

A new score predicting intraprocedural risk in patients undergoing CT-guided percutaneous needle pulmonary biopsy (CATH-score)

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Abstract. – OBJECTIVE: To develop a new score (CATH-score) for predicting intra-procedural risk in patients undergoing CT-guided percutaneous needle pulmonary biopsy.

PATIENTS AND METHODS: 100 CT-guided lung biopsies performed with a 18 Gauge (G) needle (Pilot Group) were reviewed to analyse patient-, lesion- and procedure-related variables to identify risk factors for procedural complications (pneumothorax and parenchymal bleeding) and diagnosis failure. A scoring system for predicting complications and choosing the right needle (16 G, 18 G, 21 G) was developed using risk factors weighting and prospectively applied to 153 consecutive biopsies (CATH-score Group); complications and diagnostic rates obtained were compared with a group of patients (Control Group) that underwent lung biopsy; in this group of patients the choice of the calliper of the needle was based on the operator experience.

RESULTS: lesion diameter ($p=0.03$), central location of lesion ($p=0.02$), centrilobular emphysema ($p=0.04$) and trans-pulmonary needle route ($p=0.002$) were associated with a higher complications rate in Pilot Group and were selected as risk factors to include in the CATH-score definition. Risk factors "cut-off" values were identified (Receiver Operating Characteristics curves) and risk-stratification groups were classified as follows: low (16 G, score 1), intermediate (18 G, score 2), and high procedural risk score (21 G, score 3). CATH-score usage limited complications rate despite a higher number of 16 G needle employed, with a diagnostic performance rising respect to Control Group.

CONCLUSIONS: CATH-score seems to be a valuable tool for predicting the risk of complications and choosing the right needle, in order to increase diagnostic performance in patients undergoing TTNA.

Key Words:

Lung, Biopsy, Cancer, CT.

Introduction

Indeterminate focal lung lesions (IFLLs) still represent an exciting challenge for radiologists and all medical figures involved in the management of lung diseases, such as oncologists, pulmonologists, thoracic surgeons and pathologists. Histological and immunohistochemical analysis is still recommended as "gold standard" for IFLL's nature determination¹⁻⁵. Lung tissue can be provided to pathologist through minimally invasive techniques, such as CT-guided biopsy or TTNA (trans-thoracic needle aspiration, TTNA) or EBUS- and EUS-NA/biopsy (endobronchial ultrasound-guided needle aspiration or biopsy and endoscopic ultrasound-guided needle aspiration or biopsy)^{2,3,6,7}. TTNA, performed under CT-guidance, is a valid and well-established diagnostic tool for the characterization of IFLL, providing optimal diagnostic rates, especially when lesions are malignant². Nevertheless, TTNA shows not negligible complications rate in literature and frequently reveals to be more noxious than other minimally invasive techniques such as bronchoscopy². Pneumothorax, pulmonary haemorrhage, hemothorax and chest wall hematoma are the most commonly observed complications during and after TTNA. Less frequently reported complications are hemomediastinum, cardiac tamponade, air embolism, vasovagal reaction and lesion massive bleeding⁸. Some authors tried to identify

which variables influence the rising of intra-procedural and peri-procedural complications even though most studies focused on a single specific element or complication type, and with controversial results⁹⁻¹¹. As a consequence, the “weight” of each risk factor for intra-procedural complications rate is not clearly defined in the literature. Furthermore, there is no indication about which needle size should be used for each patient or lesion. On the other hand, needle size revealed to be strictly correlated to a complications rate rising¹², even if a larger needle size offers the possibility to obtain enough tissue for molecular tests¹³. The aim of this study was to develop and test a risk factor-based score system (CATH-score) helpful in choosing the right needle for TTNA, that should lead to limit the procedural complications and to increase the diagnostic success.

Patients and Methods

Study Design and Population

This study was approved by our internal Ethical Committee and performed with respect to the Helsinki Declaration and its amendments. Written informed consent was obtained by each patient.

The study design was based on the enrolment of three different subgroups of patients (Table I): Pilot Group, CATH-score Group and Control Group.

Pilot Group

This group was built up to identify patient-related, lesion-related and procedure-related variables that increase the risk of TTNA complications and diagnostic failure, and to classify them as risk factors used in the CATH-score definition. 100 consecutive patients (62 males, 38 females;

mean age: 68 ± 12.47 ; range: 37-82; mean lesion diameter: 24.7 ± 11.5 mm; range: 8-117 mm) who underwent TTNA were retrospectively enrolled from January to September 2013. Only procedures performed with an 18 Gauge (18 G) needle were included in order to avoid selection bias. This needle size was chosen because it is the most widely used, as reported in literature¹⁴⁻¹⁸. Patient-related (age, gender, paraseptal emphysema, centrilobular emphysema), lesion-related (diameter, lobar location, distance from pleura), and procedural-related variables (percutaneous access point, trans-pulmonary needle route, patient’s decubitus) were evaluated. A statistical analysis was performed to identify which variables were statistically correlated with a higher complications rate and a lower diagnostic performance; after that, the risk factors to be introduced in the CATH-score definition were identified. A stratification of the risk was designed through the selection of “cut-off” values that identified the weight of each risk factor. After that, a points scale was assigned to each identified risk factor on the basis of its statistical weight. At the end, a scoring system (CATH-Score) was defined, in order to predict pre-procedural risk of each patient to incur in complications or missed diagnosis and helping in needle choice, as follows: low risk (score 1), intermediate risk (score 2) and high risk (score 3).

CATH-score Group

From January 2014 to June 2015, 135 consecutive patients (81 males, 54 females; mean age: 68.4 ± 13.3 ; range: 28-87) admitted in our Department to undergo TTNA (153 procedures performed) were prospectively enrolled and stratified on the basis of the identified CATH-score. For each patient pre-procedural risk was calculated before TTNA, on the basis of CATH-score, and 16G,

Table I. Pilot Group, CATH-Score Group and Control Group population characteristics.

	Pilot Group	CATH-score Group	Control Group
Males	62 (62%)	81 (60%)	61 (61%)
Females	38 (38%)	54 (40%)	39 (39%)
Total	100 (100%)	135 (100%)	100 (100%)
Mean age (yrs.)	68 ± 12.47	68.4 ± 13.3	70 ± 12.23
Age range (yrs.)	37-82	28-87	34-83
Mean lesion diameter (mm)	24.7 ± 11.5	24.3 ± 9.4	26.4 ± 12
Lesion diameter range (mm)	8-93	8-131	7-112
Mean distance from pleura (mm)	24.3 ± 24.1	24.4 ± 21.4	23.5 ± 22.9
Distance from pleura range (mm)	0-78	0-119	0-97

yrs. = years

18G and 21G needle size were prospectively used in the low, intermediate and high-risk groups, respectively.

Control Group

From January to December 2012, 100 non-consecutive patients who underwent TTNA with different needle size (16 G, 18 G, 21 G) were retrospectively enrolled and matched with the CATH-score Group in terms of similar patient-related, lesion-related and procedure-related variables.

Bioptic Procedure

All the procedures were performed with a modified Menghini needle (TSK Surecut, Oisterwijk, The Netherlands) in our Department, by the same experienced interventional radiologist (with 10 years of experience) on a 64-rows CT scanner (Lightspeed VCT, GE Healthcare; Fairfield, CT, USA). Position of the patient was chosen on the basis of the previous diagnostic CT examination, if present. A pre-procedural chest CT scan was performed (1.25 mm of thickness) in patients with a previous examination "older" than 15 days before the procedure and for those with not available previous CT examinations. Subsequently, after the positioning of the radiopaque cutaneous markers, a new CT scan was performed on the site of interest (5 cm cranial and caudal to the lesion), in order to decide the site of percutaneous access. 10-20 ml of carbocaine were intradermally administered on the access site. Percutaneous needle insertion was performed and tissue for cytological and/ or histological analysis was collected once the needle reached the lesion. If necessary, anesthesiological support was granted to the patients in terms of analgesic and oxygen therapy, monitoring vital parameters by pulse oximetry and electrocardiogram. A CT scan with 1.25 mm of slice thickness (15 cm cranial and caudal to the lesion) was performed at the end of the procedure, during forced expiration, in order to identify intra-procedural complications. Moreover, all patients underwent chest X-ray and blood count examination 3 h after biopsy, and late if necessary, to exclude peri-procedural complications.

Charts and Image Evaluation

One chest radiologist and one interventional radiologist, with 12 and 4 years of experience respectively, evaluated in consensus the medical charts, radiologic reports and intra-procedural/ immediate post-procedural CT images, as well as the subsequent chest X-rays (within

3 h after biopsy), in order to detect intra-procedural and peri-procedural complications in each group. The evidence of needle within the lesion on CT images defined technical success. For the CATH-score Group the demonstration of enough tissue material at sample taking (at least 1 tissue specimens) was also evaluated. The needle size used in each procedure performed in the Pilot and Control Group was retrieved from the radiologic reports.

Statistical Analysis

All data were presented as mean values \pm standard deviation for continuous variables, and as percentages for categorical variables and were analysed with dedicated software for statistical analysis SPSS 13.0 (SPSS Inc., Chicago, IL, USA). The association between each patient-related, lesion-related and procedural-related variables and complications as well as diagnostic success was investigated within the Pilot Group. Student's *t*-test was applied for continuous variables analysis and chi-square test was applied for categorical variables. Risk factors' weighting for CATH-score definition was investigated through the analysis of Receiver Operating Characteristics curves (ROC curves) and "cut-off" values were assessed. χ^2 -test was used to compared CATH-score Group and Control Group in terms of needle choice with respect to both procedural complications and diagnostic rate. $p < 0.05$ was considered statistically significant.

Results

Technical success was achieved for all the procedures (271) performed within the three study groups (total population of 268 patients).

Pilot Group

An overall complications rate of 65% (65/100 procedures) and a diagnostic rate of 58% (58/100 procedures) were reported, with 49/65 (75.4%) cases of pneumothorax observed. Among these cases, only thirteen (13/49; 26.5%) required chest tube placement, with a complete resolution of the pneumothorax within 24-48 h. In sixteen (16/65; 24.6%) patients parenchymal bleeding was observed, but none of them requiring blood transfusion or any other treatment. Table II shows all the considered variables and their correlation with complications and diagnostic success. Among variables,

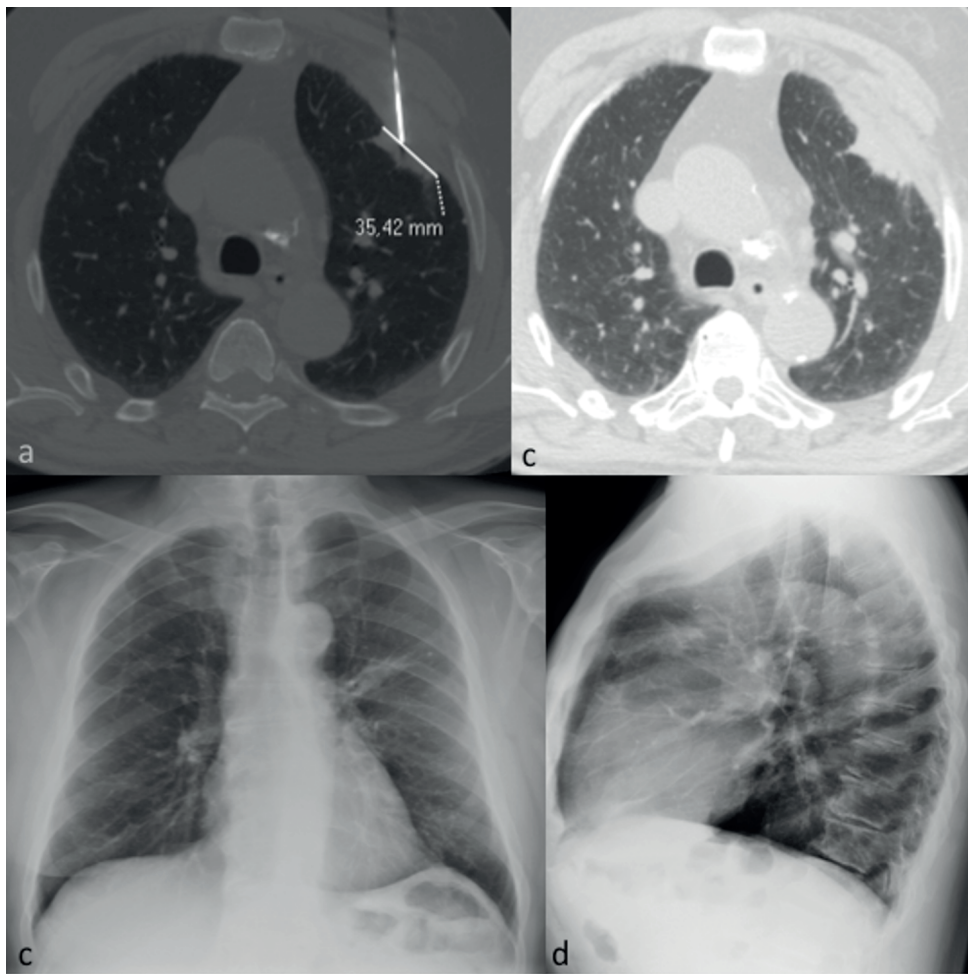


Figure 1. 65 yrs. patient with left upper lobe lesion (*a*) attached to chest wall. (Lesion diameter: 35 mm, CATH-score points: 0; Needle Route: 0 mm, score points: 0; Distance from pleura: 0 mm, score points: 0; centrilobular emphysema: absent, score points: 0; final CATH-score points: 0, CATH-score: 1, low risk. Needle to choose: 16G). Final control (*b*) shows absence of pneumothorax and parenchymal bleeding. Chest X-ray (*c*, *d*) after 3 h did not show pneumothorax nor parenchymal opacities. Final histology: lung adenocarcinoma.

lesion diameter ($p=0.03$; Student's *t*-test), central location ($p=0.02$; Student's *t*-test), as well as the presence of centrilobular emphysema ($p=0.04$; X^2 test) and trans-pulmonary needle route ($p=0.002$; Student's *t*-test) were significantly associated with a higher complications rate. These variables have been considered as risk factors in our population and introduced in the CATH-score definition. None of these variables was associated with diagnostic success. The ROC curves analysis carried out on the risk factors revealed an area under the curve (AUC) of 0.68, 0.65 and 0.71 for lesion diameter, distance from pleura and trans-pulmonary needle route respectively, showing acceptable discriminative capacity; "cut-off" values that

best stratified the risk of complications for each risk factor were the following:

- Lesion diameter (≥ 30 mm, score 0; 20-30 mm, score 1; < 20 mm, score 2).
- Lesion location (within 7 mm from pleura or peripheral, score 0; central lesion, score 1).
- Trans-pulmonary needle route (< 7 mm, score 0; 7-30 mm, score 1; ≥ 30 mm, score 2).
- Centrilobular emphysema (absent, score 0; present, score 1).

Therefore, the score scale ranged between 0 and 6 points. Three different risk-stratification groups were identified as follows: low procedural risk (score 1: 0-2 points), intermediate procedural risk (score 2: 3-4 points) and high procedural risk (score 3: 5-6 points) (Figure 1, 2 and 3).

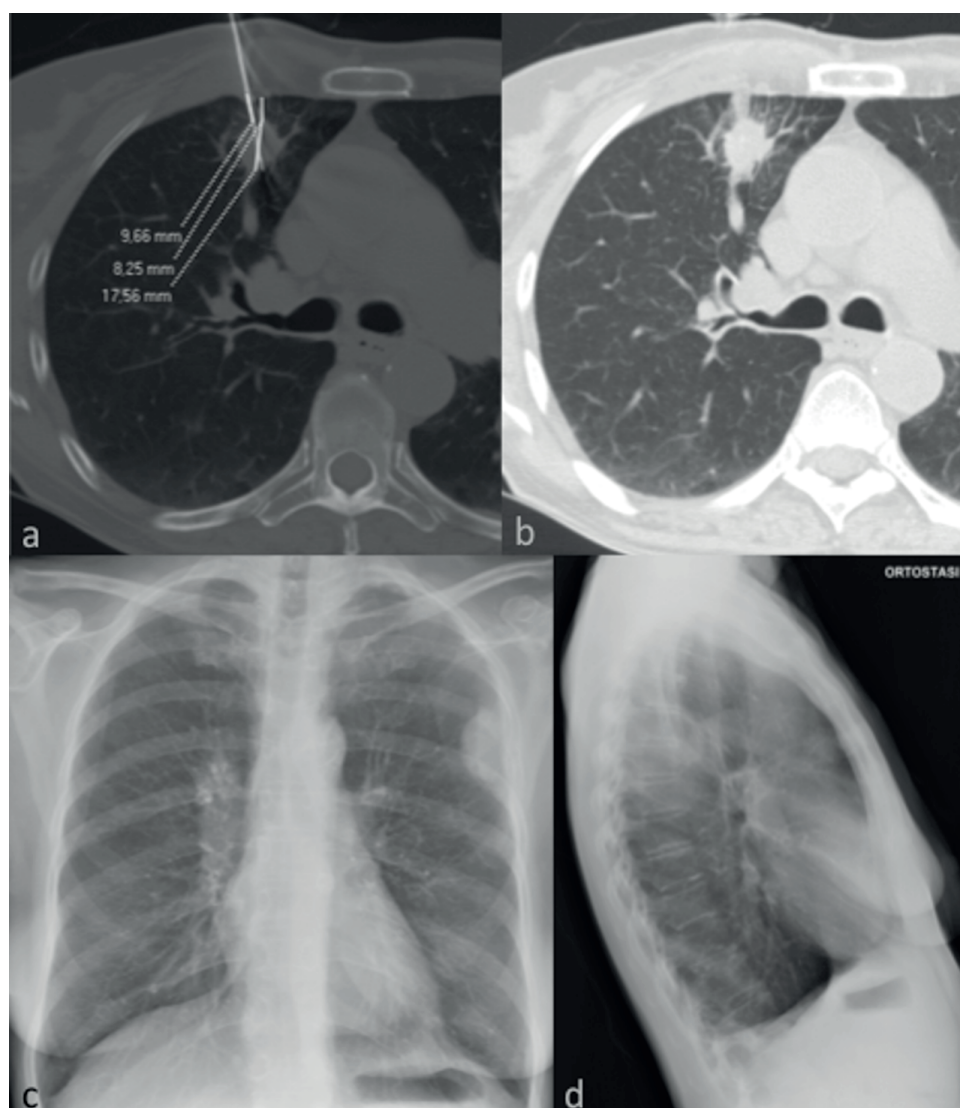


Figure 2. 68 yrs. female with a right upper lobe solid lesion (Diameter: 17 mm, score points 2; Distance from pleura: 8 mm, score points 1; needle route: 9 mm, score points 1; Centrilobular emphysema: absent, score points: 0 - CATH-score points: 4, final CATH-score: 2, intermediate risk, needle: 18 G) at CT scan (*a*). Final control (*b*) shows the presence of minimal perilesional bleeding without evidence of pneumothorax. Chest X-ray (*c*, *d*) after 3 h showed the absence of pneumothorax and confirmed the presence of a contralateral costal lesion. Patient was discharged after 2 days from procedure. Final histology: lung adenocarcinoma.

CATH-score Group

75.2% (115/153) of patients reached a score 1 and biopsies were performed with a 16 G needle, 24.8% (38/153) of patients a score 2 (18 G needle), whereas no patient obtained a score 3. An overall complications rate of 43.1% (66/153 procedures) and a diagnostic rate of 85.6% (131/153 procedures) were reported. In detail, 47/66 (71.2%) cases of pneumothorax were observed (overall pneumothorax rate: 47/153, 30.7%), with only 9/47 (19.1%) cases requiring a chest tube placement (overall tube placement rate: 9/153, 5.9%), with a

complete resolution of the pneumothorax within 24-48 h. In nineteen cases (19/66; 28.8%) parenchymal bleeding was observed during the procedures, but all of them spontaneously resolved, without requiring blood transfusion or any other treatment (overall parenchymal bleeding rate: 19/153, 12.4%).

Control Group

An overall complications rate of 68% (68/100 procedures) and a diagnostic rate of 65% (65/100 procedures) were reported. TTNA was per-

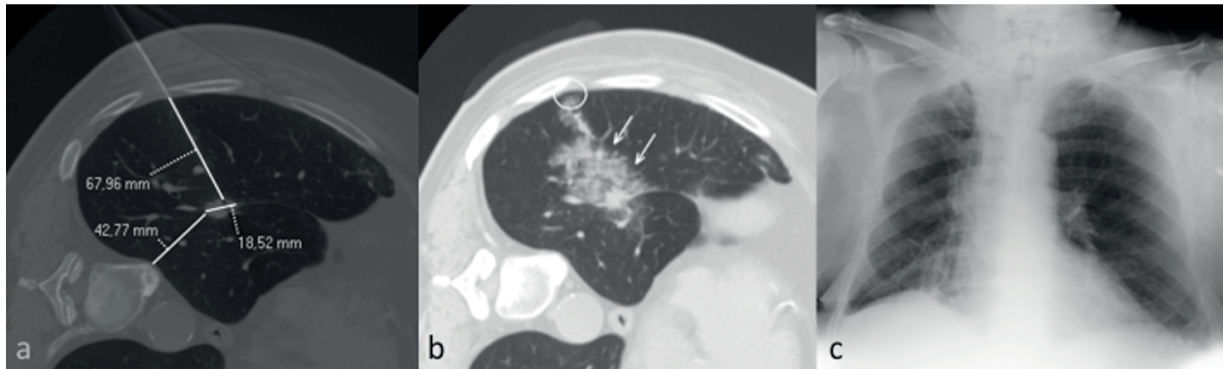


Figure 3. 76 yrs. male with a right inferior lobe solid lesion (Lesion diameter: 18 mm, score points 2; Distance from pleura: 42 mm, score points 1; needle route: 68 mm, score points 2; centrilobular emphysema: absent, score points: 0 - CATH-score points: 5, final CATH-score: 3, high risk, needle: 21 G) at CT scan (**a**). Final control (**b**) shows the presence of parenchymal bleeding (arrows) along the trans-pulmonary needle route with minimal evidence of pneumothorax (circle). No hemoptysis occurred and normal values of hemoglobin were observed after 3 and 24 h. Chest X-ray (**c**) performed at 3 h did not show presence of pneumothorax. Patient was discharged after 3 days from procedure. Final histology: lung adenocarcinoma.

Table II. Variables tested in the Pilot Group.

Variable	Complications			Diagnosis		
	Present	Absent	<i>p</i> -value	Present	Absent	<i>p</i> -value
Patient						
Age (yrs.)	69.4 ± 11.5	66.3 ± 11.9	0.08	67.3 ± 12.5	68.5 ± 13.1	0.08
Gender (M; F)	44 M; 21 F	25 M; 10 F	0.7	42 M; 16 F	22 M; 20 F	0.32
Paraseptal emphysema	5	5	0.29	4	6	0.22
Centrilobular emphysema	8	3	0.041	6	5	0.81
Pulmonary emphysema	13	8	0.73	10	11	0.28
Lesion						
Diameter (mm)	19.9 ± 7.2	30.7 ± 9.8	0.032	25.3 ± 12.3	24.4 ± 10.8	0.83
Lobar location						
Superior Right Lobe	13	10	0.33	12	11	0.52
Medium Lobe	12	4	0.36	10	6	0.69
Inferior Right Lobe	11	4	0.46	10	5	0.46
Superior Left Lobe	16	9	0.9	13	12	0.48
Inferior Left Lobe	13	8	0.74	13	8	0.68
Distance from pleura (mm)	54 ± 23.7	7.3 ± 13.6	0.022	23.8 ± 22.3	24.5 ± 23.2	0.89
Procedural						
Percutaneous access point						
Anterior Right	19	11	0.06	16	14	0.54
Posterior Right	17	8	0.72	15	10	0.82
Anterior Left	14	7	0.85	13	8	0.68
Posterior Left	15	9	0.77	14	10	0.97
Trans-pulmonary needle route (mm)	63.4 ± 25.8	27.3 ± 28.9	0.002	43.2 ± 34.3	41.4 ± 36.8	0.78
Patient's decubitus						
Prone	31	17	0.93	29	20	0.81
Supine	32	15	0.54	26	20	0.78
Right	1	2	0.24	2	1	0.75
Left	1	1	0.65	1	1	0.81

Yrs. = years; M = male; F = female.

formed by using a 16 G needle in 20/100 patients (20%), 18 G in 64/100 patients (64%), and 21 G in 16/100 patients (16%). In detail, 52/68 (76.5%)

cases of pneumothorax were registered (overall pneumothorax rate: 52/100, 52%), among whom 14/52 (26.9%) required chest tube placement

Table III. Pilot group, CATH-Score group and Control group complication rate, diagnostic rate and needle size.

	Pilot group	CATH-Score group	Control group
Complications			
Pneumothorax	49 (49%)	47 (30.7%)	52 (52%)
Chest tube placement	13 (13%)	9 (5.9%)	12 (12%)
Parenchymal bleeding	16 (16%)	19 (12.4%)	19 (19%)
Treatment	0	0	0
No treatment	16 (16%)	19 (12.4%)	19 (19%)
Other	0	0	0
All	65 (65%)	66 (43.1%)	68 (68%)
Diagnostic success	58% (58/100)	85.6% (131/153)	65% (65/100)
Needle size			
16 G	0	115 (75.2%)	20
18 G	100	38 (24.8%)	64
21 G	0	0	16

G = Gauge.

(overall tube placement rate: 14/100, 14%), with a complete resolution of the pneumothorax within 24-48 h. In 19/68 patients (27.9%) parenchymal bleeding was evident during the procedure, but none of them required blood transfusion or any other treatment (overall parenchymal bleeding rate: 19/100, 19%). 3/100 (3%) patients had both intra-procedural pneumothorax and parenchymal bleeding.

CATH-score Group vs. Control Group

Regarding to complications, CATH-score Group registered a significantly lower complications rate (43.1% vs. 68%, $p = 0.012$; X^2 test) respect to Control Group. In detail, a lower rate of patients with pneumothorax was observed (30.7% vs. 52%; $p = 0.019$) in CATH-score Group; moreover, chest tube placement rate (5.9% vs. 14%, $p = 0.023$; X^2 test) was also lower. In the CATH-score Group, a significantly higher diagnostic rate (85.6% vs. 65%, $p = 0.032$; X^2 test) was obtained. A significantly higher number of procedures by using a 16 G needle (75.2% vs. 20%, $p < 0.001$; X^2 test) and a significantly lower number of procedures by using a 21 G needle (0% vs. 16%, $p < 0.001$; X^2 test) were performed in the CATH-score Group (Table III).

Discussion

Histological assessment is the “gold standard” for pulmonary malignancy demonstration¹⁹.

Different procedural methods are available for approaching IFLLs, according to the lesion location (TTNA, EBUS- and EUS-NA/biopsy). TTNA is the most commonly used diagnostic tool for characterizing peripheral IFLLs, with a good sensitivity (88%-92%) and specificity (96%-98%) reported in literature^{2,6}. Nevertheless, TTNA may be associated with several complications such as pneumothorax, pulmonary haemorrhage, chest wall hematoma, hemothorax, hemomediastinum, as well as cardiac tamponade, air embolism and lesion massive bleeding⁸, that can potentially lead to lengthening of hospitalization and increasing costs. The most common injuries after TTNA are pneumothorax and pulmonary haemorrhage¹¹. The reported occurrence of pneumothorax is still high, ranging from 27% to 54%, with a 29.8% cases requiring a chest tube placement if pneumothorax become symptomatic or continues to increase^{8,20}. Pulmonary haemorrhage is observed in 4.0%-27% cases and may be associated with haemoptysis in 1.2%-5.0%, requiring invasive operative treatment such as endovascular embolization, when massive^{8,21}. Our study confirmed the evidence that pneumothorax and pulmonary haemorrhage are the most frequent complications after TTNA, and that no other injuries have been observed, demonstrating that other possible complications are indeed rare. In detail, a lower overall complications rate was observed in the CATH-score Group respect to the Con-

trol Group (43.1% vs. 68%), with a lower rate of pneumothorax (30.7% vs. 52%) and a significant reduction of chest tube placement (5.9% vs. 14%). Furthermore, a decrease in parenchymal bleeding rate was observed in the CATH-score Group (12.4% vs. 19% of Control Group), with no cases of severe bleeding requiring further diagnostic or therapeutic procedures. The small number of reported cases with parenchymal bleeding may explain the lack of statistical difference between the CATH-score Group and the Control Group. These data suggest that CATH-score correctly stratified patients before TTNA and helped in decreasing our complications rate, in particular when considering pneumothorax. In fact, although the rate of pneumothorax in the CATH-score group was in the range reported in literature (27%-54%), the rate of patients who required a chest tube placement was lower²⁰. The relationship between large needle size and a higher risk of complications during TTNA is well-known in literature¹². Nevertheless, it has been demonstrated that an increase in needle size raises the chances to obtain tissue for histological analysis and molecular characterization in neoplastic lesions⁶. This aspect has increasingly become important during the last decade, due to the identification of gene mutations, such as Epidermal Growth Factor Receptor (EGFR) for lung adenocarcinoma, which are associated with prognostic meaning and new therapeutic options²². In this scenario, the need of needles sized as large as possible for tissue characterization is expected to become more relevant in the next future, when molecular imaging and target molecular therapies will play a pivotal role in lung cancer management. At the best of our knowledge, there is no consensus in literature about the needle size to use to perform TTNA according to the patient and lesion. For this reason, until the end of 2013, in our Department, the needle choice was based on the operator experience, with a higher number of procedures performed by using an 18 G needle^{12,14-18}. Our results confirmed the validity of CATH-score also in the selection of needle size. The CATH-score correctly stratified our patients in regards to the needle size to be chosen for TTNA, leading to employ a 16 G needle in about 75% of the patients and to completely eliminate the usage of 21 G needles in our population. The higher number of large (16 G) needles used increased diagnostic rate significantly (85.6% vs. 65%) in the CATH-score Group respect to the Control Group. These

results suggest that CATH-score works effectively also in increasing diagnostic success and potentially providing enough tissue for molecular characterization. Nevertheless, our study is affected by some undeniable limitations. Firstly, CATH-score has been tested and internally validated in a relatively low number of patients, all referred to our Department. It is worth of note that a further analysis on larger series of patients and the external validation should be performed to definitely confirm the CATH-score potentiality. Secondly, needle (16 G, 18 G, 21 G) capability to provide enough tissue for molecular analysis was not assessed in our work but we intend to investigate this aspect in the next future.

Conclusions

The use of a CATH-score system in patients' stratification and needle size selection for TTNA may increase the diagnostic rate and protect patients from complications rising. Specifically, the CATH-score proposed in this study seems to be a valuable tool for predicting the risk of complications and for choosing the right needle, in the attempt to increase diagnostic performance and to reduce complications in patients undergoing TTNA.

Conflict of interest

The authors declare no conflicts of interest.

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