Original Research Article

POSSITIVITY RATE OF SPUTUM CYTOLOGY COMPARED TO BRONCHOSCOPY AND TRANSTHORACIC NEEDLE ASPIRATION IN LUNG CANCER PATIENTS AT WAHIDIN SUDIROHUSODO HOSPITAL, INDONESIA

ABSTRACT

Introduction: Sputum cytology is the only non-invasive method which can detect early lung malignancies. The principle of it is a finding of a cells shed from the lesion, either spontaneously or artificially. **Aim:** This study purposed to evaluate the positivity rate of sputum cytology compared to bronchoscopy or transthoracic needle aspiration (TTNA) in lung cancer patient. **Place and Duration of Study:** A prospective cross-sectional study used a medical record data using SIRS from 2022 until completed or reached the desired number of samples at Wahidin Sudirohusodo General Hospital, Makassar. **Methodology:** Patients diagnosed with lung cancers, done a sputum cytology, and bronchoscopy/ TTNA were included. The patients had consented to be included in the study and the study had passed the ethical clearance from Hasanuddin Medical University Ethical Research Committee. **Results:** A 111 patients with lung cancer, which 46 patients (41,4%) was adenocarcinoma and the other 65 patients (58,6%) was squamous cell carcinoma. Patients with a positive sputum cytology were 5 patients (4,5%), with tumor sizes ≥3cm were 107 patients (86%), and with a hemoptysis history was 59 patients (53,2%). The relationship between sputum cytology and histopathology, tumor size, and hemoptysis history were not significant (each p value >0.05). However, there were a relationship between sputum cytology and tumor location with a significant relationship between the two (p value = 0.002). **Conclusion:** Sputum cytology is not recommended for diagnosing lung cancer due to low positivity rate, but the prediction rate is high which most likely is central squamous cell carcinoma.

Keywords: Sputum cytology, bronchoscopy, transthoracic needle aspiration, lung cancer.

1. INTRODUCTION

Early detection of lung cancer based on symptoms alone is rare. Mild symptoms usually occur in those who have entered stage II to stage IV. Lung cancer cases in Indonesia are usually diagnosed at advanced stage of the disease. Early detection of it will greatly help the sufferers, especially their quality of life, even though no cure for it, up until now. By increasing public awareness about this disease, along with increasing knowledge of doctors and diagnostic equipment, early detection should be possible. The choices of examinations are clinical, chest X-ray, and sputum cytology. The principle of sputum cytology is a finding of a cells shed from the lesion, either spontaneously or artificially. Sputum can be obtained directly by cough or stimulated by inhalation.[1,2]

Sputum cytology is the only non-invasive method which can detect early lung malignancies, namely premalignant lesions or carcinomas. Sputum samples can be obtained by induction or collection. Three days pooled sputum can increase the likelihood of lung cancer detection. Saccomano's fixation (50% alcohol and 2% polyethylene glycol) is the recommended method for sample collection and fixation. Its advantages are simple, fresh sample, and done at outpatient. Its sensitivity is around 5 – 23%. Study

by Tintin et al., found the sensitivity of sputum examination with 3% NaCl inhalation of 4.3% and the Saccomano method obtained a sensitivity result of 18.3%.[2,3,4]

Sputum (phlegm) is material that is expelled from the lungs and trachea through the mouth, usually also called ecpectoratorian. Sputum expelled by a patient should be evaluated for its source, color, volume and consistency because it shows a specific pathological process. Sputum examination is necessary if pulmonary disease is suspected. The mucous membranes of the respiratory tract respond to inflammation by increasing the production of secret which often contain the related microorganisms.[2,4]

Sputum cytology is still a reliable method used to screen the lung cancer apart from clinical symptoms and low dose thorax CT scans. Some literature states that patients with hemoptysis had an increased positivity rate of it. The larger the tumor size and located at central increase the positivity rate, although not too significantly. Moreover, the type of lung tumor, namely squamous cell carcinoma, has a positive rate of sputum cytology compared to the other types.[2,3,5,6] Accordingly, the aim of this study was to evaluate the positivity rate of sputum cytology compared to bronchoscopy or transthoracic needle aspiration (TTNA) in lung cancer patient.

2. MATERIAL AND METHODS

Study Design
A prospective cross-sectional study done to compare the positivity rate from sputum cytology and from bronchoscopy/ TTNA in lung cancer patients at Wahidin Sudirohusodo Hospital, Makassar.

Subject
The data was collected from medical record using SIRS from 2022 until completed or reached the desired number of samples. Patients diagnosed with lung cancers, done a sputum cytology, and bronchoscopy/ TTNA were included. Patients who had another lung infection, had an allergy, had a chronic gastric disorder, and had sinusitis were excluded.

Data collection
The patients had consented to be included in the study and the study had passed the ethical clearance from Hasanuddin Medical University Ethical Research Committee. Several criteria used as a reference for the sputum samples for sputum cytology were the amount was 10-20 ml at a time, no or little normal oropharyngeal flora, contains <10 cells per small field of view, and contains PMN cells >25 cells per small field of view.

Statistical Analysis
The data was processed using IBM SPSS 23.0 for Microsoft Windows. Data analysis was carried out using the Chi-square test or Fisher Exact test to assess the relationship between various categorical variables, such as the sputum cytology and the type of cancer. Univariate analysis for intergroup comparisons was carried out using the log-rank test, while multivariate analysis using the Cox proportional hazards regression model was carried out under conditions that the proportional hazard assumptions were fulfilled. The significance was obtained, p value <0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

There are 108 patients with lung cancer, which 46 patients (41,4%) was adenocarcinoma and the other 65 patients (58,6%) was squamous cell carcinoma included in this study. As shown in the Table 1, patients with a positive sputum cytology were 5 patients (4,5%), with tumor sizes ≥3cm were 107 patients (86%), and with a hemoptysis history was 59 patients (53,2%).

Table 1. Patient characteristic.

Characteristic (N = 111)	N (%)
Sputum cytology	
Contain malignant cell	5(4,5)
No malignant cell	106(95,5)
Histopathology	
Adenocarcinoma	46(41,4)
Squamous Cell Carcinoma	65(58,6)
Tumor size	
<3 cm	4(14)
≥3cm	107(86)
Hemoptysis History	
Yes	59(53,2)
No	52(46,8)

The relationship between sputum cytology and histopathology, tumor size, and hemoptysis history were not significant (each p value >0.05, shown in Table 2, 3, and 4, respectively). However, there were a relationship between sputum cytology and tumor location with a significant relationship between both variables (p value = 0.002, Table 5).

Table 2. Analysis between sputum cytology and histopathology.

Sputum cytology	Histopathology		P value
	Adenocarcinoma	Squamous Cell Carcinoma	
Positive	1(20)	4(80)	0.401
Negative	45(42,5)	61(57,5)	
*Fischer Exact test			

Table 3. Analysis between sputum cytology and tumor size.

Sputum cytology	Tumor size		P value
	< 3 cm	≥ 3 cm	
Positive	0(0)	5(100)	1.000
Negative	4(3,8)	102(96,2)	
*Fischer Exact test			

Table 4. Analysis between sputum cytology and hemoptysis history.

Sputum cytology	Hemoptysis history		P value
	Yes	No	
Positive	4(80)	1(20)	0.369
Negative	55(51,9)	51(48,9)	
*Fischer Exact test			

Table 5. Analysis between sputum cytology and tumor location.

Sputum cytology	Tumor location		P value
	Central	Non central	
Positive	5(14.6)	0(0)	0.002
Negative	35(38,7)	68(100)	
*Fischer Exact test			

The types of lung cancer in this study were all non-small cell lung cancer (NSCLC) with a more squamous cell carcinomas (65 patients; 58,6%). Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for about 85% of all cases. NSCLC can be further classified based on the histological subtypes, namely adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Adenocarcinoma is the most common subtype especially in women and non-smokers. Squamous cell carcinoma is associated with a smoking history and men. Large cell carcinoma is less common and tends to grow and spread quickly. Accurate classification of NSCLC is important for determining appropriate treatment options and predicting the outcomes. Advances in molecular testing have led to the identification of genetic mutations and targeted therapy specific to certain subtypes of NSCLC, further emphasizing the importance of accurate classification.[7,8]

This study discussed the positivity rate between sputum cytology and other variables in lung cancers. In some literature, sputum cytology can still be used for initial screening of lung cancer, although the incidence rate was relatively low. In other literature, it was around 40% -57%.[7,8] Another study found a varied range from 50% to 70%.[7,8,9]

In this case, sputum cytology was closely related to the initial symptoms of a lung cancer. In some literature, lung cancer patients had hemoptysis, as a predominant symptom, whether massively or non-massively, the positivity was quite high. This was closely related to the injury process caused by lung cancer in some bronchial epithelial cells. As is well known, the main mechanism for hemoptysis in lung cancer patients was erosion of the bronchial walls resulting from lung cancer itself.[10,11] With it, the epithelial cells will be destroyed and mixed with cancer cells, which comes off and mixes with blood when coughed. This situation can be detected by sputum cytology.[11,12]

This is in line with this study. Although the positivity was less frequent, all of the positive sputum cytology was found in patients who had hemoptysis. However, patients with hemoptysis were found but were negative. This was due to various factors such as sputum mixed with blood, blood from oral cavity, sputum mixed with food and others which can interfere with the quality of the sputum. Which showed from the incidence of hemoptysis and positivity of sputum cytology was not statistically significant ($p = 0.3$).

Moreover, the size of a cancer has its own characteristics and significant relationship with sputum cytology. Several literatures, although not significant, the size of lung cancer which was quite large had a positivity rate of sputum cytology which was sufficient. Lung cancer size more than 10 cm, can be examined for sputum cytology and had positive results. The larger the size, the more likely to invades the bronchial wall and surrounding mediastinal organs. This invasiveness will damage part or all of the bronchial walls so that many bronchial epithelial cells were destroyed and mixed with the lung cancer cells. These cells will be expelled out when the patient coughs, naturally or by induction.[9,11-13]

In this study, positive sputum cytology was found, although not significant, with an average size of lung cancer above 5 cm or around 3 cm based on the cut-off value of the statistical test. This was in line with some literature which stated that the larger the size of the cancer, the greater the positivity for sputum cytology, although the results obtained were not significant for all lung cancers. However, in this study, the results showed that there was no significant relationship between tumor size and sputum cytology positivity ($p = 1.00$).

This study found that there were several squamous cell carcinomas with a negative sputum cytology. This was influenced by many factors such as sputum samples that were mixed with saliva, too little so that only a few malignant cells and epithelial cells can be taken, and no damage to the bronchial epithelium which was mixed with cancer cells. Study showed that the most common lung cancer with a positive sputum cytology was squamous cell (around 50%), followed by small cell (around 47%), adenocarcinoma (around 10%) and the other types (1%).[13-17]

Most of the squamous cell carcinoma lesion is located at the central. Central lesion is a tumor that is located in the hilum area and reaches the main terminal bronchus less than 3 cm from the trachea. Our study found that mostly the squamous cell carcinoma was located at the center. Larger size and central lesion increase the positivity of sputum cytology due to closely located with trachea. It allows expectorated sputum to be expelled directly or indirectly along with the epithelial cells mixed with the sputum.[18-21]

In this study a lot of data which was a central lesion had negative for sputum cytology. In accordance with the literature, the positivity of sputum cytology was quite small. Many factors influenced this result such as the cancer did not invasively invade the bronchial walls or most samples were inadequate. However, from our study data, the positivity of sputum cytology was highest in patients with hemoptysis, either massively or non-massively, patients with lung cancer size above 3 cm, central location and squamous cell type.[13,22-24]

There were several limitations from this study. First, there were no control over the sputum samples which affected whether the samples were pure sputum, based on the criteria, or dominated by saliva. Second, the patients had already had a definitive diagnosis of lung cancer type and received chemotherapy were not controlled. Patients received chemotherapy may had a smaller tumor sizes so that the sputum samples did not contain malignant cells. This was also one of the biases in this study. Therefore, the three samples were needed even though fit the criteria, to reduce the bias. In this case, this study showed a positive sputum cytology with a squamous cell carcinoma and centrally located lung cancer in accordance with the literature.

4. CONCLUSION

Sputum cytology is not recommended for diagnosing lung cancer due to low positivity rate, but the prediction rate is high which most likely is central squamous type lung cancer. It still can be done in area with a facility limitation.

Consent

all authors declare that 'written informed consent was obtained from the patient for publication of this manuscript and accompanying images.

Ethical approval

All authors hereby declare that all data have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. This study has an ethical approval form Medical Ethics Committee of Hasanuddin University No: 159/UN.4.6.4.5.31/PP36/2023.

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