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Efficacy of Pulmonary Ultrasound Compared to N-terminal prohormone Brain Natriuretic Peptide as a Diagnostic Tool for Congestive Heart Failure in Patients Presenting with Acute Dyspnea in the Emergency Setting

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Abstract

Objective: To determine the efficacy of using pulmonary ultrasound as a diagnostic tool in acute dyspnea of undetermined cause compared to the use of serum N-Terminal prohormone Brain Natriuretic Peptide (NT-proBNP) in the diagnosis of heart failure.

Design: Systematic literature review

Methods: Searches were conducted in PubMed and Scopus using the terms pulmonary ultrasound and congestive heart failure and studies within the last 10 years. Studies that used pulmonary ultrasound compared to BNP as a marker for the diagnosis of heart failure were included.

Results: All three studies found that the use of pulmonary ultrasound was a more specific diagnostic aid for heart failure when compared with NT-proBNP.

Conclusion: The use of pulmonary ultrasound is highly specific in guiding the clinical diagnosis of heart failure in patients presenting with acute dyspnea of an unknown cause.

Introduction

Heart failure affects 5.7 million adults in the United States.[1] Once the diagnosis is made half of the affected individuals will not live past five years. The disease also places a tremendous economic burden on society, The Center for Disease Control estimates the annual cost of hospitalizations for heart failure to be roughly 30.7 billion dollars.[1] Common risk factors for heart failure include obesity, diabetes and hypertension, all diseases that are on the rise, potentially increasing the prevalence of the disease in the not so distant future.

A diagnosis of heart failure is currently made clinically, largely based on history and physical exam. Due to the significant implications of the diagnosis, it is critical that heart failure is diagnosed as quickly as possible in dyspneic patients presenting to the Emergency Department Several imaging techniques and laboratory findings are currently being used to help the clinician make the diagnosis of heart failure, but they are not without flaws. Chest radiographs are commonly used to evaluate the lungs for several findings that are related to heart failure. These include pleural effusions, interstitial edema, alveolar edema, pulmonary venous blood diversion and a widened cardiothoracic ratio.[2] These findings are not always present during acute heart failure and the sensitivity of chest radiographs is not high enough to make a diagnosis.

A laboratory value popularly used in the diagnosis of CHF is the measure of N-Terminal pro Brain Natriuretic Peptide (NT-proBNP). This biomarker is related to the stretch of the ventricular myocytes and an elevated level demonstrates excessive ventricular work and stretch.[2] There are a number of conditions that may be associated with ventricular stretching, including acute coronary syndrome, pulmonary embolism, critical illness and old age, which makes this lab value highly sensitive but not specific.[3] NT-proBNP is able to reliably exclude heart failure in an

acute setting with a high sensitivity, however it's specificity remains variable and generally requires confirmatory diagnosis.[4]

The use of pulmonary ultrasound has been suggested as a tool to assist in making the diagnosis of heart failure in the acute setting. The examination can be easily taught to clinicians and takes about a minute to complete.[5] Ultrasound is particularly appealing as a diagnostic tool, as it is readily available, non-invasive and relatively inexpensive. It can be performed by clinicians who are familiar with the technology at the bedside making the findings available immediately for clinical application.

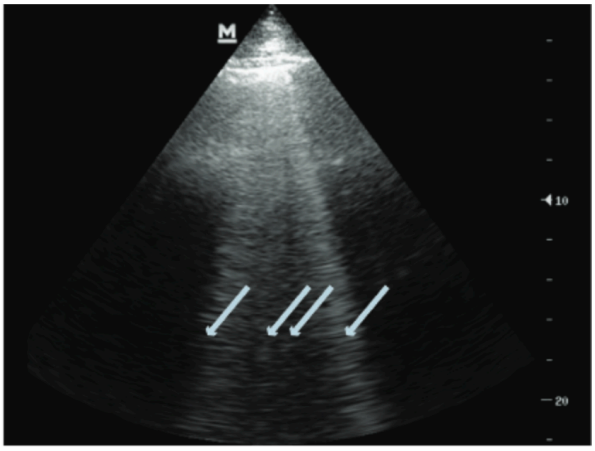

Figure 1. These arrows depict B lines on pulmonary ultrasound examination. [8]

Specifically, the presence of diffuse B lines on pulmonary ultrasound is an excellent predictor of congestive heart failure. B lines are hyperechoic vertical lines seen extending from the pleura to the bottom of the ultrasound screen, and they represent thickened interstitium and fluid-filled alveoli.[3] An example is included in figure 1. Also referred to as comet tail artifacts or lung comets, B lines extend perpendicular to the pleural line, radiating down as if in the shape of a comet's tail.[3]

When utilizing pulmonary ultrasound to assess for pulmonary edema, the thorax is divided into eight segments and assessed for B-lines in the lung. This technique is an established protocol for lung ultrasound created by Cardinale, et al and Volpicelli et al.[5,7] Using an eight zone test, when all zones are positive, the likelihood of CHF is largely increased.[3] Each thoracic zone is considered positive if three or more B-lines are identified in each of the divided zones. Subsequently, the ultrasound is considered positive for pulmonary edema when two or more of these B-line containing zones are adjacent to each other.[3] In summary, lung ultrasound is positive for pulmonary edema when there are two adjacent zones that contain three or more B lines in each zone. A visual of the pulmonary zone is included as figure 2. This indicates pulmonary congestion, a result of elevated ventricular pressures causing pulmonary interstitial edema.[4]

Figure 2. The right anterior chest wall divided into 4 zones, PSL is the parasternal line, AAL is the anterior axillary line, PAL is the posterior axillary line. Zones 5 through 8 are contralateral equivalents.[3]

The goal of this meta-analysis is to determine whether pulmonary ultrasound improves the

specificity and accuracy of the diagnosis of congestive heart failure compared to NT-proBNP. Due to the fact that NT-proBNP levels are increased in many non-CHF processes, it is not a highly specific lab and therefore a test with increased specificity such as ultrasound is preferred. A rapid and highly specific test such as ultrasound is invaluable at the bedside to rapidly diagnose congestive heart failure so that proper treatment can be initiated. The studies included in this meta-analysis compare these variables with a hope to improve their clinical utility and effectively treat patients with acute undifferentiated dyspnea.

PICO

Population: Adults presenting to the Emergency Setting with acute dyspnea
Intervention: pulmonary ultrasound
Control: NT-proBNP
Outcome: Improved specificity and diagnostic accuracy of Congestive Heart Failure

Clinical Question*:* Does the use of pulmonary ultrasound improve specificity and therefore the accuracy of the diagnosis of heart failure compared to the use of NT-proBNP (N-terminal prohormone Brain Natriuretic Peptide)?

Methods

In September of 2019, a literature review search was conducted and PubMed and Scopus were utilized to identify studies evaluating the use of bedside pulmonary ultrasound in comparison with Brain Natriuretic Peptide (BNP) for the diagnosis of congestive heart failure. The search terms "pulmonary ultrasound" and "congestive heart failure" were used. Within PubMed, 297 articles were identified based on these search terms. Within Scopus, 33 articles were found based on these keywords. We then narrowed the search and excluded 285 articles that

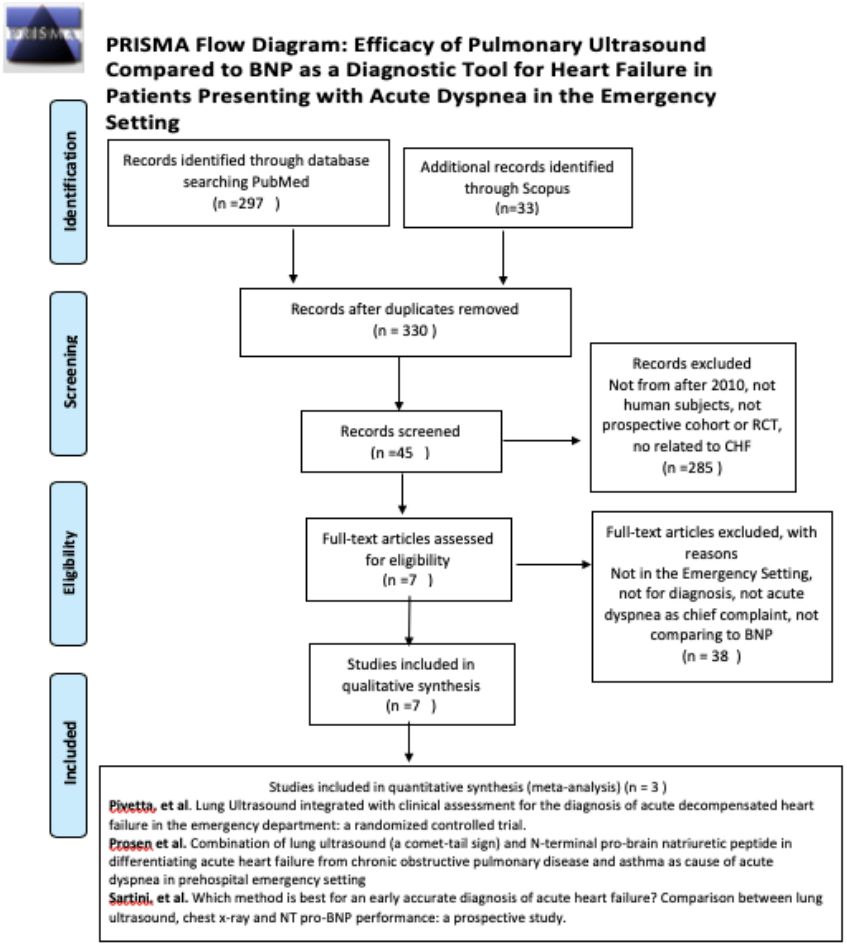

Figure 3. PRISMA Flow Diagram

were from before the year 2010, not human subjects, not prospective cohort or randomized control trials, or not related to congestive heart failure.

Following this elimination, 45 total articles which were then further narrowed down by excluding trials that did not include patients presenting to the Emergency Department with acute dyspnea as their chief complaint, and studies that did not specifically compare pulmonary ultrasound to NT-proBNP for rapid diagnosis of congestive heart failure. The remaining 10 articles were narrowed down based on the strength of statistical studies and number of subjects to 3 articles. An overview of the studies found in this review can be found in Table 1, and the Prisma flow diagram can be referenced in Figure 3. The articles included in this literature review assess the usefulness of point of care pulmonary ultrasound compared to BNP measurement in the diagnosis of congestive heart failure in patients presenting with dyspnea to the Emergency Setting.

Results

Table 1. Comparison of studies in the meta-analysis

	Study 1: Pivetta et al	Study 2: Prosen et al	Study 3: Sartini et al
Year Published	**2019**	**2011**	**2017**
Sample Size	**532**	**218**	**255**
Journal	**European Journal of Heart Failure**	**Critical Care Journal**	**Internal and Emergency Medicine**
Study Design	**Randomized control trial**	**Prospective cohort**	**Prospective blinded observational**
Duration of Study	**14 months**	**21 months**	**15 months**
Efficacy Outcomes	**Accuracy of diagnosis measured by sensitivity, specificity, PPV, NPV, AUC**	**Accuracy of diagnosis measured by sensitivity, specificity, PPV, NPV, +LR, - LR, AUC**	**Accuracy of diagnosis measured by sensitivity, specificity, PPV, NPV, +LR, -LR, AUC**

Study 1- Lung Ultrasound integrated with clinical assessment for the diagnosis of acute decompensated heart failure in the emergency department: a randomized controlled trial. Pivetta, et al.[9]

Objective: The purpose of this study was to compare the diagnostic accuracy of lung ultrasound versus chest x-ray and NT-proBNP measurements in the correct diagnosis of dyspneic patients with congestive heart failure.

Study Design: This study was a randomized, multi-center trial performed in two Italian academic hospitals, Scienza di Torino University Hospital in Turin, Italy and Careggi University Hospital in Florence, Italy. The aim of the study was to compare the usefulness of clinical examination plus lung ultrasound versus chest x-ray and NT-pro-BNP measurement in diagnosis of acute decompensated heart failure (ADHF). The patient population were patients presenting to the Emergency Department with acute dyspnea. A secondary outcome was assessing time for evaluation for evaluation with pulmonary ultrasound compared to chest Xray and pro-BNP.

There were 532 patients, deemed eligible if they were over 18 years of age and presenting with acute dyspnea defined as sudden onset of shortness of breath, not related to trauma. The criteria are described in table 2. The median age of patients was 79 years old. Patients were then randomized to be worked up as either the CXR (chest xray)/NT-proBNP group or the LUS group. Lung ultrasound (LUS) was performed by a physician, with the presence of three or more B lines in an intercostal space representing a positive area of increased lung density. The presence of three or more B lines in two or more zones bilaterally was diagnosed as diffuse interstitial syndrome. NT-proBNP levels were measured using a commercially available immunoassay.

Following initial clinical examination, the physician was asked to indicate the presumed cause of dyspnea as either ADHF (acute decompensated heart failure) or non-ADHF. CXR and NT-proBNP were eventually performed on all patients, but these results were only made available to the physician following their initial presumed diagnosis after LUS. Following hospital discharge, two expert intensivists who were blinded to LUS results reviewed medical records and confirmed ADHF based on the 2012 European Society of Cardiology guidelines for heart failure. Time needed to reach diagnosis was also measured and compared in the two groups studied (LUS and CXR/NT-proBNP).

Table 2. Inclusion and Exclusion Criteria for Study 1

Study Design *Pivetta, et al 2015*	
Inclusion Criteria	Exclusion Criteria
Patients presenting to the Emergency Department with acute dyspnea >18 years of age	Patients already mechanically ventilated with positive pressure (invasively or non-invasively) at time of first evaluation, or acute dyspnea in the context of trauma

Study Results: Patients in the group where lung ultrasound was utilized integrated with clinical assessment to diagnose ADHF showed higher sensitivity and specificity (93.4%, 95.2%) than evaluation with CXR and NT-proBNP (85%, 88.7%). Diagnostic accuracy was also deemed higher as demonstrated by an area under the receiver operating characteristic curve (AUC) of 0.95 compared to AUC of 0.87 with the CXR/ NT-proBNP approach. Results are organized in table 3.

The clinical usefulness of each approach was assessed by evaluating net benefit using decision curve analysis. Net benefit quantifies diagnostic gain by showing the benefit of a true positive minus the harm of a false positive for ADHF. Net benefit calculations revealed that lung ultrasound with clinical assessment would reduce diagnostic errors of ADHF by 7.98 cases per 100 patients. This was compared to CXR/NT-proBNP with clinical assessment which was shown to reduce diagnostic errors by only 2.42 cases per 100 patients. Assessment with CXR/NT-proBNP also results in higher false negative diagnoses and false positive diagnoses. Time needed to formulate the diagnostic hypothesis of ADHF was also significantly reduced with LUS approach.

Overall, the study shows that integration of lung ultrasound with clinical assessment is more accurate and also offers more benefit than the current recommended diagnostic method of clinical evaluation, CXR and NT-proBNP in patients in the ED presenting with acute dyspnea.

Table 3. Results of Study 1; *Pivetta et al 2015*

Integrated Evaluation Measurements	CXR/NT-proBNP (N=260)	LUS (N=258)
Sensitivity	85% (95% CI 76.5–91.4%)	93.4% (95% CI 87.5–97.1%),
Specificity	88.7% (95% CI 82.5–93.3%)	95.2% (95% CI 89.8–98.2%),
PPV	83.3% (95% CI 74.7–90%)	95% (95% CI 89.4–98.1%),
NPV	89.9% (95% CI 83.8–94.2%)	93.7% (95% CI 87.9–97.2%)
AUC	0.87 ($p<0.01$)	0.95 ($p<0.01$)

Study Critique: Some limitations in interpreting the results include the absence of standard criteria to determine the final diagnosis of ADHF. This study utilized review of medical records by two expert physicians/intensivists with another physician reviewing cases that were disagreed upon. The study was unable to perform interobserver measurements for lung ultrasound performed by different physicians. However, the authors state that LUS has been shown to have high repeatability and reproducibility amongst performers even if they are inexperienced sonographers. In another study performed by the same group, a high agreement was demonstrated between both experienced and naïve lung ultrasound operators in both acquiring and interpreting ultrasound images.

Overall, the study had a large patient study group with 532 patients, was a randomized control trial, and was generalizable in terms of results. The patient population was diverse with multiple comorbidities which is representative of most patients presenting to the Emergency Department with ADHF. The ultrasound operators were of varying experience, which represents the variety of clinicians in the Emergency Department who may be either expert or new to sonography.

Study 2- Combination of lung ultrasound (a comet-tail sign) and N-terminal pro-brain natriuretic peptide in differentiating acute heart failure from chronic obstructive pulmonary disease and asthma as cause of acute dyspnea in prehospital emergency setting. Prosen, et al.

Objective: To study the diagnostic accuracy of bedside lung ultrasound (presence of comet-tail signs), NT-proBNP and clinical assessment in the differentiation of ADHF related dyspnea from other pulmonary related dyspnea.

Study Design: This was a prospective cohort study performed at the Center for Emergency Medicine in Maribor, Slovenia between July 2007 and April 2010. The primary aim of this study was to determine the diagnostic accuracy in using the presence of bilateral B-lines on point of care lung ultrasound compared to NT-proBNP in assessment of dyspneic patients in the pre-hospital setting.

The average age of the group of patients studied was 70.9 years old. There were 218 patients included in the study, who were deemed eligible if they presented with shortness of breath as their primary complaint. Patients were excluded if they were age <18 years, had a history of renal insufficiency, trauma, or currently were presenting with severe coronary ischemia, pneumonia, pulmonary embolism, carcinoma, pneumothorax, pleural effusion, drug intoxication, anaphylactic reaction, upper airway obstruction, bronchial stenosis or GERD. Inclusion and exclusion criteria are listed in table 4.

Levels of NT-proBNP were measured using a portable Cardiac Reader device. Bedside lung ultrasound was performed using a SonoSite portable ultrasound machine. Ten emergency physicians performed ultrasound and identified the presence or absence of 3 or more B lines in eight zones of the lungs. A positive result was deemed two or more positive zones bilaterally of eight measured zones (this is per Cardinale et al and Volpicelli et al examination definitions). All physicians who participated had attended a Critical Ultrasound provider course. Measurements of NT-proBNP and ultrasound examinations were performed upon arrival to the emergency department and before any medications were given.

It is the standard of care at this hospital to perform a bedside pulmonary ultrasound in patients presenting with acute dyspnea. Physicians in the prehospital setting were blinded to the results of NT-proBNP but knew the results of the ultrasound. The study also included internists and cardiologists who were blinded to either ultrasound findings or NT-proBNP at the point of admission or discharge respectively.

Table 4. Inclusion and Exclusion Criteria for Study 2

Study Design *Prosen, et al 2011*	
Inclusion Criteria	Exclusion Criteria
Shortness of breath as primary complaint (defined as sudden onset of dyspnea without history of chronic dyspnea or increase in severity of chronic dyspnea)	Age <18 years, history of renal insufficiency, trauma, severe coronary ischemia, pneumonia, pulmonary embolism, carcinoma, pneumothorax, pleural effusion, drug intoxication, anaphylactic reaction, upper airway obstruction, bronchial stenosis and GERD

Study Results: Ultrasound examination alone proved to be more accurate in the accurate diagnosis of ADHF and was statistically significant. This was in comparison to both NT-proBNP and clinical assessment alone with modified Boston criteria scoring. Lung ultrasound examination had 100% sensitivity and 95% specificity in accurate diagnosis of ADHF, in comparison to NT-proBNP with 92% sensitivity and 89% specificity. Comparison of the methods was made using the x^2 test with Bonferroni correction. Results are further explained in table 5.

Ultrasound examination was found to have an odds ratio of 53.7 with a p value of <0.001 and 95% confidence interval for the presence of HT. This was in comparison to NT-proBNP measurement with an odds ratio of 14.3 and p-value of <0.001. These results demonstrate that ultrasound exam was found to be the strongest predictor of ADHF amongst ten significant variables that were assessed including orthopnea, rales, and NT-proBNP measurement.

Table 5. Results of Study 2; *Prosen et al 2011*

Measurement	NT-proBNP	Ultrasound examination
Sensitivity	92% (95% CI 88 to 95)	100% (95% CI 98 to 100)
Specificity	89% (95% CI 84 to 92)	95% (95% CI 91 to 100)
NPV	86% (95% CI 82 to 90)	100% (95% CI 98 to 100)
PPV	90% (95% CI 85 to 94)	96% (95% CI 93 to 100)
LR+	8.36 (95% CI 1.72 to 33.86)	20 (95% CI 1.98 to 89.94)
LR-	0.09 (95% CI 0.02 to 0.23)	0
AUROC	0.90 (95% CI 0.84 to 0.94)	0.94 (95% CI: 0.90 to 0.97)
OR	14.3 (95% CI 8.1 to 29.4)	53.7 (95% CI, 28.6 to 83.5)

Study Critique: One limitation of this study is that it was performed in a prehospital setting. However, in Slovenia where it was performed, there are medical doctors on the ambulances who performed the ultrasound and drew the serum markers for NT-proBNP so in essence it was a similar setting to an emergency department.

The study demonstrated that ultrasound alone has higher sensitivity and specificity than NT-proBNP alone and could be used as a diagnostic tool itself for accurate diagnosis of CHF. The study also revealed that the combination of ultrasound with NT-proBNP has 100% sensitivity, 100% specificity, 100% NPV and 100% PPV for differentiating heart failure compared to other pulmonary causes in the prehospital setting. They suggest that if ultrasound shows B lines, NT-proBNP should be measured following sonography to confirm the diagnosis.

There were five patients who had false positive results with ultrasound examination who then went on to have NT-proBNP values of less than 1000 pg/mL and a history of COPD/ asthma. This suggests that in a small portion of patients, it is still necessary to confirm the absence of ADHF with an NT-proBNP value. While in the majority of cases the study revealed that ultrasound examination could be used alone, to achieve complete confidence in the diagnosis of ADHF, measurement of NT-proBNP should be performed as well.

Overall, this study highlights the fact that pulmonary ultrasound can be utilized in the prehospital setting for rapid identification of B lines indicating interstitial pulmonary edema and therefore ADHF. This is vital information that can be relayed to the emergency department physician upon arrival to the Emergency Department in order to initiate prompt and appropriate treatment of ADHF.

Study 3: Which method is best for an early accurate diagnosis of acute heart failure? Comparison between lung ultrasound, chest x-ray and NT pro-BNP performance: a prospective study. Sartini, et al.

Objective: To compare and evaluate the performance of chest radiography, NT-proBNP and lung ultrasound in identification of acute heart failure in patients presenting to the ED with shortness of breath.

Study Design: This as a prospective observational study performed at the emergency department of the University Hospital of Sienna from January 2011 to February 2013. The aim of this study was to compare the accuracy in diagnosing heart failure to chest X-ray and NT-proBNP.

The average age of the patients was 79.98 years. There were 225 patients in this study. Inclusion criteria for this study included patients over 18 years of age, presenting with acute dyspnea (<24 hours) or worsening shortness of breath over a four day period not related to trauma. Exclusion criteria for this study included age less than 18 years or dyspnea following trauma. The criteria are available in table 6.

NT-proBNP was analyzed with ECLIA, Roche Methodics. The NT-proBNP level was considered indicative of heart failure when greater than or equal to 300 pg/ml following the European Society of Cardiology recommendations. Lung ultrasound was obtained upon initial presentation to the emergency department within two hours. The Esaote MyLab30 and MyLab70 ultrasound machines were used with a variable-band convex array (3.5-5MHz). Six transverse

scans of each hemithorax were performed. A positive region was defined by the presence of 3 or more B-lines in transverse intercostal planes in two or more regions. The ultrasound was performed by emergency room physicians who were blinded to the clinical data. Each physician had previously performed at least 50 examinations supervised by an expert before starting the study. The results were reviewed by an independent panel of experts made up of two cardiologists and an emergency room physician who collected all of the data to determine the final diagnosis.

Table 6. Inclusion and Exclusion Criteria for Study 3

Study Design, *Sartini et al 2017*	
Inclusion Criteria	Exclusion Criteria
Age >18 years, presenting with acute dyspnea (sudden onset <24h) or worsening of shortness of breath over a 4 day period not related to trauma	Age <18 years, dyspnea following trauma

Study Results: The study found that lung ultrasound was more specific than NT-proBNP for aiding in the diagnosis of heart failure. The study showed that the specificity of ultrasound is greater than that of NT-proBNP. The sensitivity of lung ultrasound was 57.73% and specificity was 87.97%. The sensitivity of NT-proBNP was 97.59% and the specificity of 27.56%. Results are presented in table 7.

This study also reviewed the use of chest x-ray as the sole diagnostic method of heart failure. Chest x-ray had a sensitivity of 74.49% and a specificity of 86.26%. The researchers also compared the use of two diagnostic tools simultaneously and finally three diagnostic tools at a time. These comparisons increased sensitivity and specificity as would be expected. Overall, the study found that no test alone could be used to make the diagnosis of congestive heart failure. However, the researchers did recommend a step-wise process that starts with chest x-ray and lung ultrasound and a follow up measure of NT-proBNP if the diagnosis is still uncertain.

Table 7. Results of Study 3; *Sartini et al 2017*

Measurement	NT-proBNP	Ultrasound examination
Sensitivity	97.59 % (95 % CI 91.57–99.71)	57.73% (95 % CI 47.28–67.70)
Specificity	27.56 (95 % CI 20.01–36.19)	87.97 % (95 % CI 81.20–92.96)
NPV	94.59 % (95 % CI 81.81–99.34)	74.05 % (95 % CI 66.49–80.69)
PPV	46.82 % (95 % CI 39.21–54.54)	77.78 % (95 % CI 66.4–86.73)
LR+	1.351 (95 % CI 20–1.51)	4.80 (95 % CI 2.94–7.83)
LR-	0.09 (95 % CI 0.02–0.35)	0.48 (95 % CI 0.38–0.61)
AUROC	75.5%	84%

Study Critique: The study enrolled 42 patients who had previously received diuretic therapy in the prehospital setting prior lung ultrasound, however, they also measured both sensitivity and specificity in those who had not been treated. In the patients who had not been treated ultrasound had a higher sensitivity and specificity when compared to the entire study population as would be expected.

This study divided the hemithorax into 6 regions but found that studying only four provided higher yield information. They based this finding on the dependent nature of pulmonary edema. This is a limitation of the study as other studies used 8 quadrants to evaluate each hemithorax. Cardinale et al and Volpicelli et al have set up defined quadrants and findings that allow for a consistent pulmonary ultrasound evaluation. The lack of following these established criteria is a limitation of this study.

The study also identified a small sample size of patients given the frequency of patients with dyspnea presenting to the emergency room. They suggested enrolling more patients to

improve the ability to generalize the findings. A larger sample size will improve any studies ability to generalize findings and this is an area that could be improved in the study of pulmonary ultrasound use and the diagnosis of heart failure.

Overall, this study did an excellent job of isolating the variables and blinding the observers to other findings. It also showed that lung ultrasound can be accurately performed even by providers with minimal training.

Discussion

Congestive heart failure is a growing cause of morbidity and mortality. As with all medical maladies, making the diagnosis quickly and accurately is imperative for positive outcomes. The diagnosis of heart failure is unique in that it is often made based on clinical suspicion rather than a clearly defined laboratory test. In patients presenting to the emergency department with acute dyspnea, a rapid and accurate diagnosis of heart failure can decrease the time needed to treat patients which will in turn lead to improved long-term outcomes.

NT-proBNP has been used to improve the accuracy of a heart failure diagnosis but is limited in its ability to accurately rule in CHF by a myriad of factors. Examples of artificially high and low causes of BNP have been defined by Yoo, BS[11] in table 8. While this biological marker has utility, a more definitive test is needed. Ultrasound is a commonly used technology that is easily adaptable to aid in the diagnosis of heart failure. With minimal additional training the use of bedside ultrasound can provide a fast and reliable view of the lungs and be used to enhance the clinical diagnosis of heart failure leading to faster treatment and improved outcomes. The aim of our study was to compare the diagnostic utility of pulmonary ultrasound to NT-proBNP in accurately reaching the diagnosis of heart failure.

Table 8. Factors Affecting BNP; *Yoo, BS 2014*

Factors that can account for high BNP levels and no CHF
- Age, Sex, Renal Failure, Myocardial Infarction, Acute large pulmonary embolism
Factors that can account for low BNP levels with CHF
- Obesity (BMI>30 kg/m^2), Flash pulmonary edema, CHF secondary to causes upstream from the left ventricle (Acute mitral regurgitation, Mitral stenosis), Stable NYHA class I patients with low ejection fractions

All three studies showed that pulmonary ultrasound was a more specific diagnostic aid than NT-proBNP. Ultrasound has the advantage of allowing an indirect visualization of the thorax and potential pathology such as fluid accumulation. This is compared to the serum marker NT-proBNP, which is only an indirect measure of the response to pathology. In all three studies

NT-proBNP was found to have a lower specificity compared to the use of pulmonary ultrasound. These findings are significant as they show that pulmonary ultrasound is an effective tool in making the diagnosis of heart failure.

The limitations of this review include the setting ultrasound was performed. The aim was to determine the use of pulmonary ultrasound in the emergency room in acute dyspneic patients with an unclear diagnosis. Pivetta et al. and Sartini, et al. reflected this in their studies. However, Prosen et al. performed their pulmonary ultrasound and serum markers in a prehospital setting, while they still found ultrasound to be a better diagnostic aid, the prehospital environment and the emergency room are unique settings which may limit the transferability of the results.

Another limitation identified is the procedure used during pulmonary ultrasound. A standardized approach has been established but Sartini, et al. deviated from this technique possibly altering the results of their study. It would be beneficial for future studies to utilize a consistent pulmonary ultrasound technique such as created by Cardinale, et al and Volpicelli et al. In this review, only one study was a randomized control trial (Pivetta et al), this may be seen as a limitation. Additional randomized control trials would lend enhanced credibility to the use of lung ultrasound in the diagnosis of heart failure.

To evaluate the overall utility of pulmonary ultrasound as a diagnostic test, likelihood ratios were calculated for each study using sensitivity and specificity and compared in Table 9. A positive likelihood ratio gives a quantifiable value to determine the likelihood that a disease state is present given a positive result from the diagnostic test. In all of the studies in this review the positive likelihood ratio of ultrasound was higher when compared to the positive likelihood ratio of NT-proBNP. The positive likelihood ratios demonstrate the favorable use of pulmonary ultrasound in making the diagnosis of heart failure compared to NT-proBNP.

Overall, this meta-analysis demonstrates that pulmonary ultrasound is a highly specific test that can be used in practice in the assessment of patients presenting emergently with acute dyspnea. The presence of three or more B-lines in two adjacent thoracic zones confers high specificity for acute decompensated heart failure. Pulmonary ultrasound results in fewer false positives than NT-proBNP and is therefore incredibly useful at the bedside to aid in the diagnosis of CHF. The ramifications of this conclusion are that pulmonary ultrasound can and should be used as a diagnostic aid in the initial assessment of patients with acute dyspnea.

Table 9. Positive Likelihood Ratios of BNP and LUS

	Positive LR BNP	Positive LR LUS
Pivetta, et al[9]	7.5	19.5
Prosen, et al[6]	8.36	20
Sartini, et al[10]	1.35	4.80

Conclusion

These studies show that lung ultrasound is an effective tool compared to the serum marker NT-proBNP in aiding in the diagnosis of heart failure. NT-proBNP has a lower specificity and less utility in initial diagnosis. In regard to pulmonary ultrasound, each study found that the presence of three or more B-lines in two adjacent thoracic zones confers a high specificity to the diagnosis of heart failure. This demonstrates that lung ultrasound is an effective tool for use in the assessment of the patient with acute dyspnea of undetermined cause. This meta-analysis shows that pulmonary ultrasound should be used in patients presenting to the emergency department with undifferentiated acute dyspnea before the use of NT-proBNP. If the pulmonary ultrasound results are equivocal an NT-proBNP can be ordered to aid in diagnosis as a second line diagnostic tool. This stepwise protocol prevents unnecessary lab orders with results that may not yield useful information.

Resources:

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