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ORIGINAL ARTICLE

Pulmonary Hemorrhage after Percutaneous Transthoracic CT-Guided Core Needle Biopsy: Assessment of the Risk Factors.

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ABSTRACT

Objective: the aim of this study is to assess the severity and risk factors associated with pulmonary hemorrhage complicating percutaneous transthoracic CT-guided core needle biopsy. **Patient and Methods:** this retrospective study was approved by our scientific and ethical committee. A total of 312 CT-guided lung biopsies done from December 2016, to September 2019 were included in this study. Pulmonary hemorrhage was assessed for each procedure. The severity of pulmonary hemorrhage was categorized into Grade 0 defined as no pulmonary hemorrhage, grade 1 as needle tract hemorrhage 2 cm or less, grade 2 as hemorrhage more than 2 cm, grade 3 as lobar hemorrhage or greater, and grade 4 as hemothorax. Grade 2 or higher was considered as high grade hemorrhage. **Results:** Pulmonary hemorrhage occurred 97(31%) out of the 312 after lung core biopsies. Grade I hemorrhage occur after 57 (18.3%) procedures, grade II after 37 (11.8%) procedures, grade III after 2 (0.6%) procedures and grade IV occur only after one procedure (0.3%). Grade II and more hemorrhage occur after 40 (13%) procedures and were considered as high grade hemorrhage. High grade hemorrhage was statistically significant to occur more with female sex, lesions less than 3 cm, non-subpleural location and co-axial technique (*P* <0.05). Emphysema and age were not a significant risk factor for high grade hemorrhage (*P* >0.05). **Conclusion:** pulmonary hemorrhage complicating CT-guided core needle lung biopsy is common. Significant risk factors associated high grade hemorrhage includes female sex, lesions less than 3 cm, non-subpleural location and co-axial technique.

Keywords: CT (computed tomography); pulmonary; percutaneous; core biopsy.

INTRODUCTION

Percutaneous trans-thoracic computed tomography guided lung biopsy is well-known method in the investigation and management of pulmonary nodules and masses. The diagnostic yield of this technique is better than bronchoscopy in the assessment of pulmonary nodules and masses especially in peripheral lesions [1,2].

Percutaneous trans-thoracic computed tomography guided lung biopsy is expected to play an increasingly important role in guiding lung cancer management in the coming years. This is because of the higher proportion of adenocarcinoma among current lung cancer that is more likely to be peripheral and not reachable by bronchoscopy [3,4]. Also the advance in genomic technology increases the recommendation for re-biopsy for molecular analysis of non-small lung cancers that progress or recur [5,6]. Moreover the referral for the lung biopsy will increase after the advent of lung cancer screening [7].

Pneumothorax and pulmonary hemorrhage are the most common complications of percutaneous trans-thoracic computed tomography guided lung biopsies [8]. These complications become more frequent and of greater consequences due to increased use of transthoracic computed tomography guided needle biopsy in targeting small lesions especially in old patients with multiple co-morbidities [9]. Risk factors for pneumothorax after these procedures have been extensively reported; however less is known about the predisposing factors for pulmonary hemorrhage that can be life threatening [10,11]. In two recent studies there is controversy about emphysema and co-axial versus non-coaxial technique as predisposing factors for pulmonary hemorrhage complicating lung core needle biopsy [12,13].

The aim of this study is to assess the severity and risk factors associated with pulmonary hemorrhage complicating percutaneous transthoracic computed tomography guided core needle biopsy.

PATIENT AND METHODS

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All thoracic intervention procedures were performed at radiology department, Chest Disease Hospital, state of Kuwait. A total of 312 percutaneous trans-thoracic computed tomography guided lung biopsy done at our department from December; 2016, to September, 2019 were included in this study. All patients were referred from thoracic surgery outpatient clinic and all of them were admitted at thoracic surgery wards at our hospital prior to the intervention procedure.

Pre-procedure assessment: A recent CT chest was required for all patients to determine the biopsy approach. PET/CT and or MRI diffusion with ADC mapping were sometimes required to avoid the necrotic parts of the lesion. The following laboratory parameters were required before doing the lung biopsy: platelet count > 80 000/ mm^3, and I.N.R $\leq$ 1.5. Antithrombotic drugs as Aspirin were withheld for 5-7 days before the procedure.

Technique: Percutaneous trans-thoracic computed tomography guided lung biopsy were performed with CT-guidance by using a 64-section MDCT scanner (GE HD 750,General Electric Medical System, Milwaukee, USA). Core needle biopsies were performed with 18- or 16-Gauge needles (Bard Monopty Disposable Core Biopsy Instrument, BARD BIOPSY SYSTEM/ Biopince ARGON MEDICAL DEVICES INC.). Core needle biopsies with coaxial technique were performed with 17 or 15 -gauge BARD TRUGUID disposable coaxial biopsy needle with depth stop, BARD BIOPSY SYSTEMS. For lesions in close proximity to the mediastinal vasculature, a pre-procedural or intra-procedural contrast–enhanced chest CT was performed if it had not been carried out previously. At the procedure, a biopsy trajectory was chosen that would avoid needle transgression of intervening vascular structures and if possible lung parenchyma distal to the lesion. If applicable, a needle skin entry site should avoid injury to intercostal vascular bundle. All percutaneous trans-thoracic computed tomography guided lung biopsies were done under complete aseptic condition and under local anesthesia. Biopsy was suspended in cases of persistent hemoptysis. A minor low-grade parenchymal pulmonary hemorrhage during biopsy was not considered a sufficient call to postpone the intervention procedure.

Study variables: Those included evaluation of variables as potential risk factors of pulmonary hemorrhage. Patient-related variables included age, sex and emphysema. Lesion related variables included lesion size, morphological characteristics and location. We categorized lesion size into 1-3 cm and above 3 cm. Morphological characteristics were categorized into subsolid, solid and consolidative. Lesion location was categorized into; lesions that abut the pleural were considered sub-pleural while other lesions were considered non-subpleural. Technique related variables included coaxial and non-coaxial technique using needle gauge (18-G and 16-G), co-axial needle usage (17-G and 15-G), number of passes (1 pass and 2 or more), and pleura-needle angle (90 degree and less than 90 degree). Pulmonary hemorrhage is defined as newly developed post-procedural consolidative/ground-glass opacity on post-intervention CT images. Pulmonary hemorrhage was assessed for each procedure. The severity of pulmonary hemorrhage was categorized according to a grading scheme adopted by Tai, et al (13). Grade 0 was defined as no pulmonary hemorrhage, grade 1 as needle tract hemorrhage 2 cm or less in width, grade 2 as hemorrhage more than 2 cm in width but sublobar, grade 3 as lobar hemorrhage or greater, and grade 4 as hemothorax. In consensus with grading adopted by Tai et al., we considered grade 1 hemorrhage which is quiet often as a low grade hemorrhage and hemorrhage of grade 2 or higher as higher grade hemorrhage.

Statistical Analysis: SPSS software (version 13.0; IBM) was used. Univariate analysis with Chi Square, Fisher exact tests for categoric variables and the student *t* test for continuous variables were done. An odds ratio (OR) and (95% confidence interval) which is a statistical test that quantifies the strength of increased association between two events was calculated. *P* value <0.05 was considered indicative of a statistically significant difference.

RESULTS

Pulmonary hemorrhage occurred after lung core biopsies in 97(31%) out of the 312 cases included in this study. Grade I hemorrhage (figure 1) occurred after 57 (18.3%) procedures, grade II hemorrhage (figure 2) occurred after 37 (11.8%) procedures, grade III hemorrhage (figure 3) occurred after 2 (0.6%) procedures and grade IV hemorrhage (figure 4) occurred only after one procedure (0.3%). Grade II and more hemorrhage occurred after 40 (13%) procedures and were considered as high grade hemorrhage while low grade or no hemorrhage followed 272 (87%) procedures. Analysis of the patient related risk factors (table 1) demonstrated that the mean age was not significantly associated with high grade hemorrhage, represented 51.8±8.1 years in no / low grade hemorrhage and 54.3±11.3 years in high grade pulmonary hemorrhage (*P* value 0.18). Female sex was significantly associated with high grade pulmonary hemorrhage, represented 136 cases (50%) in No/low grade hemorrhage and 29 cases (73%) in high grade hemorrhage (OR 2.64, *P* value 0.010). Emphysema was not significantly associated with high grade hemorrhage, represented 54 cases (20%) in No/low grade hemorrhage and 13 cases (32.5 %) in high grade hemorrhage (OR 1.94, *P* value 0.07). Analysis of the lesion related risk factors (table 2) showed that high grade pulmonary hemorrhage was significantly more likely to occur in lesions less than 3 cm in (size), represented 29 cases (72.5%) in high grade hemorrhage (OR 3.01, *P* value 0.003) and in lesions with non-subpleural location, represented 34 cases (85%) in high grade hemorrhage (OR 4.82, *P* value 0.001). Lesion above 3 cm and sub-pleural location were statistically protective against occurrence of high grade pulmonary hemorrhage. The analysis of the technique related risk factors (table 3) showed that only the co-axial technique was significantly more likely associated with high grade pulmonary hemorrhage, represented 33 cases (82.5%) in high grade hemorrhage (OR 2.65, *P* value 0.02). While the needle gauge, number of passes and pleural needle angle were not significantly associated with high grade hemorrhage(*P* >0.05).

Table (1): shows analysis of patient related risk factors for pulmonary hemorrhage

Patient-related variables	No/low grade hemorrhage (n=272)	High grade hemorrhage (n=40)	OR (CI 95%)	*P Value*
Age (mean ± SD)	51.8±8.1	54.3±11.3	----	0.18 **
Female sex	136(50%)	29(73%)	2.64 (1.26-5.49)	0.01*
Emphysema	54(20%)	13(32.5%)	1.94 (0.94-4.02)	0.07

*Statistically significant
** Student test

Table (2): shows analysis of lesion related risk factors for pulmonary hemorrhage

Lesion-related variables	No/low grade hemorrhage (n=272)	High grade hemorrhage (n=40)	OR (CI 95%)	*P Value*
Lesion size				
1-3 cm	127 (47%)	29(72.5%)	3.01 (1.44-6.27)	0.003*
> 3 cm	145(53%)	11(27.5%)	0.33 (0.16-0.69)	0.003‡
Lesion morphology				
Solid	210 (77%)	30(75%)	0.89 (0.41-1.91)	0.76
Subsolid	11(4%)	4(10%)	2.64 (0.79-8.72)	0.11
Consolidation	51(19%)	6(15%)	0.76 (0.30-1.91)	0.57
Lesion locarion				
Subpleural	125(46%)	6(15%)	0.21 (0.08-0.51)	0.001‡
Non-subpleural	147(54%)	34(85%)	4.82 (1.95-11.85)	0.001*

*Statistically significant risk factor for pulmonary hemorrhage
‡Statistically significant protective factor against pulmonary hemorrhage

Table(3): shows analysis of technique related risk factors for pulmonary hemorrhage

Technique-related variables	No/low grade hemorrhage (n=272)	High grade hemorrhage (n=40)	OR (CI 95%)	*P Value*
Biopsy type				
Non-coaxial	98 (36%)	7 (17.5%)	0.38 (0.16-0.88)	0.02‡
Coaxial	174 (64%)	33 (82.5%)	2.65 (1.13-6.22)	0.02*
Needle gauge				
16 G	87 (32%)	14 (35%)	1.15 (0.57-2.30)	0.70
18 G	185 (68%)	26 (65%)	0.87 (0.43-1.75)	0.70
Number of passes				
1 pass	181 (67%)	27 (68%)	1.05 (0.51-2.12)	0.91
2 or more	91 (33%)	13 (32%)	0.96 (0.47-1.94)	0.91
Pleural needle angle				
<90°	149 (55%)	21 (53%)	0.91 (0.46-1.77)	0.79
90°	123 (45%)	19 (47%)	1.10 (0.56-2.13)	0.79

*Statistically significant
‡ Statistically significant protective factor against pulmonary hemorrhage

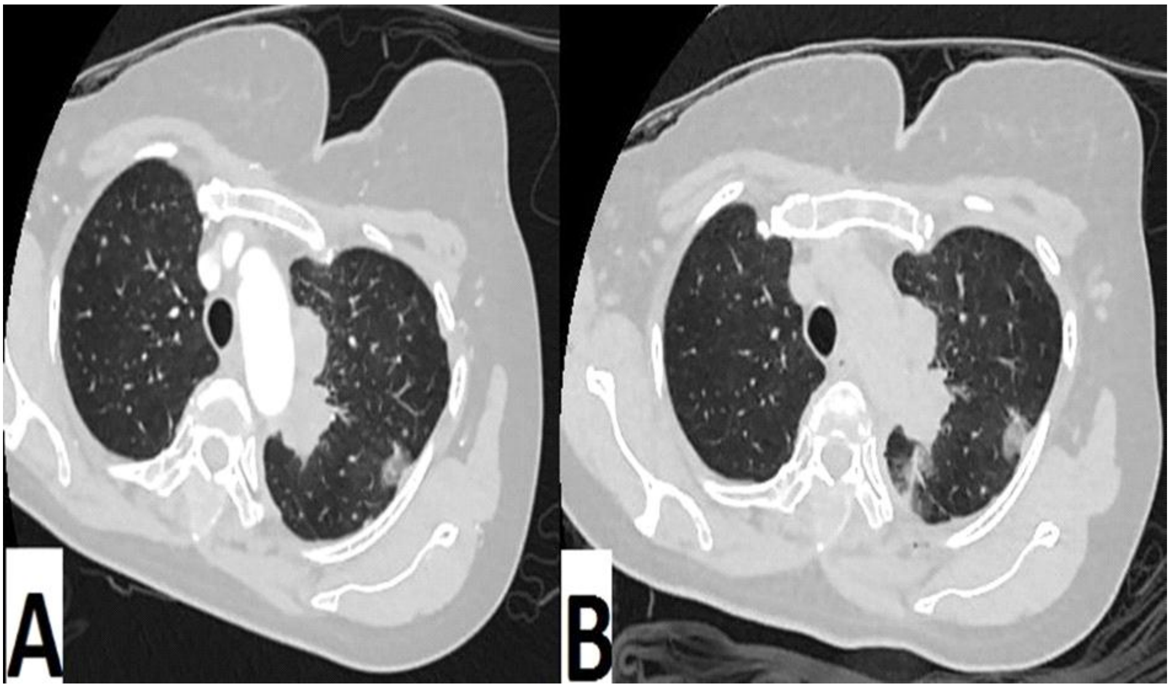

Figure (1): Grade I pulmonary hemorrhage before (a) & after (b) core needle biopsy from left pulmonary nodule.

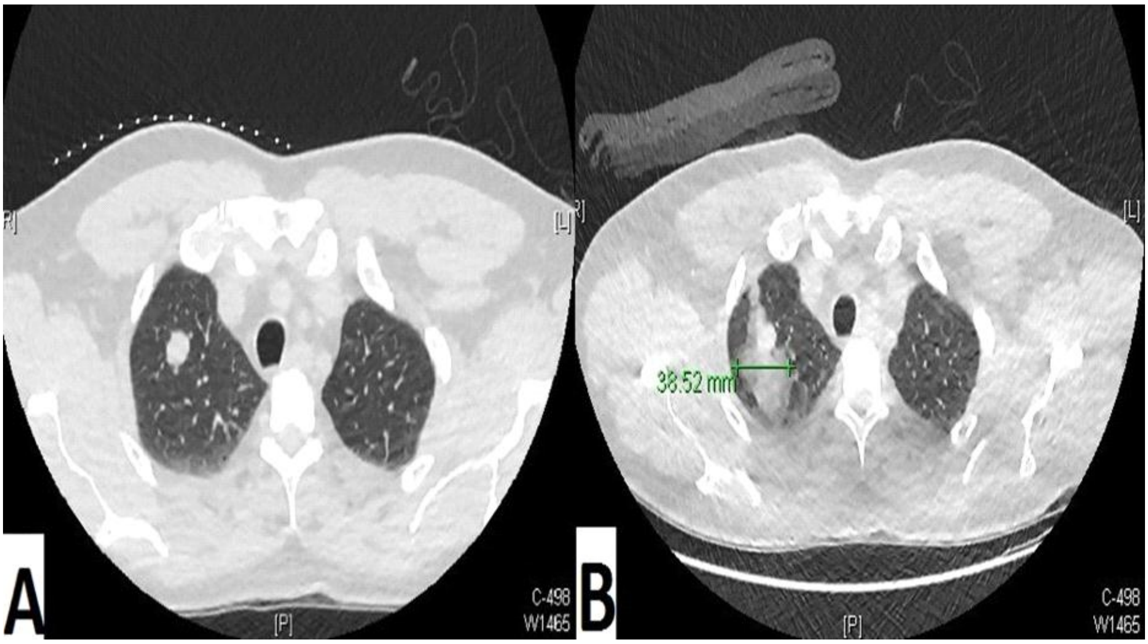

Figure (2): Grade II pulmonary hemorrhage before (a) & after (b) core needle biopsy from right pulmonary nodule.

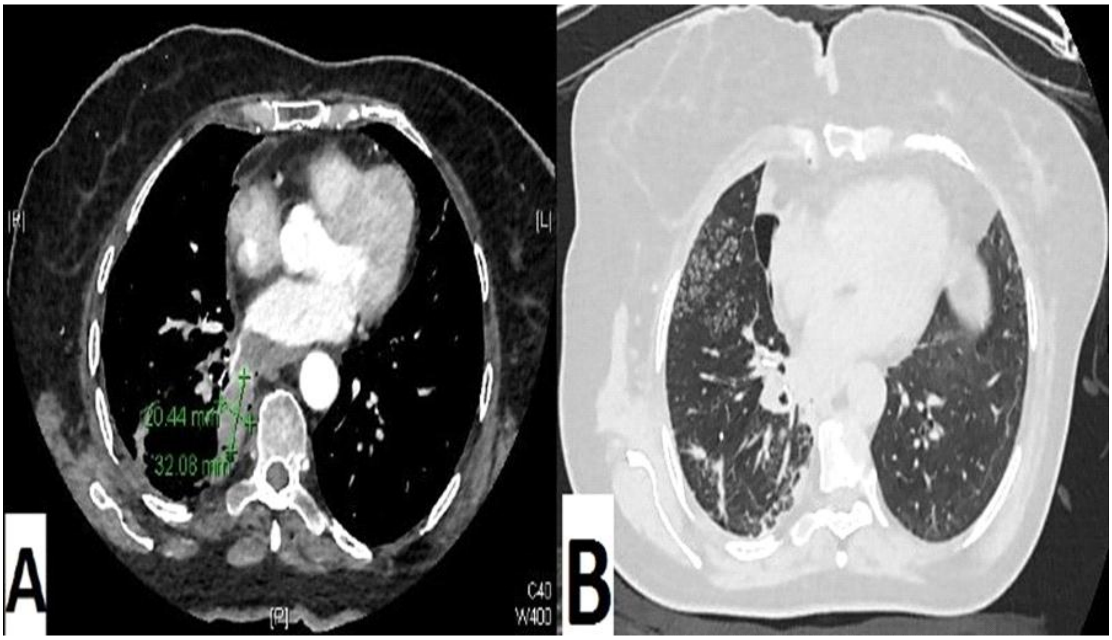

Figure (3): Grade III pulmonary hemorrhage before (a) & after (b) core needle biopsy from right pulmonary mass.

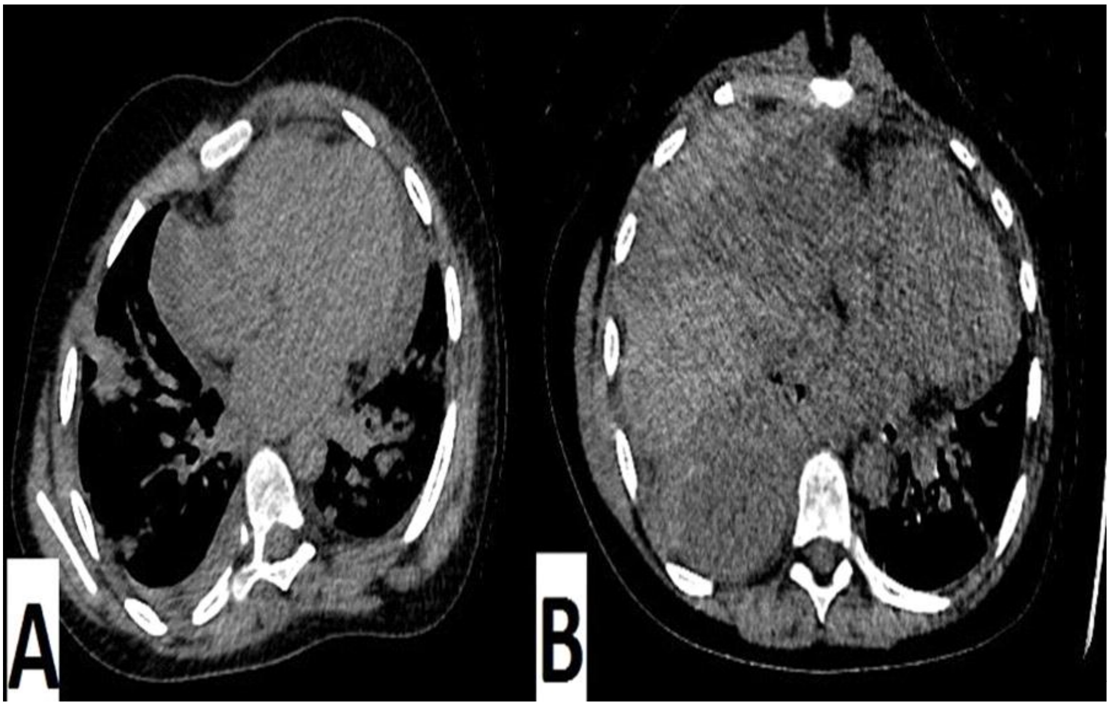

Figure (4): Grade IV pulmonary hemorrhage before (a) & after (b) core needle biopsy from right pulmonary nodular consolidation.

DISCUSSION

In the present study pulmonary hemorrhage complicating core needle lung biopsy occurred in 97 out of 312 patients (31%). These results are similar to that of Khan and his colleagues [14] and slightly lower than that of Tai and his colleagues [13] who reported 27% and 41% of pulmonary hemorrhage after transthoracic CT-guided lung biopsy respectively. In contradistinction to these results; Chassagnon and his colleagues [15] reported pulmonary hemorrhage in 60% in their study. High grade hemorrhage in our study occurred in 40 patients (13%) similar to the 17% reported by Tail et al [13]. Grade IV pulmonary hemorrhage was seen in our study in one patient only (0.3%) which is comparable to the hemothorax rates of 0.1-0.4 % reported in other studies [14,16]. However in contradistinction to the study of Tai et al [13] who had 5 hemothorax patients; one of them needs surgical intervention to control the bleeding. Hemothorax occurred only in one patient in our study and was managed conservatively with pigtail insertion and no need for surgical intervention.

In the present study the mean age was 51.8±8.1 year for no / low grade pulmonary hemorrhage and was 54±11.3 year for high grade pulmonary hemorrhage. We did not found significant difference between age of no / low grade pulmonary hemorrhage and high grade pulmonary hemorrhage groups (P >0.05). This is dis-concordant to the results of other investigators who found that older age is significantly associated with high grade pulmonary hemorrhage [13,14,17]. However in another recent study [18] the diagnostic accuracy and complications of CT guided transthoracic needle lung biopsy were similar in older patient (80 years and above) and younger patients.

In our study female sex was significantly associated with high grade pulmonary hemorrhage. This is in agreement with other studies [13,14,17].

In one study emphysema was significantly associated with high grade pulmonary hemorrhage. The authors of this study hypothesized that because patient with emphysema have destruction of airspace walls distal to terminal bronchioles, there may be increased potential space for the hemorrhage to expand [13]. In contradistinction to these results; the authors of another study stated that emphysema is not as significant risk factor for high grade pulmonary hemorrhage complicating lung core needle biopsy [12]. This is in agreement with the results of the present study as we found emphysema was not significant risk factor for the occurrence of high grade pulmonary hemorrhage (P >0.05).

In this study lesions smaller than 3 cm and those with non-subpleural location were significantly associated with high grade hemorrhage (P <0.05). This is concordant with other previous studies [14,13,17]. Deeper and smaller lesions are more technically challenging to access leading to increased needle dwelling time and needle excursion with motion with subsequent sheering of the vessels resulting in increased hemorrhage [19]. In contradistinction to other studies [13,19] we did not observe significant association between sub-solid lesions and high grade pulmonary hemorrhage.

In one study co-axial technique was significantly associated with high grade hemorrhage. The author of this study postulated that this may be due to increasing needle dwell time associated with co-axial technique [13]. This is in agreement with our study. We found significant association between co-axial technique and high grade hemorrhage (P <0.05). On the other hand in another study pulmonary hemorrhage complicating core needle biopsy showed insignificant difference between coaxial and non-co-axial techniques [12]. In agreement with another study [13] the rest of technique related factors namely needle gauge, number of passes and pleural needle angle were not significantly associated with high grade pulmonary hemorrhage as in our study (P >0.05).

In conclusion percutaneous transthoracic CT guided core needle biopsy is safe procedure. Pulmonary hemorrhage complicating this procedure is common but can be managed conservatively with no need for surgical intervention. Emphysema is not significant risk factor for high grade pulmonary hemorrhage. Significant risk factors for high grade pulmonary hemorrhage include female sex, lesions less than 3 cm, non-subpleural location and co-axial techniques.

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