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Thoracic ultrasonography: A new method for the work-up of patients with dyspnea☆

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KEYWORDS
Ultrasound;
Lung;
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Abstract *Objective:* Differential diagnosis of dyspnea is vital for the management of respiratory failure, where routine parameters can now be integrated with thoracic ultrasound data. The objective of this study was to evaluate the validity and accuracy of this approach in a department of internal medicine.
Materials and methods: We enrolled 152 patients consecutively hospitalized with a diagnosis of dyspnea. After clinical evaluation, chest radiography, biochemical assays (NT-proBNP), and emergency treatment, patients underwent ultrasound examination of the lungs. Results were considered positive if the total number of lines B was higher than 8. The ultrasound examination and NT-proBNP assay were repeated after 48 h. The gold standard was the clinical diagnosis of heart failure made by medical experts in accordance with AHA guidelines.
Results: The group of patients with positive ultrasound findings had a higher frequency of heart failure diagnoses (X^2 92.5, $p < 0.005$) and significantly higher values of NT-proBNP (10,384 ng/l vs 3889 ng/l, $p < 0.05$). Moreover, the decrease in the number of B lines at 48 h was significantly greater ($p < 0.005$) among patients treated for heart failure. There were no significant changes in the values of NT-proBNP ($p = 0.37$).
Discussion: In conclusion we have shown that even in a department of internal medicine, lung ultrasonography is a useful tool for diagnosing respiratory insufficiency and monitoring its response to therapy.

Sommario La diagnosi differenziale di dispnea è fondamentale per la gestione dell'insufficienza respiratoria in cui, ai parametri routinari, può essere ora affiancata l'ecografia toracica. L'obiettivo di questo studio è stato valutare la validità e l'accuratezza di questa metodica anche in un reparto di medicina interna.
Materiali e metodi: 152 pazienti ricoverati conseguentemente con diagnosi di dispnea sono stati esaminati dopo valutazione clinica, radiografia del torace, dosaggi bioumorali (NT-proBNP) e terapia d'emergenza. L'esame ecografico polmonare è stato considerato positivo qualora il numero totale di linee B fosse superiore ad 8. L'esame ecografico e il dosaggio

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dell'NT-proBNP sono stati ripetuti dopo 48 ore. Il gold standard di riferimento è stato la diagnosi clinica di scompenso cardiaco fatta da medici esperti secondo le linee guida dell'AHA.
Risultati: Il gruppo di pazienti che mostrava un esame ecografico positivo riceveva in percentuale maggiore la diagnosi finale di insufficienza cardiaca (X^2 92.5; $p < 0.005$) e valori significativamente più elevati di NT-proBNP (10,384 ng/l vs 3889 ng/l; $p < 0.05$).

Inoltre la diminuzione delle linee B a 48 ore era significativamente maggiore ($p < 0.005$) nel gruppo di pazienti trattati per scompenso cardiaco mentre non vi erano cambiamenti significativi nei valori di NT-proBNP ($p = 0.37$).
Discussione: In conclusione abbiamo dimostrato che anche in un reparto di medicina interna l'ecografia polmonare è uno strumento diagnostico utile per le gestione dell'insufficienza respiratoria e il suo monitoraggio durante la terapia.

Introduction

Dyspnea is one of the leading causes of hospitalization in internal medicine departments, in terms of both frequency and utilization of diagnostic and therapeutic resources. The causes of dyspnea include left heart failure-cardiogenic pulmonary edema, chronic obstructive pulmonary disease (COPD), lung cancers and infectious diseases, pulmonary embolism, and other less common causes. Distinguishing between cardiogenic and noncardiogenic causes is essential for proper treatment [1]. Differential diagnosis can be based on the results of the physical examination, conventional radiology (standard chest X-ray), ECG, and biochemical assays (BNP and NT-pro-BNP). The diagnostic value of each of these methods has been thoroughly evaluated in the literature [2]. These traditional techniques can now be integrated with the results of ultrasound evaluation of the lung parenchyma for the presence of B lines, which are an indication that the so-called pulmonary alveolar-interstitial syndrome [3]. The number of lines B is a semi-quantitative indicator of extravascular lung water [4,5].

Objective of the study

The clinical significance of thoracic sonography in the evaluation of lung diseases has been amply demonstrated in the literature [6]. Use of this technique has traditionally been limited to the detection of pleural effusion and evaluation of the chest wall, but the indications have recently been expanded. Interest in this technique has arisen primarily in emergency departments and in intensive care and trauma units, where speed, ease of execution, and bedside examination capability are crucial. For this reason, all previous studies have been conducted in these areas, which are characterized by a high prevalence of severe trauma. The types of disease investigated varies with the areas in which the studies were conducted: the prevalence of pneumothorax, acute respiratory distress syndrome (ARDS), and massive cardiogenic pulmonary edema seems to be lower in internal medicine wards, where-according to the estimates of the emergency department of Padua Hospital, over 60% of all cases of dyspnea are cardiogenic, and exacerbations of COPD account for the other 30%. The remaining 10% have various causes (e.g., pulmonary embolism without secondary pulmonary edema, lung cancer, interstitial pulmonary disease, and infections). We evaluated the hypothesis that lung ultrasound can be a reliable diagnostic tool in internal medicine patients, whose clinical conditions are generally less severe and have already been stabilized and treated in emergency settings.

Materials and methods

This observational study included 152 patients admitted consecutively to our internal medicine department for dyspnea during the period November 2007—March 2008. All had undergone clinical examination, chest X-ray, NT-proBNP assays and received some form of treatment (non-standardized) in the emergency room. Upon their arrival on the internal medicine ward (T0), patient histories were collected and physical examination, chest radiography, 12-lead ECG, and thoracic ultrasound were performed. After 48 h (T48), each patient was reassessed with thoracic ultrasound and measurement of NT-proBNP levels. Informed consent was obtained from all participants.

Cases of cardiogenic dyspnea were definitively identified, in accordance with the guidelines of the AHA [7], by a panel of medical experts after review of the participants' clinical, radiological, and biochemical data (gold standard). These reviewers were unaware of the results of the sonographic examination. Each diagnosis of heart failure was also validated retrospectively by two double-blinded cardiologists, who examined the patient's medical records, but not the lung sonograms.

To assess intra- and inter-operator variability, thoracic sonography was performed twice, by 2 different operators. The two examinations were done within minutes of one another, under double-blind conditions, and the examiners were unaware of the clinical diagnosis. Each examination lasted less than 3 min. All examinations were performed using the department's ultrasound scanner (Toshiba Aplio XV) with a 3.5-MHz convex probe. Each included frontal and longitudinal scans along the parasternal, mid-clavicular and mid-axillary lines, done with the patient in the supine or semi-sitting position. In each case, we considered the number of B lines (also known as comet-tail artifacts), that is the vertical artifacts originating from the pleural line and extending downward to the bottom of the screen. Results were considered positive when the number of B lines was greater than 8. Assays of atrial natriuretic peptide levels

Table 1 Clinical parameters.

Clinical parameters	Orthopnea	Jugular turgor	Rales	Peripheral edema	Hepatomegaly
Sensitivity	0.55	0.34	0.55	0.55	0.12
Specificity	0.67	0.90	0.73	0.63	0.87
PPV	0.72	0.84	0.76	0.70	0.60
NPV	0.49	0.47	0.51	0.48	0.39
LLR+	1.65	3.40	2.07	1.50	0.95
LLR−	0.67	0.73	0.60	0.70	1.00
Accuracy	0.60	0.55	0.62	0.58	0.42

	Paroxysmal nocturnal dyspnea	Dyspnea on exertion	Nighttime cough	Tachycardia (>120 bpm)
Sensitivity	0.17	0.81	0.19	0.11
Specificity	0.93	0.27	0.87	0.90
PPV	0.80	0.63	0.69	0.63
NPV	0.42	0.47	0.41	0.39
LLR+	2.55	1.10	1.43	1.06
LLR−	0.88	0.71	0.93	0.99
Accuracy	0.47	0.60	0.45	0.42

were performed with the immunoassay method used in the laboratory of Padua Hospital (Boehringer Elecsys® proBNP). Echocardiography was performed by a cardiologist using the same scanner used for lung sonography. All data were analyzed with SPSS software for Windows, version 14.0 (Chicago, IL).

Results

On their arrival in the internal medicine ward, the 152 patients had a mean capillary O_2 saturation of 89.8%, which is consistent with the sub-acute nature of their conditions. At discharge 68 patients had a diagnosis of heart failure; the other 84 had different diagnoses. Using the medical experts' clinical diagnosis of cardiogenic/noncardiogenic dyspnea as the gold standard, we assessed the diagnostic accuracy—in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and positive and negative likelihood ratios (LLR + and −)—of thoracic sonography, NT-proBNP assays, and the main clinical, echocardiographic, and radiological variables.

The results of the physical examination are reported in Table 1. These clinical data confirm the low diagnostic accuracy previously reported in the literature. Table 2 shows the results of thoracic ultrasound and NT-proBNP assays, both of which displayed high sensitivity (97%). The echocardiographic findings (Table 3) showed low sensitivity and moderate specificity, suggesting that they might be used to confirm the diagnosis, together with pulmonary ultrasound and NT-proBNP assays. Chest X-ray findings (Table 4) also showed good specificity but low sensitivity.

The patient group with positive findings in the thoracic ultrasound examination had a significantly higher rate of heart failure diagnoses (X^2 92.5, $p < 0.005$); the same was true for NT-proBNP values (41 X^2, $p < 0.005$). Patients with positive pulmonary ultrasound findings had significantly higher NT-proBNP values than those with negative ultrasound findings (10 384 ng/l vs 3889 ng/l, $p < 0.05$). Therefore, the lung ultrasound findings showed positive correlation with the clinical diagnosis and with the biochemical data. Reductions in the number of B lines during treatment were significantly greater in the group of patients treated for heart failure ($p < 0.005$), while this was not the case for the reduction in NT-proBNP values ($p = 0.37$). Therefore, ultrasound seems to be a more promising tool for short-term patient follow-up. The results of lung sonography were characterized by very good intra- and inter-operator concordance (expressed as the K coefficient of Cohen: 0.98 and 0.9, respectively) (Table 5).

Discussion

This study highlights the usefulness of thoracic sonography in diagnosing cardiogenic forms of dyspnea, even in sub-intensive settings like that of an internal medicine ward. Compared with clinical, echocardiographic, and radiological findings, lung ultrasound displayed specificity and sensitivity that validate its use. Its sensitivity was similar to that of laboratory values (NT-proBNP), indicating that both of these methods are useful means for excluding cardiac causes of pulmonary edema. The atrial natriuretic peptide assay is still preferable to thoracic ultrasound given its greater repeatability and the broader base of evidence that supports its use. Thoracic ultrasound is rapid and easy to perform, but it is also operator-dependent, although its use is justified by excellent intra- and inter-operator agreement. However, it can be done at the bedside, even in

Table 2 Lung ultrasound and biochemical parameters.

Parameters	B lines	NT-proBNP
Sensitivity	0.97	0.97
Specificity	0.79	0.44
PPV	0.79	0.58
NPV	0.97	0.95
LLR+	4.64	1.74
LLR−	0.04	0.07
Accuracy	0.87	0.68

Table 3 Echocardiography parameters.

Echocardiographic parameters	Increased EDV	Increased *M/V* ratio	Reduced EF
Sensitivity	0.43	0.29	0.45
Specificity	0.89	0.56	0.81
PPV	0.69	0.35	0.67
NPV	0.73	0.48	0.64
LLR+	3.96	0.65	2.36
LLR−	0.64	1.28	0.68
Accuracy	0.72	0.43	0.65

EDV: End-diastolic volume; *M/V*: Mass/Volume; EF: Ejection fraction.

Table 4 Chest X-ray parameters.

Chest X-ray parameters	Cardiomegaly	Cephalization	Pulmonary Edema	Pleural effusion
Sensitivity	0.78	0.35	0.35	0.45
Specificity	0.50	0.80	0.97	0.77
PPV	0.70	0.73	0.94	0.75
NPV	0.60	0.44	0.49	0.47
LLR+	1.57	1.73	10.43	1.91
LLR−	0.43	0.81	0.67	0.72
Accuracy	0.67	0.53	0.59	0.57

emergency conditions, and because it does not involve the use of ionizing radiation, it can be repeated without the risk of radiation-induced biological damage.

For this reason, it seems to be a useful technique for accurate semi-quantitative assessment of free water in the extravascular space. Pulmonary ultrasound also provides information on the pleural space (effusion) with higher sensitivity and specificity than plain radiographs. It is also important to recall that ultrasound is effective for identifying not only B lines but also lung consolidation caused by infections or trauma. Finally, the real-time ultrasound image evolves rapidly, in parallel with the patient's clinical condition: as noted in the literature [8—10], B lines appear and disappear very quickly, and unlike chest radiographs and NT-proBNP levels, they can be used to monitor treatment responses during patient follow-up. Ultrasound can thus be used as a guide for adjusting the intensity and duration of therapy. In our opinion, the transient nature of the B lines may be responsible for the high number of false negative results in our study. Data in the literature refer to patients who have been evaluated during the acute stages of their illness and prior to emergency treatment, whereas our study involved patients who had already been stabilized. In these cases, the ultrasound picture might also have improved.

Table 5 Significance of Cohen's K coefficient.

K	Concordance
$0 < k < 0.2$	Insufficient
$0.2 < k < 0.4$	Low
$0.4 < k < 0.6$	Fair
$0.6 < k < 0.8$	Good
$0.8 < k < 1.0$	Excellent

Comparison with echocardiography deserves separate consideration: transthoracic echocardiography seems to be a very accurate technique for evaluating cardiac function and highly specific for identifying acute cardiogenic pulmonary edema. However, it requires greater technical skills than pulmonary sonography, and it also takes longer to perform. Moreover, the results are often invalidated by a poor ultrasound window, which does not allow proper visualization of the cardiac chambers. And unlike thoracic ultrasound, it provides only indirect data on the lung parenchyma (as do natriuretic peptide levels). From a pathophysiological point of view, only direct ultrasound scans of the lung parenchyma can demonstrate interstitial imbibition or, in more severe cases, filling of the pulmonary alveoli. Combined use of the two techniques (along with clinical, biochemical, and radiological findings) is always advisable to maximize the accuracy of the etiological diagnosis. In our opinion, variations are likely to involve the timing rather than the indications for these examinations: the second-level tests can be performed later when the patient's condition is more stable and the techniques used more favorable.

Conclusions

This study confirms the usefulness of thoracic ultrasonography in the management of patients with dyspnea, even in sub-acute settings like internal medicine wards. Pinpointing the cause of dyspnea and early identification of cardiogenic forms are still among the most significant diagnostic challenges in these patients. The thoracic ultrasound examination is characterized by good sensitivity, rapid changes as the clinical picture evolves, rapid execution and repeatability, factors that make it an ideal tool for the management of patients with cardiogenic dyspnea. In particular,

this examination is more sensitive than chest radiography and echocardiography, and it exhibits sensitivity and specificity similar to that of the NT-pro-BNP assay, but it also offers more rapid changes with the resolution of the clinical picture.

Conflict of interest statement

The authors have no conflict of interest.

Appendix
Supplementary data

Supplementary data related to this article can be found online at doi:10.1016/j.jus.2011.06.009.

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