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# BLUE protocol ultrasonography in Emergency Department patients presenting with acute dyspnea ☆

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ABSTRACT

*Objective:* Dyspnea is a common Emergency Department (ED) symptom requiring prompt diagnosis and treatment. The bedside lung ultrasonography in emergency (BLUE) protocol is defined as a bedside diagnostic tool in intensive care units. The aim of this study was to investigate the test performance characteristics of the BLUE-protocol ultrasonography in ED patients presenting with acute dyspnea.
*Method:* This study was performed as a prospective observational study at the ED of a tertiary care university hospital over a 3-month period. The BLUE-protocol was applied to all consecutive dyspneic patients admitted to the ED by 5 emergency physicians who were certified for advanced ultrasonography. In addition to the BLUE-protocol, the patients were also evaluated for pleural and pericardial effusion.
*Results:* A total of 383 patients were included in this study (mean age, 65.5 ± 15.5 years, 183 (47.8%) female and 200 (52.2%) male). According to the BLUE-protocol algorithm, the sensitivities and specificities of the BLUE-protocol are, respectively, 87.6% and 96.2% for pulmonary edema, 85.7% and 99.0% for pneumonia, 98.2% and 67.3% for asthma/COPD, 46.2% and 100% for pulmonary embolism, and 71.4% and 100% for pneumothorax. Although not included in the BLUE-protocol algorithm, pleural or pericardial effusion was detected in 82 (21.4%) of the patients.
*Conclusion:* The BLUE-protocol can be used confidently in acute dyspneic ED patients. For better diagnostic utility of the BLUE-protocol in EDs, it is recommended that the BLUE-protocol be modified for the assessment of pleural and pericardial effusion. Further diagnostic evaluations are needed in asthma/COPD groups in terms of the BLUE-protocol.



## 1. Introduction

Dyspnea is a common and life-threatening symptom among patients admitted to Emergency Departments (EDs). Therefore, the rapid and accurate diagnosis of the pathology causing dyspnea is essential [1,2]. The many potential causes of dyspnea makes it difficult to form a simple algorithm for dyspnea diagnosis [3]. Although traditional methods, such as physical examination and chest X-rays, are the most frequently used methods in the differential diagnosis of dyspnea, they remain insufficient for final diagnosis. Chest computerized tomography (CT) is currently the most sensitive and feasible modality for diagnosing most lung pathologies, such as pneumonia, pneumothorax, pulmonary thromboembolism, and interstitial lung diseases; however, CT has significant limitations, such as exposure to ionized radiation, limited application in certain patients, such as pregnant women, the necessity of transferring a potentially unstable patient to the tomography unit, and difficulty in accessing CT equipment [2].

Lung ultrasonography (LUS)[1] has been used successfully as a bedside diagnostic tool for diagnosing thoracic and cardiovascular pathologies, especially for acute decompensated heart failure, pneumonia, pneumothorax, pulmonary thromboembolism (PTE), pleural-

*Abbreviations:* BLUE, Bedside Lung Ultrasonography Examination; ED, Emergency Department.

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[1] LUS: lung ultrasonography.

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pericardial effusion, and empyema [4]. This method has been shown to produce superior results compared with other methods, such as physical examination, chest X-rays, and CT, in studies conducted using LUS [5]. LUS is also advantageous because it can be performed at bedside, carries no risk of ionizing radiation, and can easily be implemented by emergency physicians, who can interpret findings together with other clinical signs and symptoms [6].

The bedside lung ultrasonography in emergency (BLUE)[2] protocol is an algorithm developed by Lichtenstein as a systemic approach to the diagnosis of patients with dyspnea in intensive care units (ICUs) with 90.5% diagnostic accuracy. Although the BLUE protocol is highly effective in diagnosing dyspneic patients, it was developed for use in intensive care patients [6]. Few studies have examined the utility of LUS with the BLUE protocol in the diagnosis of patients presenting with acute dyspnea in EDs. The aim of this study was to investigate the test performance characteristics of the BLUE protocol in detecting the causes of dyspnea in ED patients presenting with acute dyspnea.

## 2. Materials and methods

### 2.1. Study design

This prospective cross-sectional study was conducted at a tertiary care university hospital with an annual census of about 55.000 ED visits covering a period of 3 months between December 01, 2012 and February 28, 2013.

All consecutive patients aged >18 years admitted to the ED with a primary complaint of acute dyspnea and who consented to participate were included in this study. Patients younger than 18, patients who refused to participate and were not given a definitive diagnosis during follow-up, patients who underwent cardiopulmonary arrest during stabilization, or patients with trauma, pneumonectomy, diffuse interstitial lung disease, tracheal stenosis, or fat embolism were excluded from the study. In cases where a patient presented on readmission for dyspnea, only the first visit was included in the study (Fig. 1). The characteristics of the dyspneic ED patients included in the study are given in Table 1.

The primary emergency medicine physician (named ED physician) responsible for patient care performed initial clinical evaluation and management. All patients were initially evaluated for vital signs, medical history, physical examination, 12-lead ECG, arterial blood gas determination, if appropriate, and necessary laboratory tests. Patients who were hemodynamically unstable were enrolled only after stabilization.

After the primary clinical assessment of the patients by the primary ED physician was complete, as part of the study protocol, the patients underwent LUS using the BLUE protocol by another physician named "US physician." US physicians were blinded to the patients' medical history, physical examination, and laboratory/imaging tests. They were not involved in diagnostic or therapeutic decisions.

US physicians performed the LUS ultrasonography generally within 5 min without interrupting the management of the patient. Of the 383 patients, 178 were admitted during the daytime, and their ultrasound examinations were performed by IK and BG. The ultrasound examinations of 205 patients who were admitted at night were performed as follows: 45 patients with OH, 21 with BB and OH, 42 with GC, 28 with GC and BB, 23 with HAD, 17 with HAD and BB, and 29 with BB, IK, and GC. The ultrasound images were not saved.

US physicians recorded ultrasound findings on the patient study form and marked the diagnosis on the BLUE protocol algorithm as pulmonary edema, pneumonia, asthma/COPD, pulmonary embolism, or pneumothorax. Although not included in the BLUE protocol algorithm, the patients were also evaluated for pleural and pericardial effusions by US physicians.

[2] BLUE: Bedside Lung Ultrasound Examination.

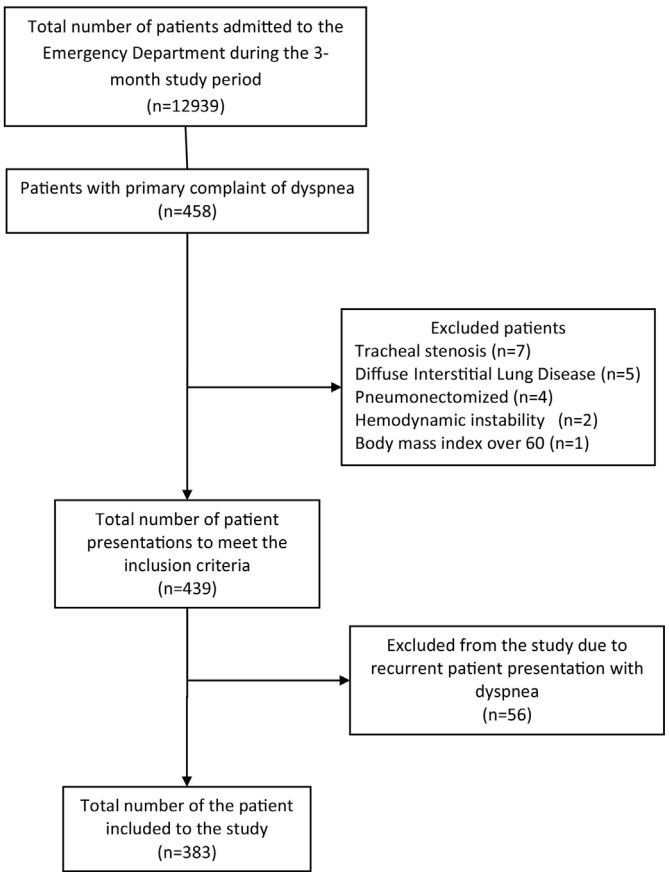


**Fig. 1.** Patients' flow chart.

**Table 1**
Characteristics of the dyspneic Emergency Department patients included to the study ($n$ = 383).

| Study patients characteristics | | |
|---|---|---|
| Age, years (min–max) | | 65.5 (19–96) |
| Sex, n (%) | Female | 183 (47.8%) |
| | Male | 200 (52.2%) |
| Co-morbidity, n (%) | Hypertension | 90 (23.5%) |
| | COPD[a]/asthma | 89 (23.2%) |
| | Coronary artery disease | 71 (18.5%) |
| | Diabetes mellitus | 62 (16.2%) |
| | Congestive heart failure | 56 (14.6%) |
| | Lung malignancy | 28 (7.3%) |
| | Other malignancies | 36 (9.4%) |
| | Bronchiectasis | 2 (0.5%) |
| | Other diseases | 11 (3%) |
| Follow up | Discharge | 192 (50.1%) |
| | Admitted to the hospital | 126 (32.9%) |
| | Admitted to ICU | 46 (12.0%) |
| | •Death in ICU (10 patients) | |
| | Voluntarily discharged | 19 (5.0%) |

[a] COPD: chronic obstructive pulmonary disease.

Blinded US physicians registered the diagnosis for each patient in the patient case file after performing the lung ultrasonography. US physicians did not share their BLUE protocol lung ultrasonographic findings or diagnosis with the primary ED physicians. The primary ED physicians evaluated the patients routinely based on ED management.

The reference standard for each diagnosis, detailed laboratory tests, and imaging modalities were completed for each patient. These reference standards are given in Table 2. The tests included electrocardiography, cardiac biomarkers echocardiography (by a cardiologist) for congestive heart failure (CHF), infection findings,

**Table 2**
Diagnostic modalities ordered for the definitive diagnosis and results of the tests.

| Diagnostic modalities | The number of patients | Percentage |
|---|---|---|
| Chest X-ray, n (%) | 382 | 99.7% |
| Normal | 124 | 32.4% |
| Abnormal | 258 | 67.4% |
| Increased cardiothoracic index | 99 | 25.8% |
| Obscured costodiaphragmatic sinus | 93 | 24.3% |
| Infiltration | 83 | 21.7% |
| Massive pleural effusion | 33 | 8.6% |
| Pneumothorax | 7 | 1.8% |
| Hilar opacity | 9 | 2.3% |
| Fibrous band formation | 8 | 2.1% |
| Elevated right diaphragm | 1 | 0.3% |
| Echocardiography by a cardiologist, n (%) | 147 | 38.4% |
| Normal | 45 | 11.7% |
| Low ejection fraction, hypokinetic or akinetic wall | 73 | 19.1% |
| Normal ejection fraction, diastolic dysfunction | 26 | 6.8% |
| Dilated right ventricle, right ventricle strain sign, compatible with pulmonary embolism | 1 | 0.3% |
| Pericardial effusion | 2 | 0.5% |
| Respiratory function test, n (%) | 101 | 26.4% |
| Normal | 5 | 1.3% |
| Obstructive pattern | 60 | 15.7% |
| Reversible pattern | 34 | 8.9% |
| Restrictive pattern | 1 | 0.3% |
| Bilateral lower extremity venous Doppler ultrasonography, n (%) | 64 | 16.7% |
| Normal | 58 | 15.1% |
| Deep vein thrombosis | 6 | 1.6% |
| Thorax computed tomography, n (%) | 66 | 17.2% |
| Normal | 8 | 2.1% |
| Infiltration | 19 | 5.0% |
| Pulmonary embolism | 12 | 3.1% |
| Atelectasis | 8 | 2.1% |
| Malignancy | 7 | 1.8% |
| Cardiomegaly | 8 | 2.1% |
| Pericardial effusion | 8 | 2.1% |
| Pleural effusion | 23 | 6.0% |
| Diffuse interstitial infiltration | 1 | 0.3% |

chest X-rays, microorganism isolation (if possible), CT (if necessary) for pneumonia, history, respiratory functional tests, and responses to bronchodilator treatment for asthma and chronic obstructive pulmonary disease (COPD), thorax CT angiography for pulmonary thromboembolism, chest X-rays and CT (if necessary) for pneumothorax.

All of these diagnoses were *discharged* diagnoses, since definite diagnosis was made after the discharge of patients from the hospital. There were no disagreements or uncertainties. BLUE protocol diagnosis was clear, and it was dependent on images obtained from the patients' US examinations.

The final clinical diagnosis was made by attending emergency physicians (for 215 ED patients before discharge from the ED), attending consultant physicians (for 126 hospitalized patients before discharge from the hospital), and an ICU team (for 46 ICU patients before discharge from the ICU) (Table 1). These final diagnoses were considered the gold standard. Lastly, the final discharged diagnoses of the patients were compared with the BLUE protocol algorithm diagnosis.

### 2.2. Ultrasound examination

LUS was conducted by 5 ED physicians who had been previously certified by basic and advanced US education and had at least 2 years of ED and US experience. These ED physicians were also informed by 2 h of theoretical lectures regarding LUS and the BLUE protocol. After attending 2 h of theoretical training, they performed 10 supervised LUS examinations according to the BLUE protocol. They were blinded to the patients' medical history and were not involved in diagnostic or therapeutic decisions.

As a rule, LUS was performed within 30 min of admission or after stabilization of patients who were hemodynamically unstable. In LUS, longitudinal examinations were performed using a microconvex probe at 2–6 MHz frequency (Fujifilm Fazone CB®, Japan). While performing LUS according to the BLUE protocol, 4 BLUE points (upper and lower BLUE point, phrenic point, PLAPS point) were examined for each hemithorax in the supine or semi-recumbent position (Fig. 2a, b, and c).

Examination of each BLUE point involves identifying the pleura between the two ribs (bat sign) first. After detection of the pleura, the *lung sliding* sign, which is a normal finding occurring as a result of movement of the visceral and parietal pleural onto each other, was evaluated. In patients with lung sliding, the A and B lines were checked. The A lines, reverberation artifacts of the pleura, appear as horizontal hyperechoic lines in normal LUS. On the other hand, the B lines appear as hyperechoic lines, which originate from the pleura, in the form of a beam continuing to the end of the screen, erasing the A lines and shifting with the movement of the pleura. One or two B lines can be seen in each quadrant of each normal lung, but it is always pathological if there are >3 in one quadrant. If there are more than three B lines in a section, this is called a B + finding (Fig. 2d and e).

In patients with lung sliding and a presence of A lines, lower extremity deep venous analysis was performed. Patients with thrombus were evaluated as pulmonary thromboembolism according to the BLUE protocol.

In patients with normal venous examination, the PLAPS (posterolateral alveolar and/or pleural syndrome) finding was investigated using the scanning PLAPS point, where pleural effusion and pulmonary filtration are seen as the best (Fig. 2f). This was diagnosed as pneumonia in the presence of PLAPS and as asthma or COPD (chronic obstructive pulmonary disease) in the absence of PLAPS. Cases were diagnosed as pulmonary edema in the presence of lung sliding and bilateral B lines (Fig. 2e).

In patients without lung sliding, pneumonia was diagnosed in cases of B line detection (B′ profile), and the lung point sign was examined in cases of A line detection (A′ profile). Patients with the lung point sign were diagnosed with pneumothorax. In the absence of this finding, the diagnosis could not be established according to the BLUE protocol. These patients were also evaluated for the M-mode seashore finding.

Patients were diagnosed with pneumonia after detection of the A line in one hemithorax and the B line in another hemithorax (A/B profile), or in cases of infiltration during placing of the US probe on the thorax (C profile) without examining lung sliding.

In addition to all BLUE protocol steps, patients were also evaluated for pleural and pericardial effusions to obtain better diagnostic utility of the BLUE protocol for the differential diagnosis of acute dyspneic patients.

Ultrasonographic diagnosis of the patients was recorded on the patients' study charts. Definitive diagnosis of the patients was compared with the ultrasonographic diagnosis.

### 2.3. Statistical analysis

All data were analyzed using the Statistical Package for Social Science for Windows 17.0 (SPSS Inc., Chicago, USA) software. Descriptive variables were expressed as median and interquartile ratios and percentage distributions. The statistical significance level was accepted as $P < 0.05$. Sensitivity, specificity, and positive and negative predictive values were calculated using a chi-square table design.

## 3. Results

All 458 patients admitted to the ED with primary complaints of dyspnea for 3 months were initially included in the study. Of them,

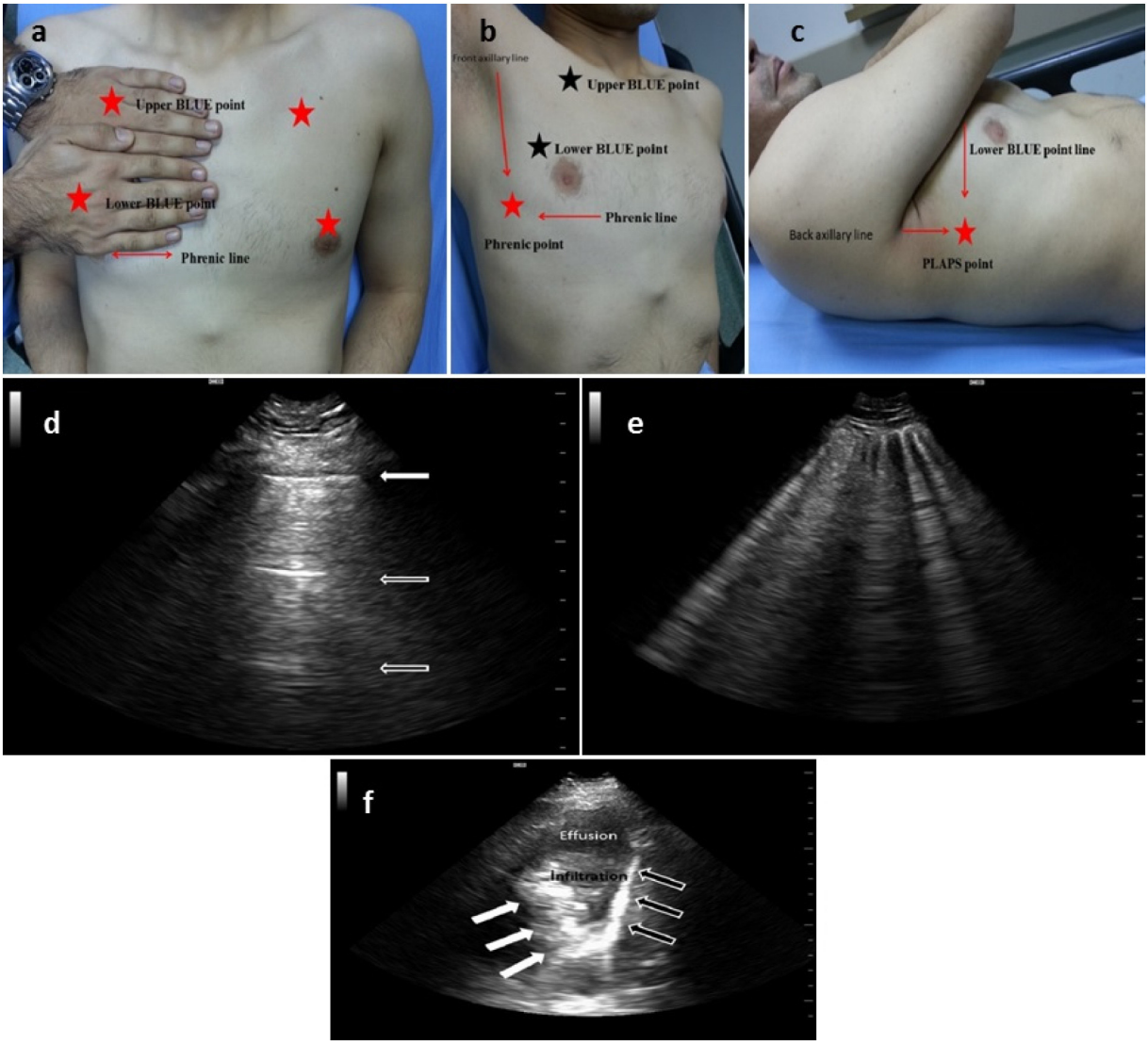


**Fig. 2.** a. Upper and lower BLUE points, b. phrenic point and c. PLAPS point, d. Bat sign and normal lung surface. White arrow is the pleura and black arrows are A lines e. multiple B lines, f. Typical PLAPS examination. Infiltration, pleural effusion and the diaphragm (black arrows) are seen. White arrows indicate aerolated lung border due to infiltration.

75 patients met the exclusion criteria and were therefore excluded from the study. A total of 383 patients (200 male and 183 female, mean age 65.0) were ultimately included in the study. Detailed information related to the characteristics of the dyspneic ED patients included in the study is given in Table 1.

Standard tests and diagnostic imaging modalities were ordered for definitive diagnosis, and the results of the test are given in Table 2. In order to be better understood, all ultrasonographic findings obtained by the BLUE protocol algorithm were given as the number and percentage of patients according to the profiles in Fig. 3.

According to the BLUE protocol, lung sliding was found in 365 patients (95.3%) and absent in 18 patients (4.7%). Among the 365 patients with bilateral lung sliding, the A profile was detected in 221 (57.7%) patients, the B profile in 96 (25.1%) patients, the AB profile in 39 (10.2%) patients, and the C profile in 9 (2.3%) patients. In accordance with the BLUE protocol, the 221 patients with a normal lung sign (bilateral lung sliding with A lines) were evaluated by venous analysis for the diagnosis of pulmonary thromboembolism. Among these patients, thrombosed veins were detected in 6 (1.6%) patients. Beyond these patients, PLAPS signs were present in 23 (6.0%) patients.

In patients in whom the lung sliding signs were abolished, we found the A′ profile in 11 (2.9%) patients, the B′ profile in 5 (1.3%) patients, the AB profile in 1 (0.3%) patient, and the C profile in 1 (0.3%) patient. Among the A′ profile patients, lung point signs were in 5 (1.3%). Diagnosis could not be made in 6 (1.6%) of the 383 patients using the BLUE protocol algorithm (Fig. 3).

The B profile was detected by LUS in 96 (25.1%) of the 383 patients; these patients were categorized as having alveolar interstitial syndrome (including pulmonary edema, non-cardiogenic pulmonary edema, acute respiratory distress syndrome, diffuse interstitial pulmonary disease, interstitial pneumonia, pulmonary contusion, pulmonary fibrosis). Of these 96 patients with the B profile, 85 had a definite diagnosis of pulmonary edema, while 7 patients had a diagnosis other than pulmonary edema. Although the definitive diagnosis of 12 patients was pulmonary edema, the B profile was not observed by LUS. As a result of diagnostic tests, 97 patients' definitive diagnosis was acute pulmonary edema. The sensitivity and specificity of the BLUE protocol for pulmonary edema were 87.6% and 96.2%, respectively (Table 3).

A final diagnosis of pneumonia was made in 91 out of the 383 patients. By the BLUE protocol, 75 (20.3%) patients were diagnosed with pneumonia. Pneumonia was detected by the BLUE protocol in

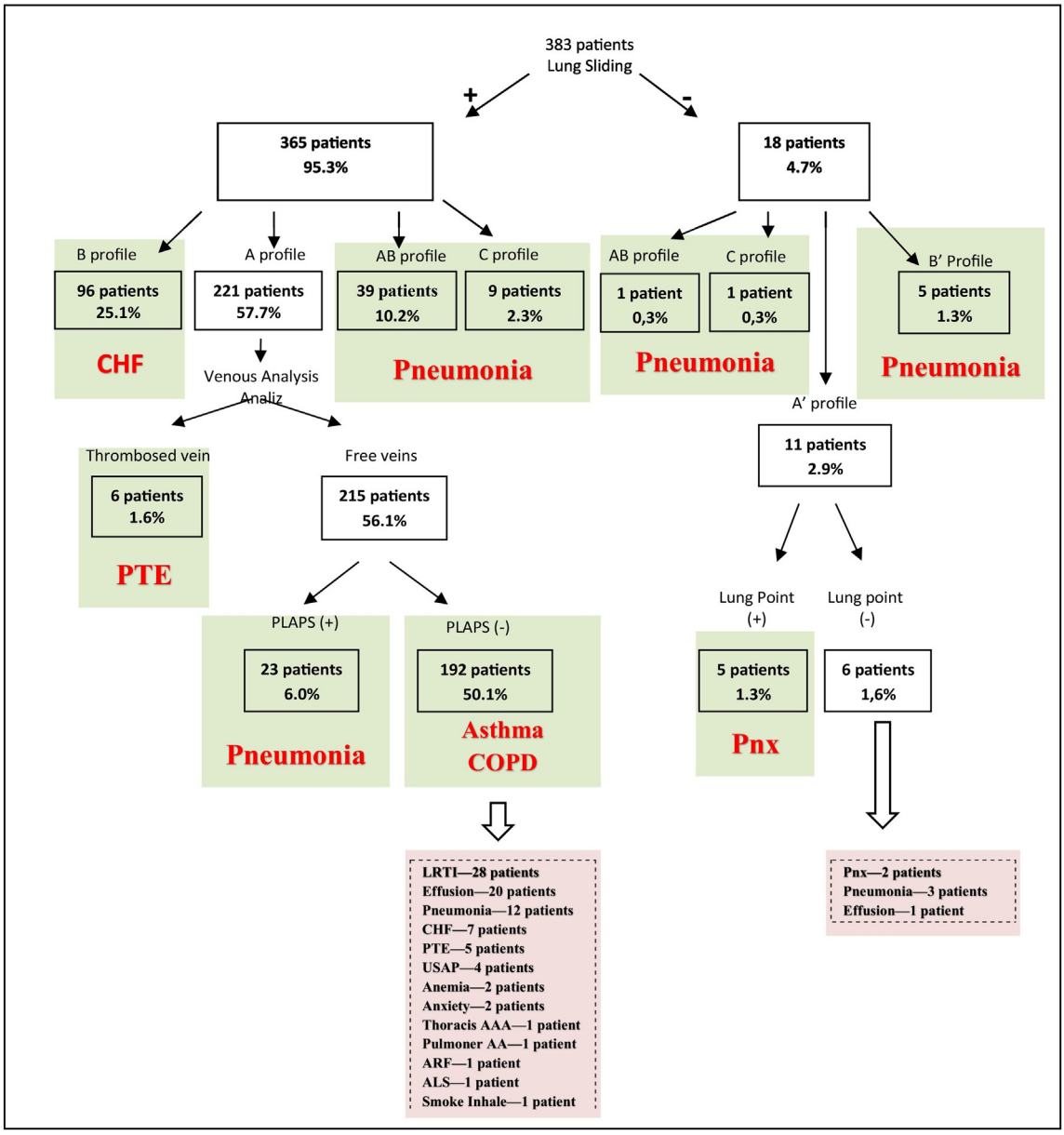


**Fig. 3.** The ultrasonographic findings of the study patients according to profiles in BLUE protocol algorithm after establishing the discharged definitive diagnosis. Dashed striped boxes indicate the definitive discharged diagnosis of the patients included to related upper boxes. (CHF: congestive heart failure, PTE: pulmonary thromboembolism, Pnx: pneumothorax, COPD: chronic obstructive pulmonary disease, LRTI: lower respiratory tract infection, AAA: abdominal aortic aneurysm, ARF: acute renal failure, ALS: amylotrophic lateral sclerosis).

23 (100%) of the 23 patients with PLAPS, 38 (95.0%) of the 40 patients with the AB profile, 9 (90%) of the 10 patients with the C profile, and 5 (100%) of the 5 patients with the B′ profile. Pneumonia was also detected in 1 patient with no lung sliding with the AB profile and in 1 patient with the C profile. Sixteen pneumonia patients were not detected by the BLUE protocol. The sensitivity

**Table 3**
Sensitivities and specificities of BLUE protocol ultrasonographic findings according to the BLUE protocol diagnosis.

| Diagnosis | BLUE protocol ultrasound findings | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) | Positive predictive value (%) (95% CI) | Negative predictive value (%) (95% CI) |
|---|---|---|---|---|---|
| Cardiogenic pulmonary edema | Bilateral diffuse B lines together with lung sliding | 87 (79–93) | 97 (94–98) | 91 (84–95) | 95 (93–97) |
| Pneumonia | PLAPS, AB profile, C profile, B′ profile, or Local B lines | 82 (78–89) | 98 (97–99) | 96 (88–98) | 94 (92–96) |
| COPD/asthma | Bilateral diffuse A lines together with lung sliding | 96 (90–87) | 75 (70–80) | 61 (56–66) | 98 (95–99) |
| Pneumothorax | Presence of A lines without lung sliding finding, absence of B lines, and presence of lung point finding | 85 (42–99) | 100 (99–100) | 100 (99–100) | 99 (98–99) |
| Pulmonary embolism | Presence of venous thrombosis in lower extremity venous examination together with bilateral diffuse A lines | 46.2 (19–74) | 100 (99–100) | 100 (100–100) | 98 (96–99) |

of the BLUE protocol for pneumonia was 82.4%, while its specificity was 99.3% (Table 3).

A final diagnosis of asthma-COPD was established in 109 patients. As a result of the BLUE protocol, excluding 23 patients with the PLAPS sign and 6 patients with thrombosed vein from the 221 patients with A profile, isolated the A profile was detected in 192 (50.1%) of the 383 patients, and a final diagnosis of asthma-COPD was made in 107 (55.7%) of the 192 patients. The sensitivity and specificity of the BLUE protocol for asthma-COPD were 98.2% and 69.0%, respectively (Table 3).

Of these 192 patients with an isolated A profile who were grouped as asthma/COPD diagnosis according to the BLUE protocol, only 107 had a definite diagnosis of asthma/COPD, while the remaining 85 patients had a different diagnosis. Among these 85 patients, there was lower respiratory tract infection (LRTI) in 28 patients, isolated pleural, isolated pericardial, or pleural+pericardial effusion in 19 patients, pneumonia in 12 patients, pulmonary edema in 7 patients, pulmonary thromboembolism in 5 patients, unstable angina pectoris (USAP) in 4 patients, symptomatic anemia in 2 patients, anxiety in 2 patients, malignant pleural disease in 1 patient, aortic aneurysm in 1 patient, pulmonary artery aneurysm in 1 patient, acute renal failure (ARF) in 1 patient, amylotrophic lateral sclerosis (ALS) in 1 patient, and bronchospasm due to smoke inhalation in 1 patient.

A total of 6 (46.2%) of the 13 patients with a final diagnosis of pulmonary thromboembolism were diagnosed using the BLUE protocol. Seven patients in whom venous thrombosis could not be detected with LUS were diagnosed with other pathologies. According to the BLUE protocol, 6 of these patients were in the COPD group, and 1 patient was in the pulmonary edema group. The sensitivity of the BLUE protocol for pulmonary thromboembolism was 46.2%, and its specificity was 100% (Table 3).

The final diagnosis of 7 patients was pneumothorax. A total of 5 (71.4%) of these patients were diagnosed with pneumothorax using the BLUE protocol. Two patients in whom the A′ profile was detected but no lung point finding was obtained could not be diagnosed according to the BLUE protocol. A sea-shore finding was also investigated in addition to the lung sliding findings. The sea-shore finding was obtained in all 7 patients. In addition, the sea-shore finding was also detected in 10 pneumonia patients with no lung sliding (B′ profile), 6 patients with no diagnosis, and 1 patient with isolated pleural effusion. The sensitivity and specificity of the lung point for pneumothorax were 71.4% and 100% (Table 3).

Using LUS, pleural, pericardial, or pleural+pericardial effusion was detected in 82 (21.4%) of the 383 patients. There was pleural effusion in 40 of the 92 patients with a final diagnosis of pulmonary edema, in 13 of the 91 patients with pneumonia, in 1 of the 13 patients with pulmonary thromboembolism, and in 2 of the 5 patients with acute renal failure. There was malignant pleural effusion in 8 patients, and pericardial effusion in 4 patients.

According to the BLUE protocol algorithm, 6 patients (1.6%) could not be diagnosed. A final diagnosis was established by US in these patients. There was pneumonia in 3 patients, pneumothorax in 2 patients, and malignant pleural effusion in 1 patient.

The BLUE protocol algorithms performed in ED patients with dyspnea established the correct diagnosis at a mean rate of 77.5% across all disease categories causing acute dyspnea in EDs.

## 4. Discussion

The BLUE protocol is a method developed to diagnose patients with dyspnea in ICUs. In this study, we evaluated the utility of the BLUE protocol in the ED. The rate of correct diagnosis of the BLUE protocol algorithms in all diseases was 77.5%. The overall accuracy of the original BLUE protocol study presented by Lichtenstein was 90.5% [6].

The overall diagnostic accuracy of our study was lower than that of the Lichtenstein study. This was due to the fact that dyspneic patients who presented to the ED had a broader spectrum of diagnoses, such as lower respiratory infections, pleural/pericardial effusions, acute coronary syndrome, anemia, anxiety, and neuromuscular diseases, except than BLUE protocol diagnosis (heart failure, pneumonia, pulmonary embolism, pneumothorax, and asthma/COPD). On the other hand, lung ultrasound examination was very useful in differentiating the underlying important pathologies, such as heart failure, pneumonia, and pneumothorax, in the ED.

According to this result, the BLUE protocol is suitable for the differential diagnosis of dyspneic patients presenting to the ED as well as intensive care patients. We successfully applied the BLUE protocol to our dyspneic ED patients. The most important limitation with regard to the application of the BLUE protocol in the ED was that patients with pleural and pericardial effusion. The evaluation of massive pleural and/or pericardial effusion could provide important contributions to diagnostic evaluation.

The other major problem with regard to the application of the BLUE protocol in the ED was the inability to detect various pathologies, especially where primary lung parenchyma is not affected, such as bronchitis, acute coronary syndrome, anemia, anxiety, and neuromuscular diseases. Since no pathology is detected by LUS, these patients were misdiagnosed as asthma/COPD. Nevertheless, the demonstration of the absence of parenchymal disease (no pulmonary edema, no pneumonia, no pneumothorax, etc.) with LUS may provide important insights into the clinician's diagnosis.

In our study, we also evaluated pleural and pericardial effusions. Pathologies that result in dyspnea originate from many different underlying conditions, many of which arise from cardiopulmonary diseases, as well as from pleural pathologies. Lung ultrasonography can also be applied for the diagnosis of effusion in accordance with the BLUE protocol. Our data demonstrate that pleural effusion can arise from a number of distinct pathologies in ED patients.

According to the BLUE protocol, patients with no pathology in the lung (A profile) are diagnosed as asthma or COPD [7]. In the study by Lichtenstein et al., there were bilateral A lines in 72 of the 83 asthma/COPD patients. In their study, 97% sensitivity and 87% specificity were reported for the diagnosis of asthma/COPD by A lines in LUS [6]. In a study conducted by Zanobetti et al., there were normal LUS findings (A lines) in 157 of the 404 patients presenting with dyspnea to the ED, and most of these patients were diagnosed with asthma/COPD and bronchitis [2]. In another study, only 8 (14.3%) of the 56 patients with B+ lines were diagnosed with asthma/COPD [8]. In our study, detection of the A profile in LUS had a sensitivity of 98.2% and a specificity of 67.3% in asthma/COPD diagnosis. The most important reason for the lower specificity value in our study compared with the literature is that the A profile can also be obtained in non-asthma/COPD patients who present with dyspnea to the ED. When the BLUE protocol algorithms were reviewed, patients who presented with acute dyspnea complaints to the ED and who had no pathology in the lung parenchyma but had other conditions, such as acute coronary syndrome, anemia, anxiety, aortic aneurysm, bronchitis, pulmonary artery aneurysm, or ALS, were also classified in the asthma/COPD group. For this reason, we suggest BLUE plus protocol that additional diagnosis could also be investigated before definitively diagnosing asthma/COPD primarily in patients who present with dyspnea to the ED and in whom the A profile is detected by LUS (recommended by us, given in Fig. 4).

One of the significant studies of ultrasound to evaluate undifferentiated dyspnea in the ED reported by Laursen showed 88% sensitivity for the final diagnosis. However, the inclusion criteria of this study were different from our study [9]. Laursen et al. included tachypneic patients with oxygen saturation of <95% who needed oxygen therapy. In our study, all patients with a complaint of dyspnea who presented to the ED were taken consecutively. We believe that the general inclusion of all dyspneic patients decreased the sensitivity of our study.

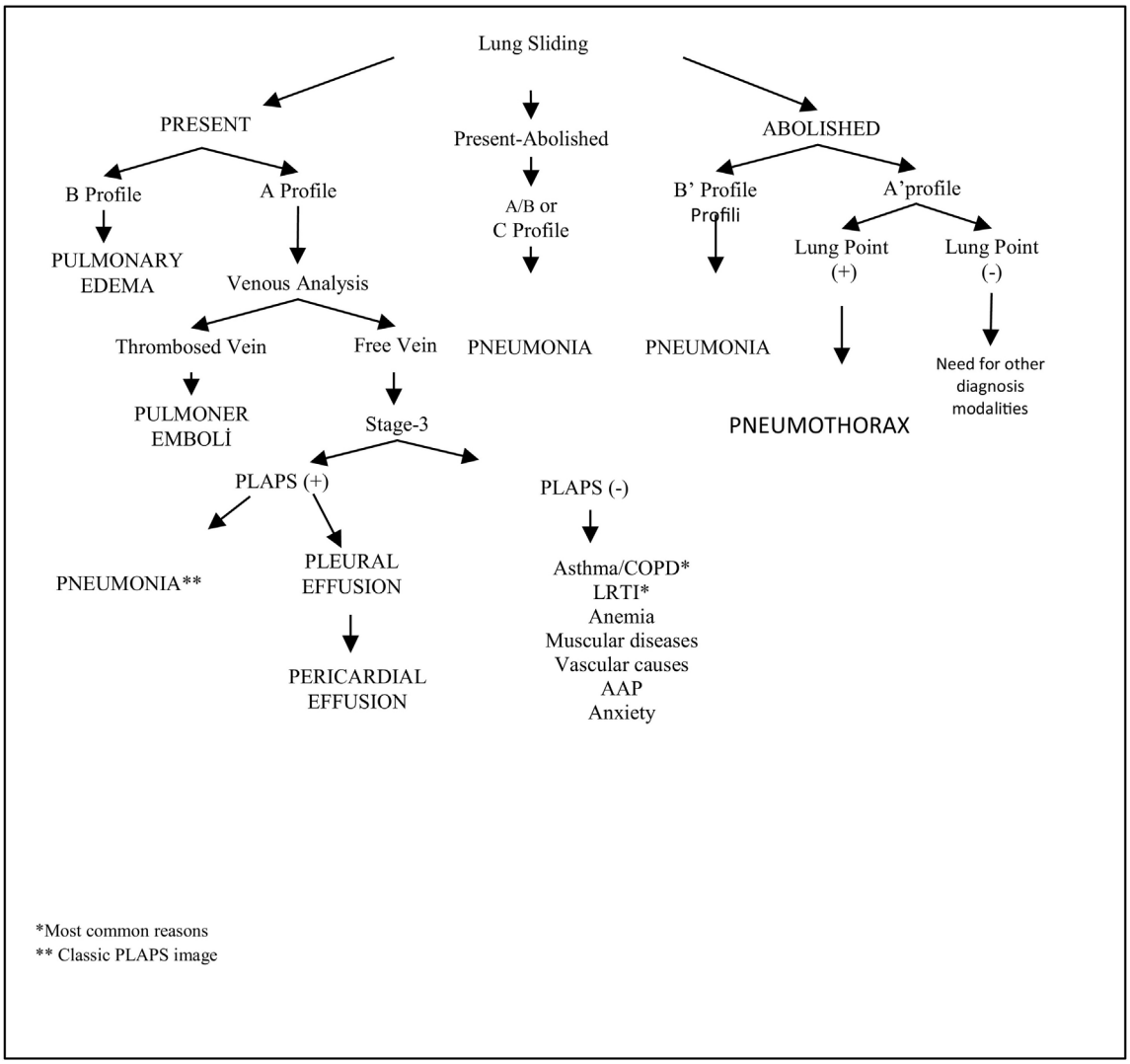


**Fig. 4.** BLUE plus protocol *recommended by the authors.*

Faccini et al. found that the sensitivity and specificity of B lines alone were 85% and 84%, respectively, in heart failure. The overall sensitivity and specificity increased after inclusion of Pro-BNP and thoracic impedance in the same diagnostic model with B lines [10]. High diagnostic accuracy (97% sensitivity, 97.7% specificity) has been achieved by adding LUS to existing diagnostic methods in heart failure [11]. The sensitivity and specificity of bilateral diffuse B lines for the diagnosis of CHF in our study were similar to those reported in the literature. Sensitivity and specificity can be increased in CHF with the addition of US to other diagnostic and treatment methods.

In our study, pneumonia was detected in all patients with PLAPS and B′ finding, 39 of the 40 patients with the AB profile, and 9 of the 10 patients with the C profile. Three patients who were diagnosed with pneumonia using the BLUE protocol had a final diagnosis of causes other than pneumonia. One of these patients was diagnosed with CHF, another was diagnosed with malignant pleural and pericardial effusion, and another was diagnosed with acute renal failure. In a study investigating the diagnosis of pneumonia with LUS, the sensitivity and specificity of LUS in pneumonia diagnosis were 85.5% and 88.1%, respectively [12]. In another study conducted by Nazerian, in which pneumonia was investigated with US, the sensitivity and specificity of LUS in pneumonia diagnosis were 82.8% and 95.5%, respectively [13]. In the same study, sensitivity and specificity increased when patients with pleuritic chest pain were examined. In our study, the sensitivity and specificity of LUS in pneumonia diagnosis were 85.7% and 99.0%, respectively, when all the data were evaluated. In this study, unlike other studies, doctors practicing LUS conduct US and establish diagnosis without knowing patients' clinical characteristics. Since physicians who make a preliminary diagnosis by examining patients before LUS can better diagnose pneumonia, the rate of true diagnosis may be higher if physicians taking the history of patients perform a physical examination prior to LUS.

In another study conducted by Le Gal and published in 2006, the sensitivity and specificity of venous pressure US performed in patients with high clinical suspicion for PTE were 39% and 99%, respectively, for the diagnosis of PTE [14]. In our study, the sensitivity of the BLUE protocol in detecting PTE was 46.2%, while the specificity was 100%. This finding is in accordance with the literature. Although thrombus most commonly originates from deep femoral veins in patients with PTE, embolism may develop from popliteal, pelvic, or femoral veins, and rarely from upper extremity veins [15]. Therefore, the addition of clinical scoring systems, such as Well's score, to the BLUE protocol may be a way to increase the sensitivity of PTE diagnosis.

In order to establish pneumothorax diagnosis using the BLUE protocol algorithms, lung sliding findings should disappear first, after which lung point findings must be detected. In a study conducted by Chung et al., the sensitivity and specificity of the detec-

tion of no lung slidings finding alone in diagnosing pneumothorax were 80% and 94%, respectively [16]. In our study, the sensitivity of lung sliding findings in pneumothorax diagnosis was 100%, while the specificity was 97.1%. In a study conducted on patients with a final diagnosis of pneumothorax in 2005, the sensitivity of the lung point finding in pneumothorax diagnosis was 79%, while the specificity was 100% [17]. Considering only the lung point finding in our study, the sensitivity of the BLUE protocol in pneumothorax diagnosis was 71.4%, whereas the specificity was 100%. The low sensitivity of the lung point finding in pneumothorax diagnosis might be due to the difficulty in detecting lung point sign. Although it is difficult to detect, lung point findings are necessary for the diagnosis of pneumothorax, since it disappears in diseases other than pneumothorax.

Pleural effusion and pericardial effusion were also evaluated as potential causes of dyspnea in our study. Since the BLUE protocol indicates that pleural effusion is due to pneumonia in 90% of cases, it is not recommended to investigate additional causes of effusion in the PLAPS point. In addition to the diagnoses based on the BLUE protocol algorithms, pleural, pericardial, or pleural+pericardial effusion were detected in 59 patients in our study. A total of 45 of these patients were in the CHF group, 13 patients were in the pneumonia group, and 1 patient was in the PTE group. The ED management of these patients with pleural effusion was not changed. On the other hand, isolated pleural, pericardial, or pleural +pericardial effusion was detected in 23 patients. The management of these patients was modified as a result of these findings. There was pleural effusion in 12 patients. A total of 10 of these patients had malignant pleural effusion, 1 had PTE, and 1 had CHF. There was malignant pleural+pericardial effusion in 7 other patients, and pericardial effusion in 4 patients. It should be kept in mind that pleural effusion detected with LUS may be due to pneumonia or may have other causes. We suggest that pleural or pericardial effusion should be monitored closely even after the completion of the BLUE protocol. Patients presenting with dyspnea to the ED should be evaluated carefully, since this can change diagnosis and patient management. Pleural and pericardial effusion should be evaluated in ED patients with the A profile (Fig. 4).

### 4.1. Limitations

The primary limitation of this study was that lung CT could not be performed in all patients for ethical reasons. The differential diagnosis was established in these patients by clinical evaluation, laboratory findings, and other imaging methods. The second limitation is that LUS was performed only by doctors experienced in US and in advanced LUS. The third limitation is that US images obtained by the 5 blinded US physicians were not saved or reviewed for accuracy. The fourth limitation is that we only focused on a specific protocol, the BLUE protocol, rather than considering which applications make sense for particular patients. While we agree that the BLUE protocol was improved by considering pleural and pericardial effusions, other US examinations, such as the assessment of EF and RV size being the most relevant, were not investigated in our study. The fifth limitation is that this was a single-centered study. Further studies are necessary and should include a multi-center design. The sixth limitation is that patients with interstitial lung disease in whom findings resembling pulmonary edema were obtained in LUS were excluded from the study. However, this is a rare cause of dyspnea. Finally, the last limitation is that the number of patients with pneumothorax ($n = 7$) and PTE ($n = 13$) was relatively small despite the fact that the number of patients included in the study was high ($n = 383$).

## 5. Conclusion

The BLUE protocol algorithm designed for intensive care patients can also be used confidently in the evaluation of acute dyspneic ED patients, especially in the diagnosis of heart failure, pneumothorax, pneumonia, and pulmonary embolism. However, as the most important result of our study, we believe that the BLUE protocol can fail in the diagnosis of asthma/COPD with low sensitivity and specificity values when evaluating ED patients with acute dyspnea. Further diagnostic evaluations are needed in asthma/COPD groups in terms of the BLUE protocol. For better diagnostic utility of the BLUE protocol in EDs, it is recommended that the BLUE protocol be modified for the assessment of pleural and pericardial effusions.

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## Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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