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The Role of Flexible Bronchoscopy in Diagnosis of Bronchogenic Carcinoma

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ABSTRACT:
Aim: the use of outpatient instrument (flexible bronchoscopy) to improve cancer diagnosis earlier with no hospital stay giving much time to early diagnosis and early management and follow up of bronchogenic cancer patients and to rule out which patient need further intervention or management.

Patients and Methods: A retrospective study of 160 patients where a flexible bronchoscopy is done in suspected cases of malignant lung lesion in relation to history, examination, chest x-ray and refer them to their age, sex , location and social status and habits including smoking, and sampling of sputum, lymph nodes and pleural fluid cytopathological exam and comparing the results with the transnasal or transoral fibroptic bronchoscopic procedures whether they were wash (brushing not done), biopsies and postbronchoscopic sputum cytological exam using Olympus fibroptic bronchoscopy.

Results: The patients arranged in two groups according to bronchscopic findings into visible and invisible tumors and central tumors and peripheral tumors groups according to radiologic findings. Best results in visible and central tumors, with the squamous cell carcinoma was the highest yield.

Key wards: Fibroptic bronchoscopy, wash, CXR,biopsies, invisible and visible intrabronchial tumors, Olympus, cytologic exam and formalin solution.

Introduction

Bronchogenic carcinoma

Incidence

In brief; carcinoma of the lung is the commonest malignant tumor in males and the 5th most common tumor among females.(1)

Pathology:

The term lung cancer is used for tumors arising from the respiratory epithelium (bronchi, bronchioles, and alveoli). Four major cell types make up 88% of primary lung neoplasms according to WHO classification. These are:

1. Squamous cell carcinoma (Epidermoid carcinoma).
2. Small cell carcinoma (Oat cell anaplastic carcinoma).

3. Adenocarcinoma (including bronchioloalveolar).
4. Large cell carcinoma (large cell carcinoma).

Ninety percent of patients with lung cancer are current or former cigarettes smoker. Epidermoid & small cell cancers usually present as central masses with endobronchial growth, while adenocarcinoma and large cell cancers tend to present as peripheral nodules or masses, frequently with pleural effusion. Epidermoid and large cell cancers cavitates in 10-20% of cases. Bronchioloalveolar carcinoma, a form of adenocarcinoma arising from peripheral airways, can present as a single mass, diffuse, multinodular lesion or a fluffy infiltrate. (2)

Etiology:

1. Cigarettes Smoking: tumor promoters ingested via cigarette smoking. (3)
2. Chronic Obstructive Pulmonary Disease (COPD): is also smoking-related, further increases the risk. (4)
3. Genetics: while lung cancer does not have a clear pattern of Mendelian inheritance, several features suggest a potential for familial tendency. First-degree relatives of lung cancer probands have a 2-3 fold excess risk of lung cancer or other cancers, many of which are not smoking-related.
4. Occupational& other exposures:

a- Established human carcinogens: aluminum products, arsenic, asbestoses, ether and depleted uranium.

b- Suspected human carcinogen: cadmium, silica, and welding fumes.

c- Environmental exposure:

- Air pollution, carbon monoxide, sulfur oxides
- Diesel exhaust.
- Electromagnetic field.
- Radioactive ore &chromium mining. (5)

5.Diet: epidemiological studies demonstrated increased risk among low ß-carotene diet.

Clinical manifestations

The signs and symptoms are caused by:

1) Local tumor growth.
2) Invasion or obstruction of adjacent structures.
3) Growth in regional lymph nodes through lymphatic spread.
4) Growth in distant metastatic sites after hematogenous spread.
5) Remote effects of tumor products (paraneoplastic syndrome).
6) 5-15% is asymptomatic.

Central or endobronchial growth may cause cough, hemoptysis, wheezes, stridor, dyspnea and postobtructive pnemonitis. Peripheral growth may cause pain from pleural & chest wall involvement, cough, dyspnea, & symptoms of lung abscess from tumor cavitations.

Regional spread in the thorax may cause tracheal obstruction, esophageal compression with dysphagia, recurrent laryngeal nerve paralysis with hoarseness, phrenic nerve paralysis with elevation of hemidiaphragm &dyspnea, sympathetic nerve paralysis with Horner’s syndrome (enophthalmos, ptosis, miosis, &ipsilateral loss of sweating).

Pancoast's (or superior sulcus tumor) syndrome result from local extension of a tumor in the apex of the lung with involvement of 8th cervical & 1st & 2nd thoracic nerves, with shoulder pain that radiates in the ulnar distribution of the arm, often radiological destruction of 1st and 2nd ribs.

Other problems include Superior Vena Cava Syndrome; pericardial and cardiac extension with resultant tamponade, arrhythmias, or cardiac failure.

Lymphatic obstruction with resultant pleural effusion. In addition, bronchioloalveolar carcinoma can spread transbronchially.

Extrathoracic Metastatic Disease is found at autopsy in>50% of Epidermoid carcinoma. It may occur in every organ.

Paraneoplastic syndromes are common and the followings are non-metastatic extrapulmonary manifestation of bronchial carcinoma:

1. Endocrine:
   - Inappropriate ADH secretion (usually small cell cancer).
   - Ectopic ACTH secretion (usually small cell cancer).
   - PTH-related peptide secretion causing hypercalcemia (usually squamous cell cancer).
   - Carcinoid syndrome (adenocarcinoma and small cell carcinoma).
   - Gynaecomastia (Estrogen-like secretion).
2. Neurological:
   - Polyneuropathy.
   - Myelopathy.
   - Cerebellar degeneration.
   - Myasthenia (Eaton-Lambert syndrome).
3. Others:
   - Digital clubbing.
   - Hypertrophic pulmonary osteoarthropathy.
   - Nephrotic syndrome.
   - Polymyositis and dermatomyositis.
   - Eosinophilia. [6]

Staging:

American Joint Committee on Cancer Staging System For Lung Cancer

Stage	TNM
IA	T1NOMO
IB	T2NOMO
IIA	T1N1MO
IIB	T2N1MO
IIIA	T3N1MO
	T1-3N2MO
IIIB	T4 Any N MO
	Any T N3MO
IV	Any T Any N M1

TNM Definitions

T TX Positive malignant cell, but primary tumor not visualized by imaging or bronchoscopy.

TO No evidence of primary tumor.

Tis Carcinoma in situ.

T1 Tumor≤3cm, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus.

T2 Tumor with any of the following features of size or extent:

- >3cm in greatest dimension.
- Involves main bronchus,≥ 2cm distal to carina.
- Invade visceral pleura.
- Associated with atelactasis or obstructive pneumonitis that extends to the hilar region but does not involve entire lung.

T3 Tumor of any size that directly invades any of the following: chest wall (including superior sulcus tumors), diaphragm, mediastinal pleura, parietal pericardium; or tumor in the main bronchus<2cm distal to the carina, but without involvement of carina; or associated atelactasis or obstructive pneumonitis for entire lung.

T4 Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, esophagus,
vertebral body, carina; or tumor with a malignant pleural or pericardial effusion, or with satellite tumor nodule(s) within the ipsilateral primary-tumor lobe of the lung.

N NX Regional lymph node can't be assessed.

NO No regional lymph node metastasis.

N1 Metastasis to ipsilateral peribronchial and/or ipsilateral
hilar lymph nodes, and intrapulmonary nodes involved
by direct extension of the primary tumor.

N2 Metastasis to ipsilateral mediastinal &/or subcarinal lymph node(s).

N3 Metastasis to contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s).

M MX Presence of distant metastasis can't be assessed.

MO No distant metastasis.

M1 Distant metastasis present. [7]

Diagnosis:

1.History and examination.
2.Non-invasive modalities:
i-chest radiography:
A. Localizes the site of tumor.
B. Shows local extent and effects of disease.
C. Show areas of atelactasis and consolidation.
D. Show proximity to pleural surface.
E. Rib destruction in advanced disease.
ii-sputum cytology:
Samples obtained may be induced by saline nebulisation or collected as a 3-day pool of sputum produced from spontaneous coughing in the morning.
iii-high resolution CT scan of chest and upper abdomen for of evidence of lesion, malignancy features, lymph nodes (LN), and adjacent structure.
iv-Positron Emission Tomography (PET):
Is valuable in staging and detection of distant disease.
v-bone scan for bony metastasis.
vi-MRI of chest offers few advantages over CT scan.
3. Invasive modalities:
A. Bronchoscopy: is an endoscopic visualization of tracheobronchial tree. Is of 2 types:
a- Rigid one.
b- Flexible one:(DISCUSSED BELOW):
Bozzini in 1806 created an endoscopic instrument utilizing a wax candle as a light source.
Following Edison's development of a miniature electric lamp, the first successful removal of an aspirated foreign body was performed.
In 1897, Gustav Killian "the father of bronchoscope" used an external light source and a head mirror to remove an aspirated pork bone from 63 years old farmer under cocaine anesthesia.
Algernon Coolidge in 1898 passed a uretheroscope through a tracheal fistula and removed a portion of a displaced tracheal cannula from the right main bronchus.
Einhorn in 1902 used an auxiliary tube to carry a light that opens the area of distal lighted endoscope.
Endoscopy as an art and science reached a peak in what might be called Philadelphia School of Bronchoesophygology by Chevalier Jackson.
The development of a flexible instrument had its origin in 1930s when Lamm demonstrated that an image could be transmitted through flexible glass threads.
Hopkins in 1954 developed coherent flexible fiber image bundle for endoscopy.
Ikeda in 1968 described and used 1st flexible fibroptic bronchoscopy in humans and since then flexible instruments of varying length and diameters with accompanying forceps have been developed.
The cytological diagnosis of bronchogenic ca. had attained a high degree of accuracy in many institutions (reported as high as 96%). Because cytology oftenly proven to be of value, specimens should be obtained routinely at bronchoscopy. [8,9,,10,11]

Flexible bronchoscopy is generally performed as an outpatient. The tracheobronchial tree up to the 2nd or 3rd subsegmental bronchi is visualized. The options available to secure a diagnosis include:

- Direct biopsy.
- Brushing.
- Saline lavage for cytology.
- Transbronchial needle aspiration with or without fluoroscopic guidance.

Autofluorescence Bronchoscopy:

It has been found that malignant bronchial mucosa have a different autofluorescence intensities under blue light (wave length 442nm). This led to development of LIFE (Light Imaging Fluorescence Endoscopy)-Lung system whereas normal mucosa appears green, premalignant and malignant tissue appears brown-red.

The role of LIFE currently is in:

- Preoperative screening for synchronus squamous ca.
- Follow-up of postoperative patients.
- Monitoring patient undergoing local, endobronchial treatments for early stage disease.
- Obtaining tissue for molecular biological studies of carcinogenesis and monitoring areas of intraepithelial dysplasia in chemoprevention trials.

INDICATIONS OF FIBROPTIC BRONCHOSCOPY:

Diagnostic:

1. Lung cancer.
2. Positive sputum cytology.
3. Paralyzed vocal cords.
4. Localized wheeze.
5. Unexplained pleural effusion.
6. Hemoptysis.
7. Cough.
8. Diffuse interstitial infilterates.
9. Immunocompromised patients with pulmonary infiltrates.
10. Ventilator-associated pneumonia
11. Endotrachial tube position/patency.
12. Atelactasis.
13. Tracheoesophagel fistula.
14. Acute inhalation injury.
15. Bronchography.

Therapeutic:

1. Mucus plug.
2. Acute lobar collapse.
3. Difficult intubation.
4. Foreign body removal.

5. Hemoptysis.
6. Brachytherapy.
7. Laser ablation.
8. Electrocautry.
9. Stent placement.
10. Balloon dilation.

Advantages of Fibroptic Bronchoscopy:

1. Patient tolerance.
2. Topical anesthesia.
3. Field of view.
4. Angle of deflection.
5. Versatility.
6. Ambulatory settings.
7. Ventilator-dependant settings.
8. usefulness in:

- Cervical spine disorders.
- Subsegmental intervention.
- Transbronchial needle aspiration.
- Brachytherapy.
- Immunotherapy.

Disadvantages of flexible bronchoscopy:

1. Instrument channel size.
2. Sterilization.
3. Maintainenance.

Flexible bronchoscopy has become commonplace in the evaluation of numerous pulmonary disorders. The external diameters of the flexible bronchoscopes range from 2.2 to 6.2 mm., with associated instrument channel ports varying in size from 1.2 to 3.2 mm.. The most commonly used flexible bronchoscope in adult population is the 5.8mm. external and 22mm. internal diameter instrument. The field of view is 90 to 120 degrees, with an upward angle of deflection of 160 to 180 degrees and a downward angle of deflection of 100 to 130 degrees. In contrast to rigid instrument, the flexible bronchoscope facilitates diagnostic and therapeutic interventions at the fourth- or fifth-order bronchial level.

In addition to these subsegmental interventions, there are several distinct advantages of flexible bronchoscope over its rigid counterpart, not the least of which is patient tolerance. Performing the procedure in an outpatient setting with topical anesthesia is possible only with flexible bronchoscopy. Furthermore, patients with cervical spine disorders or aneurysms of thoracic aorta can generally be evaluated with flexible bronchoscopy, whereas these diseases are contraindications to rigid one.

Myriad instruments may be introduced through the bronchoscope's accessory port. Standard biopsy forceps, brushes, curettes, or needles are commonly used to evaluate endobronchial lesions. The accuracy of diagnosing carcinoma with bronchoscopy is dependant on the number and types of specimens obtained. Peribronchial tissues may be sampled by transbronchial biopsy (either forceps or needle aspiration). Transbronchial needle aspiration is performed with an ensheathed 21-guage needle through the instrument channel and should be performed prior to brushings, washings, or lavage to decrease the false-positive rate. In addition, the false-negative rate is at least 15%. Brushings are generally performed after tissues have been directly sampled. Use of the 7-mm. brush results in a higher yield of cellular material than does use of 1.7-mm. brush. Removing the bronchoscope and the brush as a unit increases the diagnostic yield; removing the brush through the instrument channel frequently loses tissue and may contaminate the channel for subsequent diagnostic interventions. Grasping forceps or basket extractor is commonly used for removal of airway foreign bodies. Suction traps facilitate recovery of samples for cytology, microbiologic stains, and culture and sensitivity. Several new techniques have been applied, such as laser therapy, phototherapy, cryotherapy, immunotherapy, and brachytherapy. Many of these techniques occasionally require fluoroscopy for localization prior to intervention.

Contraindications of Bronchoscopy:

There are very few absolute contraindications for bronchoscopy. Most are relative contraindications and deal with coagulopathy, recent myocardial ischemia, or the risk of increasing intracranial pressure in patients who are in high risk situations. All of these problems can be addressed and with replacement of any clotting deficiencies, as well as judicious use of local anesthesia and sedation, these relative contraindications can usually be overcome. The main risk during brochoscopy is compromising the airway of the patient. When dealing with difficult situations such as a tracheal stenosis or tumor, the bronchoscopist must ensure an airway before proceeding with the examination, reverting to rigid bronchoscopy if necessary.

Complications;

Although rare, complications of bronchoscopy do happen. Crucial steps before the procedure should include workup of any comorbid cardiac disease or coagulopathy, and careful consideration of the underlying pathology and the possible consequences of bronchoscopic intervention. As essential step to any procedure should involve informed consent with a detailed education of the patient of the possible complications and the probable effect on the patient.

Most large series on flexible bronchoscopy quote morbidity from 0.05 to 0.1% and mortality around 0.01%. Morbidity was generally defined as respiratory compromise, symptomatic bradycardia, hypotension, syncope, or arrhythmias. Although manipulation of the instrument may be responsible for some of these manifestations, most agree that the majority of morbidity lies in the administration and reactivity to the premedication and local anesthesia.

This risk of rigid bronchoscopy is much more significant, with the largest series quoting a morbidity of 5.1% with 1.1% being construde as major. The main contradistinction between rigid and flexible bronchoscopy lies in the fact that the majority of the increase of morbidity is due to selection of more complex patients and more complex pathology with the likelihood of interventional procedures. This

morbidity reflects the increased ability of palliative procedures using the rigid scope in the increased risk of subsequent complications. This mortality rate of most large series on rigid bronchoscopy parallels that of flexible bronchoscopy.

B.Percutaneous Transthoracic Needle Biopsy.
C.Cervical Mediastinoscopy.
D.Left Anterior Mediastinotomy and Extended Cervical Mediastinoscopy.
E.Scalene Node Biopsy.
F.Video-Assisted Thoracic Surgery (VATs).
G.Thoracotomy: if all above fail. [12,13]

Determination Of Operability And Resectability:

A. Inoperable Tumors:

1. Contralateral hilar and mediastinal lymph node involvement as seen by CT scan.
2. Distortion and stenosis of the esophagus as seen by barium swallow indicate metastatic involvement of posterior mediastinal nodes.
3. The detection of oat cell carcinoma during cytological examination of sputum.
4. Positive biopsy from a palpable scalene lymph nodes.
5. A positive needle biopsy or cytology from pleural effusion.
6. The presence of distant metastasis detected clinically and proven by biopsy.
7. The undifferentiated anaplastic small cell carcinoma when diagnosed preoperatively.

B. Unresectable Tumors:

1. Massive involvement of intrathoracic structures as atelactasis of an entire lung evident by plain chest radiographs.
2.A paralyzed vocal cord, tumor of the trachea, widening of carina, a positive wash, brush, biopsy of oat cell carcinoma as demonstrated by bronchoscopy.
3. A tumor situated less than 2cm from carina.
4. A persistent filling defect, narrowing or obstruction of superior vena cava and pulmonary vessels as demonstrated by angiography.

Treatment:

1. SurgicalTreatment: either:
a. definitive surgical treatment which is usually possible in stage I, II and IIIA. It involves radical pneumonectomy, pneumonectomy, bilobectomy or lobectomy.or:
b.palliative surgical treatment : the role of surgery for the palliation of patients with unresectable tumors is debatable. There are specific situations, such as a remitting lung abscess distal to an obstructing tumor, massive hemoptysis or painful invasion of chest wall (ribs or vertebrae) that have led surgeons to consider and perform palliative or incomplete resections in the hope of improving the patient's symptoms. Methods of palliation include extended resection, lobectomy or segmentectomy.

Possible Methods of Raising the Resectability Rate:

A well-selected cases being associated with a higher resection rate and vice versa. The resection rate will be influenced also by the approach of the surgeon, a bold aggressive policy should result in a higher rate.

Patients who present with extrapulmonary intrathoracic manifestations should not be considered blindly an absolute contraindication to surgery, involvement of the phrenic nerve indicates more extension of the lesion, but this should not constitute an absolute bar to resection. A palliative form of resection including the area of adjacent pericardium could still be performed.

Involvement of recurrent laryngeal nerve indicates more extension of the tumor or lymphatic spread to adjacent lymph nodes, but it may still be possible to do a palliative resection. A positive ipsilateral hilar and mediastinal lymph nodes determined in any patient preoperatively by mediastinoscopy or mediastinotomy or at the time of thoracotomy was considered by many in the past to preclude resection. However, of complete hilar and mediastinal nodes dissection in conjunction with lobectomy or pneumonectomy have been encouraging. Tumors involving tracheal wall, carina, determined preoperatively by bronchoscopy are considered by some surgeons to be inoperable. Tracheal sleeve pneumonectomy, supra-aortic left pneumonectomy are well tried methods performed in these situations to extend the scope of resectability. Superior sulcus tumor invading the chest wall(clinically and radiologicaly evident) do not preclude a palliative extended resection. It is also possible to perform extended resection in cases of direct invasion of chest wall other than the apex provided such invasion does'nt involve vertebral bodies, transverse processes and sternum.

In cell type; the oat oat cell carcinoma is considered non-surgical lesion and should be treated by radiation. An encouraging results have been obtained by preoperative cobalt radiotherapy followed by radical surgical resection. Recently surgery is considered as a first line of treatment in patients with small cell carcinoma.[14]

2.Adjuvant radiotherapy:

There are insufficient randomised data to defend the use of adjuvant radiotherapy for resected stage III (N2/N3) disease.

The use of radiotherapy in consequence after chemotherapy(induction chemoradiotherapy), with or without surgery; has long been used to cosolidate the local component of treatment for stage III non-small cell lung cancer.

3.Chemotherapy:

As several studies began documenting the efficacy of platinum regimens as primary treatment for advanced (stageIV) non-small cell cancer, platinum-based combination chemotherapy became the preffered adjuvant choice.

Induction chemotherapy for stage IIIA(N2)/B non-small cell cancer increases survival.

4.Immunotherapy:

Several years ago it was reported that intrapleural administration of BCG in early post-operative period reduce the rate of recurrent tumor in patient with stage I lung cancer, but role of BCG immunotherapy remain controversial, with large randomized studies indicating that this therapy offers little if any benefit.

If a tumor suppressor gene, such as P53 is mutated, gene therapy trials to replace or modify this mutation are underway and have been shown to be safe when used in a clinical environment.[14,15]

Aims Of Study:

To focus a light on the importance of flexible bronchoscopy in:

- Early detection of lung cancer.
- Follow up of the patients.

Patients And Methods

This is a retrospective study of 160 patients proved to have bronchogenic ca. in Surgical Specialties Hospital in Medical City/Baghdad.
Period of study conducted from 1st of Dec. 2004 to 31st of Dec. 2005.
History, examination, ECG, CXR, PFT & follow up course of those patients were studied.

Sex Distribution:

Males were 112 cases; whereas females were 48 cases. M: F ratio 2.3:1 as shown in figure (1) below.

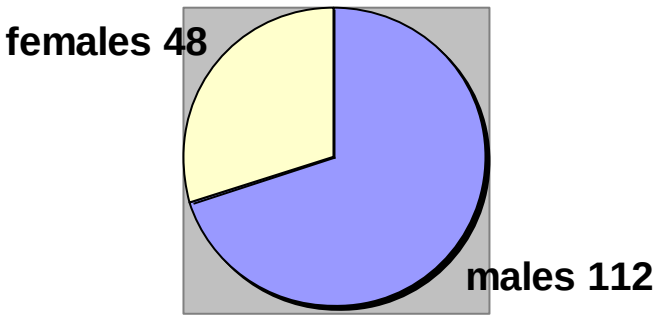

fig. (1) sex distribution

Smoking Habit:

Patients who had a positive history of heavy smoking constituted 136 ones (85%) and the remaining 24 patients (15%) were either ex-smoker or non-smokers as shown in figure (2).

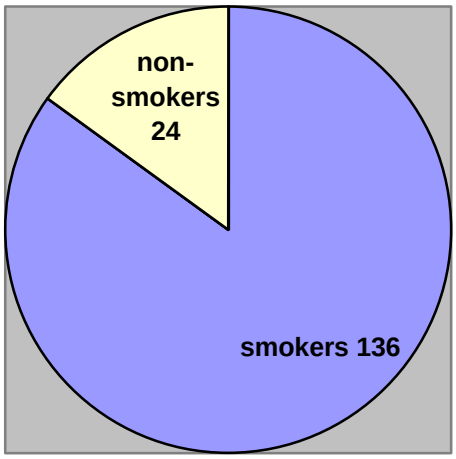

fig. (2) relation of smoking to bronch. Ca.

Age Incidence:

The age range of patients was 28-83 years with a peak incidence at 60-69 years old age as shown in table (1).

Table (1); age distribution of lung cancer patients.

Age Group	Number
30-39	2
40-49	19
50-59	42
60-69	74
70-79	22
80-89	1

Symptoms:

Symptoms distribution shown in table (2) below.

Table (2); symptoms of patients proven to have bronchogenic ca.

Symptoms	Patieint's No.	ercentage
Cough	148	92.5%
Weight Loss	112	70%
Hemoptysis	62	38.75%
Pain	48	30%
Dyspnea	50	31.25%
Dysphagia	5	3.125

Physical Examination:

All have abnormal physical findings. Table (3) below incidence of physical findings in bronchial ca.

Table (3); physical findings in ca. lung.

Findings	Patients No.	Percentage
Svc Syndrome	20	12.5%
Lymph Nodes	28	17.5%
Hoarseness	12	7.5%
Clubbing	145	90.5%

CXR:

Was abnormal in 144 patients (90%) and normal in 16 patients (10%) as shown in table (4) below.

Table (4); the number, percentage, and possible TNM staging of chest X-ray findings of 160 lung cancer patients.

Chest X-Ray Findings		Number	Percent	TNM
Hilar Shadow/Central Tumor		14	8.75 %	T1-T3,N1-2
Pulmonary Shadow	Central	70	52. 5 %	T1-T3
	Peripheral	14		
Pleural Effusion		34	21.25 %	T4
Lung Cavity		10	6.25%	------
Others		2	1.25%	------
No Abnormal Finding		16	10%	------
Total		160	100%	

More over lung cancer predilection is more in the right lung than left (2:1), and more in the upper lobes than lower lobes (3:1) particularly in right upper lobe (42 %).

Sputum Cytology:

Done in 148patients (92.5%) with positive results in 112 patients (70 %) and 80 % are squamous cell carcinoma.

Pleural Fluid Cytology:

Done in 22 patients (13.75 %) with positive results in 20 patients (90 %).

LYMPH NODES BIOPSY:

Done in patients with palpable cervical LN, they were only 16 patients, with 100 % positive results.

Flexible Bronchoscopy:

Procedure:

Done transorally or transnasally under local anesthesia. After proper visualization of the trachea, carina, right and left main bronchi and bronchial tree, specimens obtained and properly studied for cytological evaluation.

The flexible bronchoscope used in this study is Olympus.

For patients with visible intrabronchial lesion 3 biopsy specimens obtained by biopsy forceps and then small amount of normal saline solution is injected into the site of the lesion and the aspirate is collected for cytological examination.

Brushing had not performed.

For those with invisible intrabronchial lesions; the instrument passed as far as possible to the segmental bronchus from which the bleeding came or the tumor is expected and 3 specimens obtained blindly by passing the forceps as far as possible and taking biopsy specimens from that pulmonary segment.

For those whom biopsy is not taken or cannot be taken postbronchial sputum cytology were sent.

Washes were taken through the bronchoscope.

Biopsy specimens obtained by biopsy forceps through the flexible bronchoscope; preserved in 1% formalin solution and sent for histopathology.

Results

The diagnosis of bronchogenic carcinoma was established in 138 patients out of 160 patients of the study by histopathological and cytological examination of intrabronchial biopsy and bronchial wash respectively with diagnostic sensitivity of 86%.

The diagnostic sensitivity is increased by 5% reaching up to 91% by post-bronchial sputum cytological study. The rest of the patients in this study were diagnosed by other methods that include: needle biopsy, scalene nodes biopsy and open lung biopsy.

The patients in this study were divided into 2 groups according to visibility of tumor by bronchoscope:

1. In the 1_{st} group with visible intrabronchial tumor by bronchoscope (98 patients), biopsied in 92 patients and the remaining 6 patients the biopsy is not taken probably because of the bronchospasm and risk of bleeding.

The histological study of the 92 patient's biopsy specimen, was diagnostic in 86 patients with diagnostic sensitivity of 93.5%.

All of the 98 patients with visible intrabronchial tumor had cytological study of bronchial wash sample with positive results in 60 patients, giving a diagnostic sensitivity of 61%.

2. The 2_{nd} group of 62 patients with invisible tumor, bronchial wash was taken in all of them with positive results in 24 patients with a diagnostic sensitivity of 60%.

Biopsies were taken blindly (from suspected bronchus according to radiological findings or from the bronchus from which bleeding came) in 41 patients with positive results in only 3 of them and diagnostic sensitivity of only 17%.

Postbronchoscopy sputum cytology was positive in 3 out of 22 patients in the 1_{st} group; whereas it is positive in 2 patients out of the 62 patients of 2_{nd} group with a sensitivity of 13.22% of 1^{st} group and 3.25% in the 2_{nd} group; these shown in table (5) below.

Table (5); incidence of visible intrabronchial tumor and the results of biopsy, wash, sputum cytology& sensitivity of each.

Visibility Of Tumor	Patients No.	Specimens	Patients No.	Positive Results	Sensitivity
Visible Intrabro. Tumor	98	Biopsy	92	86	93.5%
		Wash	98	90	92%
		Combined	98	90	92%
		Postbronchoscopy Sputum Cytology	22	3	22.5%
Invisible Intrabro. Tumor	62	Biopsy	41	7	17%
		Wash	62	24	60%
		Combined	62	26	42%
		Postbronchoscopy Sputum Cytology	62	2	3.25%
Total	160				91%

Regarding Cxr:
The results shown in table (6) below.
Table (6); The relationship between CXR centrality and bronchoscopic visibility.

Cxr Findings	Patients No.	Bronchoscopic Visibility	Positive Diagnostic Test	Test Sensitivity
Central Tumor	84	80	78 Cases	88.5%
Peripheral Tumor	22	2	1 Case	4.5%

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Regarding Cell Types:

The highest group with positive results of biopsy and wash was those with squamous cell carcinoma and small cell carcinoma came in the next order as shown in table (7).

Table (7); shows the relation between cell type and test sensitivity of specimens obtained.

Cell Type	Patient's No.	Positive Biopsy Results	Test Sensitivity Of Positive Biopsy Results	Positive Wash Results	Test Sensitivity Of Positive Wash Results	Combined Biopsy + Wash Results	Test Sensitivity Of Combined Biopsy + Wash Results	Postbronchial Sputum Examination Results	Test Sensitivity Of Postbronchial Sputum Examination Results	Diagnosis By Other Means
Small Cell	**42**	**21**	**50%**	**53**	**83%**	**36**	**85%**	**2**	**5%**	**7**
Squamous Cell	**69**	**40**	**58%**	**52**	**75%**	**58**	**84%**	**4**	**6%**	**10**
Adenocarcinoma	**29**	**11**	**38%**	**18**	**62%**	**19**	**66%**	**1**	**3%**	**8**
Large Cell	**16**	**8**	**50%**	**7**	**43%**	**9**	**56%**	**1**	**6%**	**3**
Other Types	**4**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**3**
Total	**160**	**80**	**50%**	**112**	**70%**	**122**	**76%**	**8**	**5%**	**31**

Discussion

Development of flexible bronchoscopy had added new dimensions to the diagnosis of lung cancer and the age: Mean age was 62 years with highest proportion in the age group (60-69); this is comparable to Al-Qassir results (61year) and Well's et al (61 year) and different from Al-Alusi, Eman and Al-Khafagi. [16, 17, 18, 19, 20]

GENDER:

Male: female ratio is 2.3:1 this result is identical to Hirmiz and near the Iraqi Cancer Registry Center"3:1" and to recent Iraq studies conducted by Al-Alusi , Elhassani and reducing pattern for the last decades as shown by Elhassani 9:1 and Al-Alusi (7.7:1).

The ratio is more or less the same in USA (2:1&1.3:1 at 1990 and 2004, respectively), while the other races and ethnicities sharing the same ratio in our study as following: China 2:1, Philippine 3:1, Japan 2.8:1, Korea 3.3:1 and Vietnam 2.3:1. [1,14,18, 21,22,23,24]

SMOKING:

Smokers were 85%. This is near Elhassani results, American Thoracic Society/European respiratory Society comments that: smoking account for 80%-90% of all cases of lung cancer and it is easier to prevent than cure. (25,26)

CXR:

Remains a key for suspicion. It was abnormal in 90% of patients with nearly more than ½ of cases is in the right lung; these results are comparable to text of medicine and surgery and other conducted studies in Iraq. (18,19, 20)

SPUTUM CYTOLOGY:

Positive in 70%; this is away from studies conducted in Iraq 42%, 33.7%, 54%; while foreign studies were ranging from 20% to 80%, the least for peripheral and greatest for central tumor specially if associated with hemoptysis. (18, 19, 25,27)

FLEXIBLE BRONCHOSCOPY:

Done in all cases, positive in 138 cases (86%). In general the sensitivity of bronchoscopy for cancer detection ranges from 20-80%.

In our study the right main bronchus was the commonest site of visible intrabronchial tumor, and squamous cell carcinoma was the commonest cell type and the bronchial wash was the most reliable single procedure in the diagnosis of bronchogenic carcinoma and the diagnostic yield increased whenever combined with forceps biopsy. 55% of patients have a central tumor on CXR, 50% are visible on bronchoscopy and 49% of them yield positive bronchoscopic diagnostic procedure to about 88.5% sensitivity; whereas it is only peripheral in 22 cases on CXR and only 2 visible intrabronchial tumor (1.25%) and only 1 of them (0.6%) have a positive bronchoscopic diagnostic procedure.

Performing fibroptic bronchoscopy 1st will identify the endobronchial cancers but CT scan required in 95 patients to detect parenchymal tumor and the fibroptic bronchoscopy required to confirm 4 endobronchial cancers and to identify the last endobronchial cancer from the 95 other cases.

Adding sputum cytology as a diagnostic screen for identifying which patients undergo fibroptic bronchoscopy substantially reduces the number of tests needed to diagnose cancer while maintaining a high early rate of cancer detection.

In one study; cell types frequency was as such: squamous cell carcinoma (67.8), adenocarcinomas (17.7), large cell carcinoma (6.2), small cell carcinoma (8.9); adenosquamous and carcinoid (1.3% for each).

When bronchoscopy reveals endobronchial tumor, biopsy is best accomplished with either a forceps or brush biopsy with sensitivities in the range of 80-100%.

Positive endobronchial findings are more common with squamous and small cell cancer because of their central location; whereas a normal bronchoscopic examination is usually seen with peripheral lesions and the diagnostic sensitivity of bronchoscopy varies from 37-98%. The use of fluoroscopy to guide a transbronchial biopsy or needle aspirate and lavage improve diagnostic accuracy to 80%.

The diagnostic sensitivity of bronchoscopy in lung cancer detection by Driesin and associates reached to 91% for central and 73% for peripheral lesions (done under fluoroscopy guidance).

Richardson et al made a diagnosis of lung cancer in 41 out of 52 patients (79% sensitivity) with peripheral lesions.

In 1970 Ikeda reported the result of 360 patients with lung cancer examined with 5.5mm. Machida broncho-fibroscope; visual findings of carcinoma obtained in 83% and positive sputum cytology or transbronchial biopsy histopathology in 89% of all cases.

Brush biopsy sensitivity of 50% in study of Chandhary and associates.

Kvales and colleagues reported that Post bronchoscopy sputum and bronchial wash examinations didn't add significantly to diagnostic yield; while in Solmon's group he found that Post bronchoscopy sputum and wash yield only one additional neoplasm in 46 patients in the study. [7,12,28,29,30,31,32,33,34,35]

N.B: in our study fluoroscopy and brush biopsy were not in use.

Conclusions

1. Major problem in dealing with bronchogenic carcinoma is the late medical consultation and delayed recognition of the disease as shown by high percentage of patients with tumor with late diagnosis.
2. Flexible bronchoscopy is an important diagnostic aid.
3. Flexible bronchoscope is very dependable diagnostic aid in the diagnosis of centrally located tumor.
4. Wash and forceps biopsy has a high accuracy rate in diagnosis and in combination yield the highest diagnostic accuracy.
5. Post bronchoscopy sputum cytology is important in the diagnosis.

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