



Patterns of Care and Treatment Pathways for Non-Surgically Managed Early and Locally Advanced Non-Small Cell Lung Cancer Patients at Ain Shams University Clinical Oncology Department: A Retrospective and Descriptive Analysis

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Abstract

Background: Lung cancer is the leading cause of cancer death worldwide, but little is known about how patients with this disease are managed nationally. In our study we aim to study patterns of care and radiotherapy approaches of non-surgically managed early and locally advanced non-small cell lung cancer (NSCLC) patients in Ain Shams University Clinical Oncology Department (ASUCOD).

Patients and Methods: In this retrospective analysis we included patients who met the following criteria; age ≥ 18 years, non-metastatic, histologically confirmed NSCLC patients who did not undergo surgical resection with at least 6 months of follow up data. We collected data from Clinical Oncology department archive at Ain Shams University Hospital. Our primary objective was to identify the patterns of care and radiotherapy approaches for these patients in ASUCOD from January 2015 to December 2018.

Results: 86 patients met our inclusion criteria. Median age at diagnosis was 61 years. 95.3% were male and only 4.7% were female. Most of the patients were stage III; 40.7% were stage IIIA, 41.9% were stage IIIB, and 9.3% were stage IIIC, while only 8.1% were stage II. 41 patients were treated radically, 37 palliatively and 8 received supportive care. Overall median progression free survival (PFS) in our patients was 9.23 (7.4-13.6) months and median overall survival duration (OS) was 13.4 (9.6-18.0) months. In radically treated patients, 68.3% received sequential chemoradiotherapy (sCRT), 29.3% received concurrent chemoradiotherapy (cCRT), and 2.4% received definitive radiotherapy alone (RT). Median PFS and OS durations of radically treated patients were 16 months and 23.3 months, respectively. Median PFS and OS durations for palliatively treated patients were 6.1 months and 8.6 months, respectively. Paclitaxel / Carboplatin was the most common regimen used with definitive RT. Most of the patients received radiotherapy dose of 60Gy/30Fr (73.2%).

Conclusion: Most patients presenting at our centre are locally advanced and less than half of them were treated radically. Sequential chemoradiotherapy was the commonest treatment modality. There is a need to improve outcomes via early diagnosis, improving patients access to treatment particularly radiotherapy. Further studies in other local centres are needed to complete the picture nationally.

Keywords: Non-Surgically managed, Non-metastatic, Early, locally advanced, Non-Small Cell Lung Cancer

Introduction:

Lung cancer continues to be the leading cause of cancer-related deaths worldwide. Unfortunately, 50% to 60% of cases has been diagnosed with metastatic or advanced stage in different countries [1].

Despite improvements in survival for many other types of cancer in recent years, 5-year survival for lung cancer has remained relatively poor, mainly because by the time a diagnosis is made, lung cancer is often advanced and treatment options are limited [1].

Additionally, Stage III non-small cell lung cancer (NSCLC) includes a highly heterogeneous group of patients with differences in the extent and localization of disease. Many aspects of the treatment of stage III

disease are controversial. Unfortunately, the data supporting treatment approaches in specific patient subsets are often subject to a number of limitations; for example, that the trials involved heterogeneous patient populations; the definition of stage III disease has changed over time; and early studies were frequently inadequately powered to detect small differences in therapeutic outcome, were not randomized, or had limited duration of follow-up. Major improvements in therapy, including the use of more active chemotherapy agents and refinements in radiation and surgical techniques, also limit the interpretation of earlier clinical trials. Finally, improvements in pre-treatment staging have led to reclassification of patients with relatively

minimal metastatic disease as stage IV rather than stage III, leading to a prolonging in the apparent overall survival of both stage III and IV patients. Unavoidably, locally advanced NSCLC management guidelines from various groups do have some differences reflecting the opinions and treatment philosophy of the physicians involved in their generation [2].

Despite multimodality treatment, the prognosis for unresectable stage III NSCLC remains poor, with five-year OS rates of approximately 15 percent. Therefore, newer treatment paradigms have evolved, for example, incorporation of immunotherapy [3].

Aim of the work:

This retrospective observational study aims to describe the pattern of care and treatment pathways including radiotherapy approaches for non-metastatic unresected NSCLC in Ain Shams University Clinical Oncology Department (ASUCOD) from January 2015 till December 2018.

Patients and Methods:

This is a retrospective descriptive study conducted at Ain Shams University Hospital Clinical oncology department, conducted on non-surgically managed early and locally advanced NSCLC patients.

Study period:

The data was collected for patients presenting to ASUCOD between January 2015 to December 2018.

Study population:

Inclusion Criteria:

- 1) Age ≥ 18
- 2) Histologically confirmed NSCLC (Adenocarcinoma, squamous cell carcinoma, large cell or undifferentiated carcinoma)
- 3) Early and locally advanced NSCLC patients stages (T1N1, T2N0-1, T3N0) (T3N1 – T4N0-N1 – or any T N2 or N3 positive).
- 4) Medical records available at the participating site reflect at least 6 months of follow up from the date of diagnosis (unless patient died within the first 6 months of diagnosis).

Exclusion Criteria:

- 1) Current or previous malignant disease within 3 years except cervical intraepithelial neoplasia, non-melanoma skin cancer and very low risk prostate cancer found as incidental finding and not requiring treatment
- 2) Patients underwent radical surgical resection.

Sampling method: consecutive method

Sample size:

Between January 2015 and December 2018, all available files of NSCLC patients in Ain Shams university hospital archive were checked and all patients who had non metastatic NSCLC at time of diagnosis and didn't go for surgical management and match all inclusion were enrolled in this study. 433

patient files were pulled, 83 patients did not complete their work up and treatment at Ain Shams University clinical oncology department (ASUCOD) and 253 patients were metastatic hence excluded. 97 patients had localized disease of which 11 patients were surgically managed and only 86 patients were included in this study.

Variables

- ❖ Patient demographic characteristics collected at diagnosis which included: age, gender, governate and smoking history.
- ❖ Patient clinical characteristics were evaluated which included co-morbidities, performance status (PS) estimated using Eastern Cooperative Oncology Group score.
- ❖ Investigations done for diagnosis and staging were reviewed: pathology report, immunohistochemistry report if available, computed tomography (CT) chest, Abdomen and pelvis, magnetic resonant imaging (MRI) Brain with contrast, bone scan, positron emission tomography (PET/CT) and pulmonary function test.
- ❖ Cancer Clinical data at diagnosis that included histopathology, grade, laterality and staging based on Union for International Cancer Control TNM Classification 8th edition.
- ❖ Therapeutic treatment regimens were captured: treatment intent: palliative, radical, or best supportive care, method of administration: concurrent or sequential, chemotherapy regimen: first line, second line. Number of cycles, dose of radiotherapy, fractionation scheme, radiotherapy technique.
- ❖ Follow up data: All patients' files were reviewed thoroughly for follow up protocol in order to determine progression, outcome and any complications

Follow up and assessment of response were reported through:

- CT of the chest, abdomen, and pelvis
- MRI Brain (if brain metastasis at diagnosis)
- PET/CT (if done at baseline)

Assessment of treatment outcomes for all patients were reviewed through:

- Progression free survival (PFS): refers to the duration from the date of diagnosis till confirmed evidence of clinical or radiological progression. This progression reported according to RECIST criteria.
- Overall Survival (OS): refers to interval from date of diagnosis till death due to any cause.

Statistical analysis:

The statistical package for the social sciences (SPSS) version 22 (IBM Corporation, Armonk, NY, USA) and MedCalc version 19.4.0 (MedCalc software Ltd, Ostend, Belgium) software for Windows were used for statistical analysis. Power of significance was evaluated as P value < 0.05 was considered significant.

Results:

Demographic and clinical characteristics of the study group

Of the 86 cases involved in this study, 41 were treated radically, 37 received active treatment (chemotherapy or radiotherapy) with palliative intent and 8 received only supportive measures. Most of the patients 93% had predicted PS ≤ 2 . The most frequently observed co-morbidities were hypertension (25.6%) and diabetes mellitus (23.3%). While near half of the patients (44.2%) had no associated comorbidity (table 1).

Table 1: Demographic & clinical characteristics of the study sample

	Palliative (N=37)	Radical (N=41)	Supportive (N=8)	Total (N=86)
Age				
Median (Range)	62 (50, 85)	61 (38, 80)	62 (52, 85)	61 (38, 85)
< 60	15 (40.5%)	18 (43.9%)	3 (37.5%)	36 (41.9%)
60-75	17 (45.9%)	21 (51.2%)	4 (50.0%)	42 (48.8%)
>75	5 (13.5%)	2 (4.9%)	1 (12.5%)	8 (9.3%)
Gender				
Females	0 (0.0%)	3 (7.3%)	1 (12.5%)	4 (4.7%)
Males	37 (100.0%)	38 (92.7%)	7 (87.5%)	82 (95.3%)
Governate				
Greater Cairo	34 (91.9%)	36 (87.8%)	7 (87.5%)	77 (89.5%)
Others (Delta, Suez Canal, Upper Egypt)	3 (8.1%)	5 (12.2%)	1 (12.5%)	9 (10.5%)
Smoking history				
Current smoker	28 (75.7%)	26 (63.4%)	4 (50.0%)	58 (67.4%)
former smoker	6 (16.2%)	7 (17.1%)	3 (37.5%)	16 (18.6%)
Never smoked	0 (0.0%)	3 (7.3%)	1 (12.5%)	4 (4.7%)
unknown	3 (8.1%)	5 (12.2%)	0 (0.0%)	8 (9.3%)
Pack-years				
Median (Range)	60(40, 120)	40 (0, 450)	80.0(0, 80)	48.5(0, 450)
Baseline ECOG score				
0-1	18 (48.6%)	32 (78.0%)	1 (12.5%)	51 (59.3%)
2	16 (43.2%)	9 (22.0%)	4 (50.0%)	29 (33.7%)
3-4	3 (8.1%)	0 (0.0%)	3 (37.5%)	6 (7.0%)
Baseline CCI				
2	23 (62.2%)	22 (53.7%)	6 (75.0%)	51 (59.3%)
3-4	13 (35.1%)	18 (43.9%)	2 (25.0%)	33 (38.4%)
> 4	1 (2.7%)	1 (2.4%)	0 (0.0%)	2 (2.3%)
Comorbidities				
Hypertension	8 (21.6%)	12 (29.3%)	2 (25.0%)	22 (25.6%)
Diabetes	8 (21.6%)	12 (29.3%)	0 (0.0%)	20 (23.3%)
COPD	3 (8.1%)	1 (2.4%)	0 (0.0%)	4 (4.7%)
IHD	2 (5.4%)	3 (7.3%)	0 (0.0%)	5 (5.8%)
CHF	2 (5.4%)	2 (4.9%)	0 (0.0%)	4 (4.7%)
Hepatitis	2 (5.4%)	1 (2.4%)	1 (12.5%)	4 (4.7%)
CVA	1 (2.7%)	1 (2.4%)	0 (0.0%)	2 (2.3%)
CKD	0 (0.0%)	2 (4.9%)	0 (0.0%)	2 (2.3%)
Other comorbidities	3 (8.1%)	4 (9.8%)	1 (12.5%)	8 (9.3%)

ECOG PS: Eastern Cooperative Oncology Group; CCI: Charlson Comorbidity Index; COPD Chronic obstructive pulmonary disease; IHD Ischemic heart disease; CHF Congestive heart failure; CVA Cerebrovascular accident; CKD Chronic kidney disease; Others: TB, Bronchial asthma, Connective tissue disease, Rheumatoid arthritis

Disease characteristics of the study group

The most frequently observed histology among study group (n=86) was squamous cell carcinoma (52.3%), followed by adenocarcinoma (32.6%),

undifferentiated carcinoma (11.6%) and large cell carcinoma (3.5%). Among these patients (n=86), 8.1% had early stage (stage II) at diagnosis while 40.7% had stage IIIA disease, 41.9% had stage IIIB, 9.3% had stage IIIC disease.

Only 36.0% of patients, were staged using PET/CT while the rest 64.0% were staged using CTs. No one had been staged by invasive staging techniques (endoscopic bronchial ultrasound EBUS, mediastinoscopy).

36.0% of patients had well and moderately differentiated disease while 64.0% of patients had poorly differentiated and undifferentiated disease.

Over half of the patients (55.8%) had right side tumor while (44.2%) had left side tumor (table 2).

Table 2: Disease characteristics for study population

	Palliative (N=37)	Radical (N=41)	Supportive (N=8)	Total (N=86)	P value
Pathology					0.017
Adenocarcinoma	7 (18.9%)	20 (48.8%)	1 (12.5%)	28 (32.6%)	
Large cell carcinoma	2 (5.4%)	1 (2.4%)	0 (0.0%)	3 (3.5%)	
Squamous cell carcinoma	25 (67.6%)	16 (39%)	4 (50.0%)	45 (52.3%)	
undifferentiated carcinoma	3 (8.1%)	4 (9.8%)	3 (37.5%)	10 (11.6%)	
Stage					0.035
Stage II	1 (2.7%)	6 (14.6%)	0 (0.0%)	7 (8.1%)	
Stage IIIA	14 (37.8%)	19 (46.3%)	2 (25.0%)	35 (40.7%)	
Stage IIIB	18 (48.6%)	12 (29.3%)	6 (75.0%)	36 (41.9%)	
Stage IIIC	4 (10.8%)	4 (9.8%)	0 (0.0%)	8 (9.3%)	
Grade					0.787
GI-II	14 (37.8%)	15 (36.6%)	2 (25.0%)	31 (36.0%)	
GIII-IV	23 (62.2%)	26 (63.4%)	6 (75.0%)	55 (64.0%)	
Tumor laterality					0.542
Left lung	16 (43.2%)	17 (41.5%)	5 (62.5%)	38 (44.2%)	
Right lung	21 (56.8%)	24 (58.5%)	3 (37.5%)	48 (55.8%)	
Imaging modality used for staging					0.079
CT	23 (62.2%)	24 (58.5%)	8 (100.0%)	55 (64.0%)	
PET-CT	14 (37.8%)	17 (41.5%)	0 (0.0%)	31 (36.0%)	
Pulmonary function test					0.578
Done	4 (10.8%)	3 (7.3%)	0 (0.0%)	7 (8.2%)	
Not done	33 (89.2%)	38 (92.7%)	8 (100.0%)	78 (91.8%)	

Chemotherapy regimens and cycles

Among the study group who received chemotherapy (n=74), Gemcitabine/Cisplatin was the most used regimen (41.9%) as 1st line treatment with an average of 4 cycles. 19 patients (25.7%) only received 2nd line chemotherapy and Docetaxel was the most frequent 2nd line regimen used in 63.1%. Among patients who received concurrent chemoradiotherapy (cCRT), Paclitaxel/Carboplatin was the most frequent regimen (50%), followed by Etoposide/Cisplatin regimen (16.7%). Platinum single agent was used concurrently with radiotherapy (RT) in (25 %) of patients who received cCRT. (table 3).

Table 3: Chemotherapy regimens used in study population

First-line chemotherapy		N= 74
Gemcitabine + Cisplatin	31 (41.9%)	
Gemcitabine + Carboplatin	26 (35.1%)	
Paclitaxel + Carboplatin	7 (9.4%)	
Etoposide + Carboplatin	5 (6.8%)	
Etoposide + Cisplatin	3 (4.1%)	
Carboplatin	2 (2.7%)	
Number of cycles:		
Median (Range)	4.00 (1.00, 9.00)	
Second-line chemotherapy		N= 19
Docetaxel	12 (63.1%)	
Paclitaxel + Carboplatin	5 (26.3%)	
Paclitaxel	1 (5.3%)	
Gemcitabine	1 (5.3%)	
Chemotherapy given with RT		N= 12
Paclitaxel + Carboplatin	6 (50%)	
Etoposide + Cisplatin	2 (16.7%)	
Etoposide + Carboplatin	1 (8.3%)	
Carboplatin	2 (16.7%)	
Cisplatin	1 (8.3%)	

Radiotherapy techniques and doses

Among patients who received definitive radiotherapy with or without chemotherapy (n=41), 37 were treated with 3DCRT (3dimensional conformal radiotherapy) technique. 3 were treated with VMAT (Volumetric modulated arc therapy). While 1 received IMRT (intensity modulated radiotherapy) technique

Among patients who were treated radically (n=41), 34 patients (82.9%) completed the intended definitive radiotherapy dose, of which 30 patients received 60Gy/30Fr., 3 received 64Gy/32Fr – 66Gy/33Fr and only one patient received 50Gy/25Fr. (table 4).

As for patients who received palliative dose of radiotherapy with or without chemotherapy (n=10). 8 were treated with 3DCRT and 2 patients treated with 2D RT. Doses used were as follow: 6 received 39Gy/13Fr, 2 received 39.6Gy/22Fr, and 2 patients didn't complete the prescribed dose (30Gy/10fr) (20Gy/5Fr) for unknown reason.

Table 4: Definitive Radiotherapy doses used in study population

		N=41
Intended dose Completion		
Completed	34 (82.9%)	
Not completed	7 (17.1%)	
Radiotherapy dose		
60Gy/30Fr	30 (73.2%)	
64Gy/32Fr	2 (4.9%)	
66Gy/33Fr	1 (2.4%)	
50Gy/25Fr	1 (2.4%)	

Survival outcomes:

Median progression free survival for the whole study cohort was 9.233 [CI= 7.4-13.56]. (Figure 1). For the radically treated group median PFS was 16 months [CI= 12.9- 24.7] and for the palliatively treated this was significantly lower at median of 6.13 months [CI= 4.13 – 8.57] (p< 0.0001) (Table 5)

In the radically treated group, outcomes were better in those who received cCRT with a median PFS of 17.5 months versus 15.6 months in the sCRT group. Lowest figures were noticed in patients treated with radical radiotherapy alone where median PFS was 12.9 months. (p= 0.5712)

As regards overall survival, median OS of the whole study group was 13.4 months [CI 9.6- 18] (figure 2). In the radical treatment group median OS was 23.3 months [CI= 18.2 - 31.7] compared to 8.6 months [CI= 6.3 – 11.1] in the palliative group (p < 0.0001). (table 6).

Unlike PFS, median OS was lower in those who received cCRT at 20.7 months compared to the sequentially treated group which was 23.3 months (p = 0.1633).

Table 5: Mean and median progression free survival according to the aim of treatment modality (palliative, Radical, and Supportive)

Factor	Mean	95% CI for the mean	Median	95% CI for the median
Palliative	8.442	5.670 to 11.215	6.133	4.133 to 8.567
Radical	25.505	17.633 to 33.377	16.000	12.900 to 24.667
Supportive	2.088	0.506 to 3.669	1.200	0.100 to 6.733
Overall	16.871	12.026 to 21.716	9.233	7.400 to 13.567

Table 6: Mean and median overall survival according to the aim of treatment modality

Factor	Mean	95% CI for the mean	Median	95% CI for the median
palliative	10.359	7.818 to 12.901	8.633	6.267 to 11.067
radical	30.491	22.999 to 37.982	23.333	18.167 to 31.667
supportive	2.088	0.506 to 3.669	1.200	0.100 to 6.733
Overall	19.532	14.838 to 24.227	13.433	9.567 to 18.000

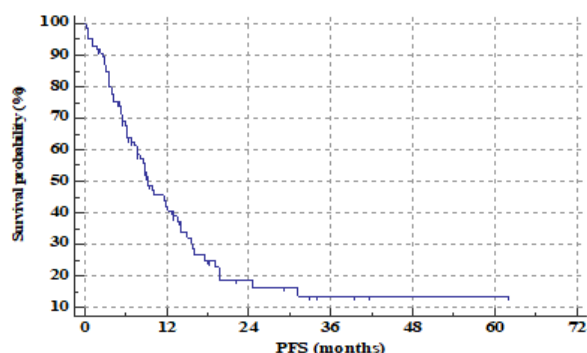


Figure 1: Median progression free survival for all study population

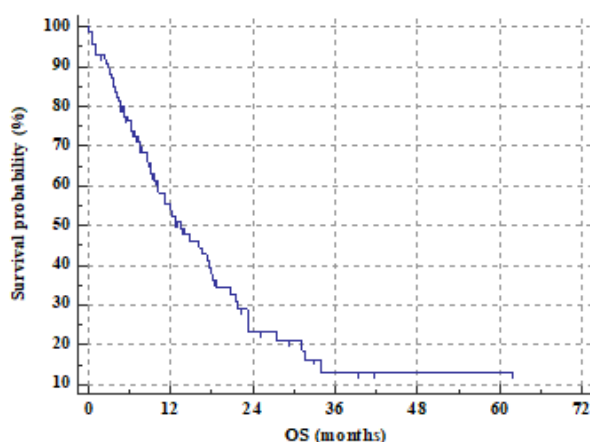


Figure 2: Median overall survival for all study population

Discussion:

Lung cancer is the most common type of cancer and the principal cause of death from cancer worldwide. In 2018, data from Globocan estimated over 2.1 million newly diagnosed cases and 1.8 million deaths globally [4]. In Egypt,, Lung cancer is estimated to be the fifth most frequent cancer in both sexes, the fourth most frequent cancer in male and eleventh in female excluding non-melanoma skin cancer, the fourth most frequent deaths in both sexes in 2018 [5].

Unfortunately, 50% to 60% of cases have been diagnosed with metastatic or advanced stage in different countries [1].

Stage III non-small cell lung cancer (NSCLC) includes a highly heterogeneous group of patients with differences in the extent and localization of disease. Many aspects of the treatment of stage III disease are controversial. Unfortunately, the data supporting treatment approaches in specific patient subsets are often subject to a number of limitations; for example, trials involved heterogeneous patient populations; the definition of stage III disease has changed over time; and early studies were frequently inadequately powered

to detect small differences in therapeutic outcome, were not randomized, or had limited duration of follow-up. Major improvements in therapy, including the use of more active chemotherapy agents and refinements in radiation and surgical techniques, also limit the interpretation of earlier clinical trials. Finally, improvements in pre-treatment staging have led to reclassification of patients with relatively minimal metastatic disease as stage IV rather than stage III, leading to a prolonging in the apparent overall survival of both stage III and IV patients. Unavoidably, locally advanced NSCLC management guidelines from various groups do have some differences reflecting the opinions and treatment philosophy of the physicians involved in their generation [2].

Despite considerable efforts, multimodality approaches and novel therapeutic techniques, yet, the prognosis of stage III remains rather unfavourable.

In our study we looked at the patterns of management and therapeutic outcomes in this group of patients. We found that from 79 patients who had stage III NSCLC, only 40 patients (50.6%) have been treated by this intensive treatment (definitive CRT) and 47.7% received any sort of radical treatment which is less than that reported in Bobbili's study, a population based study on US population of unresected stage III NSCLC patients from 2009 to 2014, at which 59% received radical treatment with CRT Despite having higher mean age of 74 years study compared to 61.4 years in our group. [6] Nevertheless, other groups reported much lower rates of radical treatment, for example in Vinod's study, which included 2365 Stage III NSCLC patients identified from the British Columbia Cancer Agency database, 61% received palliative treatment, 10.5% received best supportive care and only 19.1% received radical treatment after subtraction of surgically managed patients [7].

45.3% were females in the Bobbili's study which is different from our group at which females are minimally represented and this may be due to small sample size of our study and the scarcity of smoking among women compared to men in Egypt [8]. Bearing in mind that all represented women in our study had never smoked.

In the same study, 61.4% were stage IIIB and adenocarcinoma was the commonest represented histopathology while squamous cell carcinoma was the commonest histopathology in our study. This difference is consistent with the rise of adenocarcinoma incidence to be greater than that of squamous cell carcinomas in many countries like the US, Canada, and Japan. However, this switch has not yet been observed in other countries such as Spain, the Netherlands [9] and Egypt [10].

A Chinese group studied 579 NSCLC patients admitted at Hebei Cancer Hospital located in Northern China from January 2004 to December 2005. None of stage IIIB patients received radical treatment compared to 29.4% of stage IIIB patients in our study [11].

The Chinese group and Vinod's studies were conducted on patients between 2000 to 2007, the time when palliative treatment was commonly used in locally

advanced NSCLC. Over time, definitive CRT has become widely used strategy in locally advanced NSCLC in some countries.

However, still a small proportion of patients received radical treatment 30.8% in a population-based study on Canadian population of stage III NSCLC patients which included 1151 patients from April 1, 2010 to March 31, 2015. Median age at diagnosis was 70 (22 to 94) years and 50.2% were men. 61.2% were stage IIIA, 36.4% were stage IIIB, and 2.4% were unspecified [12].

A report from England included 6276 patients with stage III NSCLC: 3827 were stage IIIA and 2449 were stage IIIB. In Stage IIIA, 38.9% patients received radical treatment (surgery or radiotherapy), 26.7% received palliative treatment and 34.5% received supportive care. In Stage IIIB, 15.6% patients received radical treatment, 45.9 % received palliative treatment and 38.6 % received supportive care [13].

Concurrent chemoradiotherapy versus sequential treatment:

Although cCRT was established to be superior to sCRT for patients who can tolerate this approach, 68.3% of radically treated patients received sCRT. The use of the concurrent approach remains much less than that reported by several groups in different parts of the world [6, 7, 14]. In these studies, cCRT was the most common administered regimen. Definitive RT was the 2nd most common regimen followed by sCRT in patients who treated without surgery in Vinod's study for example.

After analysing this situation, it was found that, among the patients who treated with sCRT n=28 in our study

- 1) 19 patients (73.1%) were referred from another medical institution 'usually from national health insurance' after receiving chemotherapy, median number of cycles was 4 (3:14). 4 of these 19 patients had stage II NSCLC although chemotherapy has no role in their management
- 2) 3 patients received neoadjuvant chemotherapy aiming to go for surgery, but they were still not candidate for surgery after completion of chemotherapy.
- 3) 3 patients started chemotherapy till staging work up is done.
- 4) 2 patient started chemotherapy due to large target volume aiming to downsize the tumor to allow definitive radiotherapy dose administration without exceeding the tolerance dose of other surrounding organs).
- 5) Borderline PS was the reason in one patient (PS: ECOG2, age 62y, no-comorbidities) hence, he was treated with sCRT.

It was also noticed that all patients who received cCRT, started their treatment in Ain Shams University Clinical Oncology Department (ASUCOD) except one patient who was referred from national health insurance after 4 months of ending 4 cycles chemotherapy to ASUCOD where MDT decided cCRT for him. However, half of the patients who started treatment in

ASUCOD, received induction chemotherapy before starting concurrent regimen in order not to delay the patients to start anti-cancer therapy until the completion of their work up or the administrative procedures needed for radiotherapy delivery.

Through the aforementioned observations, the procedures for receiving chemotherapy seem easier than that for receiving radiotherapy in our city, and this may be due to the lack of linear accelerator devices in Egypt and the need to provide a larger number of devices and facilitate procedures for receiving radiotherapy in addition to facilitating the necessary investigations to confirm the staging before starting this intensive therapy.

Chemotherapy types used concurrently with radiotherapy:

In Bobbili's study, approximately three-quarters of patients treated with concurrent CRT, received carboplatin / paclitaxel while cisplatin / etoposide was used in a quarter [5] which is consistent with our study at which carboplatin / paclitaxel was given to 50% of patient received cCRT and cisplatin / etoposide was the 2nd most common used regimen. A multicentre phase III trial by Liang and his colleagues concluded that cisplatin / etoposide might be superior to weekly carboplatin / paclitaxel in terms of OS in the setting of concurrent chemoradiation for unresectable stage III NSCLC [15], nevertheless, A systematic review analysed these two regimens and they were comparable in terms of efficacy while toxicities showed higher rates of grade >3 thrombocytopenia and neutropenia in the carboplatin / paclitaxel regimen. There was no significant difference in response rates, OS, progression-free survival, locoregional relapse, distant metastasis and rates of pneumonitis or esophagitis [17].

Generally speaking, the most commonly used chemotherapy regimen in ASUCOD was Gemcitabine / cisplatin with a rate of 41.9% among all patients who received chemotherapy whether radically or palliatively, with or without radiotherapy.

In Ryan's [14] and Bobbili's studies [6] platinum / taxanes was the most common regimen used while in Vinod's it was cisplatin / etoposide not only in combination with radiotherapy but also in those who received palliative chemotherapy [7].

Neither TKI (tyrosine kinase inhibitor), bevacizumab, nor immunotherapy were used as a second line for patients attending ASUCOD as they are not funded for public use in this sector.

Radiotherapy dose and technique:

In term of optimal radiation dose, Sonnick and his colleagues reported that patients treated with a radiation dose > 66 Gy had significantly improved overall survival compared with those treated with < 60 Gy (HR 0.58; 0.39-0.87; P = .008) [17].

Similarly, a study compared standard-dose versus high-dose radiotherapy with concurrent chemotherapy in patients with stage III NSCLC. Results showed that 74 Gy radiation given in 2 Gy fractions with concurrent chemotherapy was not better than 60 Gy plus

concurrent chemotherapy and might be potentially harmful [18].

In our study, 59.3% received radiotherapy as part of their initial treatment.

Radically treated patients had significant higher progression free survival of 16 months (12.9-24.7) and overall survival 23.3 (18.2-31.7) months compared to palliative treatment 6.1 (4.1-8.6) months, 8.6 (6.2-11.1) months P value < 0.0001.

In He's study the median survival time for curative care, palliative care, and noncancer-specific treatment were 37.7, 11.5, and 4.5 months, respectively [12]. One possible explanation for the better figures in their group could be the fact that they included surgically managed patients (which were excluded from our study) these are potentially more fit and have earlier stage disease.

Study limitations and challenges:

1. This study is a retrospective and looked at the situation and practice in a single cancer centre (university hospital) in Cairo. Hence, these results do not necessarily reflect the actual picture in other parts and institutions in the rest of Egypt.
2. A considerable number of patients involved in our study were referred initially from other centres particularly the National Health institute hospitals after having been started on treatment or completed part of it with no option for ASCOD to change the treatment plan, accordingly, the study does not reflect accurately ASUCOD preference of treatment.
3. Data collection from patients' records was a laborious procedure; some files could not be retrieved, some files had missing values and documentation was not always in clear handwriting.

Conclusion:

Most patients presenting at our centre are locally advanced and less than half of them were treated radically. Sequential chemoradiotherapy was the commonest treatment modality. There is a need to improve outcomes via early diagnosis, improving patients access to treatment particularly radiotherapy. Further studies in other local centres are needed to complete the picture nationally.

List of abbreviations:

ASUCOD: Ain Shams University Clinical Oncology Department

CT: Computed tomography
 CRT: Chemoradiotherapy
 cCRT: Concurrent chemoradiotherapy
 EBUS: Endoscopic bronchial ultrasound
 ECOG: Eastern Cooperative Oncology Group
 IMRT: Intensity modulated radiotherapy
 MRI: Magnetic resonant imaging
 NSCLC: Non small cell lung cancer
 OS: Overall Survival
 PET/CT: Positron emission tomography
 PFS: Progression free survival
 PS: Performance status

RT: Radiotherapy
 sCRT: Sequential chemoradiotherapy
 SPSS: Statistical package for the social sciences
 VMAT: Volumetric modulated arc therapy
 3DCRT: 3dimensional conformal radiotherapy

Competing interests:

Authors of the study declare they have no conflict of interest

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Authors' contributions:

CG: Material preparation and data collection, Software, analysis and writing first draft of the manuscript and editing final version. AA: participated in study design, coordination, Visualisation, supervision and helped to draft the manuscript. KA: participated in study design, analysis and supervision. KN: participated in study design, analysis and supervision. All authors read and approved the final manuscript.

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