ORIGINAL ARTICLE

PANCOAST TUMORS: 11-YEAR SINGLE-CENTRE EXPERIENCE

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Abstract

***Introduction**: Pancoast tumors encompass any tumor located on the lung apex, extending into structures in the thoracic inlet and, often, leading to the characteristic clinical syndrome. The main goal of this study is to analyze the response to multimodal treatment and outcome of patients with Pancoast tumors.*

***Materials and Methods:** We performed a retrospective cohort single center study of patients with superior sulcus non-small cell lung carcinomas who underwent surgery between January of 2011 and February of 2022.*

***Results:** A total of ten patients were considered, 80,0% were male with a mean age of 53,6 (±6,6) years. At diagnosis, two tumors were stage II and eight were stage III. Histopathology revealed eight were adenocarcinomas and two were sarcomatoid carcinomas.*

All patients underwent neoadjuvant treatment before surgery. Nine patients received lung lobectomy, with en bloc resection comprising, predominantly, the chest wall (80,0%) and brachial plexus (30,0%). In one patient, surgery was aborted.

Surgical histopathology showed free surgical margins were achieved in eight patients (80,0%). Two patients achieved full tumoral remission (ypT0N0, 22,2%), two tumors were stage I (22,2%), two were stage II (22,2%), two were stage III (22,2%) and one tumor was stage IV (11,1%).

Mean disease-free survival was 83,9 (CI95% 42,1-125,8) months. 3-month disease-free survival rate was 88,9% and 1-year and 5-year disease-free survival rates were 63,5%. After the first-year follow-up, there was no evidence of disease progression. Mean overall survival was 115,7 (CI95% 89,3-142,1) months. At 3-month, 1-year and 5-years, overall survival was 88,9%.

***Conclusion:** Although considering the small sample of patients, the survival of Pancoast tumors in our institution exhibits a positive outcome, when compared to current literature, Significant improvements have been reported recently, in understanding the nature of Pancoast tumors, emphasizing the importance of a multidisciplinary approach but still, further research is required.*

***Keywords:** Superior sulcus tumor; Pancoast tumor; Shaw-Paulson; Thoracotomy; Surgery*

INTRODUCTION

Pancoast or superior sulcus tumors are a unique type of lung carcinoma (3-5%)[1-3] located in the apex of the lung with distinctive clinical symptoms due to the invasion by contiguity of the structures of the thoracic inlet.[1,2,4] Hence, by definition, these tumors are classified as T3 or T4 (according to the 8th TNM classification).[5]

Primarily, the most common symptoms are shoulder pain, which may radiate along the ipsilateral arm, typically along the anatomic distribution of the ulnar nerve due to brachial plexus disruption as well as anterior thoracic pain caused by intercostal nerve invasion or chest wall destruction. However, depending on the exact location of the tumor, the invaded structures diverge, determining different presenting clinical features.

A primary trait in Pancoast tumors is upper rib invasion with consequent bone destruction, leading to anterior chest wall pain and deformation. Diagnostic imaging beginning with chest radiography reveals osteolytic lesions adjacent to the lung apex tumor, highlighting suspicion to this type of malignancy.

Pancoast tumors located in the anterior compartment of the thoracic inlet may invade early the first intercostal nerves and subclavian vein. They may present with pain radiating along the anterior chest wall and venous thrombosis. Infrequently, they may also lead to superior vena cava syndrome.

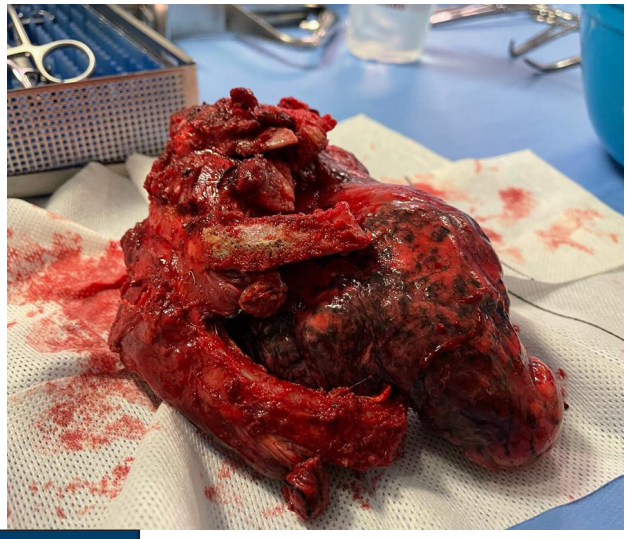

Figure 1 *En bloc resection of upper lobe and chest wall*

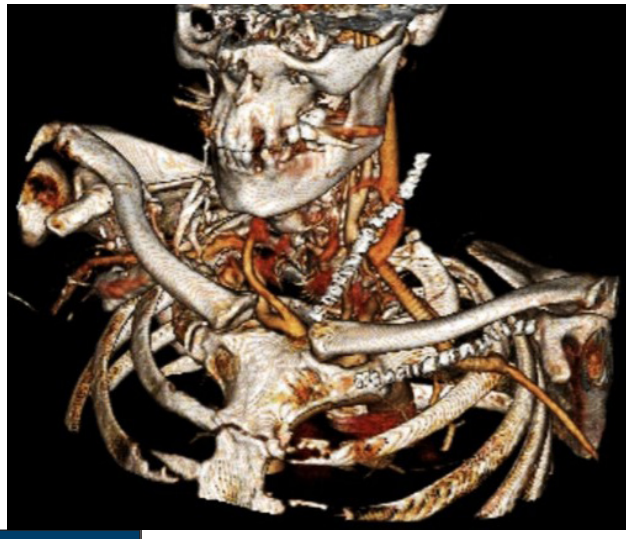

Figure 2 *Carotid axillary arterial bypass prior to tumoral resection*

Table 1 **Baseline Characteristics**

	n	%
Gender		
Female	2	20,0
Male	8	80,0
Mean Age (SD)	**53,6**	
Mean Tobacco Exposure (pack-years)	**41**	
ECOG Performance Status		
Score 0	7	70,0
Score 1	3	30,0
Comorbidities		
Chronic obstructive pulmonary disease	2	20,0
Oropharyngeal cancer	1	10,0
Chronic ischemic heart disease and Arterial Hypertension	1	10,0
Affected Lung		
Upper Right Lobe	6	60,0
Upper Left Lobe	4	40,0
Histopathology		
Adenocarcinoma	8	80,0
Sarcomatoid Carcinoma	2	20,0
Stage at the diagnosis (8th TNM)		
IIB	2	20,0
IIIA	6	60,0
IIIB	1	10,0
IIIC	1	10,0

Table 2 **Treatment Modality**

	n	%
Neoadjuvant Chemotherapy	**1**	**10,0**
Neoadjuvant Chemoradiotherapy	**9**	**90,0**
Surgery		
Lobectomy + Lymph node dissection	1	10,0
Lobectomy + En bloc resection + Lymph node dissection	8	80,0
Chest wall excision	8	80,0
Brachial plexus excision	3	30,0
Sympathetic chain excision	1	10,0
Subclavian artery excision	2	20,0
Exploratory Thoracotomy	1	10,0

When located in the middle compartment, compression or invasion of the brachial plexus (predominantly C8-T1 nerve roots) results in pain and paresthesia in the ipsilateral upper limb and atrophy of the intrinsic muscles of the hand. The tumor may also affect structures such as the subclavian artery or the phrenic nerve with subsequent diaphragm paralysis.

Tumors lying in the posterior compartment cause pain along the axillary region and medial compartment of the arm. They may infiltrate the sympathetic chain and stellate ganglion, resulting in Horner's syndrome, composed of the clinical triad of ipsilateral ptosis, miosis and anhydrosis. In late stages, involvement of the spine and vertebral bodies may be identified.[1,6]

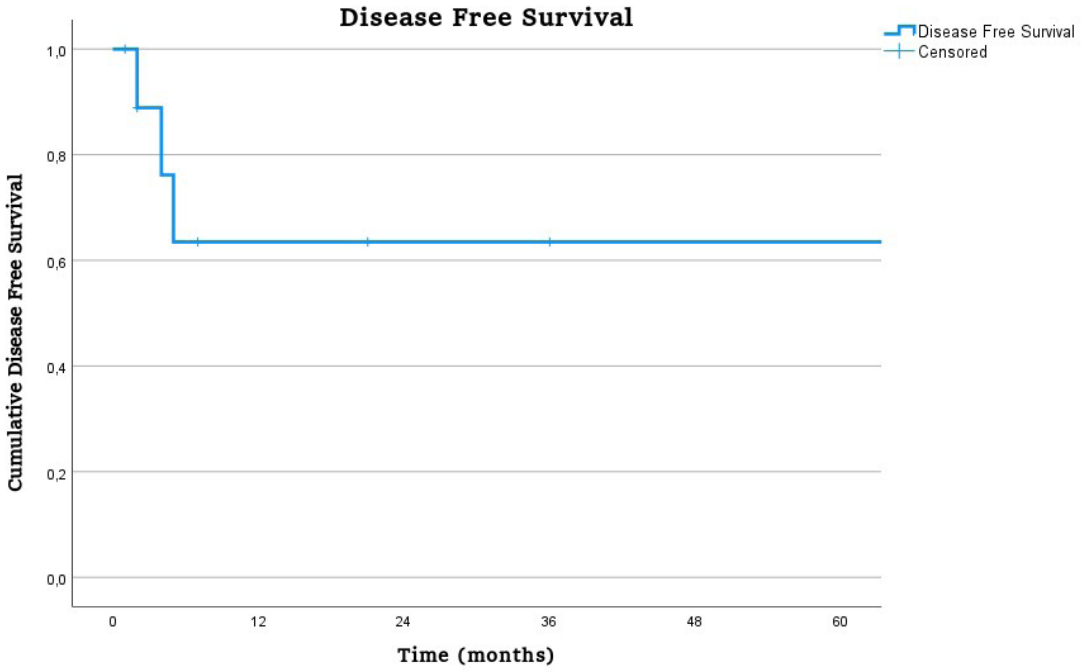

Figure 3 *Disease-Free Survival*

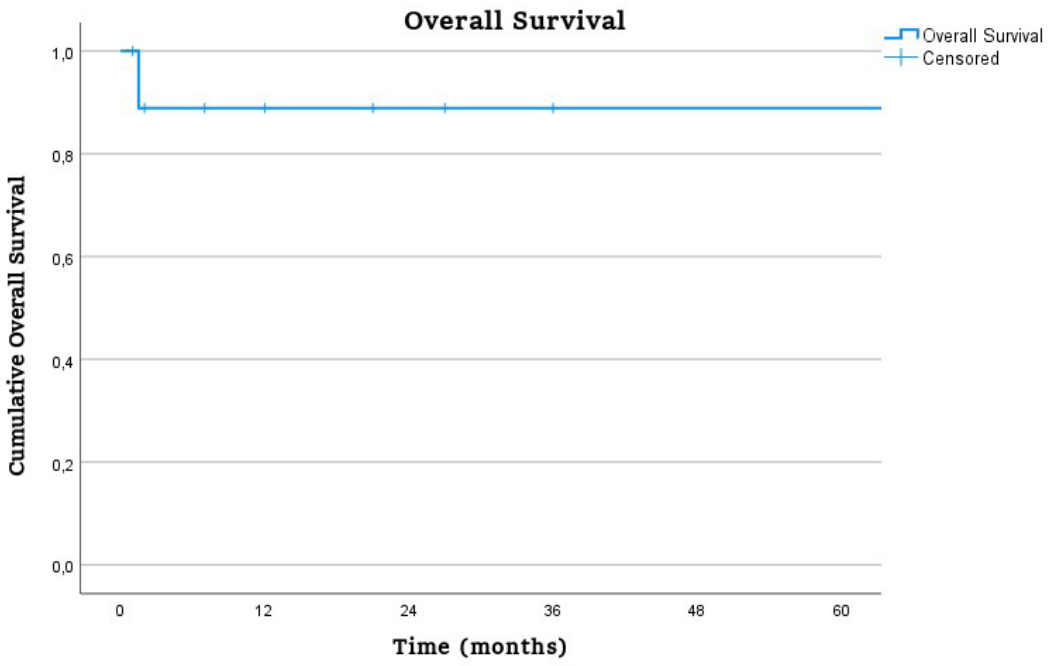

Figure 4 *Overall Survival*

Table 3 Detailed pathological response to multimodal treatment

Pre-treatment TNM	Post-operative TNM	Resection	Final Stage
cT3N0M0	ypT0N0	R0	ypT0N0
cT3N0M0	ypT3N0	R1	IIB
cT3N2M0	ypT0N0	R0	ypT0N0
cT4N0M0	ypT1N0	R0	IA
cT4N0M0	ypT3N0	R0	IIB
cT4N0M0	ypT4N0	R0	IIIA
cT4N1M0	ypT1N0	R0	IA
cT4N1M0	ypT3N1	R0	IIIA
cT4N3M0	ypT3N0M1a	R0	IVA

Table 4 Clinical presentation

Clinical Presentation	At diagnosis	After surgery n (%)
Asymptomatic	1 (10,0)	2 (25,0)
Pain (ipsilateral upper limb)	8 (80,0)	0
Paresthesia (ipsilateral upper limb)	2 (20,0)	4 (50,0)
Decreased strength (ipsilateral upper limb)	1 (10,0)	3 (37,5)
Ptosis	1 (10,0)	1 (10,0)
Horner Syndrome	1 (10,0)	2 (25,0)

For many years, Pancoast tumors were considered unresectable and thought to have a fatal prognosis.[2,7-9] Recent improvements in the management for Pancoast tumors led to the endorsement of a triple-modality treatment based on neoadjuvant chemoradiotherapy and radical surgical resection,[2,6] with encouraging results in the disease-free and overall survival.[3,8,10]

The main surgical goal is complete resection, encompassing an en bloc upper lobectomy with excision of all invaded components. Its location and proximity to vital structures constitutes a surgical technical challenge.[7]

The present study reviewed the clinical features and management of patients with Pancoast tumors referred to our center for surgical treatment over the past decade. The aim is to report our experience and present the survival outcomes for this subset of lung tumors.

METHODS

A retrospective cohort study was conducted to identify all patients with superior sulcus non-small cell lung carcinomas who underwent surgery at the Thoracic Surgery Department, between January of 2011 and February of 2022.

This study only comprised primary non-small cell lung carcinomas and excluded secondary pulmonary lesions.

We analyzed clinical hospital records and compiled the following items: personal demographic characteristics and smoking habits, clinical presentation, histologic tumor type and cTNM (status at diagnosis), neoadjuvant and adjuvant regimen treatments, surgical procedure and extent of resection, resolution of symptoms, overview of hospital stay, status of disease after multimodal treatment and at the last follow-up consultation and, if applicable, date and site of relapse.

When not available, follow-up information was obtained by direct communication with the patient or the referring physician. No patient was lost during follow-up.

Pancoast tumors were staged according to the 8th edition of TNM staging system for non-small cell lung carcinoma.

A complete response to treatment was considered if ypT0N0, along with free surgical margins, were reported after pathological examination.

Overall survival was defined as the period between the date of surgery and date of the patient's death. Disease-free survival comprehends the time between the date of surgical treatment and evidence of disease relapse (locoregional or metastatic).

Categorical variables were presented in absolute value and percentage format and the continuous variables with mean value and standard deviation. The survival outcomes were analyzed with the Kaplan Meyer method. Statistical analysis was performed using IBM SPSS 27 software.

RESULTS

During the eleven-year period considered in this study, we identified eleven patients with Pancoast tumors. Ultimately, one patient was excluded due to the diagnosis of breast cancer metastasis.

Hence, this study encompassed ten patients, with male predominance (80,0%) and a mean age at the time of diagnosis of 53,6 (±6,6) years. All patients were smokers with a mean amount of 41,0 (±28,5) pack-years. Four patients had major comorbidities (namely, chronic obstructive pulmonary disease, oropharyngeal cancer, chronic ischemic heart disease and, arterial hypertension). Moreover, all presented with a performance status of 0-1, according to Eastern Cooperative Oncology Group (ECOG) score. The demographic features are compiled in table 1.

Preoperative evaluation for all patients included clinical history, physical examination, routine blood tests, electrocardiogram and echocardiogram, chest x-ray and spirometry. Pulmonary function test evaluation showed mean values of FEV1 of 92,0% (±10,1) and DLCO of 61,9% (±9,0).

Oncologic diagnosis and staging integrated whole body computed tomography scan (CT), brain magnetic resonance imaging (MRI) and 18-fluorodeoxyglucose positron

emission tomography (PET) whole-body scan, bronchoscopy and, transthoracic biopsy of the tumor, when feasible.

Preoperative mediastinal lymph node evaluation was performed in 70,0% (n=7) of patients through endobronchial ultrasound (30,0%) and mediastinoscopy (40,0%). Status of N+ disease was found in 40,0% (n=4) of patients, as demonstrated in table 3.

Angiography and upper limb MRI were carried out only in selected cases of suspected neurovascular invasion (40,0%, n=4) in order to confirm structural involvement, define extent of disease and delineate the surgical strategy.

There was no evidence of distant metastatic disease in our sample of patients.

At the time of diagnosis, two of the Pancoast tumors were classified as stage II and eight as stage III (8th TNM classification). Histopathology study was conducted in all cases and showed eight were adenocarcinomas and two were sarcomatoid carcinomas.

The most frequently observed symptom at presentation was pain (80,0%) followed by paresthesia (40,0%) in the ipsilateral upper limb. Only one patient presented with Horner's syndrome, as depicted in table 4.

Nine patients received combined neoadjuvant chemoradiotherapy and one patient received neoadjuvant chemotherapy.

In one case, the surgical procedure was aborted because surgical findings rendered it inadvisable (tumoral invasion denoted the need for pneumonectomy and extensive resection of vascular and airway structures). Consequently, the patient completed selected treatment with definitive chemoradiotherapy. The treatment regimens are summarized in table 2.

Shaw-Paulson incision was the approach used in all cases. Surgery consisted of lung lobectomy and mediastinal lymph node dissection, in addition to en bloc resection of the invaded structures, comprising the chest wall (80,0%) and the brachial plexus (30,0%), as illustrated in figure 1. In two patients (20,0%), the need for vascular resection was anticipated and an arterial bypass was performed prior to the procedure, as shown in figure 2.

The mean pleural drainage time was 5,8 (±2,6) days. Mean hospital stay was 7,6 (±3,0) days.

One death (10,0%) was accounted postoperatively, linked to the development of aspiration pneumonia and declining respiratory capacity (50th postoperative day). No other major complications were identified.

A complete surgical resection (R0) was achieved in eight of the nine patients who underwent surgical resection. Histological evaluation showed an overall evidence of tumor downstaging with neoadjuvant systemic treatment and surgery, as demonstrated in table 3.

Postoperative oncologic staging in the nine patients who underwent surgical resection highlighted two patients (22,2%) who achieved full tumoral remission as well as two tumors in stage I (22,2%), two in stage II (22,2%), two in stage III (22,2%) and one tumor in stage IV (11,1%).

The later corresponded to a lung adenocarcinoma located in the right upper lobe with suspected infiltration of the first two ipsilateral ribs, the transversal processes of the first two dorsal vertebras as well as lymph nodes located in the right paratracheal and the aortopulmonary stations (cT4N3M0). The patient completed induction chemoradiotherapy with a good therapeutic response, demonstrating complete regression in terms of lymph node and vertebral invasion although maintaining second rib destruction. At this time, the tumor was classified as ycT3N0M0. Surgical treatment allowed for en bloc lobectomy and second rib excision. Histopathology revealed malignant infiltration of the second rib, with no signs of direct invasion and established complete resection of local disease, classifying the tumor as pT3N0M1a (stage IV). The patient underwent adjuvant chemotherapy and, presently, three years after the surgical intervention, remains alive with no evidence of disease progression.

Solely, three patients underwent adjuvant chemotherapy after surgery.

Additionally, the patient in which surgical procedure was aborted, presented full radiological remission, after definitive chemoradiotherapy.

Following surgical treatment, the most common presenting symptom was paresthesia (40,0%), as observed in table 4. Surgery allowed for positive clinical results, specifically in pain management. Two patients achieved complete clinical resolution.

The mean follow-up time after surgery was 32,3 (±42,8) months. One patient relapsed locally after five months while one patient experienced distant metastization four months after the surgical procedure.

Mean disease-free survival was 83,9 (CI95% 42,1-125,8) months. 3-month disease-free survival rate was 88,9% and 1-year and 5-year disease-free survival rates corresponded to 63,5%. After the first follow-up year, no disease progression events were detected in our sample of patients.

Mean overall survival was 115,7 (CI95% 89,3-142,1) months. At 3-month, 1-year and 5-years, overall survival was 88,9%. The Kaplan Meyer curves of disease-free and overall survival are represented in figures 3 and 4, respectively.

DISCUSSION

Pancoast tumors are rare, representing less than 5% of non-small cell lung carcinomas, with the majority accounting to adenocarcinoma.[4,11] The most important risk factor contemplated is cigarette smoking. [11]

Clinical presentation may vary extensively contingent of the structures affected in the thoracic inlet. Some syndromes are typically correlated with superior sulcus tumors, and although not required for the diagnosis, should evoke an in-depth investigation, specifically Horner's syndrome due to invasion of cervical sympathetic innervation or Pancoast syndrome, owing to infiltration of the brachial plexus.[1,2,12,13]

The Pancoast tumors management is still considered a challenge due to the aggressive nature of the disease and the complex anatomy of the region compromised.[4,7,8] Thus, this subtype of tumors conveys the importance of an individual assessment in a multidisciplinary setting to decide the best course of action.

Optimal therapeutic strategy considered at present is a trimodal approach with chemoradiotherapy and resection surgery encompassing all invaded structures, with encouraging results in controlling the malignant growth.[2,4,7,8,14,15]

The importance of neoadjuvant treatment is magnified by the fact that less than 50% of Pancoast tumors are considered resectable at presentation.[1,12]

Two large phase II trials, SWOG 9416 (launched by the North American Southwest Oncology Group) and JCO 9806 (by the Japan Clinical Oncology Group), showcased that induction chemoradiotherapy allowed for significant reduction in tumor size, achieving a radiologic partial response in 42% and 61% of patients, respectively. The positive pathologic response to chemoradiotherapy was associated with a high rate of complete surgical resection, attained in 87% (SWOG 9416) and 89% (JCO 9806) of patients. Both studies also displayed a 5-year overall survival, reaching 44% (SWOG 9416) and 56% (JCO 9806).[2,4,7,14,16–19]

The induction with chemoradiotherapy can be safely administered, increasing the chance of pathologic tumor remission and sustained survival.[4,7]

Additional studies, such as Goldberg et al (2005), Mara et al (2007), Fischer et al (2008) and Kappers et al (2009), have also highlighted the role of neoadjuvant chemoradiotherapy in allowing for R0 resections, in 76 to 100% of cases. Dual induction therapy in conjunction with surgery improved the rate of 5-year overall survival, at 37 to 59%.[4] In a more recent study, Lin et al (2021), confirmed the aforementioned results with complete resection achieved in 97% of patients submitted to trimodality treatment and a 5-year overall and disease-free survival rate of 50,1% and 47,1%, respectively.[15]

Additionally, chemoradiotherapy was associated with a higher rate of disease-free and overall survival when compared with single systemic neoadjuvant treatment.[3,7–10] Wright et al (2001) showed the superiority of induction chemoradiotherapy when compared to induction radiotherapy, in terms of complete surgical resection (93% vs 80%) and overall survival of 84% vs 49%, at the 4-year period.[4,7] Tamura et al (2009) have also described a difference in complete resection rate, with a mean value of 95% in trimodality treatment compared to 62% in a bimodality treatment plan (induction radiotherapy and surgery) and 5-year overall survival between 44 to 59% with chemoradiotherapy and surgery related to 37% rate for bimodality studies.[7,20]

In our institution, preoperative induction therapy with chemoradiotherapy was generally preferred and seemed to demonstrate significant impact in the reduction of tumor size, allowing a high rate of complete surgical resection. Therefore, we report R0 in eight of the nine patients who underwent surgical resection.

Three patients underwent adjuvant chemotherapy. In two, histological examination revealed residual malignant activity, determining positive nodal disease (ypT3N1M0) in one case and bone infiltration (ypT3N0M1a) in the other, as explained beforehand. The third case showed tumor size reduction after neoadjuvant chemoradiotherapy regimen with final postoperative staging of IIB (ypT3N0M0) with free surgical margins. The only other case of stage IIB had compromised surgical margins and, as described, suffered an early postoperative death. Hence, in our study, adjuvant chemotherapy was reserved to patients with advanced oncologic stage, following surgical specimen assessment.

In this era, new targeted therapies have been developed through the analysis of molecular oncologic markers. The identification of molecular tumoral expression has expanded the therapeutic targets, allowing for an individualized treatment strategy.[21] There is still limited evidence in the application of immunotherapy in Pancoast tumors. One case report has been recently published, where neoadjuvant tislelizumab and chemotherapy were applied to a stage IIIA Pancoast tumor, having achieved a 71% tumor reduction, and complete pathologic response after surgical treatment.[21] Currently, multiple trials to test the efficacy of induction treatment of immunotherapy and chemotherapy in these subset of patients are underway and results are yet to be published (one example is the DUMAS study, a phase II, single-arm, multicentric Spanish clinical trial).

Lung cancer treatment has greatly evolved in the last decade. The advances of target therapy and immunotherapy in the treatment of lung cancer are promising and may soon change the perception of the Pancoast tumors and improve the prognosis of these patients.

Overall, the most important prognostic factors are completeness of resection, T and N status of the Pancoast tumor as well as pathologic complete response.[8,9,20]

A considerably higher survival rate was exhibited when considering only patients who possessed R0 surgical margins.[4,8] Martins et al (2015) conducted a retrospective study showcasing positive results after resection surgery with curative intent, in a Portuguese surgical center.[12] The SWOG 9416 trial had also reported an improvement from 41% of 5-year overall survival for all patients to 53% for those with complete resection.[18,19]

Therefore, complete resection is considered the most important factor dictating the survival of Pancoast patients, although highly dependent of the T stage of the tumor and response to induction treatment.[7,8,10]

The T oncologic assessment is another important factor to consider, namely T3 tumors are associated with better survival and a higher possibility to achieve complete resection when compared to T4 staged tumors.[3,7]

Ultimately, N disease is also a relevant prognostic factor. Evidence of N2 nodal involvement is associated with poor survival in Pancoast patients.[1,14]

In the Soli et al (2017) retrospective cohort, a statistically significant lower 5-year survival was observed in patients with nodal disease compared to those without nodal involvement (48% in N0 disease vs 18% in N+ disease).[8] Furthermore, Hao et al (2020) meta-analysis also highlighted that a higher N stage was associated with a worse overall survival, with statistically significant difference when compared with lower N stage groups.[3]

One of the main limitations of our study is the small sample of patients considered. Most likely related to this factor, the survival of Pancoast tumors in our institution showed better results than the present literature. It is also indicative of selective eligibility criteria for surgical treatment. Although we chose to consider a patient with N3 clinical status, the possibility of surgery was only contemplated due to radiological complete N response after neoadjuvant chemoradiotherapy and the highly symptomatic disease presentation. Subsequent histopathologic examination confirmed the achieved N0 pathological status.

A rigorous selection of candidates and careful preoperative examination is critical in determining the patients that may benefit from surgical treatment and the most adequate surgical approach.[8] The aggressive nature of the surgical procedure and the extension of the resection required also underlines the importance of an appropriate selection of patients to withstand primary surgery.

Trimodality treatment with neoadjuvant chemoradiotherapy and surgery has led to a shift in the pattern of disease progression.[4,9,10] Local recurrence has decreased to below 35% rates, in cases of complete disease-free surgical margins.[2,4,9–11] Distant metastization is today the main relapse pattern and a significant cause of death. Distant metastasis develop most commonly in the brain, with an incidence described as high as 25%. [2–4,15,20]

In Portugal, there are multidisciplinary teams dedicated to lung cancer that do not account for the input of Thoracic Surgery. Barata et al (2021) performed a nationwide analysis of perceived delays for diagnosis and staging of lung cancer and concluded that two main factors preventing faster referral to specialty consultation included poor referral network and poor communication between services.[23] Furthermore, the United Kingdom National Lung Cancer Audit (2017) highlighted that patients were most likely to undergo surgical resection if first discussed in a multidisciplinary setting based in thoracic surgical centers, due to surgical peer review during the delineating of the treatment plan.[24] It is our perception that there is a significant number of Pancoast patients in Portugal, who have not benefited from the expertise of thoracic surgeons, integrated in a multidisciplinary team approach. Oncologic care poses the need of evidence-based treatment plans tailored to the patients' needs and surgery plays a key role in the therapeutic strategy of Pancoast tumors today.

Limitations to our study are the fact it constituted a retrospective cohort and the inherent small sample of cases considered. Moreover, Pancoast tumors considered unresectable and directed to definitive systemic treatment after multidisciplinary evaluation were beyond the scope of this article.

CONCLUSION

Pancoast tumors constitute a serious malignant condition, requiring a complex multimodal treatment plan and a high-risk surgical procedure. Although frequently associated with poor prognosis, the survival rates of Pancoast tumors have greatly benefited with a multidisciplinary and multimodal approach.

Today, studies have shown complete resection can be achieved. However, further research is necessary to determine an optimal perioperative therapy modality that will be able to improve tumor regression, thereby increasing the likelihood of complete surgical resection, a major factor in long-term overall and disease-free survival. Immunotherapy and target therapy have gained a foremost role in lung cancer treatment. Currently, we await scientific evidence on the impact of new targeted therapies on this subset of tumors.

Significant improvements have been reported in understanding the nature and treatment response of Pancoast tumors. Additional research is required to establish an association between the different therapeutic modalities and the resultant impact in disease prognosis.

Moreover, further efforts are required to improve referral of Pancoast tumors from early stages of diagnosis and to establish multifaceted teams with the involvement of thoracic surgical centers in the decision-making and treatment process.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare concerning this work.

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