and radiologist specialized in chest imaging, should be considered as there is a high 30-day mortality and to date there are no evidence-based guidelines available.

Challenges and Future perspectives

The absence of a standardized definition of POP in the literature and the complexity involved in differentiating between respiratory tract colonisation and infection may be a limitation for future studies. Further prospective trials are warranted to explore the best diagnostic methods,

therapeutic options and antibiotic treatment duration in lung cancer patients diagnosed with POP.

DECLARATIONS

Ethics approval and consent to participate

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was conducted in accordance with the study protocol, the Declaration of Helsinki and applicable regulatory requirements. The local Institutional Review Board and Ethics Committee of the University Hospital Brussels approved the protocol (EC approval number: B1432021000531). In view of the retrospective nature of the study, which did not demand a deviation from standard clinical care, and the fact that all data was anonymized, informed consent from the patient or the next of kin was not essential.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All other authors declare that they have no competing interests in relation to the content published in this manuscript.

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Authors' contributions

MM: concept, study design, data collection, data analysis and interpretation, writing and revision, SW and SD: data collection and writing and revision, KV: study concept, writing and revision, JvL: writing and revision, BI: data collection, writing and revision, EV: study concept, writing and revision. All authors have given final approval of the version to be submitted

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FIGURES

Figures legends:

Fig.1 Study flowchart; 408 patients were included. Initial analyses were performed on both patients affected and unaffected by POP. Further analysis was only computed on patients diagnosed with POP. POP: post-obstructive pneumonia

Fig.2 Diagnostic accuracy of CURB-65 for prediction of 30-day mortality; On the left, ROC curve of CURB-65 for prediction of 30-day mortality; on the right, diagnostic accuracy measures of CURB-65 score greater than or equal to 2 for prediction of 30-day mortality; AUC: area under the curve.

Fig.3 Diagnostic accuracy of SMARTCOP for prediction of 30-day mortality; On the left, ROC curve of SMART-COP for prediction of 30-day mortality; on the right, diagnostic accuracy measures of SMART-COP score greater than or equal to 3 for prediction of 30-day mortality; AUC: area under the curve.

Figure 1

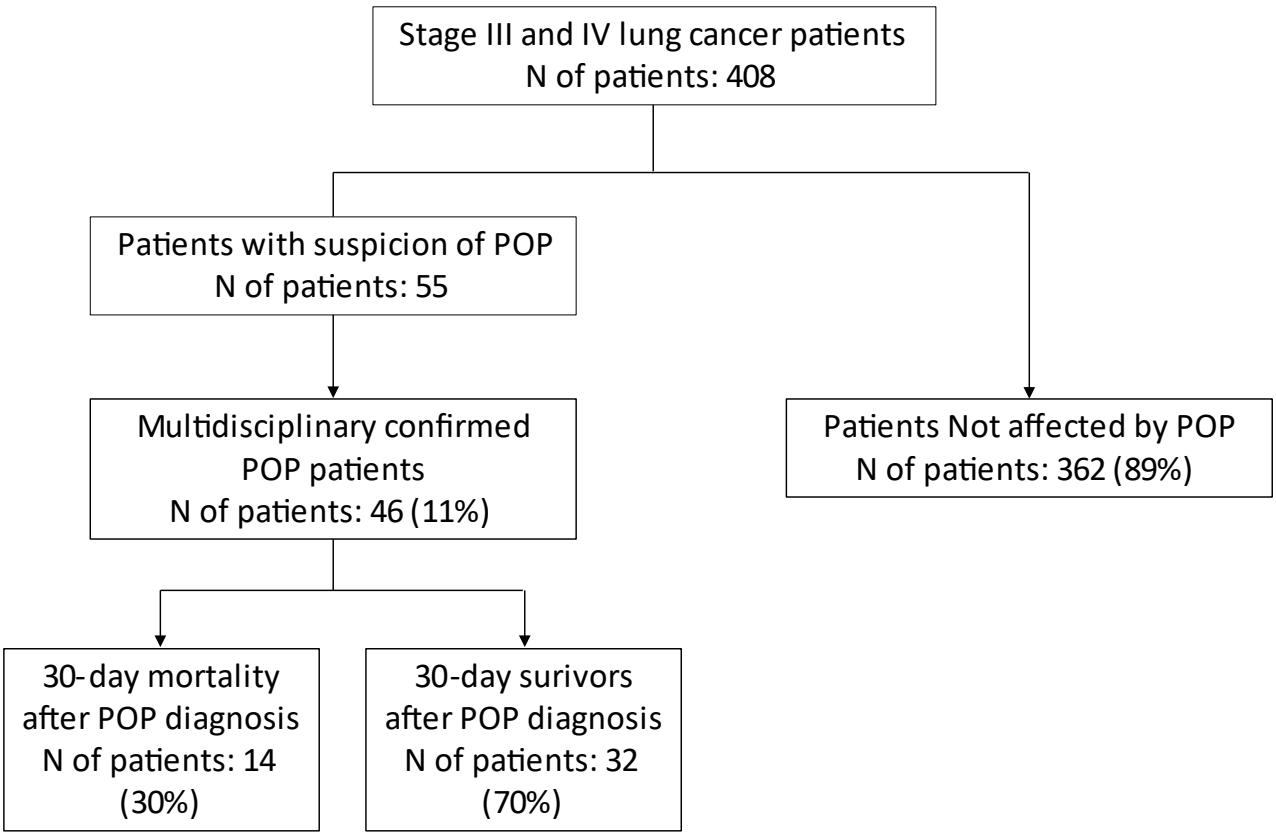
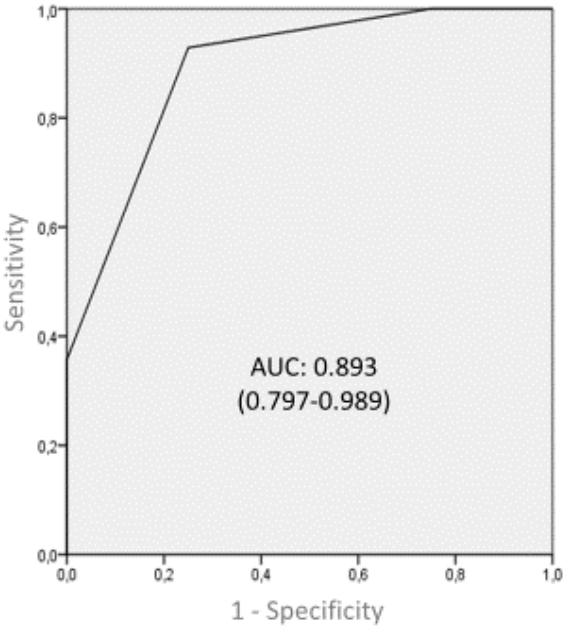
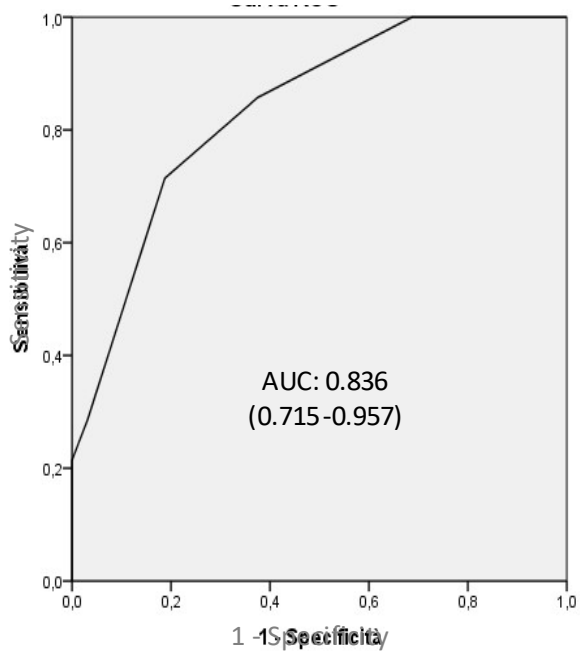

Stage III and IV lung cancer patients
N of patients: 408
Patients with suspicion of POP
N of patients: 55
Multidisciplinary confirmed
POP patients
N of patients: 46 (11%)
Patients Not affected by POP
N of patients: 362 (89%)
30-day mortality
after POP diagnosis
N of patients: 14
(30%)
30-day surivors
after POP diagnosis
N of patients: 32
(70%)

Figure 2



Diagnostic accuracy of CURB-65 score ≥ 2 for prediction of 30-day mortality	
Sensitivity	93%
Specificity	75%
Positive predictive value	62%
Negative predictive value	96%

Figure 3



Diagnostic accuracy of SMART -COP score ≥ 3 for prediction of 30-day mortality	
Sensitivity	86%
Specificity	62%
Positive predictive value	50%
Negative predictive value	91%

TABLES

Table legends:

Table 1- Baseline characteristics of patients affected by lung cancer. Parameters were expressed for the entire cohort: patients affected and unaffected by POP. POP: post-obstructive pneumonia; CCI: Charlson comorbidity index; ECOG: Eastern Cooperative Oncology Group; Data are expressed as median and interquartile range for continuous variable and numbers and proportions for categorical variables.

Table 2- Baseline characteristics of patients affected by POP; Parameters ere expressed for all patients affected by POP: patients affected by POP and deceased within 30 days from diagnosis and patient diagnosed with POP and alive at 30 days from diagnosis. POP: post-obstructive pneumonia; CCI: Charlson comorbidity index; CRP: C-reactive protein; ICU: intensive care units; DNR: do-not resuscitate; Data are expressed as median and interquartile range for continuous variable and numbers and proportions for categorical variables.

Table 3- Multivariable logistic regression analysis for the prediction of POP; CCI: Charlson comorbidity index; '-' is used for 'no observation' or 'not applicable'.

Table 4- Multivariable logistic regression analysis for discriminants of 30-day mortality; '-' is used for 'no observation' or 'not applicable'.

Table 1

Parameters	**Overall study population (n=408)**	**Population features considering POP as outcomes**	
		POP affected patients (n=46)	***Non-POP affected patients (n=362)***
Age, year	69 (62-77)	68 (62-76)	69 (62-78)
CCI, index	9 (7-10)	9 (7-10)	9 (7-10)
Karnofsky performance scale, index	80 (60-90)	80 (60-90)	80 (60-90)

ECOG performance scale, index	1 (1-2)	1 (1-2)	1 (1-2)
Sex, male (%)	255 (62%)	32 (70%)	223 (62%)
Active smoking, yes (%)	141 (36%)	18 (39.1%)	123 (35.3%)
Stage malignancy, IV (%)	296 (72%)	32 (70%)	264 (73%)
Small cell lung carcinoma, yes (%)	66 (18%)	8 (18%)	58 (18%)
Adenocarcinoma, yes (%)	218 (59%)	20 (45%)	198 (60%)
Squamous cell carcinoma, yes (%)	79 (21%)	16 (36%)	63 (19%)
Treatment: target therapy, yes (%)	30 (7%)	0 (0%)	30 (8%)
Treatment: chemotherapy, yes (%)	241 (59%)	27 (60%)	214 (59%)
Treatment: immunotherapy, yes (%)	168 (41%)	16 (36%)	152 (42%)
Hilar cancer location, yes (%)	39 (11%)	10 (24%)	29 (9%)

Table 2

Parameters	**Patients affected by POP (n=46)**	**Population features considering 30 day-mortality as outcomes**	
		Deceased patients (n=14)	***Alive patients (n=32)***
Age, year	68 (62-76)	68 (64-75)	68 (59-76)
CCI, index	9 (7-10)	9(8-10)	9 (7-10)
CRP, mg/L	121 (59-202)	123 (49-196)	120 (61-210)
Serum white blood cells, $10^3/\mu L$	12.6 (9.4-17.4)	11.9 (6.8-16.3)	16.7 (10.6-20.8)
CURB-65, score	1 (1-2)	2 (2-3)	1 (0-2)
SMART-COP, score	3 (2-4)	4 (3-5)	2 (1-3)
P/F ratio	286 (223-416)	263 (228-348)	296 (213-449)
Days of antibiotic, day	12 (7-19)	12 (5-26)	11 (7-17)
Antibiotic regimen, number	2 (1-3)	2 (1-3)	2 (1-3)
Length of hospitalization, days	11 (8-17)	9 (8-17)	12 (8-17)

Sex, male (%)	33 (72%)	9 (64%)	24 (75%)
Active smoking, yes (%)	18 (39%)	1 (7%)	17 (53%)
Stage malignancy, IV yes (%)	32 (70%)	12 (86%)	20 (62%)
ICU admission	9 (20%)	4 (29%)	5 (16%)
Readmission	13 (28%)	4 (29%)	9 (28%)
DNR orders, yes (%)	31 (67%)	13 (93%)	18 (56%)

Table 3

Term	Odds ratio	95% confidence interval	p-value
(Intercept)	0.620	-	0.011
Age	1.002	0.968 - 1.037	0.924
CCI	1.035	0.888 - 1.206	0.657
Squamous cell carcinoma	2.464	1.203 - 5.048	0.014
Hilar cancer location	2.723	1.160 - 6.390	0.021

Table 4

Term	Odds ratio	95% confidence interval	p-value
(Intercept)	0.001	-	0.002
CURB-65	73.196	5.832 - 918.735	0.001
Active smoking	0.009	0.00 - 0.400	0.015