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Superior vena cava syndrome and lung cancer: survival and prognostic factors

Abstract

Introduction: The superior vena cava syndrome (SVCS) is a set of signs related to the obstruction of the upper cava current caused by a compression, an invasion or a thrombosis of the superior vena cava. Its etiologies are numerous but dominated by neoplastic causes mainly of bronchopulmonary origin.

Aim of the work: The aim of this study is to evaluate survival and to identify the prognostic factors of superior vena cava syndrome in patients with lung cancer. We also propose to draw up the clinical profile as well as the therapeutic management in SVCS of malignant origin.

Materials and methods: A total of 108 patients with SVCS complicating primary bronchial cancer were hospitalized in the Pneumology Department at Fattouma Bourguiba University Hospital during a period of 25 years.

Results: The results showed the existence of a clear male predominance (98.1%) and an average age of 60.2 years. Smoking was found in 68.5% of cases .The superior vena cava syndrome revealed a neoplasm in 55% of cases and it was metachronous in 30.5% of cases. Median survival was 7months. In univariate study, survival was reduced in patients having general health impairment with Performans Status (PS) score≥2, signs of severity of SVCS, altered respiratory function, chronic respiratory failure, histological type of non small cell lung carcinoma and exclusive symptomatic treatment for bronchopulmonary cancer. Multivariate analysis revealed that gender, smoking, PS score and signs of severity were independent prognostic factors.

Conclusion: The management of the SVCS is multidisciplinary. It requires medical treatment whose effectiveness is still uncertain and radiotherapy which is considered the gold standard of treatment for SVCS.

Keywords: Superior vena cava syndrome, broncho-pulmonary cancer, radiotherapy, survival, prognostic factors

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Abbreviations:

SVCS, Superior vena cava syndrome; SVC, Superior vena cava; BPC, Bronchopulmonary carcinoma; NSCLC, Non small cell lung cancer; SCLC, Small cell lung cancer; CT scan, Computed Tomography N: number; WHO, World Health Organization; PS, Performans Status; FEV1, Forced expiratory volume in one second; PaO2, Partial Pressure of Oxygen in arterial blood; BMI, Body mass index; HR, Hazard ratio; CI, Confidence interval

Introduction

Superior vena cava syndrome (SVCS) is the clinical expression of superior vena cava (SVC) obstruction by extrinsic compression, vein invasion by a tumoral process, or thrombosis. The clinical manifestations are related to the increase of the venous pressure upstream of the obstruction and they depend on how fast it has been installed.[1] Many etiologies have been described and their importance has changed over the years. While in the first half of the twentieth century, infectious diseases were the main causes of the superior vena cava syndrome, mediastinal and malignant lung tumors are currently the most common etiologies. This syndrome occurs in 3 to 4% of cancer patients and in 85% of cases it is secondary to bronchopulmonary carcinoma (BPC). These cancers occupy the first place among malignant tumors in men and the third one of women. Non-small cell lung cancer (NSCLC) accounts for more than 80%

of bronchial cancers.[2] Small cell lung cancer (SCLC) is a risk factor of SVCS because of its mediastinal predilection and speed of progression.

The clinical manifestation may be discreet or, on the contrary, life-threatening.[3] The prognosis of SVCS depends essentially on the underlying cause. In BPC, the 5-year survival rate is 2 to 5%. The aim of this study is to evaluate the survival of patients with SVCS secondary to lung cancer and to identify prognostic factors.

Methods

Type of the study:

In the current retrospective study, we enrolled the records of patients followed for SVCS due to primary bronchopulmonary cancer in the Department of Pneumology, Fattouma Bourguiba University Hospital in Monastir from 1990 to 2015.

Study population:

Inclusion criteria:

We included in this study: The presence of clinical and/or radio-logical SVCS in patients with histologically confirmed primary BPC, the age≥18 years and SVCS confirmed by chest Computed Tomography (CT-scan).

Non-inclusion criteria:

We excluded all cases whose diagnosis has not been confirmed histologically, SVCS linked to secondary lung cancer, age<18 years and SVCS linked to other tumors (lymphoma) or of non tumoral origins (infections).

Survival:

It is the time between the date of diagnosis of SVCS of neoplastic origin and the date of death or the date of the latest news of the patients. The collection of patient survival data was based on medical record data for patients who died in hospital and telephone contact with the family of home-deceased patients.

Statistical analysis and study of prognostic factors:

The data collected was coded and analyzed using the SPSS version 21 software. The quantitative variables were expressed as means±standard deviations. The qualitative variables were expressed in percentages. The survival analysis was performed by the Kaplan-Meier method. The comparison of the survival according to the different prognostic variables was made by the Log-Rank test in a univariate analysis. The multivariate analysis was performed by the Cox model to identify independent factors. The model included all variables with a $p<0.2$ value in univariate analysis. The results were evaluated with a 95% confidence interval and a p value<0.05 was considered significant.

Results

a) Demographic characteristics of the studied population:

A total of 108 patients were included in our study. The general characteristics of the patients are detailed in (Table 1).

Table 1 Demographic characteristics of the studied population

	Studied population : N=108
Age (year) M±DS	60.2±11.3
Gender	
Male	106 (98%)
Female	2 (2%)
Smoking	68.50%
Year-Pack (YP)	55.1 YP±27.2 YP
Medical History	
COPD	25 (23.5%)
Diabetes	14 (12.9%)
Hypertension	12 (11.1%)

b) Clinical manifestations:

The clinical manifestations of the primary BPC as well as the clinical signs suggestive of SVCS at the time of the diagnosis are displayed in (Table 2). SVCS revealed the tumor in 60 cases (55%) and was metachronous in 33 cases (30.5%).

c) Characteristics of the primary tumor:

A histopathological confirmation was carried out in all patients. SCLC was at an extensive stage in 70.5% of cases. NSCLC was diagnosed at an advanced stage in 35 patients (54.7% of cases). The histological types along with the stage of the carcinoma are shown in (Table 3).

d) Treatment:

The management of the patients involved two components: the symptomatic treatment of the superior vena cava syndrome and the management of BPC. Symptomatic treatment of SVCS consisted on Oxygen therapy in 15 patients (13.4%), corticosteroids in 93 patients (68.1%), radiotherapy for decompression in 42 patients (38.8%), anticoagulation in 30 patients (27.7%) and diuretics in only1 patient. Management of bronchopulmonary cancer included symptomatic measures in 106 patients (98.1%), chemotherapy in 85 patients (78.7%) and curative radiation in 27 patients (25%).

Table 2 Clinical manifestations

Clinical manifestations of BPC	Number (percentage)
Chest pain	62 (57.4%)
Cough	56 (51.8%)
Dyspnea	47 (43.5%)
Hemoptysis	30 (28.7%)
Clinical signs of SVCS	Number (percentage)
Facial edema	63 (67.7%)
Collateral vein circulation	57 (61.2%)
Increased neck volume	38 (40.8%)
Distention of the veins in the neck	35 (37.6%)
Cyanosis	5 (5.3%)
Upper limbs edema	19 (20.4%)

Table 3 Characteristics of the primary tumor

Anatomopathology	
SCLC	43 (40.1%)
Squamous cell carcinoma	33 (29.9%)
Adenocarcinoma	29 (26.1%)
Large cell carcinoma	3 (2.9%)
Stages	
SCLC	
Limited stage	13 (29.5%)
Extensive stage	31(70.5%)
NSCLC	
IIIA	10 (15.6%)
IIIB	19 (29.7%)
IV	35 (54.7%)

SCLC: Small cell lung carcinoma
NSCLC: Non small cell lung carcinoma

e) Survival and prognostic factors:

A. Overall survival:

By 2015, 89 patients (82.4%) had died, 9 patients had survived (8.3%) and 10 patients had defaulted from follow-up. The median survival of our patients was 7 months. Survival at 1 and 2 years was 22% and 6%, respectively.

B. Prognostic factors:

a. Univariate study:

In univariate study, poor prognostic factors are bad general health, documented by the World Health Organisation (WHO) performans status (PS) score≥2, signs of severity of SVCS, ventilatory deficit with

forced expiratory volume in one second (FEV1)<70% of baseline in spirometry , chronic respiratory failure confirmed by Partial Pressure of Oxygen in arterial blood (PaO2)< 70 mmHg, histological type of NSCLC and exclusive symptomatic treatment for NSCLC and SCLC (Table 4).

b. Multivariate study:

Predictors of superior vena cava syndrome mortality during BPC were: Male gender, smoking, PS≥2, two or more metastases and the presence of SVCS severity signs (Table 5).

Table 4 Survival and prognostic factors in univariate study

	Number of cases	Median survival in months	p value
Age			
≤60 years	51	6 ±1.07	0.22
>60 years	57	7±0.81	
Gender			0.14
Men	107	7±0.60	
Women	1	3.5±0.60	
Smoking status			
Non-smokers or ex-smoker	34	8±1.57	
CurrentSmokers			0.13
PS Score			
<2	80	8±0.60	<10⁻³*
≥2	28	3.5±0.79	
Severity Signs of SVCS			
No	100	7±0.57	0.02*
Yes	8	3±0.91	
BMI			
<18,5	10	6±3.55	
18,5-24,99	44	7±0.68	0.07
≥25	15	10±5.87	
FEV1			
< 70%	48	6±0.83	0.04*
≥70%	23	9±1	
PaO2			
<70mmHg	17	4±0.5	
≥70mmHg	62	8±0.74	0.01*
Histology			
NSCLC	64	5±0.60	0.002*
SCLC	44	8.5±0.94	
TNM stages			
NSCLC			
IIIA	10	6±1.41	0.13
IIIB	19	9±1.8	
IV	35	5±0.54	
SCLC			
Limited	13	13±2.37	0.11
Extensive	31	7±1.04	
Treatment of NSCLC			
Symptomatic treatment	18	4±0.04	
Chemotherapy or Radiotherapy	46	9.6±0.8	<10⁻³*
Treatment of SCLC			
Symptomatic treatment			
Radio-chemotherapy	5	3	<10⁻³*
Chemotherapy	13	29±11	
	29	8.5±1.28	

* Significant BMI: Body mass index
 SCLC: Small cell lung cancer
 NSCLC: Non Small cell lung cancer

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Table 5 Independent factors of mortality in SVCS

	HR	IC 95%	P value
Male gender	13.78	1.7-111.9	0.01*
Smoking	1.78	1.1-2.9	0.01*
PS≥2	5.28	2.9-9.5	< 10⁻³*
SVCS Severity signs	2.59	1.08-6.17	0.03*

* Significant HR: Hazard ratio
CI: Confidence interval

Discussion

The SVCS is the clinical expression of superior vena cava (SVC) obstruction by extrinsic compression or thrombosis most commonly due to an invasive process. Bronchopulmonary cancer accounts for 80-85% of the most common etiology of SVCS in adults.[4] The current study investigated the prognostic factors of SVCS in patients with bronchopulmonary cancer. Despite the therapeutic progress and the fast management of the SVCS of broncho-pulmonary tumor origin, this entity remains of poor prognosis. In our study, the median survival was 7 months. Poor prognosis factors were male gender, smoking, general impairment and the presence of severity signs of SVCS. The median survival varies depending on the authors from 6 to 9 months,[3–7] which is consistent with our study (7 months). Survival at 2 years in our series was 6%.

It is reported in the literature that life expectancy in patients with tumour SVCS is 6 months, but this estimation varies widely depending on the underlying neoplastic conditions.[8,9] According to some authors, the SVCS itself is not a factor of poor prognosis since overall survival does not differ for BPC of the same histological type and same stage according to the existence or not of SVCS.[5,6,8] Most studies have found that age is an important factor influencing the prognosis of SVCS of pulmonary neoplastic origin with a survival that deteriorates with age.[3,10] In fact, Chan RCL proved in his study about 104 patients with tumour SVCS that the age under 50 years was associated with better survival in univariate study (p<10⁻³).[6] However, in our series, age 60 or younger is correlated with a shorter median survival (6 months versus 7 months), but the difference was statistically insignificant. This could be explained by the predominance of the 61-70 age groups.

Smoking is the main risk factor for bronchopulmonary cancer. The absence of smoking in our series is correlated with better survival but the difference was statistically insignificant. Several studies have shown that the survival of non-smoking patients with SVCS of pulmonary tumors was better than that of smokers. Indeed, Piers NF and al found better overall survival in non-smokers with a significant difference (p=0.038).[5] The general condition assessment of the patient is an essential step in the management of bronchopulmonary cancer with SVCS. The therapeutic decision depends on the general condition. In our series, patients with a PS of two or more had lower survival than patients with good general health (p<10⁻³). Several studies have shown that good general health is associated with better survival.[3,5,7,10–12] Indeed, Piers NF and al found that a good PS score of 0 or 1 was positively correlated with global survival (p=0.03).[5]

According to the literature review, the degree of bronchial obstruction negatively influences the survival of patients with BPC associated with chronic obstructive pulmonary disease. This association is frequent since both pathologies carry the same risk factor (tobacco).[13,14] In our patients, FEV 1<70% was associated with lower survival with statistically significant difference (p=0.04). In addition, median survival was lower (4±0.5 months versus 8±0.7 months) in chronic respiratory failure (p=0.01). The review of the literature regarding survival as a function of the histological type has shown variable results. Several studies have shown that the survival of patients with NSCLC is better compared with those with SCLC.[8,9] On the other hand, Wilson LD reported in his study that the prognosis of SVCS with neoplastic origin depends on histological type of the tumor and its response to treatment. He concluded that SCLC was correlated with better survival.[8]

In our series, patients with SCLC had a longer median survival than those with NSCLC (8.5 months versus 5 months) with a statistically significant difference. The presence of metastasis is an important prognostic factor for SVCS of neoplastic origin.[3,5,9–11] Survival in our patients was better for localized or locally advanced stages but the difference was statistically insignificant. Concerning cancer treatment, a better survival was noted under chemotherapy (8 months) with a statistically significant difference in case of NSCLC (p<10⁻³) and in case of SCLC (p<10⁻³) in our series. According to Wilson LD,[8] a complete regression of symptoms of SVC obstruction is visible under routine chemotherapy in 80% of patients with SCLC and 40% of those with NSCLC. However, Rowell NP, in a systemic review of 2 randomized studies and 44 observational studies, concluded that in patients with bronchopulmonary cancer, there was no significant difference in SVCS remission rate or in overall survival depending on the treatment prescribed: chemotherapy alone or chemo-radiotherapy.[15]

The main independent prognostic factors vary between studies. The study of Piers NF allowed to identify some independent factors of good prognosis: a good general state (PS=0 or 1), the absence of metastases and the absence of smoking.[5] Indeed, the PS is an important prognostic factor found in multi-variate analysis in several studies.[3,5] Smoking was a risk factor for mortality.[5,6] Early tumor stage and absence of metastasis were positively correlated with a better overall survival.[5] In our series, the predictive factors for SVCS mortality in bronchopulmonary cancer were: male gender, smoking, general impairment with PS≥2, two or more metastases, and SVCS signs of severity.

Conclusion

The etiologies of SVCS are numerous dominated by neoplastic causes mainly of bronchopulmonary cancer. Despite therapeutic progress of the SVCS of broncho-pulmonary tumor origin, this entity remains of guarded prognosis. The independent factors of poor prognosis were male gender, smoking, general impairment and SVCS signs of severity. Early detection and adequate treatment of SVCS is the key to a better survival among patients with bronchopulmonary cancer.

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Conflict of interest

Authors declare that there is no conflict of interest.

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