BONUS DIGITAL CONTENT

Medicine by the Numbers

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Dyspnea Due to Acute Heart Failure Syndrome

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Narrative: Dyspnea is a common acute symptom in patients presenting to the emergency department and who are ultimately diagnosed with acute heart failure syndrome (AHFS).[1] However, in patients with undifferentiated dyspnea, an accurate diagnosis of AHFS may be difficult with the standard initial evaluation that includes patient history, physical examination, electrocardiography (ECG), chest radiography, and natriuretic peptide testing. This systematic review and meta-analysis comprehensively evaluated the diagnostic accuracy of the clinical assessment and index tests that physicians may use to distinguish AHFS from other clinical conditions in patients presenting to the emergency department with dyspnea.[2]

This review included 57 mostly prospective or cross-sectional studies, 52 unique cohorts, and a total of 17,893 patients.[2] There was no single historical variable, symptom, or physical examination finding that could significantly reduce the likelihood of AHFS. An S3 gallop marginally increased the likelihood of AHFS (positive likelihood ratio [LR+] = 4.0; 95% confidence interval [CI], 2.7 to 5.9) but was an insensitive finding. None of the abnormal ECG findings substantially increased or decreased the probability of AHFS. The presence of radiographic findings that represented edema moderately increased the likelihood of AHFS (LR+ = 4.8 to 6.5; *Table 1*), but a negative chest radiograph was unhelpful. Serum B-type natriuretic peptide (BNP) testing increased the probability of AHFS (LR+ > 5.0) but only at markedly elevated concentrations (more than 800 pg per mL [800 ng per L]; *Table 2*); both BNP and serum N-terminal proB-type natriuretic peptide (NT-proBNP) testing were useful at excluding AHFS at very low concentrations (less than 100 pg per mL [100 ng per L]). Bedside lung ultrasonography of three or more B-line artifacts in two bilateral lung zones had the greatest discriminatory value among index tests (LR+ = 7.4; 95% CI, 4.2 to 12.8; negative likelihood ratio [LR–] = 0.16; 95% CI, 0.05 to 0.51). Bedside

TABLE 1

Notable Pooled Test Performance Characteristics

	N	n	% AHFS (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
Chest radiography							
Kerley B lines	2	814	46.8 (43.4 to 50.2)	9.2 (6.5 to 12.5)	98.8 (97.3 to 99.6)	6.5 (2.6 to 16.2)	0.88 (0.69 to 1.13)
Interstitial edema	3	2,001	48.3 (46.2 to 50.5)	31.1 (28.2 to 34.2)	95.1 (93.6 to 96.3)	6.4 (3.4 to 12.2)	0.73 (0.68 to 0.78)
Cephalization	5	1,338	54.0 (51.3 to 56.6)	44.7 (41.1 to 48.4)	94.6 (92.6 to 96.3)	5.6 (2.9 to 10.4)	0.53 (0.39 to 0.72)
Alveolar edema	3	2,001	48.3 (46.2 to 50.5)	5.7 (4.7 to 6.9)	98.9 (98.4 to 99.3)	5.3 (3.3 to 8.5)	0.95 (0.94 to 0.97)
Lung ultrasonography							
Positive B-line scan*	8	1,914	48.2 (46.0 to 50.5)	85.3 (82.8 to 87.5)	92.7 (90.9 to 94.3)	7.4 (4.2 to 12.8)	0.16 (0.05 to 0.51)
Bedside echocardiography							
Restrictive mitral pattern†	1	125	43.2 (34.9 to 52.0)	81.5 (68.6 tp 90.7)	90.1 (80.7 to 95.9)	8.3 (4.0 to 16.9)	0.21 (0.12 to 0.36)

AHFS = acute heart failure syndrome; CI = confidence interval; LR = likelihood ratio.

*—Defined as ≥ 2 bilateral lung zones with ≥ 3 B lines per intercostal space.

†—Defined as E/A ratio > 2 or E/A ratio between 1 and 2 and deceleration time (DT) < 130 msec; DT < 130 msec alone if atrial fibrillation.

echocardiography of visually estimated reduced ejection fraction was somewhat helpful (LR+ = 4.1; 95% CI, 2.4 to 7.2), and the finding of restrictive mitral pattern was highly predictive of AHFS (LR+ = 8.3; 95% CI, 4.0 to 16.9).

TABLE 2

Notable Interval Likelihood Ratios of BNP and NT-proBNP Values

BNP value (pg per mL)	n	Interval LR (95% CI)	NT-proBNP (pg per mL)	N	Interval LR (95% CI)
0 to 100	617	0.14 (0.12 to 0.18)	0 to 100	150	0.09 (0.05 to 0.17)
800 to 1,000	130	5.00 (3.21 to 7.89)			
1,000 to 1,500	160	7.12 (4.53 to 11.18)			
1,500 to 2,500	105	8.33 (4.60 to 15.12)			
2,500 to 5,001	65	8.91 (4.09 to 19.43)			

BNP = brain natriuretic peptide; CI = confidence interval; LR = likelihood ratio; NT-proBNP = N-terminal proBNP.

Caveats: Patients presenting to the emergency department with dyspnea are different than patients presenting to the primary care clinic with more subacute, less severe dyspnea. Although this possible spectrum bias may potentially influence study validity, the review analyzed all emergency department patients who presented with dyspnea and did not discriminate between time courses of presenting illness.[2] Therefore, index test operative characteristics should maintain applicability, but considering the likely lower AHFS prevalence (and lower pretest probability) in the clinic population, relatively more tests may be required to confirm AHFS in the primary care clinic setting.

The estimation of each index test's diagnostic accuracy was limited by the lack of a true, objective criterion or "gold" standard against which the test was measured. The criterion standard for AHFS was typically a subjective assessment by two or more physicians with data from the clinical record. The review did not evaluate the diagnostic accuracy of historical elements, symptoms, or examination findings in combination, also known as clinical gestalt.[2] Clinical gestalt likely outperforms these diagnostic elements in isolation and plays an important role in determining the pretest probability of AHFS.

The studies that were included in the review varied in quality.[2] Differences in inclusion and exclusion criteria among the included studies put them at varying degrees of risk for spectrum bias, and the consideration of pooled results should factor in the moderate to high statistical heterogeneity among included studies. With regards to the natriuretic peptide analyses, this review did not consider age as a variable that may alter BNP and NT-proBNP values. Age-stratified NT-proBNP cut points have since been demonstrated to be moderately useful in the diagnosis of AHFS.[3]

The accuracy of lung ultrasonography will be provider-dependent, but emergency physician sonographers in most included studies were workshop-trained only. Furthermore, trainees may rapidly achieve procedural competency,[4] and lung ultrasonography has been shown to have fair predictive value for pulmonary edema from AHFS when performed by novices and experts.[5] Lastly, the performance of lung ultrasonography is likely time-sensitive because B-line artifacts appear to decrease coincident with treatment for lung edema caused by AHFS[6] or other etiology.[7]

Conclusion: The individual components of the clinical history and physical examination, ECG, and chest radiography are not useful independently for confirming or excluding the diagnosis of AHFS in patients presenting to the emergency department. BNP concentrations above 800 pg per mL are helpful for establishing the diagnosis. BNP and NT-proBNP results are also valuable in ruling out AHFS when concentrations are below the threshold of 100 pg per mL. Lung ultrasonography, although provider-dependent, may be learned quickly and appears to have the best combination of test characteristics to confirm or exclude the diagnosis of AHFS.

This series is coordinated by Dean A. Seehusen, MD, MPH, *AFP* Assistant Medical Editor, and Daniel Runde, MD, from the NNT Group.

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Author disclosure: No relevant financial affiliations.

References

1. Adams KF Jr, Fonarow GC, Emerman CL, et al.; ADHERE Scientific Advisory Committee and Investigators. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J*. 2005;149(2):209-216.
2. Martindale JL, Wakai A, Collins SP, et al. Diagnosing acute heart failure in the emergency department: a systematic review and meta-analysis. *Acad Emerg Med*. 2016;23(3):223-242.
3. Januzzi JL Jr, Chen-Tournoux AA, Christenson RH, et al.; ICON-RELOADED Investigators. N-Terminal pro-B-type natriuretic peptide in the emergency department: the ICON-RELOADED study. *J Am Coll Cardiol*. 2018;71(11):1191-1200.
4. See KC, Ong V, Wong SH, et al. Lung ultrasound training: curriculum implementation and learning trajectory among respiratory therapists. *Intensive Care Med*. 2016;42(1):63-71.
5. Chiem AT, Chan CH, Ander DS, Kobylivker AN, Manson WC. Comparison of expert and novice sonographers' performance in focused lung ultrasonography in dyspnea (FLUID) to diagnose patients with acute heart failure syndrome. *Acad Emerg Med*. 2015;22(5):564-573.
6. Martindale JL, Secko M, Kilpatrick JF, et al. Serial sonographic assessment of pulmonary edema in patients with hypertensive acute heart failure. *J Ultrasound Med*. 2018;37(2):337-345.
7. Noble VE, Murray AF, Capp R, Sylvia-Reardon MH, Steele DJ, Litepol A. Ultrasound assessment for extravascular lung water in patients undergoing hemodialysis. Time course for resolution. *Chest*. 2009;135(6):1433-1439. ■