

## Quality of life survey and palliative care in lung cancer patients

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### Abstract

**Aim.** In patients with advanced and/or inoperable bronchial tumors, methods of palliative care such as radiotherapy, chemotherapy, brachytherapy and cryotherapy, singly and/or in combination, aiming at extending the survival time and improving the quality of life, were examined. **Methods.** One hundred and sixty three (163) patients, with mean age 67.9 yrs (range 22-25) and a male/female ratio at 1.34/1, treated between 2000-2004 were studied. Eighty one (81) patients receiving only cryotherapy presented a two-year survival rate at 19.3%, whilst eighty three (83) patients treated with radiotherapy or brachytherapy and/or chemotherapy showed a two-year survival rate at 25%. Sixty-five percent (65%) of patients only cryotreated had improvement in at least one or more Karnofsky and WHO indices. **Results.** Eighty percent (80%) of patients who received cryotherapy accompanied with supplementary palliative treatment showed amelioration of their clinical status. **Conclusion.** It seems that for patients with advanced or inoperable lung tumors, cryotherapy associated with additional palliative care may influence the survival time and improve their quality of life. *Hippokratia 2006; 10 (4): 163-166*

**Keywords:** *Quality of life, lung cancer, palliative care*

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### Introduction

Many patients with locoregional non-small (NSCLC) or small (SCLC) cell lung cancer presenting primary or metastatic tumors, may require palliative treatment with radiotherapy, endobronchial irradiation (brachytherapy), chemotherapy and cryotherapy. All these methods relieve the severity of symptoms and improve the quality of life.

The role of external beam radiotherapy in alleviating symptoms such as hemoptysis, cough, dyspnea and chest pain has been already studied<sup>1,3</sup>.

Eighty five percent (85%) of endobronchial lung cancer tumors are considered as inoperable when diagnosis is established, and therapy remains largely palliative<sup>4</sup>.

In thirty percent (30%) of patients with central airway obstruction in the sequel of lung cancer, the clinical figure is presented with dyspnea, atelectasis and pneumonia. The treatment of choice for these tumors include chemotherapy combined with radiotherapy<sup>4</sup>.

The goal of our study was to examine methods of palliative care, singly and/or in combination, along with an up-to-date brief literature review, in patients with advanced or inoperable bronchial tumors, in order to either prolong the survival time or to improve the quality of life for such a patient.

### Materials and methods

One hundred and sixty three (163) patients with bronchial lung tumors treated between 2000 and 2004, were studied. Types of palliative care which had been applied were as follows: radiotherapy, brachytherapy, chemotherapy and cryotherapy.

Eighty one (81) patients (group A) received only cryotherapy and eighty two (82) patients received cryotherapy plus supplementary palliative treatment such as radiotherapy, brachytherapy or chemotherapy.

Clinical evaluation of the patients as well as evaluation for their quality of life indices were performed prior to

and after each treatment.

During the investigation, the same protocol was used for all patients. This included: age, sex, stage of the tumor, histopathological type, method of palliative care, quality of life (Karnofsky index, WHO performance status), habits of smoking, type of breath, presence of dyspnea and familial history.

Patients' classification was performed by means of Karnofsky index (Table 1) based on their clinical performance. Parameters taken into account aiming at cryotherapy's application are included in Table 2. Among these parameters quality of life was considered of great importance to select the convenient type for palliative treatment (radio-, brachy-, chemo- or cryotherapy).

**Table 1.** Presentation of Karnofsky index (scale 0-100)

Karnofsky Index	
100	Normal
90	Able to carry out normal activity
80	Normal activity with effort
70	Cares for self
60	Requires occasional assistance
50	Requires considerable assistance
40	Disabled
30	Severely disabled
20	Very sick
10	Moribund
0	Dead

**Table 2.** Considered parameters for establishing cryotherapy

Cryotherapy Research Study		
Date of Follow up	SVC. Obs. Sympt.	Actual FER
Weight	Anaemia	Predicted %
Drugs-Steroids	Depression	Actual Pefr ml/sec
Inhalers	Cough	Predicted %
Nebuliser	Haemoptysis	Kamovsky scale
Treatment since seen	Chest Pain	WHO Performance
Asymptomatic	Actual FEV	Dyspnoea
Dysphagia	Predicted %	Quality of life
Anorexia	Actual FVC-ml	Future Planning
Stridor	Predicted %	

The mean age of patients recruited was 67.9 years (range 22-85) and the male/female ratio was at 1.34/1.

For statistical analysis the t-test and the theory of z-approximation to binominal distribution were used. The level of significance was set at  $P < 0.05$ .

**Results**

The TNM staging for all participants prior to start

of palliative curative treatment, was as follows: a) stage I and II: 7.3%, b) stage IIIa: 26.8%, c) stage IIIb: 28.4%, d) stage IV: 37.5%.

Histopathological results showed: 1) squamous carcinomas: 65.2%, 2) adenocarcinomas: 15.4%, 3) large cell carcinomas: 1.8%, 4) small cell carcinomas: 10.8%, 5) undifferentiated 1.8%, 6) benign: 3.75% and 7) melanomas: 1.25%.

Karnofsky index, WHO performance status, FEV1 and FVC measurements before and after treatment, revealed that among patients of group A receiving only cryotherapy, a percentage 65% of patients (they were all in the final stage presenting a great airway obstruction) displayed improvement in one or more among parameters mentioned above. Thirty-five percent (35%) of the patients in group A showed no amelioration or died the days after.

Eighty percent (80%) of the patients in group B (cryotherapy plus supplementary palliative care) showed improvement, whilst in 20% of patients there was no change regarding their clinical performance and their quality of life.

The over two years survival rates were found at 19.3% and 25% regarding the first (A) and the second (B) group of patients respectively.

Based on the evidence of these categorical data, the 95% confidence intervals (CI) for the true percentage of patients who, after palliative treatment, had represented amelioration of their clinical picture, were found between 54.61% and 75.38% for the first (A) group as well as between 71.34% and 88.66% for the second (B) group of patients recruited. Percentages of patients who displayed improvement of their clinical performance and therefore of their quality of life, were compared between the two groups. Patients with amelioration were significantly fewer ( $p=0.015$ ) for the group A compared to those for the group B.

Also, on the basis of the data given, for the percentage of patients who survived for over than two years there was not found statistically significant difference ( $p=0.388$ ) between the two groups.

**Discussion**

Radiation therapy when established in advanced or inoperable bronchial tumors, results in effective palliation of chest symptoms such as dyspnea, cough, hemoptysis and chest pain, something which has been already shown in a six-month follow-up study.<sup>1</sup>

Repeated courses of radiotherapy present no complications in patients requiring palliative care for locally recurrent disease.<sup>5</sup> Pain attributed to skeletal or hepatic metastases, is sufficiently alleviated with radiotherapy, while the method may be also applicable in superior vena cava syndrome and spinal cord compression when surgical approach is not indicated.<sup>6</sup>

Endobronchial irradiation (brachytherapy) is a type of palliative care where a highly radioactive source-iridium 192 (<sup>192</sup>Ir) is bronchoscopically placed (by means

of a flexible bronchoscope) at the desired position<sup>7-9</sup>. The above procedure is accompanied with little morbidity<sup>10</sup>, but the optimal dosage regimen and frequency for brachytherapy have not been determined as now as yet<sup>7</sup>. Nevertheless, a high dose rate (HDR) may include one to six fractions at an interval of one to three weeks with a dose at 2 to 30 Gy per fraction<sup>7</sup>. It should be reported that high dose-rate endobronchial brachytherapy is particularly indicated for treatment of intra-mural tumors<sup>11</sup>.

Previous studies<sup>12,13</sup> proposed that brachytherapy can be applied following a high dose of external beam radiotherapy which failed to relieve symptoms for unresectable lung carcinomas. According to more recent literature<sup>14</sup>, brachytherapy may be combined with external beam radiation, chemotherapy and Nd:YAG laser therapy, to enhance the palliative treatments of patients.

Indications for brachytherapy are as follows<sup>7</sup>: a) potentially curative treatment of early superficial lung cancer, b) treatment of primary non-resectable bronchial carcinomas with curative intent and c) removal of obstruction for primary or recurrent endoluminal lung cancer.

Disadvantages of endobronchial irradiation are pulmonary hemorrhages, bronchial fistula, necrotic cavitations and severe radiation fibrosis<sup>7,15,16</sup>. Location of the tumor has a significant role in manifestation of the aforementioned disadvantages<sup>14</sup>. Computed tomography (CT-scan) should be performed prior to brachytherapy's application especially when tumors involves the mainstem bronchi and upper lobes<sup>14</sup>. Moreover, if pulmonary arteries are invaded by the tumor, the bronchial wall is considerably destroyed and mediastinal invasion also occurs, these patients should be excluded from treatment with endobronchial brachytherapy<sup>14</sup>.

Patients of our study who received brachytherapy combined with cryotherapy showed no complication.

Also, it is well known that lung cancers which are among the most frequent and lethal tumors are mainly treated by surgery or by chemotherapy. A previous study<sup>17</sup> showed that there is a number of curative combinations with cisplatin, vindesine and mitomycin-C against NSCLC non-operative tumors. Patients treated with chemotherapy may survive from 19.7 to 36.4 months more compared to the ones who didn't receive this type of therapy - the latter usually survive from 8.5 to 21.4 months<sup>18,19</sup>. Disadvantage of chemotherapy is the toxicity of the pharmaceutical agents, while complications and side effects observed in the sequel of the application of this method may be attributed to recrudescence of the illness and not to the type of the applied palliative treatment. This is supported by a study<sup>20</sup> showing that if chemotherapy is well tolerated, quality of life is preserved for a longer time, compared to cases where this therapy cannot be given. Therefore, the crucial point lies in the selection of patients who could respond to chemotherapy. The participants of the present study treated with

chemotherapy, showed no toxicity complications.

Cryotherapy is a type of palliative care for lung cancer patients, aiming at destroying obstructive malignant airways lesions. This method which consists in the application of extreme cold for local destruction of tissue, is performed under general anesthesia by means of a flexible cryoprobe using nitrous oxide as a cryogen through a fiberoptic bronchoscope<sup>21,22</sup>. Tumors relatively short in length, located in trachea, mainstem or proximal lobe bronchi can be resected with Nd-YAG laser<sup>23</sup>. Cryotherapy offers an alternative to Nd-YAG laser for either resection of the above tumors<sup>23</sup> and management of tracheobronchial obstruction<sup>21</sup>. Non-critical malignant airway obstruction, hemoptysis, superficial early lung cancer and removal of (water containing) foreign bodies can also be treated with cryotherapy<sup>7</sup>. Mechanisms of injury related to this method include formation of intracellular and extracellular ice crystal producing cell's death<sup>7</sup>. Cellular's membrane permeability is damaged, cytoplasm is found to be hypertonic and dehydrated with a toxic sodium ( $\text{Na}^+$ ) ions concentrations and a pH value at  $\sim 4$ , both implying dislocation of cell's proteins, lipids and enzymes.

Furthermore, endothelial cell damage and thrombosis, resulting from the extreme cold application required by the method, are both implicated in circulation's failure causing tissue's death<sup>7,24-26</sup>. Even if cell's death following cryotherapy is attributed to necrosis or apoptosis, the exact mechanisms of action are not totally understood<sup>27</sup>. Necrosis was found to be maximal 2h following treatment (65% of positive cells) while a second peak had been observed after 4 days (77% of positive cells)<sup>27</sup>. Apoptotic cells were presented around the central necrotic area in a maximal rate 8 hours (47% of positive cells) following treatment. Given that chemotherapy produces apoptosis in a lesser degree without this effect to be time-dependent, the potential benefit to combine cryo- and chemotherapy has already been suggested<sup>27</sup>. According to another recent study<sup>28</sup>, cryotherapy may also be proposed as a neo-adjuvant treatment, while the dose-dependent effects of this method are shown. Specifically, immunohistochemical staining of cleaved caspase-3 had a lesser efficiency in the induction of apoptosis in one vs three cycles of freezing<sup>28</sup>.

Also, one or two sessions<sup>25</sup> of cryotreatment were considered successful for lung cancer patients with obstructive malignant central airway lesions, metastatic melanoma and benign granulation tissue, while for early bronchial cancer repetitive sessions were required. Removal of obstruction is observed from hours to days after cryotherapy's application<sup>7</sup> - the second session takes usually place two weeks after the first one. Therefore, cryotherapy cannot be considered as an urgent method for severe life - threatening situations.

Advantages of cryotherapy are as follows<sup>21</sup>: a) being inexpensive, b) safe for the operator and for other members of the team, c) no danger for bronchial wall perforation or endobronchial fires and d) it may be

done under local anesthesia.

According to a very recent study<sup>29</sup>, news techniques such as percutaneous cryotherapy (PCT) for treatment of thoracic cancer masses have been developed. Six months after the application of this kind of palliative therapy, 86% of masses were found to be reduced or to have a stable size<sup>29</sup>. Bleeding or bronchial damage were not observed<sup>29</sup>, morbidity was low and freezing was extended close to mediastinal tumors<sup>29</sup>, which are all very important for patient's survival.

Besides, we suggest that according to new tentatives<sup>7,25,30</sup> the evidence to manage early lung cancer by means of endobronchial irradiation (brachytherapy) and cryotherapy should be seriously considered, something which can be very useful especially for patients with cardiac problems and impaired lung function.

In our study, cryotherapy was well tolerated except benign tumors. Bleeding was presented in two participants, after completion of cryo-treatment, but surgical intervention was not considered as necessary to be performed.

In conclusion, for subjects with advanced or inoperable lung tumors receiving palliative care, the need for quality of life assessment is of basic importance.

It appears that cryotherapy combined with supplementary palliative treatment may influence the survival time and offer significant increase concerning the number of patients who display improvement of their quality of life.

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