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Research Article

Comparison of Fine Needle Aspiration versus Core Biopsies for Pulmonary Nodules

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Abstract

Purpose

To evaluate efficacy and complication rates associated with pulmonary fine needle aspirate (FNA) and core needle biopsies (CNB) utilizing CT guidance.

Materials and Methods

This retrospective study included 776 patients, 18 and over who underwent CT guided tissue acquisition of a pulmonary nodule at a single center from 6/1/2017 – 4/30/2020. Complications occurring within 24 hours of biopsy were recorded along with procedure and nodule related characteristics.

Results

The average age of the 776 included patients was 65.2 years (SD+/-11.4 years). Of these, 678 (87.4%) had CNB only, 55 (7.1%) had FNA only, and 43 (5.5%) had both. Of the 733 that had CNB or FNA only, 13.6% experienced complications serious enough to warrant intervention, 13.3% in the CNB group and 18.2% in the FNA group. There was no statistically significant difference in rates of complications that warranted intervention between the CNB and FNA groups (OR=1.452, CI=0.707, 2.983). Diagnostic yield was better in the CNB group (p<0.0001).

Conclusion

No difference in clinically significant complication rates were identified when comparing FNA and CNB for CT guided pulmonary nodule biopsy. Superior diagnostic yield of CNB was statistically significant and may be considered as a first line technique in the appropriate clinical setting.

Keywords: Core Needle Biopsy; Diagnostic Yield; Fine Needle Aspiration; Pulmonary Nodule; Pneumothorax

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Introduction

CT guided lung tissue sampling conducted by interventional radiology are instrumental in aiding diagnoses and guiding therapy for primary and secondary pulmonary disease [1]. The Fleischer Society guidelines for management of solid and subsolid nodules aim to reduce the number of unnecessary follow-up examinations while providing greater discretion to radiologists, clinicians, and patients to make management decisions [2]. However, for patients with incidentally detected solid nodules larger than 8mm, follow up imaging or tissue sampling is recommended. As nodules become larger, their morphology becomes more distinct, and management should be strongly influenced by appearance of the nodule rather than the size alone. Once a nodule is determined to require tissue sampling, central versus peripheral nodule locations dictate the main technical approach used, either transthoracic (for peripheral lesions) or endobronchial (for centrally located lesions) [3]. Transthoracic pulmonary nodule biopsies are a fundamental element of most interventional radiology practices. This approach is primarily performed utilizing CT guidance; providing a safe, simple, and well tolerated procedure [4]. Fine needle aspiration (FNA) and core needle biopsy (CNB) are two common primary techniques used in tissue sampling under CT guidance. CT guided biopsies are considered minimally invasive, however there remains an inherent risk, and determining the safest approach is vital [5,6].

The main complications in lung biopsies are pneumothorax or hemothorax [7]. Studies show variable biopsy-related pneumothorax rates, ranging from 2.8%–50%, and rates of pulmonary hemorrhage ranging from 6.2%-47%. These wide ranges may be due to differing definitions, criteria, or time windows in which complications are reported and collected. Needle types or techniques used may also vary among interventionalists and institutions [8]. Patient and nodule related factors, such as lesion size and depth may also play a role in

complication rates. Keeping these variables in mind, some studies have found similar complication rates between FNA and CNB, while others have found slightly higher complication rates in CNB. Many studies have found CNB to have superior diagnosis yield [9-12].

Determining the approach with the best diagnostic yield and lowest complications will limit repeat biopsies and associated iatrogenic risks. The purpose of this study is to compare complications associated with FNA versus CNB. Secondary objectives were to determine if diagnostic yield and other procedure-related characteristics differed between FNA and CNB.

Methods

Institutional review board approval was obtained, and patient medical records were reviewed according to Health Care Portability and Accountability Act guidelines. This retrospective cohort study included all patients 18 years old and over that underwent CT guided tissue acquisition of a pulmonary nodule at a single center's interventional radiology department from June 1, 2017, to April 30, 2020. Patients were excluded if there was radiographic evidence of a pneumothorax or hemothorax on pre-procedural CT scan. All procedures were performed or directly supervised by fellowship-trained and board-certified interventional radiologists.

Relevant clinical information was obtained from the patients' medical records and Picture Archiving and Communication System (PACS), including pertinent demographics, clinical history, biopsy details, imaging, and pathology reports. Diagnostic yield of the procedure was determined based off the pathology report. If the tissue was not representative of a lesion, then the tissue sample was classified as inadequate. Complications occurring within 24 hours of biopsy were recorded and included radiographic evidence of pneumothorax, hemothorax, or hemorrhage and clinical evidence of hemoptysis, and/or air embolism. Associated complications were classified and recorded. Data collection forms were created and managed in REDCap [13].

Logistic regression models were used to calculate odds ratios comparing rates of complications requiring intervention for FNA compared to CNB groups and both procedures compared to CNB. Continuous variables were assessed using t-tests and described by their mean with standard deviation. Categorical variables were analyzed using chi-squared tests and described with frequencies and percentages. For categorical variables with low expected cell counts, Fisher's exact tests were performed. P-values equal to or less than 0.05 were considered statistically significant. All statistical analysis was performed in SAS 9.4.

Results

A total of 776 patients underwent a CT-guided biopsy of lung nodules during the study period, including 392 (50.5%) men and 384 (49.5%) women, with an average age of 65.2 years (standard deviation [SD]+/-11.4 years). Most patients were white (84.9%), non-Hispanic (97.8%) and were current or former smokers (72.7%). The most common comorbidity was chronic obstructive pulmonary disease (COPD) with 249 (34.1%) of patients having the disease. Of 776 included patients, 678 (87.4%) had CNB only, 55 (7.1%) had FNA only and 43 (5.5%) had both (Table 1).

	CNB Only	FNA Only	Both FNA and CNB	All
Overall N (% of column)	678 (87.4)	55 (7.1)	43 (5.5)	776 (100.0)
Age at Biopsy, Mean (SD)	65.2 (11.5)	66.6 (10.7)	63.4 (11.5)	65.2 (11.4)
Gender, N (% of column)				
Female	340 (50.1)	24 (43.6)	20 (46.5)	384 (49.5)
Male	338 (49.9)	31 (56.4)	23 (53.5)	392 (50.5)
Race, N (% of column)				
White	578 (85.3)	45 (81.8)	36 (83.7)	659 (84.9)
Black	64 (9.4)	9 (16.4)	5 (11.6)	78 (10.1)
Asian	8 (1.2)	0 (0.0)	1 (2.3)	9 (1.2)
Other	28 (0.6)	1 (0.0)	1 (2.3)	30 (0.6)
Ethnicity, N (% of column)				
Non-Hispanic/Latino	661 (97.5)	55 (100.0)	43 (100.0)	759 (97.8)
Hispanic/Latino	16 (2.4)	0 (0.0)	0 (0.0)	16 (2.1)
Unknown	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
Smoking History, N (% of column)				
Missing	2 (0.3)	0 (0.0)	0 (0.0)	2 (0.3)
Never	186 (27.4)	14 (25.5)	10 (23.3)	210 (27.1)
Former	332 (49.0)	29 (52.7)	21 (48.8)	382 (49.2)
Current	158 (23.3)	12 (21.8)	12 (27.9)	182 (23.5)
Comorbidities, N (% of column)				
Congestive Heart Failure	58 (8.6)	4 (7.3)	5 (11.6)	67 (8.6)
COPD	222 (32.7)	27 (49.1)	16 (37.2)	265 (34.1)
Fibrotic Lung Disease	17 (2.5)	0 (0.0)	0 (0.0)	17 (2.2)
Restrictive Airway Disease	5 (0.7)	0 (0.0)	0 (0.0)	5 (0.6)
Bleeding Disorder	16 (2.4)	1 (1.8)	2 (4.7)	19 (2.4)
Complication Type N (% of column)				
No Complications Requiring Intervention	588 (86.7)	45 (81.8)	34 (79.1)	633 (86.4)
Pneumothorax	87 (12.8)	10 (18.2)	9 (20.9)	97 (13.2)
Hemothorax	5 (0.7)	0 (0.0)	0 (0.0)	5 (0.7)
Pulmonary Hemorrhage	20 (2.9)	5 (9.1)	5 (11.6)	25 (3.4)
Hemoptysis	6 (0.9)	0 (0.0)	1 (2.3)	6 (0.9)
Air Embolism	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 1: Patient Characteristics.

Within the CNB only group, 13.3% experienced a complication serious enough to warrant intervention. The most common complication was pneumothorax (12.8%) and pulmonary hemorrhage (2.9%). Of the 100 patients that received an intervention due to their complications, the most common intervention was admission of the patient (91.1%), followed by chest tube placement (83.3%). Within the FNA

only group, 18.2% experienced a complication serious enough to warrant intervention. The most common complications were also pneumothorax (18.2%) and pulmonary hemorrhage (9.1%). There was no statistically significant difference in rates of complications that warranted intervention, between the CNB and FNA groups (OR=1.452, CI=0.707, 2.983). There was no statistically significant difference in the number of complications patients had between CNB and FNA groups (OR=2.725, CI=0.997, 7.448). However, there were more complications observed with the use of both procedure types compared to CNB alone (OR=3.586, CI=1.296, 9.919).

Comparing procedure characteristics between the two biopsy types, the depth of the nodule from the skin was lesser in the CNB group with a mean of 7.0 cm (SD=2.7) vs 7.8 cm (SD=2.6) in the FNA group (p=0.0279) and the size of the nodule was on average larger in the CNB group, with a mean of 2.9 cm (SD=2.2) vs 1.7 cm (SD=1.4) in the FNA group (p<0.0001). The nodule was more commonly pleural based in the CNB group (p=0.0005), and diagnostic yield was better in the CNB group (p<0.0001) (Table 2).

	CNB Only	FNA Only	All	P Value
Overall N	678	55	733	
Depth of Nodule from Skin (cm), Mean (SD)	7.0 (2.7)	7.8 (2.6)	7.0 (2.7)	0.0279
Size of Nodule (cm), Mean (SD)	2.9 (2.2)	1.7 (1.4)	2.9 (2.2)	<.0001
Pleural Based Mass, N (% of column)				
No	466 (68.7)	50 (90.9)	516 (70.4)	0.0005
Yes	212 (31.3)	5 (9.1)	217 (29.6)	
Specimen Adequacy, N (% of column)				
Missing	1 (0.1)	0 (0.0)	1 (0.1)	<.0001
No	61 (9.0)	20 (36.4)	81 (11.1)	
Yes	616 (90.9)	35 (63.6)	651 (88.8)	
Location of Nodule, N (% of column)				
Left upper lobe	131 (19.3)	15 (27.3)	146 (19.9)	0.3836
Left lower lobe	152 (22.4)	8 (14.5)	160 (21.8)	
Right upper lobe	186 (27.4)	14 (25.5)	200 (27.3)	
Right middle lobe	29 (4.3)	4 (7.3)	33 (4.5)	
Right lower lobe	180 (26.5)	14 (25.5)	194 (26.5)	

Table 2: Procedure Characteristics FNA vs CNB.

*T-tests were used for comparing continuous variables; Chi-Square tests were used for comparing categorical variables.

When evaluating procedure characteristics of CNB only, patients with complications had deeper nodules from skin than those without complications (7.6 cm vs 6.9cm, p=0.0198). Those with complications had, on average, smaller nodules than the group with complications (2.2cm vs 3.1 cm, p=0.0007) and fewer patients had complications when the nodule was pleural based (p=<0.0001). Location was also significantly associated with complications, with more complications than expected occurring in the upper lobe locations (p=0.0256; Left upper lobe: 24.4% vs 18.5%; Right upper lobe 35.6% vs 26.2%). Complications were not significantly associated with other procedure related characteristics including number of passes, diagnostic yield, or needle gauge size (Table 3).

	Complication(s)	No Complications	All	P-Value
Overall N	90 (13.3)	588 (86.7)	678 (100)	
Depth of Nodule from Skin (cm), Mean (SD)	7.6 (2.3)	6.9 (2.7)	7.0 (2.7)	0.0198
Size of Nodule (cm), Mean (SD)	2.2 (1.3)	3.1 (2.3)	2.9 (2.2)	0.0007
Number of Samples/Passes, Mean (SD)	2.9 (1.1)	3.1 (1.0)	3.1 (1.0)	0.0768
Pleural Based Mass, N (% of column)				<.0001
No	78 (86.7)	388 (66.0)	466 (68.7)	
Yes	12 (13.3)	200 (34.0)	212 (31.3)	
Specimen Adequacy, N (% of column)				0.0532
Missing	0 (0.0)	1 (0.2)	1 (0.1)	
No	13 (14.4)	48 (8.2)	61 (9.0)	
Yes	77 (85.6)	539 (91.7)	616 (90.9)	
Location of Nodule, N (% of column)				0.0256
Left upper lobe	22 (24.4)	109 (18.5)	131 (19.3)	
Left lower lobe	9 (10.0)	143 (24.3)	152 (22.4)	
Right upper lobe	32 (35.6)	154 (26.2)	186 (27.4)	
Right middle lobe	4 (4.4)	25 (4.3)	29 (4.3)	
Right lower lobe	23 (25.6)	157 (26.7)	180 (26.5)	
Needle Gauge Size, N (% of column)				0.4699

16	0 (0.0)	1 (0.2)	1 (0.1)	
17	17 (18.9)	128 (21.8)	145 (21.4)	
18	63 (70.0)	420 (71.4)	483 (71.2)	
19	7 (7.8)	27 (4.6)	34 (5.0)	
20	3 (3.3)	12 (2.0)	15 (2.2)	

Table 3: Characteristics of CNB Only Procedures by Complications.

For procedure characteristics in the FNA group, only location of the nodule affected complication rates, with the right upper lobe experiencing more complications (p=0.0142) (Table 4).

	Complication(s)	No Complications	All	P-Value
Overall N	10 (18.2)	45 (81.2)	55 (100)	
Depth of Nodule from Skin (cm), Mean (SD)	8.6 (2.1)	7.6 (2.7)	7.8 (2.6)	0.2828
Size of Nodule (cm), Mean (SD)	2.1 (1.5)	1.6 (1.4)	1.7 (1.4)	0.3445
Number of Samples/Passes, Mean (SD)	3.8 (0.84)	3.2 (0.88)	3.3 (0.88)	0.225
Pleural Based Mass, N (% of column)				0.5717
No	10 (100.0)	40 (88.9)	50 (90.9)	
Yes	0 (0.0)	5 (11.1)	5 (9.1)	
Specimen Adequacy, N (% of column)				0.0747
No	1 (10.0)	19 (42.2)	20 (36.4)	
Yes	9 (90.0)	26 (57.8)	35 (63.6)	
Location of Nodule, N (% of column)				0.0142
Left upper lobe	0 (0.0)	15 (33.3)	15 (27.3)	
Left lower lobe	0 (0.0)	8 (17.8)	8 (14.5)	
Right upper lobe	5 (50.0)	9 (20.0)	14 (25.5)	
Right middle lobe	2 (20.0)	2 (4.4)	4 (7.3)	
Right lower lobe	3 (30.0)	11 (24.4)	14 (25.5)	
Needle Gauge Size, N (% of column)				0.675
Missing	0 (0.0)	2 (4.4)	2 (3.6)	
17	2 (20.0)	11 (24.4)	13 (23.6)	
18	3 (30.0)	5 (11.1)	8 (14.5)	
19	2 (20.0)	12 (26.7)	14 (25.5)	
20	3 (30.0)	11 (24.4)	14 (25.5)	
22	0 (0.0)	4 (8.9)	4 (7.3)	

Table 4: Characteristics of FNA Only Procedures by Complications.

*T-tests were used for comparing continuous variables; Fisher's exact tests were used for comparing categorical variables due to low expected cell counts.

Limitations

This retrospective study has limitations in that patients were not randomized to biopsy types and due to the nature of the study, certain data points were unable to be assessed such as the number of pleural surfaces traversed during lung biopsy. Procedure choice and acquisition were influenced by factors such as lesion size, location, distance from pleura, underlying disease such as emphysema, approach of the biopsy such as leading anteriorly or posteriorly, age of the patient, availability of a cytopathologist, and experience of the interventionalist. Another limitation to this study was the disparity in sample sizes between CNB and FNA (678 vs 55 respectively). This may be due to an underlying bias of technical preferences for the interventional radiologist performing CT guided biopsies at this institution. Further research could help determine if there is increased complication risk with specific comorbidities as well as comparing the characteristics of the two procedures and their associated likelihood of risk.

Discussion

This study's complication rates of 13.3% in the CNB group and 18.2% in the FNA group fall within ranges reported in other studies [9-12]. This study showed no difference in complication rates between FNA and CNB and no difference in complications among needle sizes in either the FNA or CNB group [10-12] This may suggest the lung is susceptible to punctures no matter how large or small the needle diameter. Marchianò et al reported an increase in pneumothorax development with larger needle size and although this is a discrepancy with this study, they noted this finding as controversial and that there was no evidence of worsening performance related to greater needle size [9].

Several studies have demonstrated that smaller lesion size can be a cause of pneumothorax and hemorrhage [10,11] The accuracy of biopsy technique decreases with diminished lesion dimensions which can lead to more passes and greater potential for complications. In this study, complication rates increased only in the CNB group when the nodule size was smaller. Size of the nodule did not impact complication rates in the FNA group. The FNA group may not have experienced higher complications with smaller nodules due to less passes, adequacy determination, size of needle, or the switching to CNB if specimen collection was inadequate with FNA.

Some studies report lesion depth as a contributing factor for complications and one analysis reported traversed lung length was found to be a factor in increased risk [9,12]. Deeper nodules require the biopsy needle to traverse more lung which can lead to further damage. In this study, deeper nodules showed an increase in complications in the CNB group, but no difference in complications was seen in the FNA group. With a larger sample size in the FNA group, this study

may have detected an increase in complications in the FNA group for deeper nodules.

This study found increased complications with lesions in the right upper lobes within the FNA and CNB groups. This correlates with a previous study that demonstrated that chest tube placement was associated with lesion depth and lung field, with a higher risk for lesions in the upper lung compared to lower and middle fields [8]. It was also noted that hemorrhage was more likely in the upper lung lobes while pneumothorax had a more homogenous distribution [11].

While some studies have shown CNB and FNA to have comparable diagnostic yield, others have shown, like this study, that CNB has a better diagnostic yield [9-11,14] Comparatively this study showed low diagnostic yield for FNA (63.6%). Other studies have shown FNA diagnostic yield ranging from 80-89% [10,14].The lower diagnostic yield for FNA in this study may be due to small sample size in the FNA group. At the institution where this study took place, an on-site cytotechnologist is present during FNA procedures to determine if there is an adequate amount of tissue to be sent to pathology. If there is not sufficient tissue, then more passes must be performed, which can lead to hemorrhage obstructing the view of the required tissue or pneumothorax altering the anatomy of the lung, which can lower the diagnostic yield. One study reported that when a cytopathologist is not present, the rate of insufficient tissue acquired may reach 20%, which would then require the patient to undergo a subsequent biopsy [10]. By comparison, CNB can be successfully performed without the need of on-site pathology.

Conclusion

This study showed that patients undergoing CNB alone did have higher complication rates with deeper and smaller nodules that were non-pleural based, yet it is difficult to interpret if FNA is better for certain nodules. For example, complications were higher for FNA with deeper nodules, but the data reports a non-significant finding likely due to the sample size being small. Therefore, the superior adequate diagnostic yield from CNB may trump the risk of complication for smaller and deeper pulmonary nodules. Use of CNB may also require less passes through a nodule and possibly fewer repeat biopsies.

Implications

Superior diagnostic yield of CNB was statistically significant and may be considered as a first line technique in the appropriate clinical setting. This could lead to a decrease in repeat biopsies and prevent delay of treatment due to inadequate tissue sampling.

Disclosures

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Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical Approval: For this type of study formal consent is not required.

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