Egyptian Journal of Chest Diseases and Tuberculosis (2016) 65, 527–530

HOSTED BY

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

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ORIGINAL ARTICLE

Fiberoptic bronchoscopic cryo-ablation of central bronchial lung cancer

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Received 2 December 2015; accepted 20 December 2015
Available online 4 January 2016

KEYWORDS

Fiberoptic bronchoscopy;
Cryotherapy;
Endobronchial tumor

Abstract *Background:* Radiotherapy and chemotherapy are the standard palliative treatments in patients with inoperable carcinoma of the lung present with obstruction of the central airway but have limited effectiveness in reopening obstructed airways. Cryosurgery is one of the several techniques that can be used to reopen an obstructed tracheobronchial lumen.

Objective: The aim of this study was to evaluate safety and clinical efficacy of flexible cryoprobe as an important option to treat the patients with inoperable obstructive central bronchial lung tumors.

Patients and methods: This study was conducted on 38 patients with central endobronchial malignant tumor. A flexible cryoprobe was used during flexible bronchoscopy. The endobronchial tumors and symptoms were assessed 2 and 6 weeks after cryotherapy.

Results: After 6 weeks, the endobronchial lesions were completely removed in 32/38 patients (~85%), partly removed in 4/38 patients (~10%), and could not be removed in 2/38 patients (~5%), with a symptomatic improvement in dyspnea, cough and hemoptysis 78%, 63.0%, 85% after 2 weeks and up to 89%, 84.0%, 100% after 6 weeks respectively.

Conclusion: Cryotherapy using fiberoptic bronchoscopy is a safe with a high efficacy technique in treating endobronchial malignant obstructive lesions.

Introduction

Lung cancer, the most frequent cause of cancer related death, is responsible for more than 1 million deaths annually [1,2].

Lung cancer represents >17% of all new cases of cancer and 28% of all cancer deaths worldwide. At the time of diagnosis, >80% of patients are inoperable, resulting in a 5-year survival rate of 15% [3,4].

Approximately 30% of inoperable patients with carcinoma of the lung present with obstruction of the central airway, which can cause distressing symptoms of cough, breathlessness, hemoptysis and recurrent infections, and may lead to gradual asphyxiation [5,6].

Palliative reopening of the affected airways often alleviates symptoms. Where the possibility of surgery has been eliminated, radiotherapy and chemotherapy are the standard palliative treatments but have limited effectiveness in reopening

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

http://dx.doi.org/10.1016/j.ejcdt.2015.12.016

obstructed airways, so, other palliative measures must be considered [7].

Interventional bronchoscopy, particularly therapeutic bronchoscopy, includes many diverse modalities, such as the Nd:YAG laser, electrocautery, argon plasma coagulation, photodynamic therapy, airway stenting, brachytherapy, and cryotherapy, which have advantages and disadvantages [7,8].

The advantage of endobronchial cryotherapy is that it has been proven effective with minimal complications. It is also relatively easy to use and economical compared with other therapeutic modalities. Cryotherapy is safe, with no danger of bronchial wall perforation, no radiation danger, no risk of electrical accidents or fires, and does not require much special training. Disadvantages include delayed results and the requirement for multiple bronchoscopies to remove debris or to retreat, which is a serious issue for cryotherapy in a patient with impending respiratory failure due to an obstructive airway lesion [8,9].

The currently available rigid cryoprobe requires rigid bronchoscopy and general anesthesia, rendering the distal upper lobe bronchial lesions inaccessible [10].

The development of a thin and flexible cryoprobe has revolutionized cryotherapy for endobronchial lesions. This new generation cryoprobe can be passed through a flexible fiberoptic bronchoscope and cryodestruct nearly all visible airway lesions [10,11].

The success of freeze injury, which is the main mechanism of cryotherapy for malignancy, depends on the cooling rate, the thawing rate, the lowest temperature achieved, and repeated freeze–thaw cycles [8,12,13].

Aim of the study

The Current short-term follow-up study aimed to evaluate safety and clinical efficacy of flexible cryoprobe as an important option to treat the patients with inoperable obstructive central bronchial lung tumors.

Patients and methods

In this study, a total of 38 patients with an endobronchial malignant lesion were recruited from Chest and Clinical Oncology departments, Tanta University.

Inclusion criteria: (1) histologically proven carcinoma of the trachea and bronchi, (2) inoperable carcinoma based on the position of the tumor, performance status or poor respiratory function. Exclusion criteria: (1) severe respiratory distress and (2) uncorrectable bleeding profile.

Patients were assessed before cryotherapy and 2–6 weeks after cryotherapy, as regards the: (1) symptomatic; dyspnea, hemoptysis and cough, (2) chest radiography, (3) respiratory function tests: forced expiratory volume in one second (FEV1), and forced vital capacity (FVC) (4) performance status, using the Karnofsky scale [14].

The New York Health Association (NYHA) classification was used for assessment of dyspnea [15]. Hemoptysis was classified as none, blood tinged, and frank hemoptysis. Cough was assessed as regards the severity and persistence (does not disturb sleep or disturbs sleep).

All procedures were carried out during flexible bronchoscopy that was done in a standard fashion with topical anesthesia (5% lidocaine) of the oral-nasopharyngeal area and conscious sedation (IV midazolam).

The distal tip of the bronchoscope was placed about 5 mm above the lesion and the appropriate cryoprobe was inserted through the biopsy channel (bronchoscope) into the tumor. A flexible cryoprobe measuring 90 cm in length and 2.4 mm in diameter was used (ERBE, Germany). The probe was cooled with CO_2 that decreases the temperature in the probe's tip to −70 °C within several seconds.

Statistical analysis

A Wilcoxon matched pairs signed rank sum test was carried out for each outcome variable to determine whether there was a difference between pre- and post cryotherapy values. Results were expressed as numeric values (%). A p value of less than 0.05 was considered significant.

Results

This study was conducted on 38 patients, M/F ratio (23/15), mean age (61.80) with a central endobronchial malignant tumor (65% located in Rt. main, Rt. LL, and Lt. UL bronchi), 60% of the tumors at the time of presentation for cryosurgery at stage IIIb or IV (23 patients), and 40% (15 patients) at stage II or IIIa Table 1.

The endobronchial lesions, after 2 weeks, were completely removed in 29/38 patients (76.31%), partly removed in 5/38 patients (13.16%), and could not be removed in 4/38 patients (10.53%). After 6 Weeks, they were completely removed in 32/38 patients (~85%), partly removed in 4/38 patients (~10%), and could not removed in 2/38 patients (~5%). So, there was an objective significant response ($p < 0.05$) of malignant endobronchial tumors to cryotherapy (using flexible cryoprobe) Table 2 and Fig. 1.

As regards the symptomatic improvement, dyspnea was improved at least one class after 2 weeks in 30/38 patients (78.94%), with more improvement after 6 weeks in 34/38 patients (89.47%). Cough was improved after 2 weeks in 24/38 patients (63.15%), with more improvement after 6 weeks in 32/38 patients (84.21%).

Hemoptysis was improved after 2 weeks in 12/14 patients (85.71%) after 6 weeks in 14/14 patients (100%), completely controlled Table 3.

Table 1 Basic characteristics of study population.

Characteristics	*N*	%
M/F	23/15	
Age	61.80 ± 8.72	
CT tumor size		
⩾3 cm	29	76.32
<3 cm	9	23.68
Lesion localization		
Rt. main bronchus	7	18.42
Rt. LL	9	23.68
Rt. UL	2	5.26
Lt. main bronchus	5	13.15
Lt. LL	6	15.78
Lt. UL	9	23.68

Table 2 Endobronchial lesions response to cryoablation.

Endobronchial lesions:	*N*	%
After 2 weeks		
Removed	29/38	76.31
Partly removed	5/38	13.16
Not removed	4/38	10.53
After 6 weeks		
Removed	32/38	84.2
Partly removed	4/38	10.5
Not removed	2/38	5.2

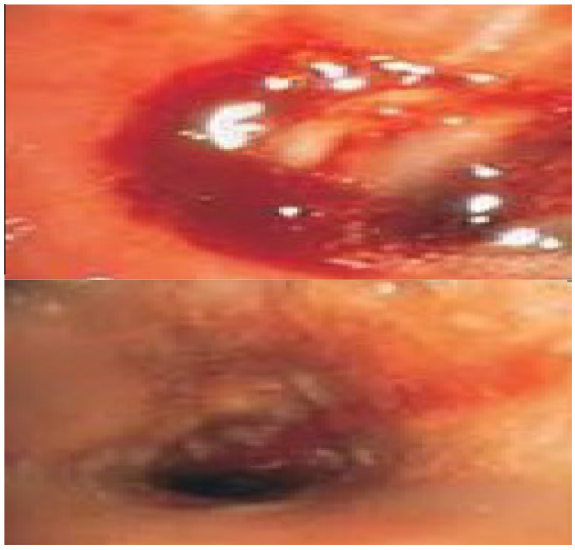

Figure 1 Before and 2 weeks after cryotherapy (completely removed).

Table 3 Symptomatic improvement, 2 weeks and 6 weeks after cryotherapy.

	N	%
After 2 weeks		
Dyspnea	30/38	78.9
Cough	24/38	63.1
Haemoptysis	12/14	85.7
After 6 weeks		
Dyspnea	34/38	89.47
Cough	32/38	84.2
Haemoptysis	14/14	100

Resolution of lung collapse in 60% of patients after 2 weeks, with resolution lobe atelectasis in ~76% ($n = 29$) of patients after 6 weeks Fig 2. Patients ($n = 9$) with persistent lung collapse included patients with partly and not removed tumors ($n = 6$), with thick secretion ($n = 3$), and with progressed extra-luminal compressive tumor ($n = 2$).

As for functional improvement, there was a significant improvement in baseline mean FVC from (1.43), to (1.91) and (2.41) after 2 and 6 weeks. There was a significant improvement in the baseline mean FEV1 from (1.21), to (1.82) and (2.94) after 2 and 6 weeks.

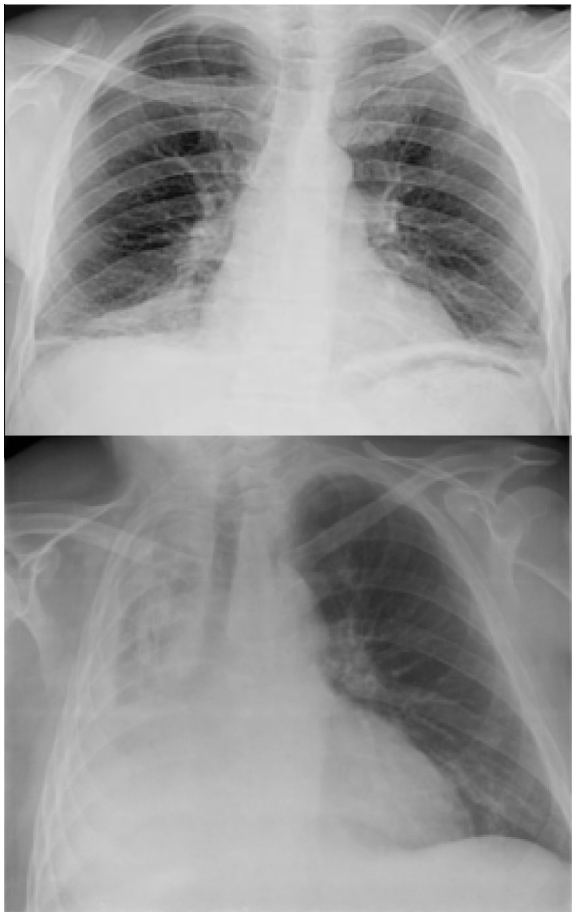

Figure 2 Chest X-ray before and after cryotherapy with Rt. lung collapse resolution.

Table 4 FVC, FEV1, and performance status before and after cryotherapy.

	Before	2 weeks	6 weeks
FVC	1.43 ± 0.57	1.91 ± 0.76	2.41 ± 0.83
FEV1	1.21 ± 0.54	1.82 ± 0.72	2.94 ± 0.98
Perf. St.	54 ± 6	60 ± 7	75 ± 8

There was a significant improvement in the baseline mean Karnofsky score from (54), to (60) and (75) after 2 and 6 weeks Table 4.

Complications: some minor complications (manageable) were reported: mild hemoptysis, blood tinged sputum (7.8%), respiratory distress (5.2%), mild fever (5.2), and post-operative atrial fibrillation (2.6%). There were no reported cases of airway perforation, cardiorespiratory arrest and infection.

Discussion

This study was conducted on 38 patients with intraluminal inoperable malignant tumors, and complete removal of tumor was achieved in 76% of cases by the 2nd week, and up to 85% by the 6th week, only in 2 out of 38 patients tumor could not

be removed. The mechanisms involved in tissue destruction by cryosurgery can be divided into immediate and delayed. Immediate mechanisms include the physical effect of intracellular ice crystal formation, the biochemical effect of cell dehydration and shrinkage, and thawing effects. The delayed effect involves vascular stasis and apoptosis [16,17].

This study showed a marked symptomatic improvement in dyspnea, cough and hemoptysis at 2 weeks and a more marked improvement at 6 weeks after cryo-ablation.

Also, the study showed an effective improvement in the lung function measured by FVC and FEV1, and a significant improvement in the performance status.

From the radiological point of view, resolution of lung collapse had occurred in 60% of patients after 2 weeks, with resolution of lobe atelectasis in 76% ($n = 29$) of patients after 6 weeks.

Our results were in accordance with, Gerard J. et al. [18], who described in this case series, cryotherapy provides a non-operative mechanism of improving airway patency and may be used in combination with other treatment modalities to provide optimal end-of-life care to patients who otherwise may not have been offered any intervention.

Maiwand et al. [5], who reported that a total of 521 patients with advanced obstructive tracheobronchial malignancy underwent cryosurgery. The tumor was shrunk or eradicated and lung atelectasis was improved. Hemoptysis, cough, dyspnea and chest pain were improved. Median survival was 8.2 months and 1- and 2-year survival was 38.4% and 15.9%, respectively.

Yu et al. [19], who investigated the effect of endobronchial cryosurgery in 92 patients with central bronchial carcinoma using CO_2 as the cryogen. Tumor complete remission (CR) was achieved in 51 (55.4%) patients and partial remission (PR) in 31 (37.7%) patients. Cough, hemoptysis, dyspnea, and chest pain were improved in 73.9%, 98.0%, 75.0%, and 50.0% of the patients.

In other studies, a symptomatic improvement has been reported with complete or partial restoration of airway potency in over 90% of patients using cryotherapy, a significant goal of therapy in the palliative management of these patients [20,21].

Limitations of this study, were small number of the study population, and results were not correlated with age, disease stage, and tumor cell type.

In conclusion, in our case series, we reported the successful use with high safety profile of cryotherapy with flexible bronchoscopy to treat central airway obstruction due to endobronchial malignant lesions. The key efficacy outcomes are improved respiratory function and quality of life.

References

[1] G.A. Silvestri, J. Jett, Bronchogenic carcinoma, in: J.F. Murray, J.A. Nadel (Eds.), 4th ed., Textbook of Respiratory Medicine, vol. 3, Elsevier Saunders, Philadelphia, 2005, pp. 1357–1382.

[2] K.S. Bilello, S. Murin, R.A. Matthay, Epidemiology, etiology, and prevention of lung cancer, Clin. Chest Med. 23 (2002) 1–25.

[3] R. Siegel, C. Desantis, K. Virgo, K. Stein, A. Mariotto, T. Smith, et al, Cancer treatment and survivorship statistics, 2012, CA Cancer J. Clin. 62 (4) (2012) 220–241.

[4] C.S. Dela Cruz, L.T. Tanoue, R.A. Matthay, Lung cancer: epidemiology, etiology and prevention, Clin. Chest Med. 32 (2011) 605–644.

[5] M.O. Maiwand, G. Asimakopoulos, Cryosurgery for lung cancer: clinical results and technical aspects, Technol. Cancer Res. Treat. 3 (2) (2004).

[6] C.T. Bolliger, P.N. Mathur, J.F. Beamis, et al, ERS/ATS statement on interventional pulmonology. European Respiratory Society/American Thoracic Society, Eur. Respir. J. 19 (2002) 356–373.

[7] A. Ernst, D. Feller-Kopman, H.D. Becker, A.C. Mehta, Central airway obstruction, Am. J. Respir. Crit. Care Med. 169 (2004) 1278–1297.

[8] J.W. Lee, Y.P. Park, S. Yang, The endoscopic cryotherapy of lung and bronchial tumors: a systematic review – can we expect a new era of cryotherapy in lung cancer?, Korean J Intern. Med. 26 (2011) 132–134.

[9] G. Asimakopoulos, J. Beeson, J. Evans, M.O. Maiwand, Cryosurgery for malignant endobronchial tumors: analysis of outcome, Chest 127 (2005) 2007–2014.

[10] P.N. Mathur, K.M. Wolf, M.F. Busk, et al, Fiberoptic bronchoscopic cryotherapy in the management of tracheobronchial obstruction, Chest 110 (1996) 718–723.

[11] J.P. Homasson, P. Renault, M. Angebault, et al, Bronchoscopic cryotherapy for airway strictures caused by tumors, Chest 90 (1986) 159–164.

[12] G.M. Fahy, J. Saur, R.J. Williams, Physical problems with the vitrification of large biological systems, Cryobiology 27 (1990) 492–510.

[13] A.A. Gage, K. Guest, M. Montes, J.A. Caruana, D.A. Whalen Jr., Effect of varying freezing and thawing rates in experimental cryosurgery, Cryobiology 22 (1985) 175–182.

[14] P.J. Hollen, R.J. Gralla, et al, Measurement of quality of life in patients with lung cancer in multicenter trials of new therapies, Cancer 73 (1994) 2087–2098.

[15] The Criteria Committee for the New York Heart Association, Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels, 9th ed., Little Brown and Company, 1994, pp. 253–255.

[16] B. Rubinsky, Cryosurgery, Annu. Rev. Biomed. Eng. 2 (2000) 157–187.

[17] N.E. Hoffmann, J.C. Bischof, The cryobiology of cryosurgical injury, Urology 60 (Suppl 2A) (2002) 40–49.

[18] Gerard J. Fitzmaurice, C. Karen, et al, Endobronchial cryotherapy facilitates end-stage treatment options in patients with bronchial stenosis: A case series, Ann. Thorac. Med. 9 (2004) 120–123.

[19] X.Y. Yu, X. Tang, H.Y. Liu, et al, Cryosurgery under bronchoscope guidance for patients with central bronchial carcinoma, Yi Shi Jin Xiu Za Zhi (Neike) 27 (2004) 37–38.

[20] I.A. Du Rand, P.V. Barber, J. Goldring, et al, British thoracic society guideline for advanced diagnostic and therapeutic flexible bronchoscopy in adults, Thorax 66 (2011) 1–21.

[21] C. Schumann, P.M. Lepper, T.F. Barth, et al, Successful immediate cryorecanalization of simultaneous high-grade tracheal, bronchial stenosis as rare manifestations of bronchial associated lymphoid tissue lymphoma, J. Thorac. Cardiovasc. Surg. 137 (2009) e17–e19.