The Third Heart Sound for Diagnosis of Acute Heart Failure

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Dyspnea is a common presenting complaint in the emergency department (ED). Rapid identification of heart failure as the etiology leads to early implementation of targeted therapies. Although having only intermediate sensitivity, the S3 is a highly specific finding among older adults with heart failure. Identification of an S3 by routine auscultation can be problematic given the chaotic and noisy ED environment, patient comorbid conditions, and intolerance of ideal positioning for auscultation. Technologies using computerized analysis of digitally recorded heart tones have recently been developed to aid the clinician with bedside detection of abnormal heart sounds. Data using these technologies and their applications in the ED are reviewed as well as implications for future use and research.

Introduction

Dyspnea is a common complaint that leads to as many as 2.5 million clinician visits per year in the United States [1]. Numerous disorders can cause this sensation of uneasy breathing or respiratory distress including heart failure, asthma, chronic obstructive pulmonary disease (COPD), metabolic acidosis, airway obstruction, neuromuscular disorders, and anxiety/panic disorder. Rapid identification of those with heart failure leads to the early implementation of appropriate, evidence-based, and symptomatic therapies.

Heart failure is a global public health issue of epidemic proportions [2] and represents a tremendous burden to overall healthcare costs. At least 5 million Americans have heart failure, and approximately 550,000 new cases are diagnosed each year in the United States alone [3]. The incidence is expected to continue to increase dramatically due to our aging population, improved survival from acute coronary syndromes, and advances in cardiovascular disease management [4–6]. Consequently, as many as 10 million people in the United States are expected to have heart failure by the end of this year [7]. With an estimated annual cost of 33.2 billion dollars, heart failure is among the costliest cardiovascular illnesses in the United States [3]. Hospitalization for heart failure exacerbation accounts for the largest care expenditure. In fact, Medicare data demonstrate an estimated cost of $5912 per discharge, more than double any cancer diagnosis [3,8•,9].

Heart failure is a complex clinical syndrome characterized by impaired myocardial performance including systolic or diastolic dysfunction, neuroendocrine system activation, and intravascular volume overload. It can be simplistically defined as a clinical syndrome resulting from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood [10]. The cardinal manifestations are dyspnea and fatigue (exercise intolerance) as well as fluid retention (pulmonary congestion and peripheral edema). A better emergency department (ED) or acute care term would be "acute heart failure syndrome" (AHFS), defined as a gradual or rapid change in heart failure signs and symptoms resulting in a need for urgent therapy [11]. These signs and symptoms are primarily due to pulmonary congestion from elevated left ventricular (LV) filling pressures and can occur in patients with preserved or reduced ejection fraction (EF). The term "diastolic dysfunction" refers to an abnormality of LV filling or relaxation; with the addition of effort intolerance and dyspnea, it is called "diastolic heart failure" or "acute heart failure with preserved EF" [12,13•14•]. AHFS admissions are about 50% female, approximately 75% will have known heart failure, and nearly 50% will have preserved EF [15–17]. The majority of heart failure in the western world is due to coronary artery disease, hypertension, and dilated cardiomyopathy.

In order to accurately diagnose this problem and avoid unnecessary health care costs, a well-defined method of diagnosis remains of primary importance. Although no "gold standard" exists, right heart catheterization and indirect measurement of EF via radionuclide scanning or

echocardiography proves to be reliable diagnostic tests. However, lack of immediate availability and cost make these studies prohibitive in the ED setting. As a result, an ED diagnosis of heart failure is often based on history and physical exam findings along with ancillary tests such as chest radiography and electrocardiography and more recently serum natriuretic peptide (brain natriuretic peptide [BNP] or proBNP) measurements.

ED Diagnosis of Heart Failure

Traditional history and physical examination findings have important shortcomings [8•]. Despite a high specificity for the presence of elevated filling pressures, jugular venous distention and a third heart sound (S3) have sensitivities of only 30% and 24% respectively [18,19]. Alternatively, the Valsalva maneuver can improve the sensitivity of physical examination for detection of LV dysfunction in a highly selected group of patients. However, this requires stable, cooperative patients that are able to hold their breath [20]. Other signs and symptoms of fluid overload such as lower extremity edema and dyspnea again raise the suspicion of heart failure, but their lack of sensitivity makes them poor screening tools [19]. In addition, chest radiography and electrocardiography are often inaccurate. Twenty percent of cardiomegaly noted on echocardiogram is missed on chest radiograph [21]. Pulmonary congestion can be minimal or absent in patients with significantly elevated pulmonary artery wedge pressures [22]. In a recent study, approximately one of every five ED patients with acute decompensated heart failure did not demonstrate signs of congestion on chest radiography [23•]. Standard electrocardiogram results also lack the sensitivity to act as a screening tool [24,25].

Even though pulmonary artery catheterization has been a widely used hemodynamic monitoring device for heart failure in critical care units, its use in the ED is very problematic. Recent studies have raised significant concerns that such catheters do not improve outcome and may have unacceptable complication rates. We are in need of noninvasive measurements of LV filling pressure applicable to both the critical care unit and ED [26–28].

Origin of S3/S4

The S3 occurs 0.12 to 0.16 seconds after the second heart sound [29] (Fig. 1). Among several proposed theories, the most likely explanation is that excessive rapid filling of a stiff ventricle is suddenly halted, causing vibrations that are audible as the S3. Pathologic states where an S3 is encountered include anemia, thyrotoxicosis, mitral regurgitation, hypertrophic cardiomyopathy, aortic and tricuspid regurgitation, and LV dysfunction [30]. The fourth heart sound (S4) occurs just before the first heart sound (S1) in the cardiac cycle. It is produced in late diastole as a result of atrial contraction causing vibrations of the LV muscle, mitral valve apparatus, and LV blood mass [31]. Disease processes that produce an S4 include hypertension, aortic stenosis and regurgitation, severe mitral regurgitation, cardiomyopathy, and ischemic heart disease [30].

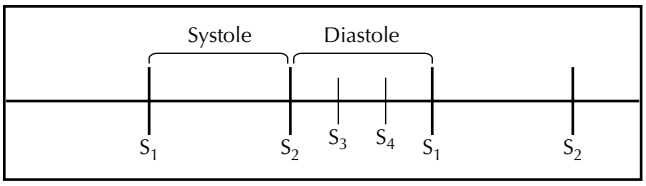

Figure 1. Location of heart sounds in the cardiac cycle.

Auscultation of the S3 and S4

Both an S3 and S4 are auscultated in similar fashion. Harvey [32] recommended the "inching" technique as a way to distinguish the often times pathologic S3 and S4 from the physiologic S1 and second heart sound (S2). In both situations, the patient is examined in the left lateral recumbent position using the bell of the stethoscope. Starting at the aortic area (where the S2 is the loudest), the examiner "inches" down to the cardiac apex, using the S2 as a reference point. If one encounters an extra sound in diastole, just after the S2, this is an S3 or diastolic gallop. The S3 is generally absent at the base, so that as the examiner moves toward the apex the S3 is encountered.

The opposite maneuver leads to the detection of an S4. Now, the examiner inches from the apex upward to the base. The S1 (heard loudest at the apex) is used as a reference because the S4 occurs in early systole, just before S1. If the stethoscope is moved away from the apex, the S4 disappears. In order to distinguish a split S1 from an S3/S4 (both lower frequency sounds than an S1) the examiner places pressure on the bell of the stethoscope. In this situation an S3/S4 will disappear, whereas a fixed split S1 will remain.

Significance of S3 and S4 Detection in Heart Failure

Identification of an S3/S4 by routine auscultation can be problematic. In the previously mentioned studies that suggest a low incidence of S3 detection in heart failure, it is possible that the physicians may have been unable to detect a sound that was truly present. Recent studies indicate that physicians are becoming less proficient at performing the physical examination, and physicians in residency programs have been shown to have poor cardiac auscultatory skills [33–37]. Furthermore, inter-observer agreement of S3 detection is poor, with board-certified cardiologists having no better agreement than house staff [38–40]. Exacerbating the difficulty of S3/S4 detection is that the ED environment is often loud, patients have many

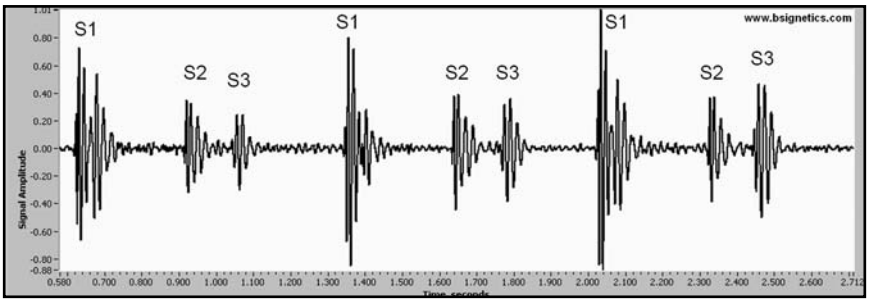

Figure 2. Phonocardiograph recording of three heart beats. Normal S1 and S2 with added S3. (*Courtesy of* Biosignetics Corp.)

confounding illnesses such as COPD and obesity that make detection difficult, and the patients may not tolerate being placed in the ideal examining position (recumbent or left lateral decubitus) because of their dyspnea and/or orthopnea. Thus, although detection of an S3/S4 may be useful as a diagnostic and prognostic tool in ED patients with dyspnea, the traditional method of auscultation is less than ideal.

The overall prevalence of an electronically detected S3 is 10% among asymptomatic adults, and its detection in older adults may be highly specific for cardiac pathology. Although detection of an S3 can be "normal" in adolescents and young adults, its detection after age 40 years is considered abnormal [30,41–43]. Traditionally insensitive for LV dysfunction, when detected, an S3 can be very predictive of elevated LV filling pressure. In a study of outpatients referred for cardiac catheterization, the detection of an S3 was the most specific finding of elevated LV end diastolic pressure (95%) [44]. Another study also found that the detection of an S3 has a high specificity and positive predictive value in detection of patients with low EFs [45]. Even more importantly, it has been suggested that patients with a detectable S3 have an increased risk of hospitalization and death compared with those patients without a detectable S3 [46–48].

It is not clear whether the presence of an audible S4 is predictive of cardiac disease. Although an electronically detected S4 increases in prevalence with increasing age, it may be less common than previously reported [49•]. Using phonocardiogaphic technology available in the 1970s, Spodick and Quarry [50] found the presence of an S4 to be no more common in patients with heart disease than those without. Previous phonocardiographic studies have found a prevalence of S4s from as low as 11% [51] to as high as 75% [52] as well as many values in between [50,53–57]. These studies may have overestimated the prevalence of S4 when compared with routine auscultation due to the overlapping low frequency sound range of the S4 (10–50 Hz) with the typical frequencies of the S1 (30–150 Hz), thus making it difficult to distinguish an S4 from a split S1 [49•].

New Technologies

Technology has recently been developed to aid the clinician with bedside detection of an S3 by digitally recording and analyzing heart tones using an electronic stethoscope or other means (Phonocardiograph and Heart Energy Signature software [Biosignetics, Inc., Exeter, NH; Inovise Medical, Inc., Portland, OR]) These provide unique and valuable information to the examining physician at the bedside about pathologic heart sounds (S3/S4) and murmurs.

One such platform converts complex multi-component non-gaussian heart sounds into simple images. It is based on an application that reads sound, vibration, or any other dynamic time-varying data files and processes them to estimate characteristic energy signatures jointly in time and frequency space. This technology allows rapid computation and provides convenient post-processing options and a graphic user interface. The Phonocardiograph Monitor displays and records heart sounds from an electronic stethoscope, as well as abnormal sound grades, intensity, and pitch (Fig. 2). The Heart Energy Signature system allows instant visual detection of abnormalities and detailed characterization of power and pitch variation for each sound component by representing the heart sound as a visual image and obtaining quantitative characteristics of power and pitch variation in time (Fig. 3). The printout can be displayed on a laptop.

Audicor (Inovise Medical, Inc., Portland, OR) is a portable acoustic cardiograph integrated with a standard 12-lead electrocardiogram (Fig. 4). Phonocardiographic evidence of heart sounds is determined by a computerized algorithm that reports several different phonocardiographic measures, including the presence of an S3 and S4 gallop, electromechanical activation time (duration from QRS onset to mitral valve closure), and LV systolic time. This method has been previously validated in studies comparing the detection of S3 and S4 to hemodynamic measurements obtained during cardiac catheterization [58]. Both V3 and V4 channels are analyzed by the algorithm for the presence of abnormal diastolic heart sounds, using the electrocardiogram as a timing marker and frequency content appropriate for the gallops.

Using this system, Collins et al. [59•] determined the sensitivity of an electronic S3 to be 34% and the specificity to be 93% and found that the presence of an electronically detected S3 in combination with an indeterminate BNP (100–500 pg/mL) increased the positive likelihood ratio (LR) for primary heart failure diagnosis from 1.3 to 2.9 and increased the positive predictive value from 54% to 80%. In a related study, Collins et al. [60•] documented

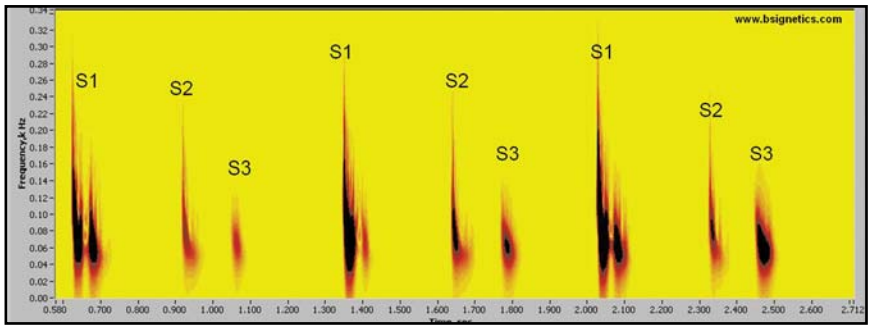

Figure 3. Heart energy signature of three heart beats. (*Courtesy of* Biosignetics Corp.)

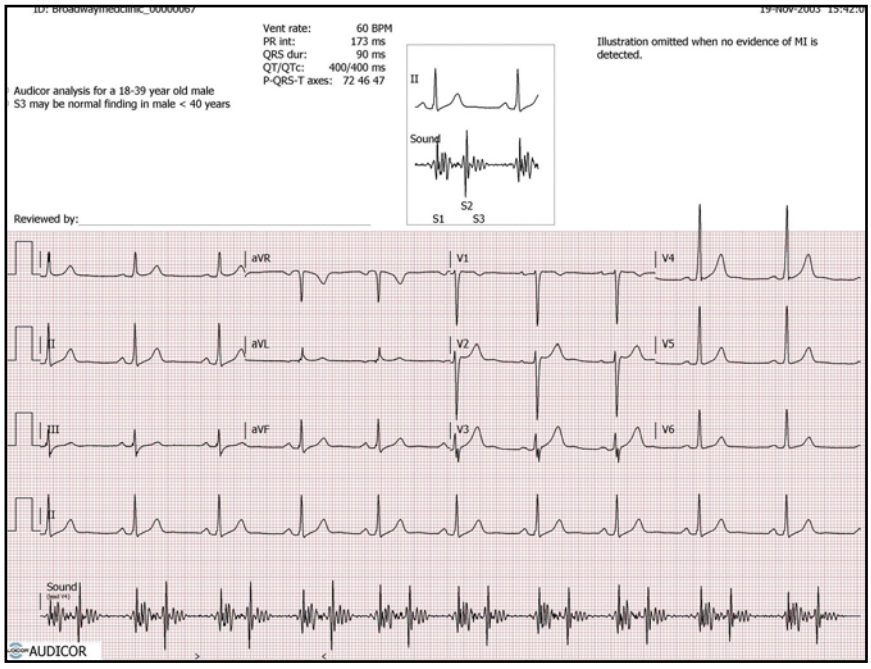

Figure 4. The Audicor system reports the presence of an S3 (*top*) and provides a sound tracing (*bottom*) in this version paired with a standard electrocardiogram. (*Courtesy of* Inovise Medical, Inc.)

the electronic presence of an S3 in over 50% of ED patients with the diagnosis of primary heart failure prior to treatment with vasodilators or diuretics. The S3 prevalence was reduced to 29% when heart sounds were analyzed following treatment with diuretics, vasodilators or both. The S4 was similarly decreased after treatment [60•].

In a recent meta-analysis, Wang et al. [8•] found that an auscultated S3 had the largest positive LR among physical exam findings (positive LR, 11; 95% CI, 4.9–25) for accurately detecting heart failure. The LR was even higher among those with underlying pulmonary disease (asthma/COPD) (positive LR, 57; 95% CI, 7.6–425) [8•]. Additionally, Shapiro et al. [61•] described a LV dysfunction index which combined S3 and systolic time interval data obtained using the Audicor system. This index (using a cutoff of > 1.87) had 72% sensitivity, 92% specificity, a positive LR of 9.0, and an accuracy of 88% in predicting LV dysfunction. When applied in patients with intermediate BNP levels (100–500 pg/mL) the LR for LV dysfunction increased from 1.1 for BNP alone to 7.1 when the summary index was added [61•]. Other preliminary results have shown an improvement in ED physician diagnostic confidence and additive independent prognostic information [59•,62].

These newer technologies for the phonocardiographic detection of added heart tones should improve significantly our ability to detect abnormal extra heart sounds in the chaotic and noisy ED environment and may potentially lead to improved diagnostic and prognostic abilities. These tools may also be used to grade the severity of heart failure, track responses to therapeutic interventions or even follow worsening disease.

Conclusions

Although the S3 gallop may be difficult to detect in the ED, its presence has a high specificity and positive LR for the presence of heart failure, even among those with underlying pulmonary disease. It can be combined with serum BNP for better diagnostic accuracy. New technologies have been developed to electronically detect the presence of added heart sounds which can be used to help differentiate LV dysfunction from other causes of dyspnea, assess response to therapy, or possibly track worsening severity of disease. The overall

utility and usefulness of these newer technologies in the ED setting needs further study, although preliminary results are promising.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Springfield CL, Sebat F, Johnson D, et al.: **Utility of impedance cardiography to determine cardiac vs noncardiac cause of dyspnea in the emergency department.** *Congest Heart Fail* 2004, **10(Suppl 2):**14–16.
2. Tsao LG, Gibson CM: **Heart failure: an epidemic of the 21st century.** *Crit Pathways Cardiol* 2004, **3:**194–204.
3. *American Heart Association: Heart Disease and Stroke Statistics—2007 Update.* Dallas: American Heart Association; 2007.
4. McCullough PA: **Scope of cardiovascular complications in patients with kidney disease.** *Ethn Dis* 2002, **12:**S3–44-8.
5. O'Connell JE, Brown J, Hildreth AJ, Gray CS: **Optimizing management of congestive heart failure in older people.** *Age Ageing* 2000, **29:**371–372.
6. Croft JB, Giles WH, Pollard RA, et al.: **Heart failure survival among older adults in the United States: a poor prognosis for an emerging epidemic in the Medicare population.** *Arch Intern Med* 1999, **159:**505–510.
7. Rich MW: **Epidemiology, pathophysiology, and etiology of congestive heart failure in older adults.** *J Am Geriatr Soc* 1997, **45:**968–974.
8. • Wang CS, FitzGerald JM, Schulzer M, et al.: **Does this dyspneic patient in the emergency department have congestive heart failure?** *JAMA* 2005, **294:**1944–1956.

This meta-analysis revealed that the presence of a detectable S3 increases the positive LR for the presence of congestive heart failure the most among physical exam findings, even in those patients with underlying pulmonary disease.

9. Hunt SA: **ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure).** *J Am Coll Cardiol* 2005, **46:**e1–82.
10. Hunt SA, Abraham WT, Chin MH, et al.: **ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society.** *Circulation* 2005, **112:**e154–235.
11. Gheorghiade M, Zannad F, Sopko G, et al.: **Acute heart failure syndromes: current state and framework for future research.** *Circulation* 2005, **112:**3958–3968.
12. Aurigemma GP, Gaasch WH: **Clinical practice. Diastolic heart failure.** *N Engl J Med* 2004, **351:**1097–1105.
13. • Bhatia RS, Tu JV, Lee DS, et al.: **Outcome of heart failure with preserved ejection fraction in a population-based study.** *N Engl J Med* 2006, **355:**260–269.

This population-based study showed that a significant proportion of patients with new-onset heart failure had a preserved EF of greater than 50% and that the 1-year mortality did not differ significantly from those with a reduced EF.

14. • Owan TE, Hodge DO, Herges RM, et al.: **Trends in prevalence and outcome of heart failure with preserved ejection fraction.** *N Engl J Med* 2006, **355:**251–259.

This study revealed that the prevalence of congestive heart failure with preserved EF may be increasing while overall mortality is unchanged.

15. Adams KF Jr, Fonarow GC, Emerman CL, et al.: **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:**209–216.
16. Cleland JG, Swedberg K, Follath F, et al.: **The EuroHeart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis.** *Eur Heart J* 2003, **24:**442–463.
17. Komajda M, Follath F, Swedberg K, et al.: **The EuroHeart Failure Survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 2: treatment.** *Eur Heart J* 2003, **24:**464–474.
18. Davie AP, Francis CM, Caruana L, et al.: **Assessing diagnosis in heart failure: which features are any use?** *QJM* 1997, **90:**335–339.
19. Stevenson LW, Perloff JK: **The limited reliability of physical signs for estimating hemodynamics in chronic heart failure.** *JAMA* 1989, **261:**884–888.
20. Zema MJ, Restivo B, Sos T, et al.: **Left ventricular dysfunction—bedside Valsalva manoeuvre.** *Br Heart J* 1980, **44:**560–569.
21. Kono T, Suwa M, Hanada H, et al.: **Clinical significance of normal cardiac silhouette in dilated cardiomyopathy—evaluation based upon echocardiography and magnetic resonance imaging.** *Jpn Circ J* 1992, **56:**359–365.
22. Mahdyoon H, Klein R, Eyler W, et al.: **Radiographic pulmonary congestion in end-stage congestive heart failure.** *Am J Cardiol* 1989, **63:**625–627.
23. • Collins SP, Lindsell CJ, Storrow AB, Abraham WT: **Prevalence of negative chest radiography results in the emergency department patient with decompensated heart failure.** *Ann Emerg Med* 2006, **47:**13–18.

This study used national heart failure registry data (ADHERE) to demonstrate a lack of chest radiograph findings in almost one of five patients with acute decompensated heart failure.

24. Rihal CS, Davis KB, Kennedy JW, Gersh BJ: **The utility of clinical, electrocardiographic, and roentgenographic variables in the prediction of left ventricular function.** *Am J Cardiol* 1995, **75:**220–223.
25. Silver MT, Rose GA, Paul SD, et al.: **A clinical rule to predict preserved left ventricular ejection fraction in patients after myocardial infarction.** *Ann Intern Med* 1994, **121:**750–756.
26. Harvey S, Harrison DA, Singer M, et al.: **Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial.** *Lancet* 2005, **366:**472–477.
27. Binanay C, Califf RM, Hasselblad V, et al.: **Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial.** *JAMA* 2005, **294:**1625–1633.
28. Richard C, Warszawski J, Anguel N, et al.: **Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: a randomized controlled trial.** *JAMA* 2003, **290:**2713–2720.
29. Sokolow M: **Physical Examination.** In *Clinical Cardiology,* 5 edn. Norwalk, CT: Appleton & Lange; 1990.
30. Reddy PS, Salerni R, Shaver JA: **Normal and abnormal heart sounds in cardiac diagnosis: Part II. Diastolic sounds.** *Curr Probl Cardiol* 1985, **10:**1–55.
31. Abrams J: **Current concepts of the genesis of heart sounds. II. Third and fourth sounds.** *JAMA* 1978, **239:**2029–2030.
32. Harvey WPL: **Cardiac pearls.** *Dis Mon* 1994, **40:**41–113.

33. Adolph RJ: **In defense of the stethoscope.** *Chest* 1998, **114:**1235–1237.
34. Craige E: **Should auscultation be rehabilitated?** *N Engl J Med* 1988, **318:**1611–1613.
35. Fletcher RH, Fletcher SW: **Has medicine outgrown physical diagnosis?** *Ann Intern Med* 1992, **117:**786–787.
36. Marcus GM, Vessey J, Jordan MV, et al.: **Relationship between accurate auscultation of a clinically useful third heart sound and level of experience.** *Arch Intern Med* 2006, **166:**617–622.
37. Weitz HH, Mangione S: **In defense of the stethoscope and the bedside.** *Am J Med* 2000, **108:**669–671.
38. Lok CE, Morgan CD, Ranganathan N: **The accuracy and interobserver agreement in detecting the 'gallop sounds' by cardiac auscultation.** *Chest* 1998, **114:**1283–1288.
39. Ishmail AA, Wing S, Ferguson J, et al.: **Interobserver agreement by auscultation in the presence of a third heart sound in patients with congestive heart failure.** *Chest* 1987, **91:**870–873.
40. Held P, Lindberg B, Swedberg K: **Audibility of an artificial third heart sound in relation to its frequency, amplitude, delay from the second heart sound and the experience of the observer.** *Am J Cardiol* 1984, **53:**1169–1172.
41. Reddy PS: **The third heart sound.** *Int J Cardiol* 1985, **7:**213–221.
42. Sloan A: **Cardiac gallop Rhythm.** *Medicine (Baltimore)* 1958, **37:**197–215.
43. Evans W: **The use of the phonocardiograph in clinical medicine.** *Lancet* 1951, **1:**1083–1085.
44. Harlan WR, Oberman A, Grimm R, Rosati RA: **Chronic congestive heart failure in coronary artery disease: clinical criteria.** *Ann Intern Med* 1977, **86:**133–138.
45. Patel R, Bushnell DL, Sobotka PA: **Implications of an audible third heart sound in evaluating cardiac function.** *West J Med* 1993, **158:**606–609.
46. Drazner MH, Rame JE, Dries DL: **Third heart sound and elevated jugular venous pressure as markers of the subsequent development of heart failure in patients with asymptomatic left ventricular dysfunction.** *Am J Med* 2003, **114:**431–437.
47. Rame JE, Sheffield MA, Dries DL, et al.: **Outcomes after emergency department discharge with a primary diagnosis of heart failure.** *Am Heart J* 2001, **142:**714–719.
48. Glover DR, Littler WA: **Factors influencing survival and mode of death in severe chronic ischaemic cardiac failure.** *Br Heart J* 1987, **57:**125–132.
49.• Collins SP, Arand P, Lindsell CJ, et al.: **Prevalence of the third and fourth heart sound in asymptomatic adults.** *Congest Heart Fail* 2005, **11:**242–247.

This study evaluated the presence of electronically detectable S3 and S4 among 1329 asymptomatic adults.

50. Spodick DH, Quarry VM: **Prevalence of the fourth heart sound by phonocardiography in the absence of cardiac disease.** *Am Heart J* 1974, **87:**11–14.
51. Bethell HJ, Nixon PGL **Atrial gallop in coronary heart disease without overt infarction.** *Br Heart J* 1974, **36:**682–686.
52. Benchimol A, Desser KBL: **The fourth heart sound in patients without demonstrable heart disease.** *Am Heart J* 1977, **93:**298–301.
53. Aronow WS, Uyeyama RR, Cassidy J, Nebolon J: **Resting and postexercise phonocardiogram and electrocardiogram in patients with angina pectoris and in normal subjects.** *Circulation* 1971, **43:**273–277.
54. Erikssen J, Rasmussen K: **Prevalence and significance of the fourth heart sound (S4) in presumably healthy middle-aged men, with particular relation to latent coronary heart disease.** *Eur J Cardiol* 1979, **9:**63–75.
55. Jordan MD, Taylor CR, Nyhuis AW, Tavel ME: **Audibility of the fourth heart sound. Relationship to presence of disease and examiner experience.** *Arch Intern Med* 1987, **147:**721–726.
56. Prakash R, Aytan N, Dhingra R, et al.: **Variability in the detection of a fourth heart sound—its clinical significance in elderly subjects.** *Cardiology* 1974, **59:**49–56.
57. Swistak M, Mushlin H, Spodick DH: **Comparative prevalence of the fourth heart sound in hypertensive and matched normal persons.** *Am J Cardiol* 1974, **33:**614–616.
58. Marcus GM, Gerber IL, McKeown BH, et al.: **Association between phonocardiographic third and fourth heart sounds and objective measures of left ventricular function.** *JAMA* 2005, **293:**2238–2244.
59.• Collins SP, Lindsell CJ, Peacock WF, et al.: **The combined utility of an S3 heart sound and B-type natriuretic peptide levels in emergency department patients with dyspnea.** *J Card Fail* 2006, **12:**286–292.

This study demonstrates that an electronically detected S3 is highly specific for heart failure and when used in combination with intermediate BNP levels increase positive LRs and the positive predictive value for the presence of heart failure.

60.• Collins SP, Lindsell CJ, Peacock WFT, et al.: **The effect of treatment on the presence of abnormal heart sounds in emergency department patients with heart failure.** *Am J Emerg Med* 2006, **24:**25–32.

This study demonstrates the potential usefulness of the electronically detected S3 in assessing response to treatment for heart failure.

61.• Shapiro M, Moyers B, Marcus GM, et al.: **Diagnostic characteristics of combining phonocardiographic third heart sound and systolic time intervals for the prediction of left ventricular dysfunction.** *J Card Fail* 2007, **13:**18–24.

This study demonstrates the usefulness of an electronically detected S3 and other noninvasive data in the assessment of LV dysfunction.

62. Collins S, Peacock F, Clopton P, et al.: **Heart Failure and Audicor Technology for Rapid Diagnosis and Initial Treatment of ED Patients with Suspected Heart Failure (HEARD-IT).** *Acad Emerg Med* 2007, **14(Suppl 1):**S164.