



## Postoperative recurrence of primary lung cancer: anatomico-clinical and therapeutic study

### Récidive tumorale post-opératoire du cancer broncho-pulmonaire primitif : étude anatomo-clinique et thérapeutique

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#### RÉSUMÉ

**Introduction:** Le cancer broncho-pulmonaire (CBP) est la première cause de mortalité par cancer dans le monde. Même après un traitement chirurgical radical le taux de récurrence de la maladie reste élevé.

**Objectif:** Etudier le profil des patients opérés pour CBP et d'identifier les facteurs pronostiques des récurrences tumorales.

**Méthodes:** Étude rétrospective incluant 67 cas de CBP, ayant bénéficié d'une chirurgie curative, hospitalisés dans le service de pneumologie Ibn Nafiss de l'hôpital Abderrahmene Mami de 2010 à 2016.

**Résultats:** L'âge moyen de la population était de 61 ans avec un sexe ratio de 21. Le délai moyen de diagnostic était de 22 jours. Le type histologique le plus fréquent était l'adénocarcinome (63%). La lobectomie était indiquée chez 63% des malades.

La récurrence tumorale a été notée chez 40% des patients. Le délai moyen entre la récurrence et le traitement chirurgical était de 12 mois. La récurrence était plus fréquente pour les adénocarcinomes et les fumeurs âgés de plus de 60 ans. La survie globale était de  $56 \pm 4$  mois. Elle était plus prolongée pour les patients jeune, avec un tabagisme inférieur à 25 PA, au stade précoce, et qui ont reçu une chimiothérapie adjuvante. La probabilité de survie était de 13% à 5 ans tous stades confondus.

**Conclusion:** Les facteurs pronostiques de récurrence après chirurgie curative du CBP sont l'âge du patient, le tabagisme, le type histologique, le stade du cancer ainsi que l'acte chirurgical.

**Mots clés :** Tumeur Poumon - Chimiothérapie - Chirurgie - Récidive – Survie- Métastase

#### SUMMARY

**Background:** Lung cancer is the leading cause of cancer mortality worldwide. Even after radical resection, the rate of recurrence of non-small cell lung cancer remains high.

**Aim:** To identify the profile of patients operated for lung cancer and to study the prognostic factors of tumor recurrence.

**Methods:** We performed a retrospective study including 67 cases of lung cancer with curative surgery, hospitalized between 2010 and 2016.

**Results:** The mean age was 61 years. The sex ratio was 21. The average time to diagnosis was 22 days. The average time to start treatment was 10 days. The most common histological type was adenocarcinoma (63%). Lobectomy was performed in 63% of the patients.

Tumor recurrence was noted in 40% of the patients. The average time between recurrence and the surgical treatment was 12 months. The most common location of recurrence was the lung (70%). Recurrence was more common among adenocarcinoma and smokers older than 60 years. The majority of locally advanced and metastatic cancers have recurred.

The average survival was  $56 \pm 4$  months. Better survival rates were observed in young patients, with less than 25 pack-years of early-stage, no lymph node involvement, and patients who received adjuvant chemotherapy. The probability of survival was 5 years for all tumor stages.

**Conclusion:** The prognostic factors for recurrence after radical resection for lung cancer were: the age of patients, smoking history, histological type, tumor stage, and surgical procedure.

**Key-words:** Lung neoplasms, Surgery, Recurrence, Survival, Chemotherapy, Metastasis

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## INTRODUCTION

Primary bronchial cancer is the leading cause of cancer mortality worldwide with an incidence of 1.8 million in 2012 (12.9% of total cancers), mostly (58%) of the cases occurred in developing countries [1]. Bronchial cancer is currently one of the main public health problems in Tunisia, with a standardized incidence rate of 31.2/100000 for men and 3.2/100000 for women [2]. The diagnosis is often done at a late stage in smoking adults presenting with rather unspecific respiratory signs. The confirmation of the diagnosis is anatomopathological. Schematically, there are two entities with clinical and therapeutic characteristics: non-small-cell cancers (NSCLC) and small-cell cancers. Despite therapeutic advances, all stages combined, NSCLC has a poor prognosis. Treatment is based on surgery, but only 20% of patients are eligible for curative surgical treatment [3]. This surgical treatment requires a complete tumor resection, and even a pneumonectomy combined with a radical mediastinal lymph node dissection or perioperative treatment to offer the patients better long-term survival prospects.

Although many patients with NSCLC surgery go into complete remission, some have tumor recurrences in various locations and within different delays after surgery. The purpose of our work was to study the clinical, anatomopathological and therapeutic profile of these patients. We also noted tumor recurrence cases and studied their prognostic factors.

## METHODS

We conducted a retrospective study, conducted on 67 patients operated for NSCLC and treated between 1 January 2010 and 31 December 2016. Patients with NSCLC confirmed by the anatomopathological study and with curative surgery were included. Patients who refused to participate, and patients whose anatomopathological study revealed small cell cancer, typical or atypical carcinoid tumor, or secondary bronchopulmonary cancer were excluded.

Data collection was initially carried out with patients through a pre-established questionnaire containing socio-demographic data, habits, medical history, the consultation period defined by the time period between the onset of symptoms and the first consultation, the diagnosis circumstances, the clinical manifestations, the body mass

index (BMI) and the general state assessed based on the performance status (PS) of the World Health Organization. Secondly, via the patients' records we recorded

- The characteristics of the NSCLC including the location of the tumor (location and extent), the bronchial endoscopy data, the histological confirmation means, the histological type, the extension analysis, staging according to the TNM 2009 classification (7th edition) of the International Association for the study of lung cancer (IASCL) and the period of positive diagnosis defined by the time between the date of hospitalization and histological confirmation [4].

- Therapeutic management data including the therapeutic delay defined by the time period between the positive diagnosis and the beginning of the specific treatment, the type of the treatment, the starting date of treatment, the date of the surgical treatment, the surgical gesture, the various post-operative complications and the ultimate response to the treatment

The response to the treatment was considered completed when all lesions disappeared, the targeted lymphadenopathy had a small 10mm axis. Tumor progression was defined as an increase of more than 20% in the size, compared to the smallest sum and/or appearance of a new lesion. Third, the patient follow-up data were collected from the medical records and, failing that, the patients or their family members were contacted via telephone.

The point date has been set on 31 December 2017. This follow-up clarified:

- Locoregional and distant recurrences: recurrence of cancer cells, in the same place or in another location in the body.

- Overall survival: the time separating randomization and death regardless of the cause of the death.

Patients were considered to be lost if they had not consulted since leaving the ward or if they did not respond to the summons. Data were captured and analyzed using SPSS version 22. The quantitative variables were expressed as a mean standard deviation. Qualitative variables were expressed as a percentage (%). The survival estimate was obtained using the Kaplan-Meier method with the calculation of the Log-Rank test for the

univariate comparison. The investigation of predictive factors of postoperative recurrence was carried out in the univariate analysis. The difference would be considered significant if  $p < 0,05$ .

The design and conduct of the study was in accordance with the general principles outlined in the Declaration of Helsinki [5]. The ethics committee of Abderrahmen Mami Hospital approved the study and all subjects have given signed, informed consent in our study.

## RESULTS

During the study period, 67 patients were included. The average age of the study population was 61,8 years with extremes ranging from 42 to 76 years. Eighty-six percent of the patients (86%) were smokers (table1). Respiratory comorbidities were noted in 16 cases. Six patients had a chronic obstructive pulmonary disease and three had a past medical history of pulmonary or pleural tuberculosis. The average consultation time was 86 plus-minus 13 days, general signs were common in our series. Deterioration of the general state was observed in 58% of patients. It was the predominant symptom followed by coughing (42%) and chest pain (40%). NSCLC was discovered accidentally in only 8 patients.

**Table 1.** General characteristics of the study population

	Number of patients	Average
Average age (years)	67	61+/-8
Men/Women	64/3	
Smoking	58/67	
Mean tobacco intoxication (Pack-year)	--	50
Passive smoking	55/67	
Histological type		
Adénocarcinoma	42/67	
Squamous cell carcinoma	21/67	
Large cell carcinoma	2/67	
Adenosis carcinoma	1/67	
Non micro cellular carcinoma (no histological specificity)	1/67	

The extension analysis was based on: - Chest CT (CT) was performed in all patients.

- Abdomino-pelvic CT was performed on 59 patients

(88%). Abdomino-pelvic ultrasound was performed on 10 patients (15%). In our series, no patients had intra-abdominal metastases.

- The search for brain locations was performed by the brain scanner (50 patients 75%) or brain MRI (14 patients 21%). Brain MRI revealed brain metastases in one patient.

Bone scintigraphy was performed in 4 patients. In one patient it showed a hyper fixation in the 6th and 7th right ribs due to a contiguous lesion. Spinal MRI was performed on 2 patients and was normal. Histological diagnosis was made on average after 152±14 days after the appearance of clinical symptoms, with extremes of 35 to 400 days. An anatomopathological confirmation of the diagnosis was made through a bronchial biopsy in 13% of the patients, transparietal biopsy in 12% of the patients, and diagnostic and therapeutic surgery in 75% of the patients.

Adenocarcinoma was observed in 63% of the cases followed by squamous cell carcinoma in 31% of the cases (Table 1). The average time between the first consultation and the start of the specific treatment was 47±4 days. The mean period between the positive diagnosis and the beginning of the treatment was 10±2 days. All patients were discussed in a multidisciplinary consultation meeting before surgical treatment, the most commonly performed surgical gesture was lobectomy (42 patients) (Table 2). After surgery, the anatomopathological examination of the surgical specimen has permitted to set up the p TNM classification (Table2)

Chemotherapy was indicated for 49 patients. It was neoadjuvant for 2 patients, adjuvant for 39 patients and associated with radiotherapy for 8 patients. Chemotherapy was exclusive in 41 cases and combined with radiotherapy in 8 cases. For the majority of our patients, the chemotherapy consisted of a platinum salt combined with a molecule of 3<sup>rd</sup> generation (Vinorelbine or Gemcitabine or Docetaxel). In the case of contraindication to Cisplatin, Carboplatin was used. Neoadjuvant chemotherapy was indicated for 10 patients, exclusive for 2 patients and combined with adjuvant chemotherapy for 8 patients. All our patients received dual therapy.

The most commonly used protocol was Cisplatin-Gemcitabine therapy. It was given to 5 patients followed by Cisplatin-Vinorelbine therapy (3 patients) and Carboplatin-Gemcitabine therapy (2 patients). In our study, 60% of the patients who received neoadjuvant chemotherapy were

stage IIIA. The post-operative dual therapies were based on Cisplatin-Vinorelbine (27 patients), Carboplatin-Vinorelbine (3 patients), Cisplatin-Gemcitabine (10 patients), Carboplatin-Gemcitabine (5 patients) and Cisplatin-Docetaxel (2 patients). The majority of our patients who received adjuvant chemotherapy were Stage IIIA (45%), and 28% of them were Stage IIB. The administered molecule was the same as the neoadjuvant chemotherapy except for a 59-year-old patient, with stage IIIA classified adenocarcinoma, who received neoadjuvant Cisplatin-Gemcitabine and Cisplatin-Gemcitabine Vinorelbine as an adjuvant.

**Table 2.** Post-operative classification and patient treatment

	Number of patients
<b>Surgical procedure</b>	
Lobectomy	42/67
Pneumonectomy	8/67
Bilobectomy	4/67
Lobectomy + parietomy	5/67
Lobectomy+ tumorectomy	2/67
Lobectomy + Fowler resection	1/67
Lobectomy + cumen resection	1/67
Lobectomy + azygos vein arch resection	1/67
Tumorectomy	1/67
Wedge resection + lobectomy	2/67
<b>pTNM staging</b>	
pT IA	10/67
pT IB	4/67
pT IIA	6/67
pT IIB	18/67
pT IIIA	25/67
pT IIIB	1/67
pT IV	3/67
<b>Therapeutic strategy</b>	
Surgery alone	15/67
Neoadjuvant CT*+ surgery	2/67
Surgery+ adjuvant CT*	33/67
Neoadjuvant CT*+ surgery + adjuvant CT*	6/67
Surgery+ adjuvant CT*+ adjuvant RT*	6/67
Surgery+ adjuvant RT*	2/67
Cerebral surgery + cerebral RT*+thoracic Surgery	1/67
Neoadjuvant CT*+ surgery+ adjuvant CT*+ adjuvant RT*	1/67
Neoadjuvant CT*+ Neoadjuvant RT* + Surgery+ Adjuvant CT*	1/67

CT\* : chemotherapy ; RT\* : radiotherapy.

It should also be noted that the adjuvant chemotherapy molecule was modified during the treatment by replacing cisplatin with carboplatin for 2 patients due to renal toxicity for one of them and digestive intolerance for the other patient. Radiotherapy was indicated for 12 patients but only 11 patients (16%) received this treatment. Adjuvant radiotherapy was indicated for 9 patients. It was indicated given the presence of a parietal or mediastinal lymph node involvement, a patient, however, was lost to follow-up before initiating the radiation therapy (Table 2).

In our series, a patient classified cT3N0M1 b, had a single brain metastasis surgery followed by brain radiotherapy then was referred to our department for surgical treatment of his primary tumor. Two cases of pulmonary metastasis were reported, one had wedge resection and the second a lobectomy associated with neoadjuvant and adjuvant chemotherapy.

The average duration of the follow-up, calculated from the date of surgery, was  $770 \pm 79$  days (extreme 9 to 2506 days). It was concluded that 43% were living in apparent good health, 22% were living in therapeutic failure, 28% were dead and 7% were lost to follow-up.

Tumour recurrence was noted in 40% of patients with locoregional (44%), distant (30%) and associated (26%) recurrences. The average time between surgical treatment and recurrence was  $12 \pm 2$  months with extremes ranging from 2 to 49 months. The recurrence locations were pulmonary (n=19), cerebral (n=7), hepatic (n=6), nodal (n=6), adrenal (n=3), osseous (n=3) and pancreatic (n=1). The average age of patients who went through a recurrence was  $60 \pm 8$  years. The study of the progression of our patients showed that 85% of the patients who had a recurrence were smokers with a mean consumption of  $43 \pm 4$  Pack-year and the majority of our patients who had tumor recurrence presented chest signs at the first hospitalization in our department (81%).

The most common histological type found in patients with tumor recurrence was adenocarcinoma (43%) followed by squamous cell carcinoma (29%);  $p=0.14$ . The broncho-pulmonary cancers that recurred were mainly locally advanced or metastatic cancers (Table 3).

The distribution of recurrences according to the surgical procedure showed that 33% of patients with lobectomy had a recurrence. In contrast, 50% of patients with pneumonectomy experienced recurrence ( $p=0.06$ ). The

association of chemotherapy with surgery was found in 89% of patients with tumor recurrence (Table 4).

**Table 3.** Recurrence distribution by stage pTNM

Stage	Number of patients	Number of recurrence	% of recurrence in every stage
IA	10	1	10%
IB	4	0	0%
IIA	6	3	50%
IIB	18	7	39%
IIIA	25	13	52%
IIIB	1	1	100%
IV	3	2	67%

**Table 4.** Proportion of recurrence for each specific treatment.

Strategy	Number of patients	Number of recurrence	% of recurrence in every group
Surgery alone	15	1	7
Neoadjuvant CT*+ surgery	2	0	-
Surgery+ adjuvant CT*	33	17	52
Neoadjuvant CT*+ surgery + adjuvant CT*	6	3	50
Surgery+ adjuvant CT*+ adjuvant RT*	6	3	50
Surgery+ adjuvant RT*	2	1	50
Cerebral surgery + cerebral RT*+thoracic Surgery	1	1	100
Neoadjuvant CT*+ surgery+ adjuvant CT*+ adjuvant RT*	1	1	100
Neoadjuvant CT*+ Neoadjuvant RT* + Surgery+ Adjuvant CT*	1	0	-

CT\* : chemotherapy ; RT\* : radiotherapy.

Chemotherapy after recurrence was indicated in 18 patients. The most widely used protocol was based on Docétaxel alone proposed for 9 patients, Vinorelbine in monotherapy was indicated in 2 patients. Combinations of a Carboplatin+ Gemcitabine, Cisplatin+Vinorelbine Cisplatin + Docetaxel and Cisplatin + Pemetrexed were indicated for one patient each. Palliative radiotherapy was indicated for 8 patients. It was performed on the brain for 6 patients. It was for a palliative analgesic purpose for 1 patient and thoracic and mediastinal for another one. A

specific surgical treatment for recurrence was indicated for 4 patients. There was a cerebral metastasectomy for 2 patients, a wedge of a contralateral pulmonary nodule for 1 patient, and a resection of the anterior arch of the second left rib associated with tumorectomy for 1 patient.

One patient was lost to follow-up before initiating a specific treatment and another patient with a bad general condition could not support the treatment of the recurrence. It should be noted that three patients had died just after the discovery of the recurrence. The starting date of the follow-up was the date of the patient's first hospitalization. The mean overall survival of our patients was 56±4 months for all histological types combined with an overall survival probability of 70% at 1 year and 13% at 5 years for all stages

Patients with early-stage NSCLC survived for longer periods of time compared to patients with advanced tumors. Pulmonary adenocarcinoma was associated with the most prolonged survival rates (56±5 months) compared to squamous cell carcinoma (50±5 months) (p=0.15). Survival benefit was shown in patients who received adjuvant and/or neoadjuvant chemotherapy compared to those treated by surgery alone (56 ± 5 months Vs 45± 6 months; p=0.23), for survival after recurrence, patients who received adjuvant chemotherapy survived longer than those who did not receive chemotherapy after chest surgery with a significant difference ((46 ±6 months Vs 15 ± 4 months; p=0.008).

In our study, it was found that surgery influenced the survival rates of our patients since the best survivals were recorded in groups of patients who underwent lobectomy. Indeed, the best lifespan from the first visit to our department was for the patient classified stage IIIA who had a lobectomy associated with a tumorectomy with a survival of 83 months followed by the patient classified IIIA who underwent an unenlarged single lobectomy and survived for 77 months. The prognostic factors that had improved the survival of our patients were the absence of mediastinal lymph nodes (58±5 months vs 52± 7 months; p=0.004) and adjuvant chemotherapy (p=0.08).

Smoking affected the overall survival in patients with NSCLC (56±5 months vs 50± 5 months) (p=0.01), especially in cases of significant tobacco intoxication (>25PA) (p=0.016). The advanced stage or the presence of metastases (58±7 months vs 51±4 months; p=0.04) harmed the survival. Age had no significant influence on

the overall survival. This last was comparable between patients over the age of 60 and younger patients ( $p=0.12$ ). Recurrence also did not have a significant impact on average survival ( $45\pm 6$  months) for patients who had a recurrence ( $p=0.43$ ).

## DISCUSSION

The diagnosis of NSCLC is based on anatomopathology. Surgery can provide the diagnosis, it is only recommended in case of a strong suspicion of bronchial cancer with the impossibility of obtaining a confirmation by less invasive means, or if a curative excision seems possible [6]. In our series, thoracotomy was used to establish the diagnosis in 75% of the patients, it was performed in 49.5% of the patients in the study of Riquet et al. [7]. According to our study, the distribution of histological types of NSCLC has changed in recent years, marked by a higher incidence of adenocarcinoma, which can be explained by the use of blond tobacco, the use of filters and the increase of nitrosamines in cigarettes.

The purpose of the extension analysis is staging the tumor. In the recommendations of the National Cancer Institute, the initial extension of the NSCLC is based on clinical examination, systematic bronchial endoscopy with biopsies and thoracic CT abdomino-pelvic with a bone window reading. If at the end of this assessment, the tumor is accessible to a locoregional treatment, a CT scan or, at best, a brain MRI will be performed. If all this initial extension balance is negative, it is necessary to complete the scans with a PET scan [8]. In our daily practice, we comply with the recommendations concerning the extension report. However, PET was not performed for patients in our study due to its unavailability in the public sector.

The TNM classification and staging guide the therapeutic attitude. The difference between our series and the French series in the number of early stages and the high rate of advanced stages can be explained by the delay in consultation in our country and the lack of NSCLC screening in our context. Indeed, the average time between the discovery of the first symptoms and the first consultation was  $86\pm 13$  days, longer than the French studies [9]. This difference can be explained by the patient's ignorance of the probable nature of these symptoms and the distance separating patients from care centers. However, the

time frame for positive diagnosis was comparable to other international series [10] but is still longer than the BTS recommendations, where it is recommended not to exceed two weeks [11]. In our department, 11% of NSCLC received curative surgical treatments. This figure is comparable to national studies [12] but, lower than a study in France where 21,7 % of the patients were operated [13]. In our series, 22% of the patients received exclusive surgical treatments, 73% received perioperative chemotherapy, 16% received radiotherapy, and only 12% received chemotherapy associated with radiotherapy and surgical treatments.

In the ESCAP-2011-CPHG study, including 741 patients with surgery, 56.9% had no other treatments, 34.7% had chemotherapy, 5.9% had radiation therapy, and 2.6% had radiation therapy [14]. The difference between the results could be explained by the later stage of the NSCLC discovery in our country. Lobectomy was the most common surgery in our series (63% of cases), and studies have shown that a lobectomy associated with a lymph node dissection is the reference procedure if the patient's respiratory state allows it [15]. At the clinical level, atypical wedge resections are generally less successful in terms of local recidivism and are reserved for patients at risk [16].

Systematic lymph node cleansing has been performed for all our patients and allows a more accurate evaluation of lymph node status that could not be performed by systematic sampling. A neoadjuvant treatment (NAT) was performed for patients who had a preoperative histological diagnosis (15% of the cases in our series). The "downstaging" after NAT may enable surgery in nearly half of the tumors initially not resectable [17] and would allow the disappearance of the lymph node invasion N2 in 20 to 30% of the cases [18]. Thoracic oncology experts may choose an adjuvant radiotherapy in cases of N2 with a capsular break or in cases of parietal invasion.

It reduces the risk of local tumor recurrence for IIIA N2 stages without a current demonstration of improved survival [19]. Oligo-metastatic NSCLC may benefit from the combination of a surgical treatment of the primary tumor and the metastasis and post-operative chemotherapy especially in the case of isolated adrenal, cerebral and pulmonary metastases [20]. In our series, two patients had metastasis surgery (brain, lung). Patient follow-up in our department after chest surgery was based on a clinical examination and a chest x-ray every three months and a

chest CT abdominopelvic and cerebral semester during the first two years then once a year.

There is no consensus on the follow-up of patients with NSCLC. The follow-up should, therefore, be tailored to the patient. In a retrospective study, the survival since surgery of operated patients under scheduled surveillance was no different from that of patients who only consulted for symptoms [21]. However, recurrence is sometimes unavoidable after a variable delay. Tumor recurrence rates range from 20% to 50% among patients with resected early-stage NSCLC [22].

In a study carried out in Switzerland, after a radical resection of 2449, 44.4% of the cases developed a recurrent distant tumor. It was local for 26% of the cases, and loco-regional and distant for 16.9% of the patients [23]. In our study, tumor progression was noted in 27 patients (40%) with a locoregional recurrence in 44% of the cases, a distant recurrence in 30% of the cases, and 7 associated recurrences (26%). These results are more encouraging than previous studies where recurrence rates were higher. A French prospective study found 70.8% of recurrence [24]. In our series, the average time between a specific treatment and tumor recurrence was  $12 \pm 2$  months. There were 5 early (6 months) and 22 delayed (6 months).

In our series, the majority of recurrences had lobectomies (51.8%). However, this does not prove that lobectomies increase the rate of recurrence since the majority of our operated patients have benefited from it (62.7%). According to the lobectomy series [25], 34% of patients developed a recurrence of the disease. Furthermore, in an earlier study, more limited resections (wedge or segmentectomy) were associated with a high risk of regional recurrence [26]. In our study, older age (older than 60), smoking, adenocarcinoma, advanced or metastatic stage, and pneumonectomy were high-risk factors for recurrence.

According to an American analysis of 293 NSCLC patients who underwent lung resection, the factors associated with a higher rate of recurrence were active smoking, cancer history, tumor size, anatomical resections, adenocarcinoma, pleural and visceral invasion, and angiolymphatic invasion [27]. Furthermore, according to a recent meta-analysis, pre-operative chemotherapy would decrease the risk of recurrence, improve overall survival, distant recurrence delay, and non-recurrent survival in resectable NSCLC [28]. In the case of local recurrence,

a surgical restart or radiation chemotherapy may be proposed depending on the extension. In our series, a specific surgical treatment for recurrences was indicated for 4 patients. Metastasis surgery was indicated for three patients.

The majority of our progressing patients received chemotherapy (66.7%). Only 2 patients received chest radiation and 6 patients received a cerebral radiation. According to Saynak, for patients with metastatic recurrence who have not received chemotherapy during their first-line treatment, the treatment of recurrence will consist of chemotherapy such as those usually offered in a first-line treatment, however, for patients who have received adjuvant chemotherapy, the therapeutic strategy is not defined [29].

As with any retrospective analysis, our study has its limitations. Although local recurrences were sometimes confirmed by biopsy, overestimation could be caused by using imaging studies to retain the diagnosis of recurrence. The mean overall survival in our study was  $56 \pm 4$  months, while the mean survival for patients with recurrence was  $45 \pm 6$  months ( $p=0.43$ ).

The survival numbers in our series were low compared to the literature due to a prolonged delay between the onset of symptoms and the first visit. Overall survival was 21.6% at 5 years, all stages, for NSCLC in the United States [30].

In our study, overall survival was higher for patients in the early stages especially in case of the absence of mediastinal lymph node involvement. Other prognostic factors found influencing the survival of our patients were young age, as well as the introduction of specific treatments essentially adjuvant chemotherapy. Smoking, the importance of tobacco poisoning ( $>25PA$ ), and the presence of metastases harmed survival chances. This matches with literature data [31;32] Mediastinal lymph nodes extension would be the most predictive factor of poor prognosis of operated NSCLC [33]. These results are consistent with our series where overall survival was better for NSCLC operated at the localized stage compared to the locally advanced or metastatic stage with a significant difference ( $p=0.04$ ).

A Phase III randomized trial demonstrated the superiority of neoadjuvant chemo-radiotherapy over neoadjuvant chemotherapy in terms of overall response rates and local control. However, there was no difference in SG between

the two arms [34]. According to the European Society for Medical Oncology Guidelines Working Group, adjuvant chemotherapy should be proposed for patients with Stage II and Stage III resected NSCLC and may be considered in operated Stage IB patients, and for a primary tumor >4 cm. Pre-existing comorbidity, operative time, and post-operative recovery should be considered in this decision [35].

Our results are close to those in the literature where survival was better for patients who received adjuvant chemotherapy compared to those who did not receive postoperative chemotherapy. We also found that the surgical procedure influenced the survival of our patients since the best survival was recorded for patients who received a lobectomy. This is consistent with studies where survival rates at 5 and 10 years were significantly worse after wedge-resection compared to lobectomy [36], the latter also showed superiority compared to segmentectomy [37].

### CONCLUSION

Recurrent broncho-pulmonary cancers were mainly at a locally advanced or metastatic stage. Adjuvant chemotherapy increased the survival chances of operated patients with recurrent cancer. In our study, it was found that surgery influenced the survival of our patients as the best survivals were recorded for patients who received lobectomy.

The increasing number of cancers discovered at an early stage and the shortening of the consultation period could explain the improvement of survival and the risk of recurrence. Therapeutic innovations and surgical techniques development have contributed to the improved prognosis of NSCLC.

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