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# Surgically treated pneumonic-type lung adenocarcinoma with long survival characteristics

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## ABSTRACT

**Aims**: Pneumonic-type lung adenocarcinoma is defined as a pneumonia-like area of infiltration or consolidation involving a region of the lung. These carcinomas, which are suitable for curative treatment options and have a long survival when detected at an early stage, may resemble infectious or inflammatory lung diseases due to their radiological appearance and clinical findings, may lead to potential delays or difficulties in diagnosis, and this may cause progression in patients who are suitable for curative treatment options.

**Methods**: A total of 41 patients which were surgically treated between 2011-2020 and diagnosed pathologically with pneumonic-type adenocarcinoma. The patents' TTF-1, type of operation, pathological stages, overall/progression-free survival, as well as overall/progression-free survival according to the type of operation and radiological appearance, were also evaluated.

**Results**: The study included 41 patients. Although overall survival times were long, there was no statistically significant defference between wedge resection and lobectomy group in overall survival by operation type. Although progression-free survival times were long, there was no statistically significant defference between wedge resection and lobectomy group in progression-free survival by operation type. There was no statistically significant difference between solid and consolidated groups in terms of overall survival and progression-free survival according to radiological appearances. There was no statistically significant difference between TTF-1 positive and negative groups in overall survival.

**Conclusion**: Pneumonic-type lung adenocarcinomas respond to curative treatments when diagnosed at an early stage. The optimal treatment method for operable patients is surgery, which is associated with prolonged survival.

**Keywords**: Lung cancer, pneumonic-type adenocarcinoma, surgical treatment

## INTRODUCTION

Non-small cell lung cancers account for 85% of all lung cancers, the most common subtype of which, especially in non-smokers, is adenocarcinoma.[1,2] The 2015 WHO classification categorizes lung adenocarcinomas into adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA) and invasive adenocarcinoma.[3]

Pneumonic-type lung adenocarcinoma is defined as a pneumonia-like area of infiltration or consolidation involving a region of the lung (**Image 1**).[4] Pneumonic-type lung adenocarcinomas can be confused with infectious pneumonias because of their appearance.[5] Histologically, it manifests with a lepidic predominant growth pattern with mucin or tumor cells in the alveolar spaces.[1] It is referred to as pneumonic-type lung cancer due to its radiological resemblance to pneumonia. Demographically, this type of cancer occurs in those aged 41-66 years, but with variations associated with gender, age or geographical region.[6,7] The 2015 WHO classification states that invasive mucinous adenocarcinomas account for most of the pneumonic-type adenocarcinomas.[3] Histologically, it is defined predominantly as mucinous, although there are also mucinosis, non-mucinosis and mixed types.[1] There is no radiological difference between the mucinosis and non-mucinosis types.[3] Pneumonic-type adenocarcinomas typically do not show lymph node metastasis or distantmetastasis, despite diffuse pulmonary involvement.[1,8] With its radiological appearance and clinical findings, pneumonic-type adenocarcinomas can mimic infectious or inflammatory pulmonary diseases that can bring about a delay or difficulty in diagnosis, resulting in disease progression

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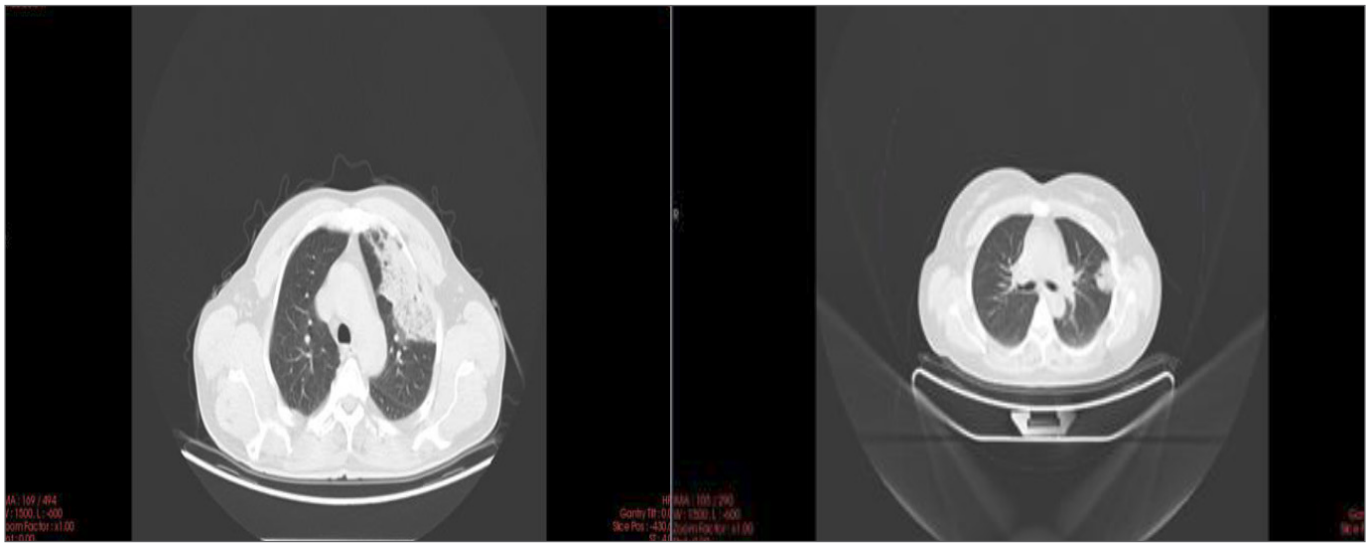

**Image 1.**Pneumonia-like area of infiltration or consolidation involving a region of the lung. 61-year-old male patient was diagnosed with invasive adenocarcinoma by transthoracic biopsy in the consolidated lesion in the upper lobe of the left lung, and left upper lobectomy was performed. Image-2: 52-year-old male patient underwent lobectomy for the consolidated lesion on thoracic computed tomography

that may result in respiratory failure prior to diagnosis. Pneumonic-type adenocarcinomas, which are suitable for curative treatment options and have a long survival when detected at an early stage, may resemble infectious or inflammatory lung diseases due to their radiological appearance and clinical findings, may lead to potential delays or difficulties in diagnosis, and this may cause progression in patients who are suitable for curative treatment options.

## METHODS

The study was carried out with the permission of Ankara Atatürk Sanatorium Training and Research Hospital Clinical Researches Ethics Committee (Date: 12.07.2023, Decision No: 2012-KAEK-15/2739). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

'Involved in the study were 41 patients who underwent surgery with a diagnosis of pneumonic-type lung cancer in our hospital between 2011 and 2020, whose reports were reviewed retrospectively. The demographic data of the patients, including age, gender, comorbidities, smoking, dates of diagnosis and progression, and pathological data were examined after being retrieved from the system, and the TTF-1, type of operation and pathological stages were recorded. The patients were restaged according to the 8th TNM classification by scanning the hospital system.

The pathology reports of the patients were categorized according to the 2015 WHO classification and those whose pathology report was diagnosed as invasive adenocarcinoma were included in the study. The pathological staging of the patients was repeated by examining the pathology reports. A total of 59 patients who were diagnosed with pneumonic type adenocarcinoma and operated on in the system screening were reached, and only 41 patients with T1a (Stage 1a) tumors were included in the study.

Patients with regular follow-up were included in the study, and total and progression-free survival status of the patients was obtained by scanning the last visit and death notification system. The type of operation was decided by the staging of the patients with PET_CT before the operation and the staging during the surgery. The primary endpoint of the study was to determine the survival rates according to the type of surgical operation. The patients operated with thoracotomy were divided into two groups according to type of operation, being the lobectomy and wedge resection groups, and were evaluated for progression-free survival and overall survival. The patients were divided into three groups: solid, consolidated and solid-consolidated, based on the radiological appearance, and were evaluated for progression-free survival and overall survival. secondary endpoint of the study was progression-free/overall survival according to radiological appearance.

### Statistical Analysis

Descriptive statistics were used to present the demographic data of the study patients. The survival analysis was carried out using the Kaplan-Meier (Log-rank) method. IBM SPSS Statistics (Version 27.0. Armonk, NY: IBM Corp.) was used for statistical analysis. A p value of $<0.05$ was considered statistically significant.

## RESULTS

The study included 41 patients, of which 21 (51.2%) were female, and 20 (48.8%) were male. The mean age of the patients was 60.8±12.6 years. Of the total, 20 of the patients had no comorbidity, while the most common comorbidity was chronic obstructive pulmonary disease (COPD) (n=7) in the remainder (**Table 1**).

**Table 1.** Characteristics of study population

| Characteristics | Number (%) | Mean±SD |
|---|---|---|
| Gender | | |
| Female | 21 (51.2 %) | |
| Male | 20 (48.8 %) | |
| Age±SD | | 60.8±12.6 |
| Comorbidities | | |
| COPD | 7 (21.9%) | |
| HT | 3 (9.4%) | |
| Asthma | 1 (3.1%) | |
| DM | 1 (3.1%) | |
| Smoking | | |
| Yes | 16 (50%) | |
| No | 16 (50%) | |
| Diagnostic method | | |
| Surgical | 22 ( 53.6%) | |
| TTBX | 17 (41.5%) | |
| FOB | 1 (2.4%) | |
| Transbronchial | 1(2.4%) | |
| TTF-1 | | |
| Positive | 9 (22%) | |
| Negative | 8 (19.5%) | |
| Not evaluated | 24 (58.5%) | |
| Radiology | | |
| Consolidation | 16 (39.0%) | |
| Solid | 15 (36.6%) | |
| Solid-consolidation | 5 (12.2%) | |
| Surgical type | | |
| Lobectomy | 30 (73.2%) | |
| Wedge | 8 (19.5%) | |
| Pneumonectomy | 3 (7.3%) | |
| Progression Status | | |
| Yes | 7 (17.1%) | |
| No | 34 (82.9%) | |
| Mortality | | |
| Alive | 38 (92.7%) | |
| Exitus | 3 (7.3%) | |

COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, HT: Hypertension, TTBX: Transthoracic biopsy, FOB: Fiberoptic bronchoscopy

Overall survival was 474±19.8 weeks and progression-free survival was 212±60.6 weeks. The patients underwent three types of surgical resection: lobectomy (n=30), pneumonectomy (n=3) and wedge resection (n=8). Overall survival according to the type of operation was 237.6±135.3 weeks in the lobectomy group and 230.5±110.7 weeks in the wedge resection group, with no statistically significant difference between the groups (p=0.75). Progression-free survival according to the type of operation was 231.5±66.8 weeks in the lobectomy group and 78±0.0 weeks in the wedge resection group, with no statistically significant difference between the groups (p=0.53) (**Figure 1**). Only three patients died during follow-up; there were no mortalities in the pneumonectomy group.

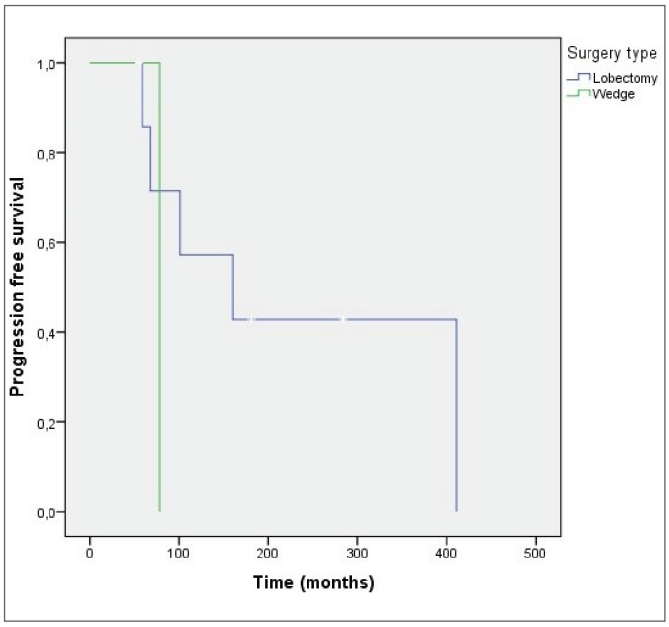


**Figure 1.** Progression-free survival according to the type of operation

Of the total, 17 patients were diagnosed by transthoracic biopsy and 21 by the surgical method, while other diagnostic methods included fiberoptic bronchoscopy, transbronchial biopsy and wedge resection.

Radiologically, the patients had three types of appearance: solid (n=15), consolidation (n=16) and mixed (solid + consolidation) (n=5). The patients underwent three types of surgical resection: lobectomy (n=30), pneumonectomy (n=3) and wedge resection (n=8).

According to the radiological appearance, overall survival was 392.8±26.2 weeks in the solid group, 482±26.7 weeks in the consolidated group, and 402.7±79 weeks in the solid+consolidated group, with no statistically significant difference between the groups (p=0.58). No progression was identified during the follow-up of the patients in the solid group according to their radiological appearance. According to the radiological appearance, progression-free survival was 305±36 weeks in the consolidated group, 394±24 weeks in the solid group and 313±81 weeks in the solid+consolidated group, with no statistically significant difference between the groups (p=0.17) (**Figure 2**).

Pathological examinations revealed eight TTF-1 negative patients and nine TTF-1 positive patients. No TTF-1 evaluation could be made for the other patients. Overall survival was 141.4 weeks in the TTF-1 positive group and 247 weeks in theTTF-1 negative group, with no statistically significant difference between the groups (p=0.628).

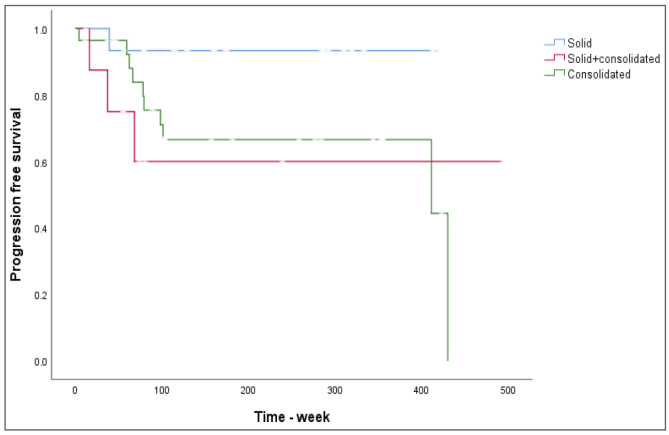


**Figure 2.** Progression-free survival according to the radiological appearance

## DISCUSSION

Pneumonic-type lung adenocarcinoma can be easily confused with pneumonia, tuberculosis or other interstitial lung diseases due to its usually non-specific symptoms, and diagnosis is sometimes delayed, especially in developing countries, resulting in diagnosis at an advanced stage.[9-11] Pneumonic type lung adenocarcinoma has a poor prognosis when diagnosed in locally advanced and advanced stages.[12] In this patient group, even increased T stage and seperate nodules adversely affect prognosis and survival.[13] Pneumonic-type lung cancer, when diagnosed at an early stage, is eligible for curative treatment options, with the most effective treatment method being surgical resection. Patients eligible for surgical resection have a high survival rate, with lobectomy being the best option when possible.[14] In the present study, concurring with literature, patients undergoing surgery had prolonged overall and progression-free survival. Although progression-free survival was longer in the lobectomy arm than in the wedge resection group, the difference was not statistically significant. There was no mortality in the pneumonectomy group.

Previous studies have identified the most effective biopsy method for this patient group as surgical biopsy or transthoracic biopsy, and this method was identified as the most common also in the present study.[15]

Previous studies have established a correlation between radiological appearance and histological subtype, reporting a consolidative pattern incidence of 33-75% in mucinous tumors.[16] On the other hand, pneumonic type adenocarcinomas present a histological appearance in a mucinous pattern in approximately 45%, a non-mucinosis pattern in 40%, and a mixed pattern in 15% of cases.[1] In the present study, in line with literature, the histological appearance of all pneumonic-type adenocarcinoma patients undergoing surgery was in the mucinous pattern.

A previous study reported a consolidative appearance incidence in 83% of pneumonic-type adenocarcinomas.[14,17] Likewise, the consolidation and mixed (solid-consolidated) groups were more common radiologically in the present study, which is consistent with the literature.

In the same study, it was shown that overall survival was better in stage 1 and 2 invasive mucinous adenocarcinomas than invasive non-mucinous adenocarcinomas, but overall survival was similar in stages 3 and 4.[18] In a study in patients with a diagnosis of invasive mucinous adenocarcinoma, it was found that spiculation, increased density, emphysema were poor prognostic factors, and pneumonic-appearing tumors had a worse prognosis than solid-appearing tumors.[19] In the present study, postoperative overall according to radiological appearance was longer in the consolidative group than in the solid group, but progression-free survival according to radiological appearance was longer in the solid group than in the consolidative group among the pneumonic-type lung cancer patients. While the difference was not statistically significant, this may be associated with the small number of cases. TTF-1 positivity is a good prognostic factor in adenocarcinoma. Previous studies have shown TTF-1 to be negative in some pneumonic-type adenocarcinoma, and to be associated with a poor prognosis.[20] In the present study, survival was longer in the TTF-1-negative patients, although there was no significant difference in survival between the two groups, which may be associated with the small number of TTF-1 cases evaluated.

## CONCLUSION

Pneumonic-type lung adenocarcinoma responds to curative treatment when diagnosed at an early stage. Since its radiology can be confused with pneumonia, early diagnosis by biopsy is important in suspected cases to prevent any delay in the start of treatment. The optimal treatment approach in operable patients is the surgical method, being associated with prolonged survival.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Ankara Atatürk Sanatorium Training and Research Hospital Clinical Researches Ethics Committee (Date: 12.07.2023, Decision No: 2012-KAEK-15/2739).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

## REFERENCES

1. Detterbeck FC, Marom EM, Arenberg DA, et al. The IASLC Lung Cancer Staging Project: background data and proposals for the application of TNM staging rules to lung cancer presenting as multiple nodules with ground glass or lepidic features or a pneumonic type of involvement in the forthcoming eighth edition of the TNM classification. *J Thorac Oncol.* 2016;11(5):666-680.
2. Saitoa S,Espinoza-Mercadob F,Liu H, et al. Current status of research and treatment for non-small cell lung cancer in never smoker females. *Cancer Biol Ther.* 2017;18(6):359-368. doi: 10.1080/15384047.2017.1323580
3. Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG. Introduction to the 2015 World Health Organization classification of tumors of the lung, pleura, thymus, and heart. *J Thorac Oncol.* 2015;10(9):1240-1242.
4. Beck KS,Sung YE,Lee KY,Han DH. Invasive mucinous adenocarcinoma of the lung: serial CT findings, clinical features, and treatment and survival outcomes. *Thorac Cancer.* 2020;11(12):3463-3472. doi: 10.1111/1759-7714.13674
5. Zhang S,Yu X,Huang Y, et al. Pneumonic-type invasive mucinous adenocarcinoma and infectious pneumonia: clinical and CT imaging analysis from multiple centers. *BMC Pulm Med.* 2022;22(1):460. doi: 10.1186/s12890-022-02268-5
6. Wislez M, Massiani M-A, Milleron B, et al. Clinical characteristics of pneumonic-type adenocarcinoma of the lung. *Chest.* 2003;123:1868-1877.
7. Li Q, Fan X, Huo JW, Luo TY, Huang XT, Gong JW. Differential diagnosis of localized pneumonic-type lung adenocarcinoma and pulmonary inflammatory lesion. *Insights Imaging.* 2022;13(1):49. doi: 10.1186/s13244-022-01200-z
8. Barlesi F, Doddoli C, Gimenez C, et al. Bronchioloalveolar carcinoma: myths and realities in the surgical management. *Eur J Cardiothorac Surg.* 2003;24:159-164.
9. Ishibashi H, Niikawa H, Ishida I, et al. Primary lung cancer incidentally diagnosed in lung biopsy for diffuse pulmonary disease. *Kyobu Geka.* 2005;58(9):813-817.
10. Huo JW, Huang XT, Li X, Gong JW, Luo TY, Li Q. Pneumonic-type lung adenocarcinoma with different ranges exhibiting different clinical, imaging, and pathological characteristics. *Insights Imaging.* 2021;12:169. doi: 10.1186/s13244-021-01114-2
11. Yoshino R, Yoshida N, Ito A, Ujiie N, Nakatsubo M, Kitada M. Surgical resection of a large invasive mucinous adenocarcinoma:A case report. *Clin Case Rep.* 2023;11(7):e7707. doi: 10.1002/ccr3.7707
12. Wei J, Tang D, Nie Y, Chen J, Peng L. Clinical characteristics and prognosis of nonsurgically treated patients with pneumonic-type adenocarcinoma. *Medicine (Baltimore).* 2019;98(18):e15420.doi: 10.1097/MD.0000000000015420
13. Kim W, Lee SM, Lee JB, et al. Prognosis for pneumonic-type invasive mucinous adenocarcinoma in a single lobe on CT: is it reasonable to designate it as clinical T3? *Korean J Radiol.* 2022;23(3):370-380. doi: 10.3348/kjr.2021.0465
14. Wislez M, Massiani M-A, Milleron B, et al. Clinical characteristics of pneumonic-type adenocarcinoma of the lung. *Chest.* 2003;123:1868-1877.
15. Yongjian Liu , Ji Li , Shibo Wang , et al. Advanced pneumonic-type lung carcinoma: a retrospective study of clinical-radiological-pathological characteristics with survival analysis in a single Chinese hospital. *Zhongguo Fei Ai Za Zhi.* 2019;22(6):329-335.
16. Régnard JF, Santelmo N, Romdhani N, et al. Bronchioloalveolar lung carcinoma: results of surgical treatment and prognostic factors. *Chest.* 1998;114(1):45-50.
17. Okubo K, Mark EJ, Flieder D, et al. Bronchoalveolar carcinoma: clinical, radiological, pathological factors and survival. *J Thorac Cardiovasc Surg.* 1999;118(4):702-709.
18. Nie K, Nie W, Zhang YX, Yu H. Comparing clinicopathological features and prognosis of primary pulmonary invasive mucinous adenocarcinoma based on computed tomography findings. *Cancer Imaging.* 2019;19(1):47.
19. Wang T,Yang Y,Liu X, et al. Primary invasive mucinous adenocarcinoma of the lung: prognostic value of CT imaging features combined with clinical factors. *Korean J Radiol.* 2021;22(4):652-662. doi: 10.3348/kjr.2020.0454.
20. Zhang Y, Wang R, Li Y, et al. Negative thyroid transcription factor 1 expression defines an unfavorable subgroup of lung adenocarcinomas. *J Thorac Oncol.* 2015;10(10):1444-1150.