Non-small cell lung cancer: how do experts want to be treated?

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Abstract

Objectives: Lung cancer is the leading cancer type among cancer deaths in the world and our country. There are some controversial issues that specialists dealing with oncology have difficulty in decision making. The aim of this study is to determine the approach of physicians of different specialties to the management of lung cancer.

Methods: In this study, an on line questionnaire was applied to specialists of lung cancer. In this questionnaire there were some lung cancer scenarios created on controversial issues, each including different stages of the disease. The scenarios were based on the hypothesis that “the participating physicians had lung cancer themselves”, and expected to answer the treatment scenarios in this wise. The participants are pulmonologists, thoracic surgeons, radiation oncologists and medical oncologists.

Results: Of the participating 170 physicians 45% were radiation oncologists, 24% pulmonologists, 23% thoracic surgeons and 8% medical oncologists. In the scenario, created to determine the approach to surgery in N2 disease, 45% of cases preferred surgery. It was also remarkable that surgery was preferred 16% in N3 diasease. In stage 1A2 disease, when pulmonary functions were insufficient for surgery, radiotherapy was preferred by 64% of cases. In the scenario questioning the decision about chemotherapy in T3N2 disease, cisplatin-etoposide vs paclitaxel-carboplatin options were preferred 32%, 26% respectively. The approach to solitary brain metastasis was 64% in favor of stereotactic radiotherapy after brain surgery. Immunotherapy was the preferred treatment when multipl brain metastasis occured in case with negative driver mutations and PDL1>1%. In oligometastatic disease, 97% of cases preferred surgery for both lung and metastatic side.

Conclusions: Although there are guidelines in the management of lung cancer, there are still controversial issues with renewed treatment protocols in some special conditions. We believe that the results of this study will highlight these issues.

Introduction

Lung cancer… The leading cause of cancer deaths, regardless of gender or ethnicity. Researches on the early diagnosis, on the best staging methods and treatment are going on in the whole world. Lung cancer was a very rare disease in 1878 at a percentage of 1% at autopsy series (1). However with the use of tobacco at the First World War, it increased rapidly so that now it is the most common type of cancer.

Efforts are on early diagnosis (2, 3). For the best treatment option, staging is also mandatory. First staging for lung cancer was described in 1940’s (4). Tumor-node-metastasis (TNM) staging is still used with some updates. The latest version is the 8th version which is approved by International Association for the Study of Lung Cancer (IASLC) and American Joint Committee on Cancer (AJCC) (5).

Among the developments in diagnosis and staging; the best treatment for early stage lung cancer is still surgery (6). However there some controversial issues in the treatment of even early stage lung cancer and

so at other stages. Despite all the literature and guidelines, sometimes clinicians make different decisions for their patients expecting the best for their condition. What about for themselves? If they were the patient, themselves, would they follow the guidelines or make some changes adding their emotion?

Complete resection of lung cancer is associated with significantly longer survival, but only about 25% of patients are candidates for surgery at the time of diagnosis (7).

Material And Methods

An on line questionnaire (attached as a supplementary document) was produced from Survey Monkey Questionnaire Programme. First part of the questionnaire was about the demographic information and status of the participiants like education, current practice. In the remaining they were tested in 8 different lung cancer scenarios and were asked to answer the questions if they were “the patient themselves”. The scenarios were created all from the discussable issues at the treatment. The whole questionnaire can be found at the end of the manuscript. Questions were prepared at the base of 8th TNM staging. The participiants were all specialists dealing with lung cancer, including pulmonologs, thoracic surgeons, radiation oncologists and medical oncologists. All the answers were collected and analysed with the same programme.

Results

Of the participating 170 physicians, 24% were pulmonolog, 23% thoracic surgeon, 45% radiation oncologist and 8% medical oncologist. Eighty six percent of the participants were between 40–49 years old. Women were more than men with a rate of 56%. The smoking data is on Fig. 1.

The interest of the physicians in lung cancer was mostly between 5–15 years (45%).

In scenario 1, they were asked if they were smoker and diagnosed as non small cell lung cancer (NSCLC), what they would do? Results of this question is in Fig. 2.

Scenario 2 was to discuss single station N2 lymph node for the decision of surgery for stage T2AN2M0 (Stage IIIA). Almost half of the TS, preferred surgery at initial treatment, even the NCCN guideline recommendation of induction chemotherapy or definitive chemotherapy (NCCN).

Scenario 3 was a stage IIIB (T2a N3 M0) squamous lung cancer. A 4 cm. peripheral left lower mass, with a concomittan left supraclavicular lymph node which had an FDG uptake at PET-CT scan and proven to be malignant with a biopsy. Nearly half of the surgeons preferred to be operated even though the malignant lymph node (43.6%).

Scenario 4: “A 1.5 cm. right upper lobe tumor is detected and your lymph nodes are proven to be benign with PET/CT and EBUS (T1b N0 M0 = Stage 1A2). If you are suitable for a lobectomy with good respiratory functions what would you prefer?” Most of the participants preferred surgery while a quarter

of radiation oncologists preferred stereotactic body radiotherapy (SBRT). If respiratory functions were limited and unsuitable for a lobectomy, most of the surgeons choosed sublobar resection, while others preferred SBRT. Nobody preferred chemotherapy (Table 1).

Table 1
Preferences of the participants for scenario 4, T1b tumor, but unsuitable for lobectomy.

	Sublobar resection	Stereotactic RT	CT*	No treatment	Total
Pulmonology	%45,0 18	%50,0 20	%0,0 0	%5,0 2	%23,8 40
Thoracic surgery	**%79,5** **31**	%20,5 8	%0,0 0	%0,0 0	%23,2 39
Medical oncology	%15,4 2	%84,6 11	%0,0 0	%0,0 0	%7,7 13
Radiation oncology	%10,5 8	**%89,5** **68**	%0,0 0	%0,0 0	%45,2 76
Total results	%35,1 59	**%63,7** **107**	%0,0 0	%1,2 2	168

P: pulmonolog **TS**: thoracic surgeon **RO**: radiation oncologist **MO**: medical oncologist *CT: chemotherapy

Scenario 5: “A centrally localized left lung tumor invading left pulmonary artery without any metastatic lymph node is detected (T4 N0 M0 = Stage 3A). Your surgeon adviced neoadjuvant therapy before a surgery. Would you choose RT, CT, or concomitant RT and CT?” Pulmologists, surgeons and medical oncologists mostly selected CT respectively (59%, 64.1%, 61.5%) whereas radiation oncologists were on the side of concomitant therapy (66.2%). The radiation dose preferences were 45 Gray for 53.4%, 60–66 Gray for the remaining radiation oncologists.

Scenario 6: “A locally advanced NSCLC is detected. You accepted to have concomitant radiochemotherapy (T3 N2 M0 = Stage IIIB). The treatment alternatives are cisplatin + etoposid, weekly paclitaxel + carboplatin, cisplatin + vinorelbin, cisplatin + gemcitabine or platin + pemetrexet.” Seventy four percent of the surgeons did not have any idea, while half of the pulmonologists preferred cisplatin + etoposid (51.3%). Weekly paclitaxel + carboplatin option was higher than other treatments for medical oncologists and radiation oncologists (46.1%, 43.4%). “What about the continuation of the therapy if you are still unresectable?” They were asked if they would get consolidation (durvalumab) therapy. The acceptance rates were as follows; pulmologists 76,9%, surgeons 56,4%, medical oncologists 92,3%, radiation oncologists 92,1%.

Scenario 7. The participant had lung adenocarcinoma. At the time of staging, brain metastasis was detected with a contrasted magnetic resonans imaging. All driver mutations were negative (EGFR, ALK, ROS-1 and PD-L1<%1). Participants were asked which treatment they would choose for the brain metastasis before the systemic therapy? Only surgery, surgery followed by a stereotactic radio surgery (SRS) for the cavity, SRS followed by surgery or SRS or whole brain RT? Most preferred option was surgery followed by SRS with a sum of 64% at all clinicians. The second part of this scenario was as follows: “Brain metastasis are 3, driver mutations positive and PD-L1 <%1. You are planned to be treated with tyrosine kinase inhibitor. Before this treatment which is your preference for brain metastasis; early cranial RT or waiting for the response of cranial metastasis to systemic treatment with close MR monitoring.” Results are at Table 2.

Table 2
Responses to scenario 7, part 2.

	Early cranial RT	**Wait for the response of cranial metastasis to systemic treatment with close MR monitoring**
Thoracic Surgeons	%51,9 20	%48,7 19
Pulmonologists	%79,5 31	%20,5 8
Medical oncologists	%15,4 2	%84,6 11
Radiation oncologists	%50,0 38	%50,0 38

Scenario 7, part 3 is about 3 brain metastasis, negative driver mutations and this time PD-L1 >%1. The treatment options are;

1. Chemothreapy followed by RT
2. Immunotherapy followed by RT
3. RT followed by Chemotherapy
4. RT, followed by immunotherapy

Most of the participants preferred answer 4 (64,1%, 43,2%, 69,2%, 64,5%).

In case of multipl brain metastasis requiring whole cranial RT, would you prefer hippocampus sparing RT to protect neurocognitive functions? Answers are at Table 3.

Table 3
Answers of the participants to the scenario requiring whole brain RT.

	Yes	No	No idea
Thoracic Surgeons	%71,05 27	%0,00 0	%28,95 11
Pulmonologists	%69,23 27	%2,56 1	%28,21 11
Medical oncologists	%76,92 10	%15,38 2	%7,69 1
Radiation oncologists	%63,64 49	**%31,17 24**	%5,19 4

Scenario 8. “You were found to have NSCLC with a single adrenal gland metastasis (oligometastatic disease) and you underwent an adrenalectomy operation. There is no progression in your lung lesion. Would you consider a radical treatment for the primary lung lesion (surgery, radical RT or RCT)?” Nearly all of the participants preferred to have a radical treatment for the lung lesion (97%).

Discussion

Guidelines are essential for decision making on cancer treatment (8). Lung cancer staging is updated in recent years and the treatment is also changing parallel to this (9).

Many of the patients, even informed in detail, don’t have much idea about their treatment strategy and they leave the choice of treatment entirely to their doctors. How about doctor patients? Having all the knowledge of diagnosis, treatment and prognosis, would they change the treatment protocols, if they were the patient? Would they decide with their emotions or by following the literature and guidelines?

Do physicians have a higher risk for cancer? Lee et al. hypothesed that physicians have a higher risk than general population due to night shifts, radiation, poor lifestyle. They researched NHI Research Database (NHIRD) which is one of the largest and most comprehensive database of it’s type in the world. In total physicians had 2.51%, general population had 2.90% cancer rate and physicians had a significantly lower cancer risk than the comparison group. The top cancers in physicians were lung, liver, colon, prostate and breast smilarly to the general population. Rotating night shifts is a risk factor for breast cancer of female. But other risk factors can not be ruled out (10).

Looking from the perspective of a patient is important (empathy). Schwartz et al, focused on early stage lung cancer treatment from the view of surgeons and patients. Since the mortality rates of early stage lung cancer is low, both surgeons and patients can prioritize quality of life when deciding the treatment.

Surgeons focus on the surgical procedure choice and the following treatment, while patients primarily focus on their physical and mental health after surgery. In this context surgeons should empathize, while they are informing their patients (11). Some of the contributers of our study mentioned that it was hard to answer the questions and that they felt depressed while they read the scenarios.

Mackillop et all. asked 118 specialists, 4 different lung cancer scenarios (12). This study demonstrated the differences of the decisions of physicians. In the case of multipl station N2, 61% preferred immediate radiation therapy, while 22% wished no immediate treatment. When the tumor is 2 cm. and no metastatic lypmh nodes, 81% choosed surgery alone, 12% surgery followed radiation therapy according to the operative findings. After a pneumonectomy, an extensive nodal involvement at the pathological evaluation, 66% wished adjuvant radiotherapy. Doctors refusing adjuvant chemotherapy mentioned the toxicity of chemotherapy as the reason of their decision. The belief that chemotherapy is ineffective was another reason for refusing. In the situation of metastatic lung cancer, 69% wished palliative radiotherapy to the metastatic painful side with or without other treatment. The ratio of doctors choosing symptomatic treatment was 20%.

Moore at al. prepared an open ended questionnaire to ask urologists, radiation and medical oncologists. The questionnaire was about the management of several common genitourinary cancer situations. They were asked to reply to consider themselves as a patient. The results demonstrated that choice of treatment was mostly influenced by specialty than re-suits of previous clinical trials in all kind of scenarios. The study found evidence of controversy among experts for the best treatment for common clinical genitourinary cancer scenarios (13).

Schnaper et al, searched for the attitude of oncologists for their own cancer in any system or organ without concern for cell type (14). They compared oncologists (medical, surgical and radiation oncologists) at different levels of training. In general as a first line therapy they were asked if they would prefer chemotherapy, surgery or radiation. Radiation therapy was preferred lower than other modalities, except radiation oncologists. Surgical oncologists preferred surgical modalities to radiotherapy as first line therapy ($p = 0.06$). In case of a relapse scenario, nonexperienced oncologists led to disenchantment and rejected various treatments, while experienced oncologists led to an increased acceptance of therapies again (14).

Conclusions

This study is unique in the literature in terms of it’s design. The questions are about some current controversial situations of lung cancer treatment. On the other hand, even treatment options are clear with the guidelines for some of the scenarios like N2 disease and surgery, many of the participants preferred surgery (45.3%). Moreover 15.8% of the doctors preferred surgery despite N3 disease which is a remarkable data.

The selection of radiotherapy for non operabl stage IA2 disease is also one of the stunning results of the study with a percantage of 63,7. Chemotherapy protocols of cisplatin + etoposid vs paclitaxel +

carboplatin were at close values for T3N2 disease (31,7% vs 26,3% respectively).

For a solitary brain metastasis 64% preferred surgery followed by a sterotactic radiotherapy. When brain metastasis are multipl, driver mutations are negative and PDL1>%1 immunotherapy has been the treatment choice. In case of oligometastatic disease almost all the participants choice was surgery for both of the organs.

In this case, it would not be wrong to say that experts do not have a complete consensus on controversial situations. These controversial topics may be discussed more in congress, events and literature.

Declarations

This study was presented at the European Respiratory Society Virtual Congress 4-8 September 2021, Barcelona, Spain. (Presented by Nimet Aksel)

This study is approved from the Medical Practice Training Committee of our hospital at 13.11.2019 (2019/16-20).

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All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Banu Yoldaş, Nimet Aksel, Esra Kıraklı & İbrahim Petekkaya].

The first draft of the manuscript was written by [Banu Yoldaş] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Medical Practice Training Committee of our hospital at 13.11.2019 (2019/16-20).

The datasets generated during and/or analysed during the current study are available in the [Banu Yoldaş] repository.

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Supplementary Document

The Supplementary Document is not available with this version

Figures

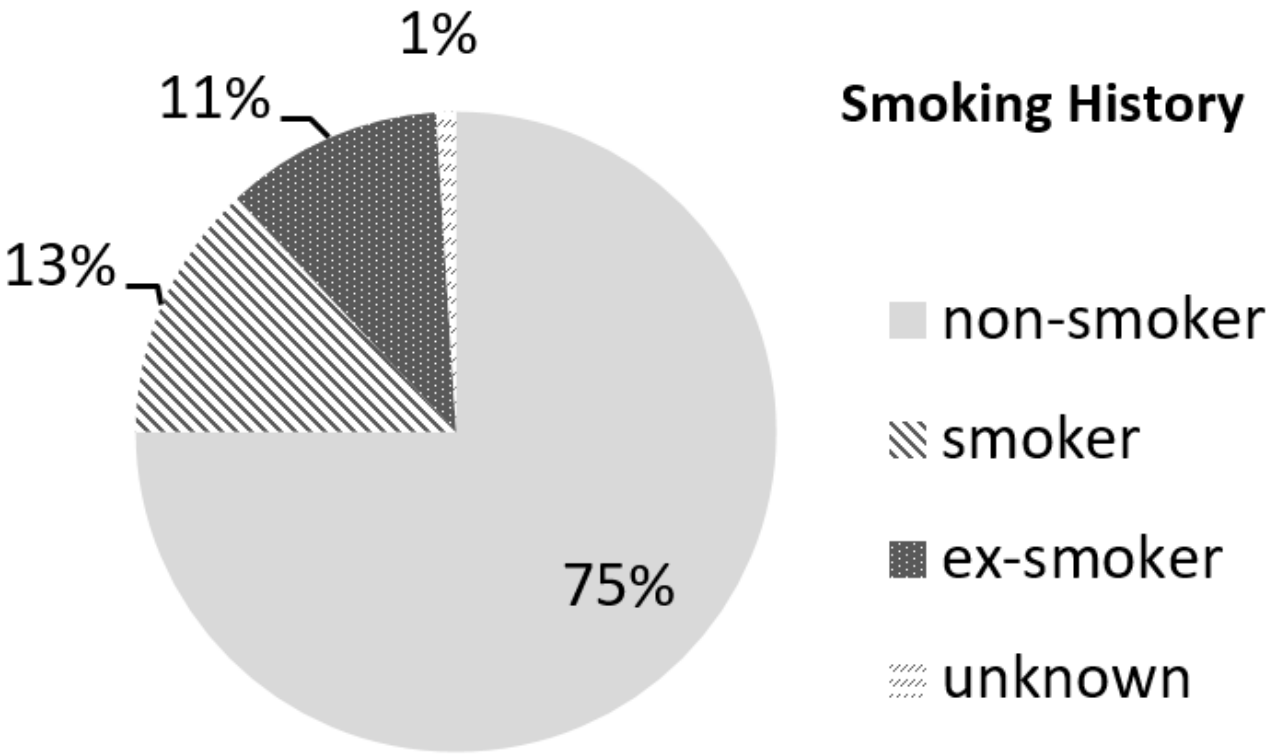

Figure 1

Smoking history of the participants.

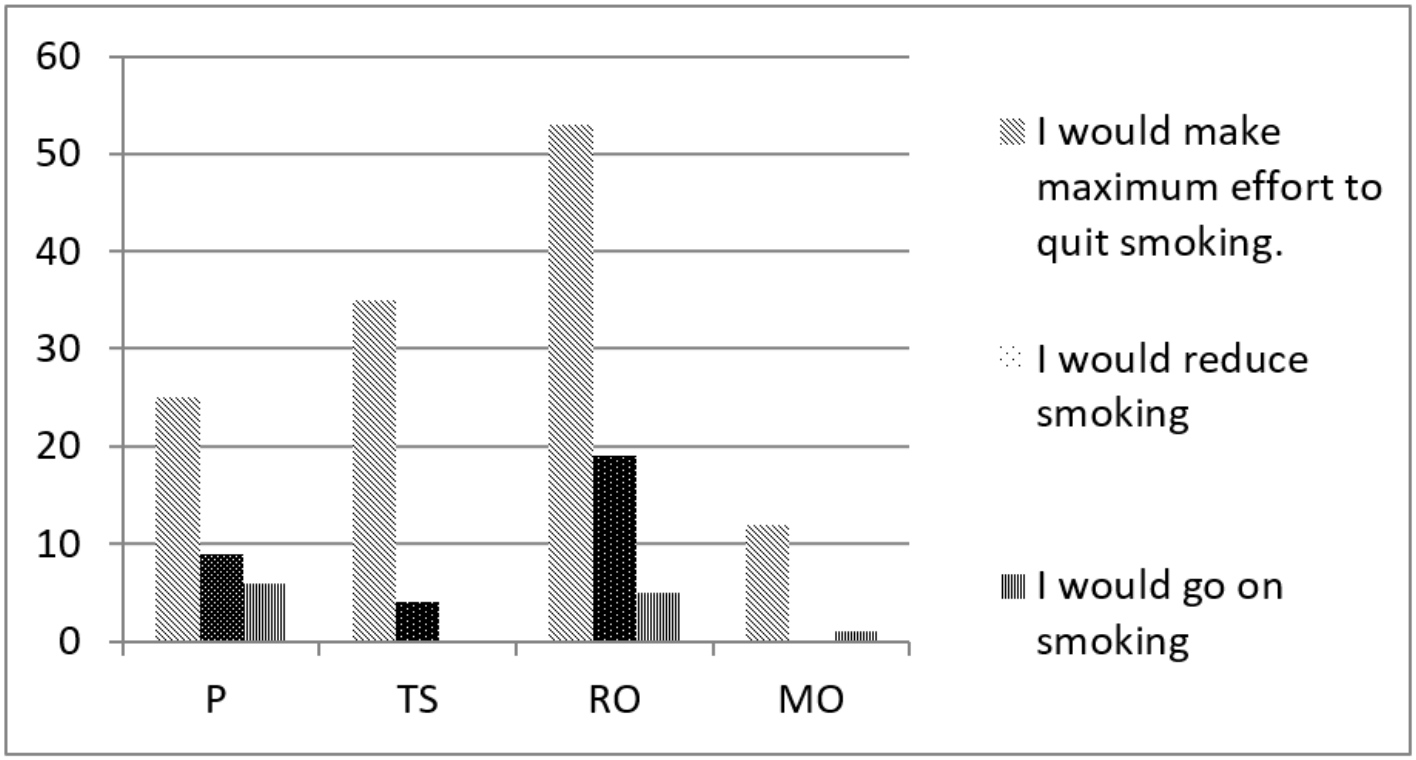

Figure 2

Participants' answers to question about smoking behaviour after the NSCLC diagnosis.