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Original Research Article

Validity of lung ultrasound with bedside lung ultrasonography in emergency protocol in diagnosing pneumonia

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ABSTRACT

Background: Pneumonia is an acute inflammation of the lung parenchyma caused by microorganisms. In 2020, pneumonia was included in the top 10 diseases requiring hospitalization in Indonesia with a mortality rate of 23% for patients treated in the intensive care unit. The diagnosis of pneumonia is based on anamnesis, physical examination, and supporting examinations. However, in practice, diagnostic procedures in patients with immobilization or patients with unstable hemodynamics are difficult to perform. Lung ultrasound (LUS) with bedside lung ultrasonography in emergency (BLUE) protocol is a simple and portable supporting examination that is known to be able to diagnose pneumonia more easily, accurately, and quickly. Therefore, a study related to the validity of LUS in diagnosing pneumonia needs to be conducted.
Methods: This study is a diagnostic test. The study was conducted over a period of 6 months (August 2023 to February 2024) at Prof. Dr. I.G.N.G. Ngoerah hospital. In this study, the validity was assessed consisting of sensitivity, specificity, and accuracy of LUS in diagnosing pneumonia. Data were analyzed using STATA MP 17.
Results: The total subjects in this study were 70 people. The sensitivity of LUS in diagnosing pneumonia was 86.8% (CI95%=74.7-94.5%) and the specificity was 70.6% (CI95%=44-89.7%), with an accuracy of 82.8%. The positive test predictive value was 90.2% (CI95%=78.6-96.7%) and the negative test predictive value was 63.2% (CI95%=38.4-83.7%). Thus, in subjects with LUS suggestive of pneumonia, pneumonia management can be done immediately. However, in subjects with LUS results not showing pneumonia, further supporting examinations are needed to confirm the diagnosis of pneumonia. Sensitivity, specificity, and accuracy varies based on age, body mass index, immunocompromised status, and degree of pneumonia
Conclusions: LUS with BLUE protocol is a valid supporting examination in diagnosing pneumonia (rule in disease).

Keywords: Ultrasound, BLUE protocol, Pneumonia, Sensitivity, Specificity, Accuracy

INTRODUCTION

Pneumonia is an acute inflammation of the lung parenchyma caused by microorganisms (bacteria, viruses, fungi, or parasites).[1] Pneumonia is one of the eight leading causes of death in the world with a mortality rate of 23% for patients treated in intensive care. Pneumonia is often

the main cause of sepsis and septic shock with rates reaching 50%.[1]

The diagnosis of pneumonia is based on anamnesis, physical examination, and supporting examinations. Diagnosing pneumonia in daily practice is also influenced by several special technical conditions, such as the failure to perform diagnostic procedures on patients with immobilization or patients with unstable hemodynamic due to the unavailability of portable diagnostic tools. Thus, diagnosing pneumonia quickly and accurately is a major challenge for clinicians.

LUS examination is a supporting examination that has been developed in diagnosing pneumonia. Several studies have stated that the use of LUS is a simple, portable, reliable tool, and is not inferior to chest X-ray to diagnose pneumonia. A systematic review states that the sensitivity of LUS when compared with CT scan, CT scan with clinical symptoms, or microbiology as the gold standard reaches 90.9%, 95%, and 53.3%, respectively. Meanwhile, the specificity of LUS reaches 89.7%, 91.3%, and 67.9%.[2] A study conducted by Parlamento et al showed that LUS is more sensitive than chest X-ray in diagnosing pneumonia in adult patients presenting to the emergency unit.[3] Another study conducted by Bitar et al also supports this, LUS is said to be superior to chest X-ray for diagnosing pneumonia in the intensive care unit.[4] The advantages of LUS compared to other diagnostic tools are that it is easy to perform, inexpensive, and there is no radiation.[3]

Accurate and rapid diagnosis of pneumonia is very important because it will affect the management and is related to patient outcomes. This study aims to determine the validity of LUS with the BLUE protocol in diagnosing pneumonia at the Prof. Dr. I.G.N.G. Ngoerah general hospital.

METHODS

This study is a diagnostic test using consecutive sampling conducted for 6 months (August 2023 to February 2024). Gold standard in this study was the doctor's diagnosis made by two pulmonologists or internal medicine consultants.

Inclusion criteria

Subjects aged ≥18 years; have at least 2 of the following pneumonia clinical features: cough, changes in sputum characteristics to purulent, body temperature ≥38^0 C (axillary)/ history of fever, chest pain, shortness of breath, signs of consolidation from physical examination, bronchial sounds and rhonchi; or patients suspected of having pneumonia based on the assessment of the doctor in charge; and receive treatment at Prof. Dr. I. G. N. G. Ngoerah general hospital in August 2023-February 2024 either through the polyclinic, emergency unit, or inpatient care were included.

Exclusion criteria

Subjects with a history of thoracic surgery, extensive subcutaneous emphysema, chest wound dressing, lung tumor, pulmonary embolism, pulmonary tuberculosis, bronchiectasis, idiopathic pulmonary fibrosis, and refused to participate after informed consent were excluded.

Ultrasound protocol

LUS was performed using SOGATA©. This examination was performed using a convex probe with a frequency of 3.5-5 MHz to evaluate three points on each hemithorax; upper BLUE point, the lower BLUE point, and PLAPS point according to the BLUE protocol (Figure 1). Ultrasonography was performed using BLUE protocol within a maximum of 3 minutes 6 seconds and within the less than 1×24 hours of the chest X-ray examination (Figure 2).

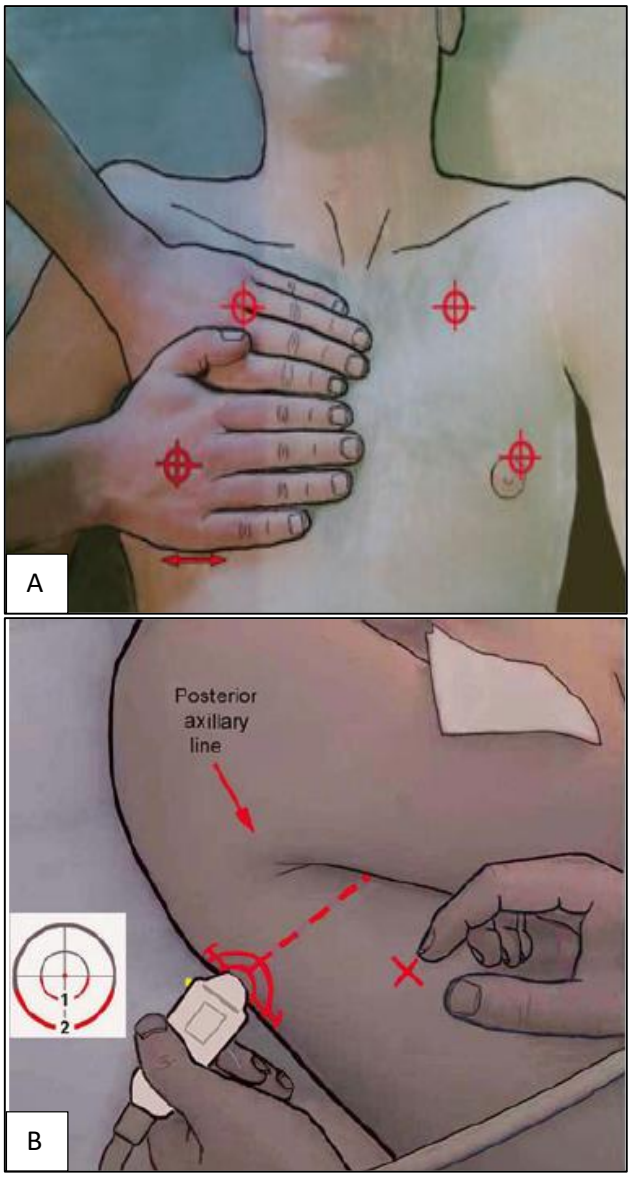

Figure 1 (A and B): Location of LUS.

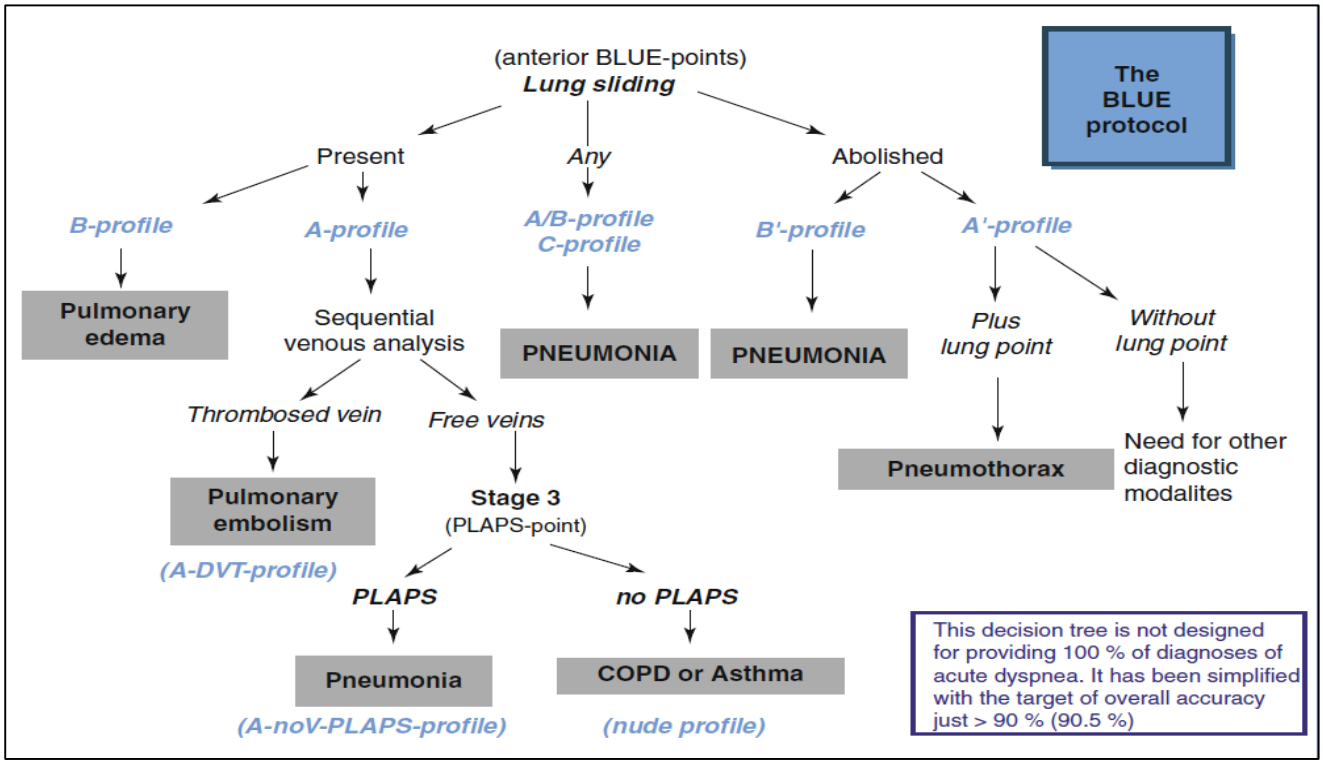

Figure 2: Scheme of BLUE protocol.

The BLUE point was determined using two hands that were the same size as the patient's hands, the upper hand touching the clavicle, without the thumb. The upper BLUE point is located between the third and fourth fingers of the upper palm. The lower BLUE point is in the middle of the lower palm (crossing downwards to avoid the heart), while the PLAPS point is the point of intersection of the posterior axillary line and the transverse line that continues from the lower BLUE point. The results of the LUS examination are documented and numbered according to the subject's serial number and will be evaluated by two radiology residents and verified by a Thoracic Consultant Radiology Specialist. Clinical data, laboratory data, chest X-rays, and the diagnosis of the patient's are not included when evaluating the LUS results. The LUS results are not included when the doctor evaluating diagnosis (blind). The evaluation of diagnosis by doctor is made based on anamnesis, physical examination, laboratory, and chest X-ray examinations.

Univariate analysis aims to describe the characteristics of the subjects and the measurement results of each research variable. Diagnostic tests are carried out to assess sensitivity, specificity, accuracy, negative predictive value, and positive predictive value. Inference is based on 95% CI of each validity indicator. Cohen's Kappa Consistency test is carried out to assess the consistency of answers between the doctors in diagnosing pneumonia and residents in interpreting the LUS results. The entire data analysis process above was carried out using STATA MP 17 software.

RESULTS

The subjects in this study were 70 people. Characteristics of the subjects in this study are presented in Table 1. Based on Table 1, most of the subjects were in the age group of 60 years (57.4%) with an average age of 60.25±16.56 years. The subjects were predominantly male (57.4%), not obese (88.57%), not immunocompromised (92.86%), and had non-severe pneumonia (60.38%).

Table 1: Characteristics of research subjects.

Characteristics	N (%)
Age (in years)	
Mean±SD	60.25±16.56
18-59	30 (42.86)
≥60	40 (57.40)
Gender	
Male	40 (57.40)
Female	30 (42.86)
BMI (kg/m^2)	
Obesity	8 (11.43)
Not obese	62 (88.57)
Immunocompromised status	
Immunocompromised	5 (7.14)
Not immunocompromised	65 (92.86)
Degree of pneumonia	
Severe	21 (39.62)
Not severe	32 (60.38)

In this study, 53 (75.71%) subjects were diagnosed with pneumonia based on the gold standard. As many as 92.45% were community acquired pneumonia, while 7.55% were hospitalized acquired pneumonia (Table 2).

The results of LUS in subjects suspected of having pneumonia are shown in Table 3. Most subjects had profile C, namely 42 (79.25%), followed by profile A-No-V-PLAPS 7 (13.21%), and profile A/B 4 (7.55%). The kappa test performed on this ultrasound result variable was 0.66, indicating substantial agreement.

Table 4 illustrates the validity of LUS with the BLUE protocol in diagnosing pneumonia. Overall, the sensitivity of LUS in diagnosing pneumonia reached 86.8% (CI95%=74.7-94.5%) and specificity was 70.6% (CI95%=44-89.7%), with an accuracy of 82.8%. The predictive value of a positive test was 90.2% (CI95%=78.6-96.7%) and the predictive value of a negative test was 63.2% (CI95%=38.4-83.7%).

In this study, an analysis of the validity of LUS was also carried out based on subject characteristics including age, BMI, immunocompromised status, and degree of pneumonia as shown in Table 5. Based on age, patients aged 18-59 years had higher sensitivity than those aged over 60 years. Based on BMI, patients with obesity had lower sensitivity, specificity, positive test predictive value, negative test predictive value, and accuracy compared to subjects who were not obese. Based on immunocompromised status, subjects with immunocompromised had lower sensitivity, specificity, positive test predictive value, negative test predictive value, and accuracy compared to subjects who were not immunocompromised. Based on the degree of pneumonia, subjects with severe pneumonia had higher sensitivity, negative test predictive value, and accuracy compared to subjects with non-severe pneumonia.

Table 2: Results of establishing a pneumonia diagnosis based on the doctor diagnosis (gold standard).

Diagnosis	N (%)
Not pneumonia	17 (24.29)
Pneumonia	53 (75.71)
Community acquired pneumonia	49 (92.45)
Hospital acquired pneumonia	4 (7.55)
Ventilator associated pneumonia	0 (0)

Table 3: LUS results of subjects suspected of having pneumonia.

LUS results	N (%)
B' profile	0 (0)
A/B profile	4 (7.55)
C profile	42 (79.25)
A-No-V-PLAPS profile	7 (13.21)

Table 4: Results of LUS validity analysis in diagnosing pneumonia with the doctor diagnosis as the gold standard.

Variables	Doctor diagnosis		Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	Accuracy
	Pneumonia	Not pneumonia					
LUS suggestive pneumonia	46	5	86.8 (74.7-94.5)	70.6 (44-89.7)	90.2 (78.6-96.7)	63.2 (38.4-83.7)	82.8
LUS not pneumonia	7	12					

Table 5: Sensitivity, specificity, positive predictive value, negative predictive, and accuracy of ultrasound in diagnosing pneumonia.

Variables	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	Accuracy
Age (in years)					
18-59	90 (68.3-98.8)	60 (26.2-87.8)	81.8 (59.7-94.8)	75 (34.9-96.8)	80
≥60	84.8 (68.1-94.9)	85.7 (42.1-99.6)	96.6 (82.2-99.9)	54.5 (23.4-83.3)	85
BMI (kg/m^2)					
Obesity	83.3 (35.9-99.6)	50 (1.26-98.7)	83.3 (35.9-99.6)	50 (1.26-98.7)	75
Not obese	87.2 (74.3-95.2)	73.3 (44.9-92.2)	91.1 (78.8-97.5)	64.7 (38.3-85.8)	84.6
Immunocompromised status					
Yes	66.7 (9.43-99.2)	50 (1.26-98.7)	66.7 (9.43-99.2)	50 (1.26-98.7)	60
No	88 (75.7-95.5)	73.3 (44.9-92.2)	91.7 (80-97.7)	64.7 (38.3-85.8)	84.6
Degree					
Severe	90.5 (69.6-98.8)	70.6 (44-89.7)	79.2 (57.8-92.9)	85.7 (57.2-98.2)	81.5
Non severe	84.4 (67.2-94.7)	70.6 (44-89.7)	84.4 (67.2-94.7)	70.6 (44-89.7)	79.5

DISCUSSION

Most of the study subjects were in the 60-year age group with a total of 40 people (57.4%) and an average age of 60.25±16.56. years. This is in accordance with research conducted by Nafae et al with 76.25% of subjects being ≥50 years old.[5] Research conducted by Elsayed et al also used subjects similar to this study with an average age of 70.6±6.9 years.[6] The dominance of male subjects in this study is also consistent with research conducted by Nafae et al and Elsayed et al with the percentage of male patients being 56.25% and 75.8% respectively.[6] The characteristics of the research subjects based on BMI were dominated by the non-obese group with a total of 62 people (88.57%), while the remaining eight people (11.43%) were included in the obese group. The characteristics of BMI in this study are in accordance with other studies conducted by Kang et al. In that study, most of the samples were non-obese groups with an average BMI about 23.9 kg/m^2.[7] Only a small number of this study subjects had immunocompromised status with a total of 5 people (7.14%), while the remaining 65 people (92.86%) were included in the non-immunocompromised group. The characteristics of this study are different from the study conducted by Karimi which did not include immunocompromised patients in his study.[8]

In this study, 53 (75.71%) of the research subjects were diagnosed with pneumonia, while the remaining 17 (24.29%) were not pneumonia. This is in accordance with the study conducted by Bitar et al. In the study, out of 92 research subjects, 73 (79.3%) were diagnosed with pneumonia.[4] A total of 49 (92.45%) of the subjects in this study were community-acquired pneumonia, while the rest were included in hospitalized acquired pneumonia. This is different from the study conducted by Bitar et al where most of the research subjects were included in hospitalized acquired pneumonia, while 15% of patients were diagnosed as community-acquired pneumonia.[4]

Most of the subjects in this study had non severe pneumonia, while the remaining 21 people (39.62%) had severe pneumonia. These characteristics are different from the study conducted by Patel et al. In that study, the subjects involved were subjects with respiratory distress.[9] While the study conducted by Sezgin involving subjects who came to the emergency unit.[10]

Based on the results of ultrasonography, most of the study subjects diagnosed with pneumonia had a profile C image, in 42 people (79.25%), followed by A-No-V-PLAPS images in 7 people (13.21%), and profile A/B in 4 people (7.55%). In this study, there was no Profile B' image obtained in subjects diagnosed with pneumonia. The results of this study are in accordance with other studies conducted by Agmy et al. In this study, most of the LUS results related to pneumonia had a profile C image (43.8%), followed by A-No-V-PLAPS (22.9%), A/B profile (20.4%), and B' profile (12.5%).[11] Overall, the accuracy of LUS in diagnosing pneumonia is 82.8%. Accuracy was lower in patients aged 18-59 years (80%), obese (75%), immunocompromised (60%), and non-severe pneumonia (79.5%). Meanwhile, higher accuracy was obtained in subjects aged ≥60 years (85%), non-obese (84.6%), non-immunocompromised (84.6%), and severe pneumonia (79.5%).

Sensitivity of LUS in diagnosing pneumonia

Overall, the sensitivity of LUS in diagnosing pneumonia reached 86.8% (CI95%=74.7-94.5%). This means that the ability of ultrasound to obtain positive results among subjects diagnosed with pneumonia is 86.8% or among 100 subjects diagnosed with pneumonia, about 87 people will be declared positive by ultrasound, while the rest are negative (false negative). These results are in accordance with the results of a study conducted by Bekgoz et al which stated that the sensitivity of ultrasound in diagnosing pneumonia was 82% (CI95%=78-89%). In this study, ultrasound was also performed with the BLUE protocol.[12] These results differ from another study conducted by Danish et al. In this study, a higher sensitivity of 88% was obtained. This may be due to differences in subject characteristics and the gold standard used in the study. All subjects in study patients treated in the intensive care unit. Gold standard used was chest x-ray and chest CT scan.[13]

There was a variation in sensitivity in this study based on the characteristics of the study subjects. This sensitivity decreased in study subjects aged ≥60 years, which was 84.8% (CI95%=68.1-94.9%). In a study conducted by Ticinesi et al with study subjects aged ≥65 years, the sensitivity of LUS in diagnosing pneumonia reached 92% (CI95%=86-97%).[14] This difference may be due to differences in LUS protocols. In this study, LUS was performed on both hemithoraxes. Lower sensitivity in subjects aged ≥60 years may also be related to immunosenescence. In elderly patients, there is a decrease in the production of quality and quantity of immune cells. The aging process affects the quality of innate immune cells such as neutrophils, monocytes, macrophages, NK cells, and dendritic cells. This will lead to atypical symptoms and chest x-ray in patients aged ≥60 years with pneumonia.[15]

Sensitivity of LUS in diagnosing pneumonia was lower in obese study subjects, which was 83.3% (CI95%=35.9-99.6%). Meanwhile, in non-obese subjects, the sensitivity reached 87.2% (CI95%=74.3-95.2%). This is in accordance with other studies stating that obesity is a factor that technically affects ultrasound results in patients with pneumonia.[16] Ultrasound waves can be attenuated by subcutaneous fat, thus affecting image quality. The waves are attenuated at a level of 0.63 dB per cm of fat. Decreased image quality begins to occur in patients weighing 250 pounds to 300 pounds (113 to 136 kg). Tissue thickness has a direct impact on ultrasound image quality.[17]

In immunocompromised patients, the sensitivity of LUS in diagnosing pneumonia is lower than non-

immunocompromised subjects, which is 66.7% (CI95%=9.43-99.2%) vs 88% (CI95=75.7-95.5%). In immunocompromised patients, there is a decrease in the absolute number of circulating neutrophils and impaired phagocytic and bactericidal activity of neutrophils. This has an impact on the atypical clinical presentation of pneumonia, including the absence of sputum production and the absence of infiltrate formation in supporting examinations.[18.]

The sensitivity of LUS in diagnosing pneumonia in subjects with severe pneumonia reached 90.5% (CI95%=69.6-98.8%), while in subjects with non-severe pneumonia the sensitivity reached 84.4% (CI95%=67.2-94.7%). This may be due to the location of the consolidation and the extent of the consolidation. In subjects with non-severe pneumonia, there is no infiltrat or multilobar consolidation. In contrast to subjects diagnosed with severe pneumonia, consolidation is generally extensive to multilobar, making it easier to identify via LUS with the BLUE protocol. The sensitivity in this study was slightly lower when compared to the study conducted by Agmy et al with a sensitivity of 93.2%.[11] The difference in the results of this study may be due to the difference in the ultrasound probe used and the differences in the characteristics of the study subjects. The subjects in that study were patients with severe shortness of breath who required intensive care.

Specificity of LUS in diagnosing pneumonia

Overall, the specificity of LUS in diagnosing pneumonia in this study reached 70.6% (CI95%=44-89.7%). This means that the ability of ultrasound to obtain negative results among subjects who do not have pneumonia is 70.6% or among 100 subjects who do not have pneumonia, about 71 people will be declared negative by ultrasound examination, while the rest are positive (false positive). This is different from a systematic review which states that the specificity of LUS in diagnosing pneumonia reaches 81.91% (CI95%=72.71-88.50%).[19] Another study conducted by Elsayed stated that the specificity of LUS in diagnosing pneumonia is 94.1%. This difference may be caused by differences in the characteristics of the research subjects and the gold standard used. In this study, all research subjects were patients with pneumonia who met the criteria for intensive care with CT scan used as the gold standard.[6] In another study conducted by Cortellaro et al a specificity of 95% was obtained (CI95%=82.7-99.4%). In this study, all subjects were patients with suspected pneumonia who entered through the Emergency Unit. Ultrasound examination was carried out for a longer period of time (five minutes). LUS was performed by evaluating ten thoracic areas, two anterior areas, two lateral areas, and one posterior area in each hemithorax.[20]

Lower LUS specificity was obtained in research subjects aged 18-59 years with 60% (CI95%=26.2-87.8%). This difference in results may be influenced by differences in the characteristics of the research subjects. As many as 80% of research subjects with immunocompromise and 75% of patients with obesity were included in the 18-59 year group.

The specificity of LUS in diagnosing pneumonia was lower in obese study subjects, reaching 50% (CI95%=1.26-98.7). Obesity is a factor that can technically impact image quality and make it difficult to take ultrasound images. Sound waves from ultrasound are attenuated at a level of 0.63 dB per cm of fat.

In immunocompromised patients, the specificity of ultrasound in diagnosing pneumonia was lower, at 50% (CI95%=1.26-98.7%). In immunocompromised patients, there was a decrease in the absolute number of circulating neutrophils and impaired phagocytic and bactericidal activity of neutrophils. This has an impact on the atypical clinical presentation of pneumonia, including the absence of sputum production and the absence of infiltrate formation in supporting examinations.[18]

The specificity of LUS in diagnosing pneumonia in subjects with pneumonia, either severe or non-severe pneumonia, was 70.6% (CI95%=44-89.7%). This value is lower than previous studies which stated that the specificity of LUS in diagnosing pneumonia reached 81.91% (CI95%=72.71-88.50%).[19] This difference may be caused by differences in the degree of pneumonia in the research subjects used.

Another study with a higher specificity value reaching 94% was conducted involving subjects with respiratory distress.[19]

Accuracy of LUS in diagnosing pneumonia

Overall, the accuracy of LUS in diagnosing pneumonia was 82.8%. Accuracy was lower in patients aged 18-59 years (80%), obese (75%), immunocompromised (60%), and non-severe pneumonia (79.5%).

In this study, the predictive value of a positive test was 90.2% (CI95%=78.6-96.7%) and the predictive value of a negative test was 63.2% (CI95%=38.4-83.7%). The predictive value of a positive test of 90.2% means that the probability of having pneumonia if the ultrasound results suggest pneumonia is 90.2%. In other words, out of every 100 subjects with ultrasound results suggestive of pneumonia, 90 subjects will be correctly diagnosed with pneumonia. Meanwhile, the negative test predictive value is 63.2%, which means that the possibility of the subject not experiencing pneumonia if the ultrasound result is not pneumonia is 63.2%. In other words, for every 100 subjects with ultrasound results that are not pneumonia, 63 subjects will be correctly diagnosed as not pneumonia. Thus, LUS is good for screening pneumonia so that empirical management and therapy for pneumonia can be given earlier. However, if the ultrasound result is not pneumonia, other supporting examinations are needed to confirm the diagnosis of pneumonia.

In previous study conducted by Sezgin the accuracy of ultrasound in diagnosing pneumonia reached 97.6% with a positive predictive value of 99.0% (CI95%=94.7-99.9%) and a negative predictive value of 92% (CI95%=85.4-95.9%). The study involved a larger number of subjects, 125 people (101 subjects diagnosed with pneumonia and 24 subjects not pneumonia). All subjects were treated in the Emergency Unit.[10] Another study conducted by Agmy et al had an accuracy of 95.8%. In this study, all subjects were subjects with severe shortness of breath who required intensive care.[11] The difference in accuracy values can also be caused by differences in the tools used. The two probes used in this study were a deep probe and a superficial probe, while this study only used one probe. In addition, differences in subject characteristics including the severity of pneumonia, immunocompromised status, and body mass index also affect the accuracy of this study.

Limitations

This is a single center study. This study also found variations in validity based on subjects' characteristic. Thus, further research related to the validity of LUS with BLUE protocol in diagnosing pneumonia can be conducted by focusing on each characteristic.

CONCLUSION

LUS with BLUE protocol is a valid examination tool used to diagnose pneumonia (rule in disease). The sensitivity, specificity, and accuracy of LUS with BLUE protocol in diagnosing pneumonia were 86.8%, 70.6%, and 82.8% respectively.

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