



Vol. 2, No. 2
May-August 2021
pp 45-48



doi: 10.35366/107222

Original research

Mediastinal lavage as a diagnostic complement for the evaluation of lung cancer patients

El lavado mediastinal como complemento diagnóstico para la evaluación de pacientes con cáncer de pulmón

Miguel Martínez-Arias,* José Morales-Gómez,† Erika Peña-Mirabal,‡
Chiharu Murata,§ Rodolfo Javier García-del Razo¶

Keywords:

Lung cancer,
mediastinoscopy, mediastinal
lavage, lung cancer staging.

Palabras clave:

Cáncer de pulmón,
mediastinoscopia, lavado
mediastinal, estadificación
del cáncer de pulmón.

ABSTRACT

Introduction: The residual liquid from the mediastinal lavage (ML) that goes to waste during the procedure application of the mediastinoscopy, could contain useful information to determine the lung cancer staging of the patients. However, its use has not been studied. The aim of the present study is to describe the lung cancer patients' prognosis, in which the presence of neoplastic cells in the residual mediastinal wash was positive, through a mediastinoscopy. **Material and methods:** A case series study was conducted, including the eligible cases found at the National Institute of Lung Disease (INER, Mexico City) and ISSEMyM Medical Center (CM ISSEMyM, Toluca City, Mexico) from 2012 through 2017. In the study, a patient was considered eligible if a mediastinoscopy was indicated to determine the lung cancer staging according to both hospitals protocols. During the biopsy sampling procedure, discarded liquid from the lavage was collected and the presence of neoplastic cells was determined through cytology. Survival rate was estimated with the Kaplan-Meier method. **Results:** 30 patients went through mediastinoscopy. Seven were excluded and the remaining 23 patients had a biopsy done. 10 patients got positive results for neoplasia, of which 7 were positive for ML. The median survival time for patients with a positive ML was of 3.8 months [95% CI: 3.0-5.0], meanwhile negative results had a median of 18 months [95% CI: 15.0-22.0] (Log-Rank test, $p = 0.011$). **Conclusion:** We consider that the N2 with ML (+) must be staged as an "occult N3". A prospective cohort study will be required.

RESUMEN

Introducción: El líquido residual del lavado mediastinal (LD) que se desperdicia durante la aplicación del procedimiento de la mediastinoscopia, podría contener información útil para determinar la estadificación del cáncer de pulmón en los pacientes. Sin embargo, su uso no ha sido estudiado. El objetivo del presente estudio es describir el pronóstico de los pacientes con cáncer de pulmón, en quienes la presencia de células neoplásicas en el lavado mediastinal residual fue positiva mediante una mediastinoscopia. **Material y métodos:** Se realizó un estudio de serie de casos, incluyendo los casos elegibles encontrados en el Instituto Nacional de Enfermedades Respiratorias (INER, Ciudad de México) y en el Centro Médico ISSEMyM (CM ISSEMyM, Ciudad de Toluca, México) de 2012 a 2017. En el estudio se consideró que un paciente era elegible si estaba indicada una mediastinoscopia para determinar el estadio del cáncer de pulmón según los protocolos de ambos hospitales. Durante el procedimiento de toma de muestras para la biopsia se recogió el líquido desechado del lavado y se determinó la presencia de células neoplásicas mediante citología. La tasa de supervivencia se estimó con el método de Kaplan-Meier. **Resultados:** A 30 pacientes se les realizó una mediastinoscopia. Siete fueron excluidos

* Centro Médico,
ISSEMyM, Toluca, Toluca
de Lerdo, México.

† Instituto Nacional de
Enfermedades Respiratorias,
Ciudad de México, México.

‡ Instituto Nacional de
Pediatria, Ciudad de
México, México.

¶ Centro Médico ISSEMyM.

Correspondence:

Dr. Miguel Martínez-Arias

E-mail: drmartzari@
hotmail.com

Received: 19/11/2020
Accepted: 04/08/2021

How to cite: Martínez-Arias M, Morales-Gómez J, Peña-Mirabal E, Murata C, García-del Razo RJ. Mediastinal lavage as a diagnostic complement for the evaluation of lung cancer patients. Rev Mex Cir Torac Gen. 2021; 2(2): 45-48. <https://dx.doi.org/10.35366/107222>



y a los 23 restantes se les realizó una biopsia; 10 pacientes obtuvieron resultados positivos para neoplasia, de los cuales siete fueron positivos para LD. La mediana de supervivencia de los pacientes con un LD positivo fue de 3.8 meses [IC de 95%: 3.0-5.0], mientras que los resultados negativos tuvieron una mediana de 18 meses [IC de 95%: 15.0-22.0] (prueba Log-Rank, $p = 0.011$). **Conclusiones:** Consideramos que la clasificación N2 con LD (+) debe ser estadiado como un "N3 oculto". Será necesario realizar un estudio de cohortes prospectivo.

INTRODUCTION

The studies that propose the actual lung cancer staging, report an estimated 5-year survival rate of 24% for N2 associated patients, while with patients diagnosed with N3 only had a 7% of survival.¹ Part of our experience differs from these estimates, since we noted that some patients with a N2 diagnosis have a much poorer prognosis, this being similar to the behavior of those diagnosed with N3. This fact makes us suspect that there could exist a subgroup in patients with N2 with a worse prognosis.

The washing and aspiration of cellular seedlings for staging of cavities is something already known in the world literature as it is the case of abdominal cavity lavage for posterior aspiration and cytology.^{2,3} If obtaining cellular seedlings, it is considered as an advanced stage, the pleural effusion when being drained and having the liquid sent to cytology, reported as positive for cancer has a fundamental aspect in the staging and prognosis for the patient with lung cancer. Pleural lavage cytology (PLC) is the microscopic study of cells obtained from a saline solution instilled and collected from the thoracic

cavity (in patients without preoperative pleural effusion) during surgery for non-small cell lung cancer (NSCLC).⁴ The solution is aspirated and the cytologic analysis is performed to determine the presence of malignant cells.

The staging of lung cancer by mediastinoscopy is recommended⁵ and widely done, and the liquid from

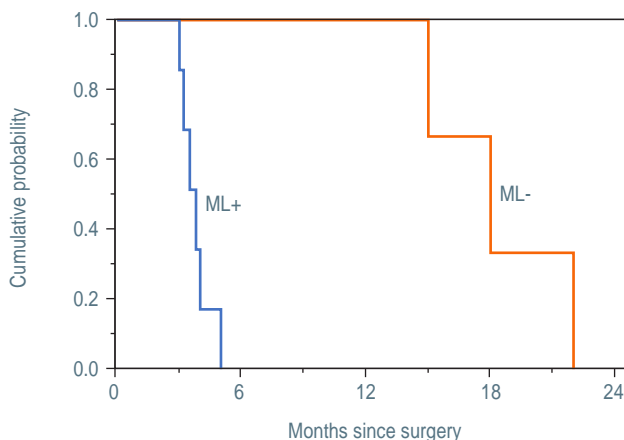


Figure 1: Survival comparison between mediastinal lavage positive and mediastinal lavage negative by use of Kaplan-Meier method. The difference was statistically significant (Log-Rank test: $p = 0.012$).

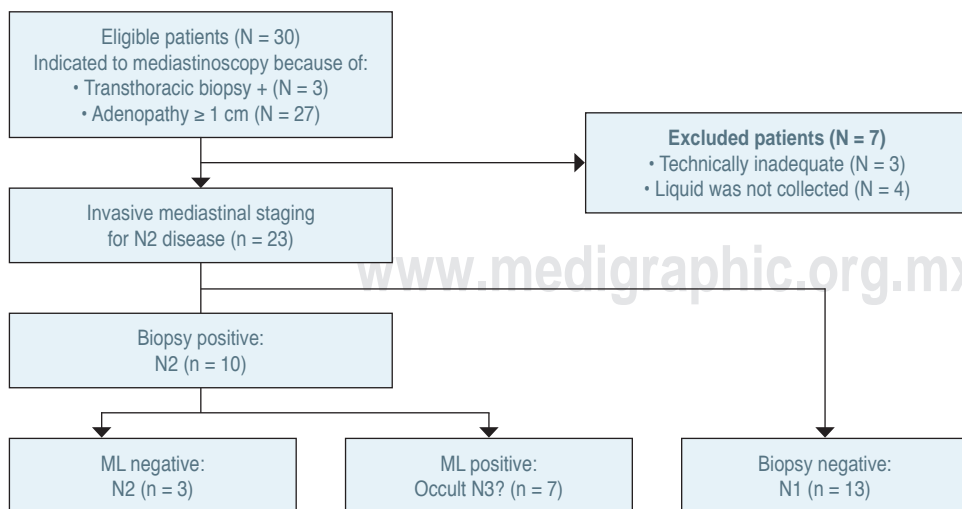


Figure 2: Patients selection process and staging in the present study.

Table 1: Contrasting the results of the mediastinal lavage and the biopsy for lung cancer positivity.

Mediastinal lavage	Biopsy		Total
	Positive*	Negative	
Positive	7	0	7
Negative	3	13	16
Total	10	13	23

*Lymphadenopathy ipsilateral to the tumor site.

ML could contain very useful information, however, this possibility has not been studied. The objective of this study is, therefore, to describe the survival rate of patients with lung cancer in relation to neoplastic cells presence in the liquid discarded from the mediastinal lavage, obtained through the mediastinoscopy, which can generate a change in staging from N2 to N3 or generate a subgroup which would represent a change in the treatment for the patients.

MATERIAL AND METHODS

The data of a series of cases with lung cancer was analyzed. The study was carried out without any modification to the surgical procedure of mediastinoscopy, only by collecting the washing fluid, which is usually thrown to waste.

The cases were selected at INER and at CM ISSE-MyM during a period lasting from August 2012 through March 2017. Patients were considered eligible if: lymph nodes larger than 1 cm in 2R, 2L, 4R, 4L and 7 for the standard Mediastinoscopy and level 5 and 6 for the extended one were found; they had a lung cancer diagnosis without staging or an extension study; and diagnosis of anterior mediastinal tumours in those cases in which no sufficient histological material had been obtained by transthoracic puncture. Patients without condition for surgery, as well as those with previous mediastinoscopy with negative results were excluded.

In all the washing procedures 50 cc of irrigation solution was applied which was aspirated by trap and container, and the sample was fixed with carbowax in a 1:1 preparation. The samples were reviewed in the pathology service where they reported the cytology by number of aspirated cells by field views. It was con-

sidered a positive result the presence of a neoplastic cell, whereas it was considered negative when not finding any neoplastic cells in all fields.

The present study did not require the local Ethics Committee authorization since the surgical procedure was not modified, no maneuver was made with the patients, no genetic study was performed on the liquid obtained and it was accepted by the Academic Committee of both Institutions for its realization.

Statistical Analysis. The ML and biopsy results were contrasted by use of a 2×2 contingency table. The median survival time of both group (ML positive and negative) was estimated by Kaplan-Meier method (Figure 1) and log-rank test was used to comparison between groups. Estimated median were reported with their CI95%. All statistical analyses were carried out by the statistical package JMP11 of SAS Institute, Inc.

RESULTS

Thirty mediastinoscopies were carried out between 2012 and 2017, from which 7 procedures were excluded due to inadequate sample taking during mediastinal lavage (3 cases) and the complete absence of mediastinal lavage (4 cases) (Figure 2). Biopsies were taken from these 23 mediastinoscopies, from which 13 came out negative and 10 cases came out positive with the biopsy for neoplastic cells. Among these 10 patients, 7 were positive and 3 were negative in ML (Table 1). The median of survival time (Table 2) in the patients with positive ML was 3.8 months [95% CI: 3-5 months], whereas in the negative ML patients group the median was 18 [15-22 months]. This difference was statistically significant (Log-rank: $p = 0.012$).

DISCUSSION

It was observed that between patients with and without ML positivity a clear difference in their survival rates,

Table 2: Survival comparison of patients: mediastinal lavage positive VS mediastinal lavage negative.

Group	n	Mediana [95%CI]	p*
Mediastinal lavage	7	3.8 [3.0-5.0]	0.012
Mediastinal lavage (+) o (-)	3	18.0 [15.0-22.0]	

*Log-Rank test.

although all of 10 cases were staged in N2 according to actual TNM classification for lung cancer.^{6,7} Seven of those 10, ML positive patients, had poor median survival time of 3.7 months [95% IC: 3.0-5.0], whereas the rest, 3 ML negative patients, presented 18 months as their median survival time [95% IC: 15.0-22.0]. The survival time of former group is similar to that of N3, rather than N2.¹

It is known that the invasion of malignant cells goes from the center to the periphery, so it is not possible to find neoplastic cells seedlings in Mediastinal tissue without prior ganglionic involvement. Indeed, we found no case with positive in ML, resulting in negative results for biopsy. Our finding allows us to propose a hypothesis that the seven cases with positive in ML were not pure N2, but N3, which we could call "occult N3", constituting a subgroup in TNM staging of Lung Cancer.

Obviously, the scope of our study is very limited, because of the study design, retrospectively reviewed case series, and besides that the number of observed patients was very few. However, we consider that our finding suggests an important issue, and it is worth to carry out a well-designed prospective cohort study to test our hypothesis.

CONCLUSION

In patients with N2 adenopathy, there is a subgroup that was reported with LM (+). This subgroup showed a

survival rate similar to the N3 group according to the current classification. We propose to have this subgroup considered a "hidden N3" for decision making in terms of treatment. It is necessary to carry out a prospective cohort study to confirm this finding.

REFERENCES

1. Groome PA, Bolejack V, Crowley JJ et al. The IASLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (7th) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2007; 2(8): 694-705.
2. Davidson W, Madan R, O'Neil M et al. Utility of peritoneal washing cytology in staging and prognosis of ovarian and fallopian tube neoplasms: a 10-year retrospective analysis. *Ann Diagn Pathol*. 2016; 22: 54-57.
3. Rossi E, Bizzarro T, Martini M et al. The role of liquid based cytology and ancillary techniques in the peritoneal washing analysis: our institutional experience. *PLoS One*. 2017; 12(1): e0168625. doi: 10.1371/journal.pone.0168625.
4. Wang CM, Ling ZG, Wu YB et al. Prognostic value of pleural lavage cytology in patients with lung cancer resection: An updated meta-analysis. *PLoS One*. 2016; 11(7): e0157518. doi: 10.1371/journal.pone.0157518.
5. Vilman P, Frost Clementsen P, Colella S et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS). *Endoscopy*. 2015; 47(06): 545-559.
6. Goldstraw P, Chansky K, Crowley J, et al. The IASLC lung cancer staging project: proposals for revision of the TNM stage groupings in the forthcoming (Eighth) Edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2016; 11(1): 39-51.
7. Dettnerbeck FC, Chansky K, Groome P et al. The IASLC lung cancer staging project: external validation of the revision of the TNM stage groupings in the eighth edition of the TNM classification of the lung cancer. *J Thorac Oncol*. 2016; 11(9): 1433-1446.