UNIVERSITY OF NAIROBI

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS

RETROSPECTIVE AUDIT OF FLEXIBLE BRONCHOSCOPY PRACTICE AT KENYATTA NATIONAL HOSPITAL - A 5 YEAR AUDIT

Dr. ABDIWELI M. BASHIR

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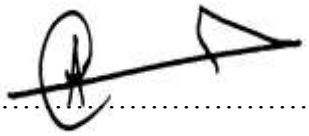
PROPOSAL SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF MEDICINE IN INTERNAL MEDICINE

DECLARATION

This proposal is my own original work and has not been presented for a degree at any other University.

Signed 

Dr. Abdiweli M. Bashir

Department of Clinical Medicine and Therapeutics,

University of Nairobi.

APPROVAL BY SUPERVISORS

This dissertation has been submitted for the degree of Masters of Medicine in Internal Medicine with our approval as university supervisors

Dr. Jared Mecha, MBChB, MMed (Nrb), MSc-RM, MPH
Consultant Pulmonologist and Lecturer
Department of Clinical Medicine and Therapeutics,
University of Nairobi

Signed ..... Date: 3/12/21.

Dr. Loice Achieng, MBChB, MMED INT MED (UoN), DLSHTM, MSC INF DIS (UoL)
Infectious disease specialist and Lecturer
Department of Clinical Medicine and Therapeutics,
University of Nairobi

Signed ..... Date: 6/12/21

Dr. Andrew Owuor, MBChB, MMed Int.Med, Dip HERMES
Consultant Physician, Respiratory & Critical Care Specialist
Kenyatta National Hospital

Signed ..... Date: 3/12/2021.

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Finally, thanks to God who has enabled me get this far.

LIST OF ABBREVIATIONS

ABG	Arterial Blood Gas
AFB	Acid fast bacilli
BAL	Broncho-alveolar lavage
BOOP	Bronchiolitis Obliterans organizing pneumonia
BP	Blood pressure
BTS	British Thoracic Society
ECG	Electrocardiogram
FB	Flexible Bronchoscopy
FOB	Fiber optic Bronchoscopy
HIV	Human Immunodefiency Virus
KNH	Kenyatta National Hospital
PTB	Pulmonary Tuberculosis
RCT	Randomized clinical Trial
RDU	Respiratory Disease Unit
SPSS	Statistical package for social sciences
TB	Tuberculosis
TBB	Trans-bronchial Biopsy
TBC	Total Blood count

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ABSTRACT

Background: Since the discovery of flexible fiber optic bronchoscopy (FB) by S. Ikeda in 1964. It has become an important diagnostic and therapeutic tool for management of chest disease. There are numerous indications for bronchoscopy including peripheral pulmonary nodule, hemoptysis, chronic cough, pleural effusion, recent or unresolved pneumonia, pulmonary tuberculosis, and lung collapse.

Routine clinical audit of flexible bronchoscopy practice is guideline recommendation of British thoracic society, the aim of these audits is to review level compliance with the guideline/standards. Compliance with the guidelines enhance standardization of practice, outcomes and patient safety. The audits review the structure, processes and outcomes of practice to ensure efficacy and patient safety.

There is paucity of data on the practice, safety and efficacy of flexible bronchoscopy in Kenya thus this will be a novel study.

Objective: To determine the flexible bronchoscopy practice at Kenyatta National Hospital.

Design: Retrospective medical audit.

Setting and Duration: The study will be conducted at Kenyatta National Hospital Respiratory Disease Unit and is anticipated to take 2 months.

Population: The study population will be medical files of patients aged 13 years and above who underwent flexible bronchoscopy in at the RDU of Kenyatta national hospital between January 2016 and December 2020.

Methods: A retrospective clinical audit of 250 flexible bronchoscopies done over the last 5 years will be conducted. The audit will review the processes and outcomes of the practices using as structured checklist to collect data needed to meet the study objectives. The process audits will review practices in pre-procedure patient preparation, anaesthetic technique, patient monitoring, indications for the procedures, sampling techniques and pattern of findings. The outcome review will evaluate the histopathologic or microbiologic yield of the specimen collected and the immediate complications.

Analysis: The data will be collected using a structured study proforma with unique study serial number to avoid duplication. Data forms will be kept in a secure cabinet accessible only to the PI. All data from the study proforma will be coded, entered and managed in a Microsoft access. Data will then be entered, cleaned and analyzed using Statistical Package for Social Sciences (SPSS version 21.0). Continuous data will be presented as means and medians while categorical data will be analyzed and presented as proportions.

CHAPTER 1: INTRODUCTION

Since the discovery of flexible fiber optic bronchoscopy (FB) by S. Ikeda in 1964, it has become an important diagnostic and therapeutic tool for management of respiratory diseases.

Flexible bronchoscopy is an easier to perform and safer compared to rigid bronchoscopy. The ease to maneuver, patient comfort and its documented safety has made flexible bronchoscopy (FB) a safer, outpatient procedure, that has replaced rigid bronchoscopy for routine diagnostic use (1). It can be performed under conscious sedation and local anesthesia thereby avoiding the attendant complications of general anesthesia and making it an outpatient procedure.

The practice of flexible bronchoscopy is not standardized even in developed world despite availability of guidelines concerned primarily with safety of the procedure(2). It is for this reason that the British Thoracic Society in its 2013 guideline on practice of diagnostic flexible bronchoscopy recommends periodic clinical audit of the practice for conformity to the standards (3).

Clinical audits and surveys on the practice of FB has shown considerable variation in physician's routines in patient preparation, drug therapy, sampling method and occurrence complications. These variability was thought to result from combination of individual experience and presence of conflicting data on some aspects of the practice. Smyth et al however noted that even audits on some aspects of the practice where standard of care was already established considerable variation was noted (2).

BTS 2001 guideline recommends a number of pre-procedure patient evaluation and preparation in order to enhance patient safety. They include pre-procedure fasting of at least 4 hours, coagulation profile and platelet count for high risk patient. These recommendations are however to be individualized (3).

The technique of anaesthesia and the choice of medication is still a variable practice among chest physicians. The practice of whether to sedate or not is even more variable. In surveys done in the US and Pakistan 96% and 98% of chest physicians reported they sedated patients when doing flexible bronchoscopy(4, 5). This was higher than the rate reported in Egypt (79%)(6). Despite this variability there is no evidence to show benefits of sedation(7).

Flexible bronchoscopy plays an important diagnostic role in the evaluation of non-resolving pneumonia, chronic persistent cough, persistent atelectasis, lung masses, hemoptysis and airway obstruction. According to Gupta AA et al in a study analyzing bronchoscopy findings in tertiary hospitals in India, trends over 34 years they noted that some of the most common indications for performing flexible bronchoscopy are suspected lung malignancy (32.2%), infections, especially *Mycobacterium tuberculosis (*18.6%), interstitial lung disease (13%), pleural effusion (3.6%), and foreign body (0.26%)(1).

In another study by Almoudi OS et all a suspicion of pulmonary tuberculosis (31%), lung mass (19%) and hemoptysis (18%) were the most common indications among Saudi patients undergoing flexible bronchoscopy(8).

Fiber optic bronchoscopy is also a valuable therapeutic tool in the management of persistent atelectasis, foreign body removal, removal/debulking of endobronchial tumors and management of emphysema by bronchoscopy lung volume reduction surgery(8).

Flexible bronchoscopy is generally considered to be safe but some intra and post bronchoscopy complications have been reported. Almoudi et al noted hypoxemia (14%), sinus tachycardia (5%), bronchospasm (3%), bradycardia (2%), apnoea (2%) and seizures (1%) as some of the complications occurring during the procedure. Complications such as pneumothorax (4%) and sepsis (1%) were reported post procedure.

The KNH RIDU has been performing bronchoscopy for over 20 years now yet there is no local data on the practice, indications, pattern of bronchoscopic findings and safety. The goal of this study will be to document the practice at KNH in terms of patient evaluation and preparation practice, monitoring, indications, anaesthetic technique, sampling procedures, patterns of findings, complications and histopathologic/microbiologic yield of samples obtained.

CHAPTER 2: LITERATURE REVIEW

HISTORICAL PERSPECTIVE

Bronchoscopy is an endoscopic procedure that visualizes the inside of the respiratory tract by placing a tube with light and camera inside the airway (9)

The discovery of bronchoscopy began during the era of Gustav Killian in 1876, with the removal of a pork bone from a farmer's airway. Chevalier Jackson laid the foundation for modern day rigid bronchoscope and S. Ikeda in 1967 helped to introduce the modern-day fiber optic bronchoscope (9).

Ikeda`s fiber-optic bronchoscope has undergone improvements over the years with advances in technology to improve airway visibility and procedure safety and comfort (9).

CLINICAL AUDIT OF BRONCHOSCOPY PRACTICE

There is a global drive to standardize professional practice including bronchoscopy through clinical audits. The British Thoracic Society in 2013 guideline on practice of diagnostic flexible bronchoscopy recommends periodic clinical audit of the practice(3). These audits are intended to evaluate the current practices and their conformity or lack of, with local (where available) and international guidelines (10).

There is no local or regionally validated guideline for the practice bronchoscopy in the region. There is also no clinical audit of the local practice of flexible bronchoscopy despites its existence over 20 years.

The clinical audit of flexible bronchoscopy practice, just like other practice audits, reviews the structure, processes and outcomes of the practice (11). The structural audit reviews resources required to deliver care, the environment, facilities, and available protocols and policies.

Processes audit involves the procedures and practices implemented by the staff in the prescription, delivery and evaluation of care. These could include practices in pre-procedure patient preparation, peri-procedure patient monitoring, practice of anesthesia including mode and choice of anaesthetic agents, indications, diagnostic sampling techniques and pattern of findings.

Outcomes audit evaluate the effect of care received by the users both in terms of diagnostic yield and complications.

Despite the promotion of clinical audits in professional practice evidence supporting its efficacy is weak to moderate and dependent on the interventional design and delivery. A Cochrane review of 140 studies on clinical audits concluded that audits can be effective in improving professional practice but the effect is small to moderate. They observed that the relative effectiveness of audits was greater when the baseline adherence to standards of the audited practice is low and when it is done as a continuous practice (10).

PRE-PROCEDURE PRACTICE

The British Thoracic guideline (BTS) 2001 makes some recommendations on patient evaluation and preparation before flexible bronchoscopy. These evaluations are not routine and are to be individualized.

Fasting

The BTS guideline recommends fasting for solid foods for 4 hours and 2 hours for clear fluids however audits have shown the practice is variable. In a survey of Adult Flexible Bronchoscopy Practice in Cairo, Madkour et al noted 59% of chest physicians in Cairo recommended fasting for 4-8 hours before bronchoscopy while a considerable number (39%) recommended more than 8 hours (6). The practice was similar in UK where a survey found 73.3% of physicians recommended fasting for 4-8 hours, 8.4% for more than 8 hours, and14.3% for less than 4 hours (12).

Cochrane reviews of 38 RCTs did not show significant evidence that shortened fluid fast resulted in risk of aspiration when compared with the standard 'nil by mouth from midnight fasting policy. The participants were however “healthy” adults (13).

Laboratory evaluation

The BTS guideline recommends coagulation profile, platelet count and haemoglobin concentration to be performed when the clinical risk for abnormal coagulation is high.

The evidence to support this recommendation is not strong, Kozak et al in a study of 274 patients, found that more that 75% of patients who developed bleeding on bronchoscopy had normal coagulation studies and no clinical risk factor for bleeding. Incidence of bleeding among those with abnormal coagulation profile was 11% (14).

Bleeding complications were not significantly predicted by the presence of clinical risk factors, type of biopsy, abnormal coagulation, platelet, hemoglobin, or creatinine values (14).

The practice is also varied with more than 50% of chest physicians in UK reporting that they do routine total blood count (TBC), 18% do clotting profile in patients undergoing bronchoscopy without trans-bronchial lung biopsy (TBB). The practice was higher when patient where scheduled for TBB with 91% requesting TBC and 88% clotting profile(2).

Madkour et al reported similar findings in bronchoscopic practices in Cairo. Half of the physicians requested for TBC whether TBB was planned or not. 65% of them also did coagulation studies even when TBB was not planned.89% ordered for coagulation profile because a trans bronchial biopsy was scheduled (15).

Even when bleeding occurred it was reported to be mild to moderate with only 3% estimated to be more than 100 milliliters. 90% of these bleeds resolved spontaneously or with local vasoconstrictor therapy(14).

Ordering of pre-procedure investigations should be based on the clinical status of individual patient so as to reduce the increasing cost of medical care and make bronchoscopy more accessible (6).

Spirometry and Arterial Blood Gas Evaluation

The BTS guideline does not give recommendation for routine pre-procedural spirometry or arterial blood gas analysis (ABG) but two thirds of the pulmonologists in the UK in a survey by Smyth et al reported that they do routine pre-bronchoscopy spirometry while 63% do routine ABG for patients with low oxygen saturations or poor spirometric measures (16). The practice is different in Egypt where only 17% did baseline spirometry and 37% routine ABG (15).

Anaesthetic practice

The technique of anesthesia and the choice of medication has remained a variable practice. This is more so on whether to sedate or not. In a survey among pulmonologists in the UK, 92% reported to giving sedation during bronchoscopy. The practice was similar in the United States and Pakistan with 96% and 98% sedation rate respectively (4, 5) but much lower among chest physicians in Egypt (79%)(15).

Despite the variation in practice there still no consensus on the benefits of sedations. Credle et al have shown that sedation was implicated in up to 50% of major complications resulting from bronchoscopy (7). Hatton et al in a double blind trial also found no difference in comfort between the patients given 70ug/kg of intravenous midazolam versus placebo (17). Putinati et al however

showed administration of intravenous diazepam resulted in significant improvement in patient tolerance to the procedure. They also indicated reduction in number of abandoned procedures due to patient intolerance, when patients were sedated (18).

The need for sedation is variable among patients and influenced by whether pre-procedure education and reassurance is given (16).

There is also variability in choice of sedatives among the chest physicians. The practice audit in the UK showed that 63% of pulmonologist used benzodiazepines only, 14% gave opioids only while 12% combined both opioids and benzodiazepines (16). The practice was however different in Egypt where there was less use of the combination (3%) and opioids only (1%) but similar in preference for benzodiazepine only (75%)(15). These practice of combined opioids and benzodiazepines has not been shown to improve tolerance to procedure when compared with either agent alone. It is also associated with increased risk of cardiorespiratory depression (19, 20).

The American College of Chest Physicians in its consensus statement (2011) recommended all physicians should use topical anesthetic, analgesic and sedative agents when feasible. This was based on its safety and effectiveness (21). Most practice audits both in Europe and Asia demonstrated compliance with these recommendations with about 94% of physicians using local anesthesia when doing bronchoscopy.

Patient Monitoring

Guidelines recommend all patients undergoing bronchoscopy should have heart rate, respiratory rate, blood pressure and oxygen saturation monitored continuously before, during and after the procedure. A practice survey in India, Egypt and UK showed some variable practices. While pulmonologists in the UK and India almost always monitored oxygen saturations, 24% of those in Egypt did not do (6). The monitoring of blood pressure during the procedure was also not universal with 90% physicians in the UK, 27% in India and 44% in Egypt reporting that they did not monitor BPs always. This was sometimes attributed to limited number of assistants during the procedure (UK)(2).

Routine ECG monitoring during procedure is not recommended unless there is a history of a cardiac disease or in case of hypoxia despite oxygen supplementation. 74.6% practitioners in North America reported they always did ECG monitoring during the procedure, this was much higher

than in Egypt (35%), UK (22%), and India (39%)(2, 6). More than 50% of physicians in the UK reported to have never done ECG monitoring during bronchoscopy, this carries the potential risk of not discovering occurrence of arrhythmias and cardiac events in predisposed patients like the elderly (2).

Topical anesthesia, sedation, mechanical obstruction by the probe can all cause hypoxemia during bronchoscopy, routine oxygen supplementation would seem logical. There is insufficient evidence to support this practice. Jones et al in a prospective study of 1051 cases evaluated whether all patients required routine supplemental oxygen therapy during bronchoscopy (22). They concluded that majority of the patients did not require routine oxygen supplementation, but recommended routine oxygen saturation monitoring.

The BTS recommends supplemental oxygen when a patient has significant desaturation i.e. change >4% or SPO_2 <90% (3). This practice was also noted to be variable with 88.9% North American chest physicians providing routine supplemental oxygen as compared to only 54% in India (4).

PROCEDURAL PRACTICE

Route of insertion

The best route insertion of the bronchoscope is still controversial with no particular preferences in the guidelines. The practice is equally varied with 75% of physicians in Cairo preferring nasal route while in Pakistan 98% preferred oral route of insertion. 43% of those in North America had no preference between the two routes.

Aguirre et al in a prospective study evaluating the routes of bronchoscope insertion and patient discomfort found no statistically significant difference between the oral and nasal routes. They reported oral route was associated with better cord visualization, less requirement for topical anesthesia and fewer insertion failures (23).

In a larger randomized study with 307 bronchoscopy case, choi et al compared oral and nasal routes for patient discomfort and found oral route was associated with less discomfort ($P<0.001$) as compared to nasal approach. They also found oral route was associated with less local anaesthetic need, less insertion site bleeding, less dyspnea and coughing. They however concluded that the route of insertion did not have significant influence on the outcome of the procedure (24).

Indications of bronchoscopy

The conventional and newer indications of diagnostic and therapeutic flexible bronchoscopy provide a greater leeway in its clinical application. The indications of flexible bronchoscopy vary from country to country depending on the disease pattern, and to the age demographics (25).

According to a North American survey, the most common indications for bronchoscopies are pulmonary mass or pulmonary nodules, hemoptysis, pneumonia, infections, interstitial lung disease and therapeutic bronchoscopy for atelectasis (4).

In a prospective study that reviewed 124 consecutive bronchoscopies done over 3 years in Saudi Arabia, the most common indications reported were pulmonary infiltrate (suspected TB -31%), lung mass (19%), hemoptysis (18%), pulmonary fibrosis (8%), and atelectasis (6%) (8).

In Nigeria, the most common indications for bronchoscopy were suspected bronchogenic cancer (33%), pleural effusion (19.2%), chronic cough (13.1%), hemoptysis (10.1%), suspected PTB (6.1%).

The burden of TB globally continues to grow with 1.5 million deaths in 2018 and 16.7% of these being among those with HIV. Bronchoscopy has been shown to have diagnostic utility in patients suspected to have TB with no sputum or sputum smear negative for AFBs. Jacomeli et al in a prospective study of 286 patients suspected to have TB but who had no sputum or were sputum smear negative found 44% to have TB after bronchoscopic BAL and culture (10).

In most audits and studies, hemoptysis is a common feature in the top five indications for flexible bronchoscopy. Bronchoscopic evaluation of hemoptysis by Mehta et al found 64% had normal findings, 4% had malignancy, 4% abscess, 2% TB, 2 tracheitis, 2% tracheal trauma and 1.2% had bleeding site with no established diagnosis (26).

Another important indication for flexible bronchoscopy is non-resolving pneumonia or chronic cough. A number of studies have looked at the utility of fiber optic bronchoscopy in evaluating non-resolving pneumonia. Feinsilver et al evaluated 35 consecutive patients who had radiographic infiltrates, cough, either temperature >38.1°C, leukocytosis, or sputum production, who had symptoms for at least 10 days and antibiotic therapy for a week without resolution of signs and symptoms. Fiberoptic bronchoscopy (FOB) was diagnostic in 86 percent (12/14) of the patients(27). Common etiologies established in the 86% were infectious (Pneumocystis

pneumonia, Cytomegalovirus pneumonia, Actinomycosis and *Mycobacterium tuberculosis*), cancer, eosinophilic pneumonia, Wegener's granulomatosis, and bronchiolitis obliterans organizing pneumonia (BOOP).

Chaudhuri et al similarly demonstrated the utility of FOB in patients with non-resolving pneumonia. Using FOB, a definitive etiological diagnosis for non-resolving pneumonia was established in 85.7% of the patients. Common etiologies for the non-resolving pneumonia were bacterial pneumonias (53%), bronchogenic carcinoma (26.67%), tuberculosis (16.67%) and 1.67% Wegener's granulomatosis(28). Gram-negative bacilli were the most common isolates (30 out of 32 cases) of bacterial pneumonia (93.75%) with *Klebsiella pneumonia* and *Pseudomonas aeruginosa* being the most predominant gram negative organisms isolated (28).

Partial or complete atelectasis is another important indication for both diagnostic and therapeutic bronchoscopy. Toolsie et al demonstrated that in a study of 149 patients undergoing bronchoscopy due to complete or near complete atelectasis that the most common cause of atelectasis based on BAL was bacterial infection (70.4%) due to predominantly gram negative organisms. Endobronchial tumors were found in 14%, commonly non-small cell carcinoma (29).

Flexible bronchoscopy has become an important diagnostic tool in the evaluation of patients suspected to have lung cancer. More than 70% of lung carcinomas are approachable via bronchoscopy. Beyond diagnosis it is also valuable tool in staging and delivery of therapeutic modalities (30).

The diagnostic yield of FOB in lung cancer is dependent on the location, size of the lesion and the experience of the bronchoscopist. The BTS recommends a diagnostic yield of 85% when definite endobronchial tumor is visible. It also recommends at least 5 biopsy samples be collected when endobronchial tumor is visible. Bronchial brushing and washing can be combined with biopsy to increase the diagnostic yield(3).

Some of the most important indications for therapeutic flexible bronchoscopy include foreign body removal, management of persistent atelectasis and endobronchial tumor management (8).

Limper et al reviewed the clinical spectrum, predisposing conditions, efficacy and complications of bronchoscopy in trachea-bronchial foreign body in adults. 98.3% (59) of the cases had foreign body that could be visualized and retrieval attempted. 96.6% of these had successful retrieval with

bronchoscopy (both flexible and rigid bronchoscopy). Rigid bronchoscopy was noted to have higher successful retrieval rate (97%) when compared to flexible bronchoscopy (61%). They found 41.7% had underlying impaired airway protective mechanism such as primary neurological disorder, trauma with loss of consciousness or sedation (31).

In another study Debeljak et al looking at common sites of foreign body location and efficacy of bronchoscopy in adults with airway foreign body reviewed results of 62 patients who underwent removal. They found that the FB were predominantly lodged in the right bronchial tree on 42 occasions (67.7%), 20 cases in the left (32.3%) and one in the trachea. The foreign bodies were successfully removed in all but 2 patients (3%) (32).

Toolsie et al looked at the role of bronchoscopy in atelectasis compared to conservative management. They reviewed 177 hospitalized patients with complete or near complete lung collapse, 149 of them underwent flexible fiber-optic bronchoscopy while 28 (16%) underwent conservative management. The primary outcome of this study was the degree of radiologic resolution, timing of bronchoscopy in relation to radiologic resolution and mortality as a secondary outcome. They noted that patient who underwent flexible bronchoscopy achieved higher rate of resolution (57%) as compared to those who underwent conservative management (28.6%). The timing of the bronchoscopic intervention whether less than 24 hours or more did not result in statistically significant difference in resolution of the lung collapse (44.3% vs 43.8% respectively). There was also no difference in all-cause mortality between the two groups (conservative vs bronchoscopic group)(29).

Bronchoscopic pattern of findings

The various studies or audits looking at the patterns of flexible bronchoscopic findings vary in the nomenclature of reporting. This is largely due to lack of standardize reporting systems globally or regionally. The Bronchoscopic Working Groups of Italian Scientific Societies has attempted to develop a standardized reporting guideline with a glossary for trachea-bronchial lesion description in order to standardize bronchoscopy practice in Italy(33).

A survey of chest physicians in Cairo noted that common bronchoscopic patterns reported include normal findings, visible occluding tumor and mucosal swelling or irregularity(6).

An audit of FOB practices in a private hospital in Greece reviewed 200 bronchoscopies for pattern of findings and histopathologic correlations of the findings. They found the a normal appearance to form 17% of the findings, bronchial mass (15.5%), inflammation (12%), bronchial stenosis (9.5%), profuse secretions (9%), focal hemorrhage (8%) (34).

Almoudi et al also had similar pattern of findings except for much higher proportion of inflammation (64%).They found normal appearance (14%), narrowed segment (31%), tumor-like mass (18.5%)(8).

Inflammatory changes reported on bronchoscopy were associated with 42% histopathologic findings of TB and 18% non-TB granuloma. Narrowed segment or stenosis was associated with 72% histopathologic findings of lung cancer, 14% with granuloma and 7% non-specific chronic inflammation. In the study, tumor-like mass was confirmed by histopathology to be lung cancer in 86% of the cases, 15% as TB and 5% as non-specific chronic inflammation(8).

Diagnostic sampling techniques

A number of diagnostic procedures can be done using flexible bronchoscope in order to establish a diagnosis of suspicious endobronchial lesions. Airway inspection is combined with one or more of the following diagnostic procedures. Endobronchial brushing, Bronchial washing, Broncho-alveolar lavage, endobronchial biopsy, trachea-bronchial biopsy and needle aspiration (35).

Most commonly used diagnostic sampling techniques including bronchial washing, bronchial brushing and bronchial biopsy. Adewole et al in a study in Nigeria where 99 patient underwent bronchoscopic diagnostic sampling, 100% had bronchial washing, 39.4% had bronchial brushing while 72 had endobronchial biopsy (39).

The practice in Saudi Arabia was 90% of the patients underwent bronchial washing and brushing and 82% had an endo-bronchial biopsy of suspicious lesions(8). These was similar to the practice in Greece where 90.4% underwent bronchial washing, 80% biopsy but lower bronchial brushing rate of 60% (34).

Hau et al found combining brushing with forceps biopsy improved the diagnostic yield in lung cancer. They also noted pre-biopsy brushing of endobronchial exophytic tumors was superior to

post biopsy brushing(36). This contrast with the findings of Chaudhary *et al* who found pre-biopsy brushing to be superior(37). Chaudhary et al argued biopsy procedure liberates tumor cells, increasing the pool of tumor cells collected during post biopsy brushing. Hau et al rationalized their findings on good visibility before biopsy as compared to post-biopsy where bleeding contaminates the limited field available for brushing, making it more difficult to identify and sample appropriate tissue.

The BTS guidelines recommend combination of brushing and washing to increase the diagnostic yield of biopsy when the endobronchial tumor is visible (3).

Outcome Audits

Diagnostic yield and efficacy

The diagnostic efficacy of bronchoscopy is influenced by the choice of patient i.e clinical indications and radiologic findings, adequate training and experience of the operator, collection and handling of the specimen for histology or microbiology(34).

Kontakiotis et al found 73.5% of bronchoscopic findings that were suggestive of cancer such as masses or nodules, stenosis or occlusion of lobar or segmental bronchus yielded a positive diagnostic result (34). These yield for cancer was lower than studies in Pakistan (93%)(5) and much higher than what was reported in Nigeria at 51%(12). The BTS recommends a diagnostic level of 85% be attained when a definite endobronchial tumor is visible(3).

Kontakiotis et al also noted “blind” sampling from 4 cases of non-diagnostic bronchoscopy were positive for malignancy (34).

Toori et al found specimen collected for microbiological sampling had an overall diagnostic yield of 24% for any organism and 20% where TB was being evaluated. Various other studies such as in Nigeria shows a bronchial washing AFB smear positivity rate of 50-90% (12). Toori et al attributed their low yield to the fact that evaluation of bronchial washing microbiological yield was not the main aim of their study and the highly selected patient population in the other studies(5).

Complications

FB is a relatively safe procedure as long as basic precautions such as appropriate patient selection, preparation, supervision, and adherence to protocol is observed (38).

Adewole et al found an overall complication rate of 5%. This rate was higher than complications rates reported in other studies. Cradle et al after reviewing 24,521 bronchoscopies performed by 250 chest physicians found a complications rate of 0.08% (7). Pue and patch reported a higher complication rate of 0.5-0.8% (38).

The commonest complications reported in most studies are epistaxis, hypoxemia, tachycardia, bronchospasms, pneumothorax, and cardiac arrest (7, 8, 12, 38).

The overall mortality rate in most studies is between 0 – 0.01% (7, 8, 12, 38).

While it is clear that the rate of complications and death is small, it is therefore prudent that physicians must exercise caution in selection of patients, review their use of sedatives and ensure availability of emergency equipment to reduce the risk of these complications or death (39).

CONCEPTUAL FRAMEWORK

Narrative

Several factors influence complications and bronchoscopic and histopathologic findings of flexible bronchoscopy. The patients' demographics, coagulation profile and clinical presentation are among the important factors associated with complications of the procedure. The demographic characteristics, clinical factors and the experience of the bronchoscopist also influence the overall diagnostic outcome of the procedure.

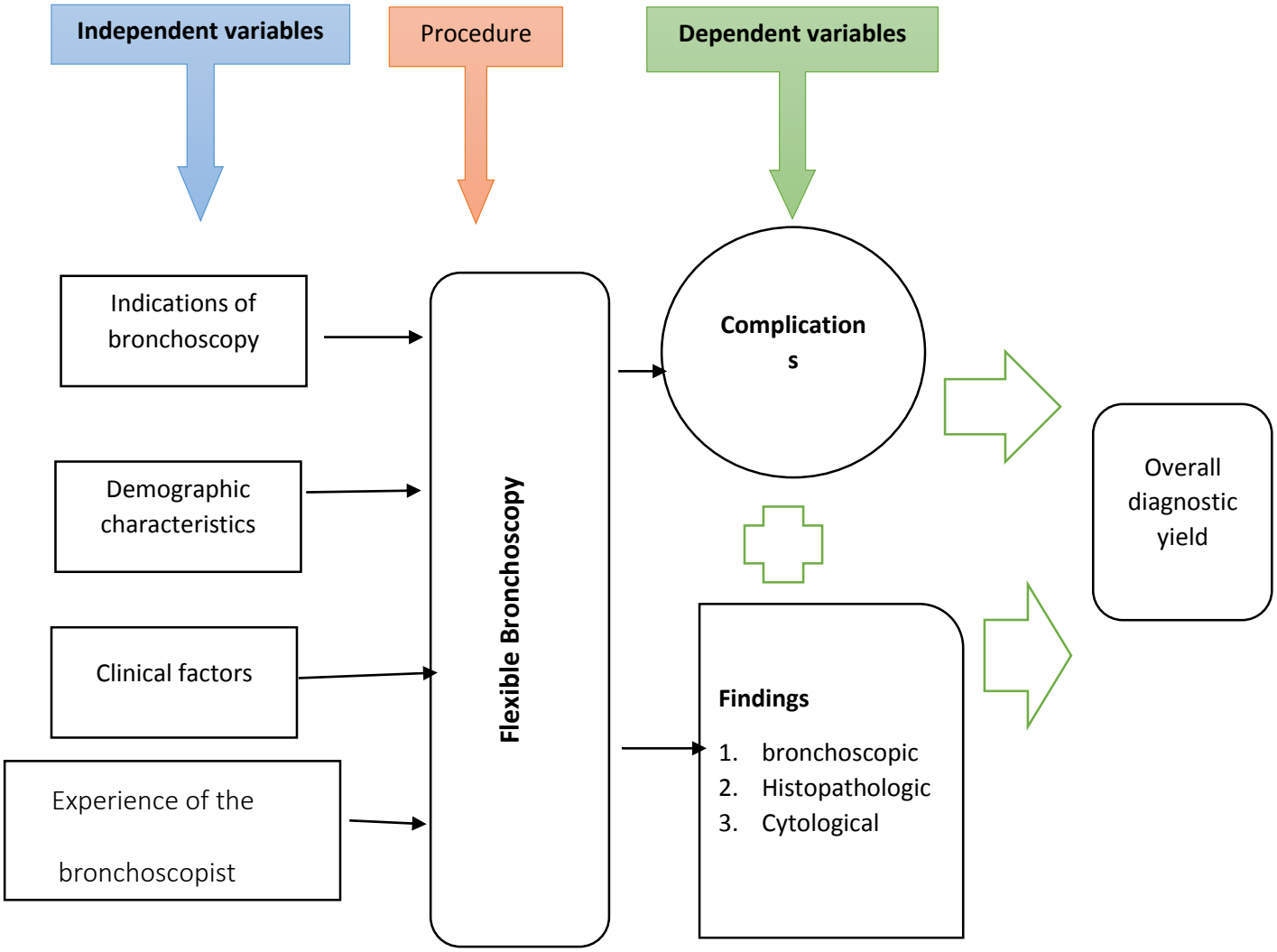


Figure 2.1: Conceptual Framework

STUDY JUSTIFICATION

The flexible fiber optic bronchoscopy (FFB), has become one of the most commonly used diagnostic procedure in Pulmonary medicine due to its enhancement in the diagnosis and understanding of lung diseases.

The practice of flexible bronchoscopy is not standardized even in developed world despite availability of guidelines concerned primarily with safety of the procedure and there are strong efforts to audit the practices in order to standardize it.

The KNH RIDU has been performing bronchoscopy for over 20 years now yet there is no local data on the practice, indications, pattern of bronchoscopic findings and safety and overall compliance with the standards.

The goal of this study will be to document the practice at KNH in terms of patient evaluation and preparation practice, monitoring, indications, anaesthetic technique, sampling procedures, patterns of findings, complications and histopathologic/microbiologic yield of samples obtained.

The findings of this study will inform us on the safety and utility of flexible bronchoscopy in our settings.

RESEARCH QUESTION

What are the flexible bronchoscopic practices at Kenyatta National Hospital, Respiratory disease unit?

STUDY OBJECTIVES

BROAD OBJECTIVE:

To determine the flexible bronchoscopic practices in Kenyatta National Hospital, Respiratory disease unit and its conformity with the standard practices.

SPECIFIC OBJECTIVES

1. To determine the most common indications for Flexible Bronchoscopy among adult patients at KNH Respiratory Disease Unit.
2. To determine the complications reported and complication rates during bronchoscopy among adult patients at KNH Respiratory Disease Unit.
3. To determine the pattern of findings of flexible bronchoscopies done on adult patients at KNH Respiratory Disease Unit.
4. To determine the diagnostic yield of Flexible bronchoscopy among adult patients undergoing flexible bronchoscopy at KNH respiratory Disease Unit.

SECONDARY OBJECTIVES

1. To determine anaesthetic technique and patient monitoring practice during bronchoscopy at Kenyatta National hospital, Respiratory Disease Unit.

CHAPTER 3: METHODOLOGY

Study Site

This study will be conducted at Kenyatta National Hospital (KNH), the largest referral hospital in Kenya, with 2000 bed capacity located in Nairobi County, Kenya. The catchment area is largely from the Nairobi metropolis with referral from all over Kenya and east Africa. It has an established weekly outpatient specialized chest clinic, Daily asthma clinic, TB clinic, MDR TB ward, Respiratory Disease ward with a bronchoscopy suite. The Respiratory Disease unit has 5 consultant chest physicians (KNH/UoN). The bronchoscopy suite has been operational since 1995 with about 786 flexible bronchoscopies done between 1995 and 2020.The study will be conducted at the KNH bronchoscopy suite and the main hospital registry where patients' details will be retrieved from the files.

Study Design

This study will be single center retrospective clinical audit. This design will allow the evaluation of indications, bronchoscopic findings, complications and overall histocytologic yield of bronchial specimen of flexible bronchoscopies that were done in the unit between January 2016 and December 2020.

Study Population

The study population will be medical files of patients aged 13 years and above who underwent flexible bronchoscopy in pulmonology unit of Kenyatta national hospital between January 2016 and December 2020.There files will be retrieved from the main KNH records office using hospital number recorded on the bronchoscopy register.

Eligibility Criteria

Inclusion Criteria

All patients aged 13 years and above who underwent flexible bronchoscopy in Bronchoscopy unit of Kenyatta National Hospital between January 2016 and December 2020.

Exclusion criteria

Patients without in-patient or out-patient identification number on the bronchoscopy register.

Sample size/sampling Method

Sample size estimation

According to health records estimates in KNH, 250 patients underwent bronchoscopy in in the 5-year period of interest. A representative sample will be drawn from this finite population and sample size will be determined as follows:

$$n = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where

n' = sample size with finite population correction,

N = size of the target population = 250

Z = Z statistic for 95% level of confidence = 1.96

P = Estimated proportion of patients with the most common indication of flexible bronchoscopy – suspected lung cancer from previous studies = 67.6% (40)

d = margin of error = 5%

$$= \frac{250 \text{ x } 1.96^2 \text{ x } 0.676 \text{ x } 0.324}{0.05^2 \text{ (250-1)} + 1.96^2 \text{ x } 0.676 \text{ x } 0.324}$$

n = 144

A minimum of 144 patient files will be sampled for this study.

Consecutive sampling of all eligible files will be carried done.

Research tools

Study data will be sourced from patient's medical records. Data collection tool will be used to collect variables of interest.

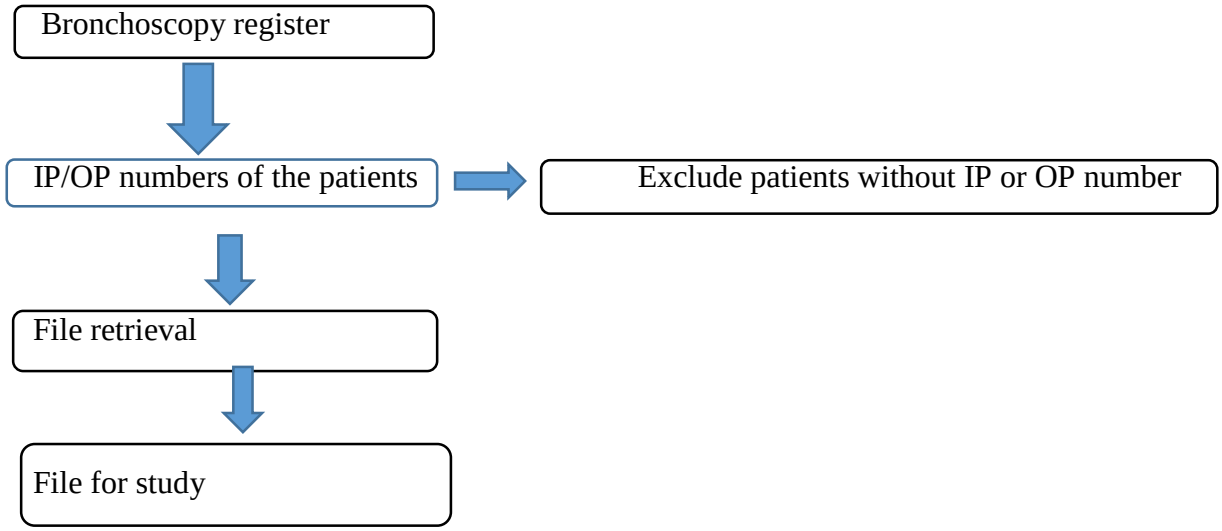
Data collection

The medical records of the patients will be reviewed at both main registry and RDU, Bronchoscopy unit of KNH. The review will be done through retrospective review of the medical records at the main registry and bronchoscopy unit by the investigator with assistance from the medical records officers using in-patient or Out-patient identification numbers from the bronchoscopy register. Missing bronchoscopy reports in the file will be supplemented by retrieving the duplicate report kept at the bronchoscopy unit. We will include all consecutive patients who underwent flexible bronchoscopy in the 5-year period and files that do not meet the inclusion criteria will be excluded. The data will be collected using a structured study proforma with unique study serial number to avoid duplication.

Secondary sources of data such as ward round notes or clinic reviews will be sought from the files with missing/incomplete histology/microbiology results for completeness of data.

During the period of data collection and analysis, measures to prevent the spread of COVID-19 such as use of sanitizers, face masks and appropriate social distancing by both the researcher and research assistants will be ensured.

Figure 3.1: Data Retrieval Flow Chart



Study variables

The study variables will include the patient's demographics (age, sex, residence, occupations, smoking history), Indications for bronchoscopy, pre-procedure investigations, anaesthetic technique and drugs of choice, bronchoscopic findings, bronchoscopic sampling procedures done, complications reported as document by the physician performing the procedure, histopathologic/cytological findings where specimen was collected.

Data Analysis

Data forms will be kept in a secure cabinet accessible only to the PI. All data from the study proforma will be coded, entered and managed in a Microsoft Excel 2016 data entry sheet. Data will then be exported into Statistical Package for Social Sciences (SPSS version 23.0) for analysis. The study population will be described by summarizing demographic and clinical characteristics into percentages and means or medians for categorical and continuous data respectively.

Indications, complications and pattern of findings will be analyzed and presented as percentages (proportions). Similarly, the overall histocytologic yield of the bronchial specimens will be expressed as percentages. It will be calculated by numbers of positive diagnosis (histologic/microbiologic results) divided by total number of specimen collected for histologic and/or microbiologic evaluation * 100.

The diagnostic yield for malignancy will also be expressed as percentage. It will be calculated as number of malignancy diagnosis made divided by total number of visible tumors reported * 100

Outcomes and complications of the procedure will be associated with age, sex, smoking history, occupation, platelet count and indications of bronchoscopy. Association with categorical variables will be done using chi square test while comparison of means will be done using Student's t test. Statistical tests will be interpreted at 5% level of significance (p value less or equal to 0.05).

Ethical Considerations

Data collection will be done after ethical approval is obtained from the Ethics Committee at the KNH. We will request for waiver of consent from the Ethics committee because the study involves review of the medical records of all patients who have undergone flexible bronchoscopy between January 2016 and December 2020 and correlate the data with CBC, Microbiology, cytology and histology results of the patients kept in the file/recorded by the primary doctors. Researcher will be collecting limited data that will be assigned a random code and the link is known only to the researchers. Results of the research will not affect clinical care of the individuals.

Absolute confidentiality will be observed. The primary researcher will keep all the data collection tools including the computer used to analyze the data under lock and key. The patients will only be identified using unique numbers to ensure confidentiality. Data obtained from this study will not be used for any other purpose other than the objectives of the study.

Study limitations

This being a retrospective study, we foresee incomplete documentation or missing files as a potential limitation.

Table 4.1: Work plan/Timelines

	April-Nov	December	Jan-feb 2021	March-April/May	May-June	July
Proposal development						
Proposal presentation						
Ethical review						
Data collection						
Data analysis						
Thesis presentation						

Table 4.2: Budget

ITEM	COST
Stationary and printing	30,000
Research assistant	20,000
Statistician	30,000
Miscellaneous	20,000
TOTAL	100,000

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APPENDICES

Appendix 1: Data Collection Form/checklist

Serial Number :

OP/IP Number :

SECTION 1: DEMOGRAPHICS			
NO	**Question**	**Response**	**Code**
1	**Identification number (IP/OP Number)**		**[ ]**
1	**Gender (GEN)**	**F=1** **M=2**	**[ ]** **[ ]**
2	**Age (A)**	**Number**	**[ ]**
3	**Residence**		**[ ]**
4	**Occupation**	**1. Employed** **2. Self employed** **3. Unemployed** **4. Not documented**	**[ ]** **[ ]** **[ ]** **[ ]**
5	**Smoking history**	**1. Current smoker** **2. Ex. Smoker** **3. Non-smoker** **4. Not indicated**	**[ ]** **[ ]** **[ ]** **[ ]**
SECTION 2: DISEASE INFORMATION			
6.	**Indication for bronchoscopy**	**1. Pulmonary infiltrate (suspected PTB or other infections)** **2. Lung mass** **3. Haemoptysis**	**[ ]** **[ ]** **[ ]**

		4. Atelectasis **5. Interstial Lung disease** **6. Chronic cough** **7. Hilar/mediastinal LN** **8. Pleural effusion** **9. Others** **10. Not documented**	
7.	**Platelet count**	**1. < 20.000/ul** **2. 20.000 – 50,000** **3. > 50,000/ul** **4. Not documented**	**[ ]**
8.	**International normalised ratio**	**1. < 1.5** **2. > 1.5** **3. Not documented**	**[ ]**
SECTION 4: BRONCHOSCOPY			
9.	**Anaethesia technique**	**1. LA with sedation** **2. LA without sedation** **3. GA** **4. Not documented**	**[ ]**
10	**Sedation drugs given**	**1. opiods** **2. Benzodiazepines** **3. Ketamine** **4. Propofol** **5. Not documented**	**[ ]** **[ ]** **[ ]** **[ ]**

11.	**Source of referral**	**1. In-patient/wards** **2. Out patient**	**[ ]**
12.	**Bronchoscopic finding (gross)**	**1. Secretions/mucus plug** **2. Inflammatory changes** **3. Narrowed segment/extrinsic compression** **4. Tumour** **5. Normal** **6. Others** **7. Not documented**	**[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]**
13.	**Bronchoscopic diagnostic procedure performed**	**1. Bronchial washing** **2. Bronchial brushing** **3. Broncho alveolar lavage** **4. Biopsy** **5. Trans-bronchial needle aspiration** **6. None** **7. Not documented**	**[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]**
14.	**complications**	**1. Hypoxemia < 90%** **2. Tachycardia>100** **3. Bradycardia <60** **4. Bronchospasm** **5. Bleeding** **6. Pneumothorax**	**[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]**

		7. Death	**[ ]**
		8. None	**[ ]**
		9. Others	**[ ]**
		10. Not documented	**[ ]**
15.	**Investigation done**	**1. Histology**	
		2. Cytology	**[ ]**
		3. Microbiology	**[ ]**
		I. M.C.S	**[ ]**
		II. TB Gene xpert/PCR	**[ ]**
		III. Gram stain	**[ ]**
		IV. ZN stain for AFB	**[ ]**
		4. None	**[[**
		5. Not documented	
16.	**Histopathological/Cytologic/microbiologic findings/Final Diagnosis**	**1. Lung cancer**	**[ ]**
		2. Non-MTB infections	**[ ]**
		3. TB	**[ ]**
		4. Chronic non-specific inflammation	**[ ]**
		5. Squamous metaplasia	**[ ]**
		6. Interstitial pneumonia	**[ ]**
		7. Chronic bronchitis	**[ ]**
		8. Sarcoidosis	**[ ]**
		9. Aspergilosis	**[ ]**
		10. normal	**[ ]**
		11. Not documented	

17	**Histologic sub-type in case final diagnosis is Lung cancer**	**1. Adenocarcinoma** **2. Squamous cell carcinoma** **3. Small cell Lung cancer** **4. Large cell carcinoma** **5. Carcinoma not otherwise classified** **6. Not documented** **7. Not applicabe**	**[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]** **[ ]**