

Principales emergencias oncológicas en el cáncer de pulmón: un análisis de un único centro

Main structural oncologic emergencies in lung cancer: a single center analysis

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ABSTRACT

Introduction: Lung cancer is the leading cause of structural oncologic emergencies (OE). The clinical outcome of patients with OE is often poor and mortality is high. The aim of this study was to evaluate the incidence, clinical presentation and outcomes of patients with structural OE in patients with lung cancer.

Method: Retrospective cohort study involving all lung cancer patients admitted with a structural OE (superior vena cava syndrome (SVCS) and metastatic spinal cord compression (MSCC)) between January 1, 2015 and November 30, 2019. Long-term outcome was evaluated at 90 days after de OE and during the follow-up time. A comparative analysis between SVCS group and MSCC was also made. Data analysis was performed using the SPSSv.25.0.0 with a significant level of $\alpha=5\%$.

Results: Of the 610 patients with the diagnosis of lung cancer, and 35 (~6%) had an OE:16 a SVCS and 19 had a MSCC. OE was the first manifestation of cancer in more than 50% of patients (8 in SVCS group and in 12 in MSCC group).The mortality rate was 66% 90 days after OE and 97% at the end of follow up. Patients with MSCC had worse outcomes when compared to SVCS, with more mortality in the first 3 months and more morbidity.

Conclusion: In this study, structural OE was the first manifestation of lung cancer in more than 50% of patients and its occurrence is associated with a worse prognosis. We need to be aware of this situation, especially in the emergency department, in order to minimize those consequences. Future studies are needed to determine the impact of early diagnosis, treatment patterns on OE outcomes and strategies for reducing structural OE related costs.

Keywords: Oncologic emergencies, Lung cancer, Superior vena cava syndrome, Metastatic spinal cord compression, Cancer symptoms, Outcomes, Mortality, Survival.

INTRODUCTION

Lung cancer (LC) is the leading cause of cancer deaths worldwide (1.3 million deaths per year)¹. Given the increasing incidence of and declining mortality rate for LC worldwide, an increase in the number of oncologic emergencies (OE) is expected²⁻⁴.

An OE is defined as any acute, potentially life-threatening condition that has developed directly or indirectly as a result of cancer or cancer treatment^{5,6}. It can be the initial manifestation of cancer in about 21% of patients⁷ and can be divided into metabolic, hematological and structural (such as superior vena cava syndrome (SVCS) and metastatic spinal cord compression (MSCC))⁸. Among structural OE in LC patients, MSCC is the most common (2.5% to 5% of patients)⁹ and devastating OE, requiring urgent diagnosis and prompt management because of rapid progression of neurological dysfunction, with poor prognosis^{9,10}. SVCS is found in 3.8% of LC patients at time of diagnosis and it can be life threatening^{11,12}.

In this study we evaluated¹ incidence of the structural OE in patients with LC admitted to our hospital², the underwent treatment after admission³ and mortality rate at 90-days and during the follow up time. We also establish a comparison between two groups: MSCC and SVCS patients in terms of overall survival and clinical outcomes.

METHODS

A retrospective cohort study was made, including all patients admitted to a single secondary care hospital between January1, 2015 and November 30, 2019, with SVCS or MSCC in patients with LC. All patients with a history of LC, as well as patients with a primary presentation of malignant disease at the emergency room were included.

Patients were divided into two different groups according to their final diagnosis: MSCC¹ and SVCS². The patients' baseline charac-

teristics (gender, age, LC histology, ECOG and number of previous treatments to LC) were documented, whether the time between LC diagnosis and OE, treatment underwent to OE, and mortality rate and outcomes during the follow up time. Follow-up ended November 30, 2019. At final follow-up, charts of all patients were reviewed for correspondence regarding mortality.

The protocol was consistent with the Declaration of Helsinki, and approval for the study was retrieved.

Statistical analysis

Data analysis was performed using the SPSS® v.25.0.0 (Statistical Package for Social Sciences). We calculated means with standard deviations (SDs) or medians with interquartile range (IQR) for categorical variables.

To test hypotheses between MSCC and SVCS, we used nonparametric tests (Mann-Whitney and Kruskal-Wallis), depending on the nature of the tested hypotheses. For survival analysis we used Kaplan-Meier curves.

In all hypothesis tested it was considered a significance level of $\alpha = 5\%$.

RESULTS

We identified 610 patients with newly diagnosis with LC between January 1, 2015 and November 30, 2019. There were 35 (6%) patients who presented with a structural OE. In this group, 16 patients (45.7%) presented with a SVCS and 19 (54.3%) with a MSCC. Table 1 provides an overview of patient characteristics divided by groups within the different categories.

Median (IQR) age was 64 (36-89) years old, 88.6% were man, 45.7% had an adenocarcinoma, 37.1% were ECOG 1 at admission and in 57.1% (n=20) the OE was the first manifestation of cancer

(in 50.0% patients with SVCS and in 63.2% patients with MSCC). In the others, the median (IQR) time between the diagnosis and the OE was 7 (1-56) months and 28.6% (n=10) were in the first two-lines chemotherapies (5 in the first and 5 in the second-line).

In the subgroup analysis (table 1) only ECOG at admission was statistically different, with worse ECOG in the MSCC group.

Table 1. Baseline characteristics of the patients with SVCS and MSCC

Characteristics	SVCS (n=16)	MSCC (n=19)	p*
Age (in years), median (IQR)	66.5 (36.0-89.0)	64.0 (49.0-78.0)	0.909
Male gender, n (%)	15 (93.8%)	16 (84.2%)	0.392
First manifestation of LC, n(%)	8 (50%)	12 (63.2%)	0.72
Time in months between LC diagnosis an OE in others, median (IQR)	5 (1-24)	13 (4-56)	0.342
Histology, n (%)			0.306
Adenocarcinoma	6 (37.5%)	10(52.6%)	
Small cell lung cancer	6 (37.5%)	5 (26.3%)	
Squamous cell carcinoma	3 (18.8%)	2 (10.5%)	
ECOG at diagnosis, median(IQR)	1.00 (0-4)	3.00 (1-4)	0.037*

Abbreviations: SVCS, superior vena cava syndrome; MSCC, metastatic spinal cord compression; LC, lung cancer; OE, oncology emergency; IQR, interquartile range.

In MSCC group, when the diagnosis was performed, 16 (84.2%) had paraparesis, 2 (10.5%) paraplegia and 2 (10.5%) present with sphincter incontinence. Only 1 patient presents with superior arm paraparesis.

After OE, 27 patients (77.1%) underwent radiotherapy (15 in the SVCS and 12 in the MSCC group), which was statistically superior (p=0.34) in the SVCS group when compared with MSCC group; 9 patients (25.7%) underwent surgery, all from the MSCC group.

The 90-day mortality rate for the patients that presented with OE caused by LC was 65.7%, and the overall mortality rate at final follow-up was 97.1 %. Median survival was 2 (range 0–37) months. No-one from the SCVC group were alive at 59 months follow up and only one person in the MSCC group still alive (Fig. 1).

During the follow up time, 15 patients (42.9%) started or restarted systemic chemotherapy (5 in MSCC group and 10 in the SVCS), with statistical differences between those two groups (Table 2) .

Table 2. Outcomes of OE patients

Outcome	SVCS (n=16)	MSCC (n=19)	p*
Start or restart systemic LC treatment, n (%)	10 (62.5%)	5 (26.3%)	0.034*
Day-90 mortality, n (%)	8 (50.0%)	14 (73.7%)	0.293
Time to death in months, median (IQR)	3 (0-37)	1 (0-12)	0.356

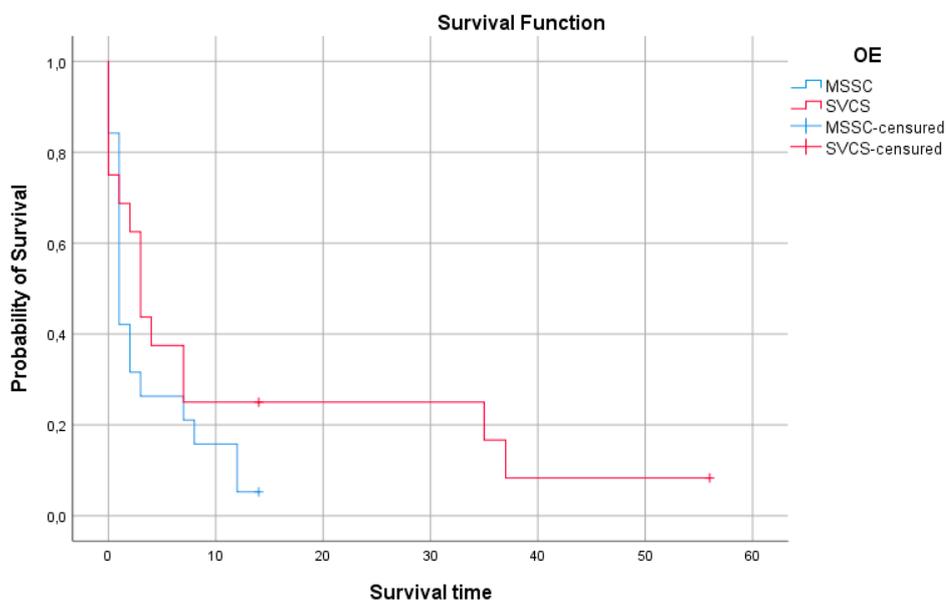
Abbreviations: SVCS, superior vena cava syndrome; MSCC, metastatic spinal cord compression; LC, lung cancer; IQR, interquartile range.

DISCUSSION

Structural OE represent a wide spectrum of disorders either resulting from the progression of a known malignancy or presenting as the initial manifestation of a previously undiagnosed malignancy⁴.

The main results of this study was: almost 6% of patients with LC had an OE during the course of the disease; MSCC was the most prevalent OE in our population; almost 90% of patients with OE were man; in more than 50% of our patients the OE was de first manifestation of cancer; patients with MSCC had a worse performance

Fig.1. Survival analysis of Oncology emergencies



status at diagnosis than SVCS patients; the majority of patients died in the first three months after OE; the day-90 mortality was superior in MSSC subgroup; there's no difference in mortality rate between the subgroups.

OE are life-threatening conditions or can lead to severe sequelae, prompt recognition can markedly reduce morbidity and mortality in the short-term and affect prognosis in the long-term¹³.

In our study almost 6% of patients with LC had an OE during the course of the disease, with is in accordance with literature⁷. MSSC occur in approximately 3% and SVCS in 2% of cancer patients during the disease, which is similar to what was found in the literature^{7,11,14,15}. However we only included patients with LC, and this difference was not in the literature^{11,14}.

In this population, OE was the initial manifestation of LC in more than 50% of the patients, and lead to diagnosis. This percentage is even bigger in the MSSC group, which is superior to what we found in the literature (~30%)¹⁶. This difference can be due to differences in the included population, because Park et al included only patients who underwent surgical treatment¹⁶.

In this study ECOG performance status at diagnosis was worse in the group of patients with MSSC when compared to SVCS subgroup. This may be since MSSC usually develops in patients with advanced cancer¹⁵⁻¹⁷. Another explanation is that the majority of patients with MSSC had important neurologic deficits at admission, which had an important impact in functionality evaluation.

The majority of patients, in this study, die during the first three months after OE and the occurrence of OE was associated with a worse prognosis, what is in accordance with the literature¹³. This is even bigger in the MSSC group, in which 90 days mortality was 74%¹⁵.

More than half of the patients with SVCS started or restarted systemic treatment but only ~27% in MSSC were submitted to systemic treatment after the OE. This could be due to de worse prognosis of MSSC or because of worse ECOG performance status at admission.

As far as we know, there're no observational orongoing clinical trials in structural oncology emergencies including SVCS and MSSC in lung cancer. In this study, we made that distinction between de structural OE and show their outcomes.

This study has several limitations. First, it is a single center study conducted in secondary care hospital, thus the results may reflect the clinical practice of this center and might not be applied to other places with different realities, like oncologic centers. This study was conducted only in patients with the diagnosis of LC. Some patients with OE admitted to the hospital die before the primary tumour is diagnosed. So, we almost certainly underestimated the true frequency of OE due to lung cancer because of under-reporting and patient migration. The sample size was low and became even smaller when we separated the two groups which may be undervalued or overvalued the results.

CONCLUSION

In this study, structural OE was present among almost 6% of patients with new diagnosis of LC and can be the initial manifestation in more than 50% of the patients. The mortality rate in this population was high which shows the worst prognosis after its occurrence. MSSC had an even worse prognosis when compared to SVCS. Future studies are needed to determine the impact of early diagnosis, treatment patterns on OE outcomes and strategies for reducing structural OE related costs.

Key messages

In patients with LC the incidence of OE was almost 6% during the course of the disease and it could be the initial manifestation of cancer, leading to diagnosis, in more than 50% of patients. Their occurrence is associated with worse outcomes, with high mortality rate.

LIST OF ABBREVIATIONS

LC, lung cancer; OE, oncologic emergencies; SVCS, superior vena cava syndrome; MSSC, metastatic spinal cord compression; IQR, inter-quartile range; SD, standard deviation; SPSS, Statistical Package for Social Sciences.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTION

Study concept and design: MV, FE.

Acquisition of data: MV

Drafting of the manuscript: MV, HM, CS, FE

Statistical analysis: MV

Analysis and interpretation of data, critical revision of the manuscript and final approval of the version to be published: MV, HM, CS, FV

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ETHICAL ASPECTS

The study followed the criteria of the Helsinki Declaration. All participants submitted a consent form to be included in this study.

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