REVIEW PAPER

The Utility of Heart Sounds and Systolic Intervals Across the Care Continuum

Acoustic cardiography is an exciting, new, easy-to-use, modernized technology that incorporates already proven techniques of phonocardiography. Application of acoustic cardiography to clinical practice can improve diagnosis and management of heart failure patients. Its clinical use should help address some of the need for robust, inexpensive, and widely accessible technology for proactive heart failure diagnosis and management. Acoustic cardiographically recorded measurements have been correlated with both cardiac catheterization and echocardiographically determined hemodynamic parameters. Heart sounds captured by acoustic cardiograms have proven to assist clinicians in assessing dyspneic patients in the emergency department by utilizing the strong specificity of an S_3 for detecting acute decompensated heart failure. Acoustic cardiography offers a cost-efficient, easy-to-use method to optimize the devices used in cardiac resyncronization therapy. The rapidly and easily obtainable information gathered by acoustic cardiography should foster its more widespread use in diagnosis and treatment of heart failure, including cardiac resyncronization therapy device optimization. (CHF. 2006;12(4 suppl 1):2–7) ©2006 Le Jacq

Heart failure (HF) currently affects over 5 million Americans, with roughly 500,000 new cases each year. It accounts for 12–15 million office visits and 6.5 million hospital days annually. Despite new and improved treatments, HF results in 300,000 deaths each year as a primary or contributory cause. The rapid growth of HF has made it a disease of epidemic proportions that has a tremendous clinical and financial impact on the US health care system. With 5-year mortality rates approaching 50%, it is the most common cause of hospitalization in patients older than 65 years and is the single most expensive diagnosis in the United States. In 2001, there were almost one million hospital discharges for decompensated HF, at a cost of more than $20 billion. The average hospital loses more than $1000 per HF admission.[1]

HF care in 2006 has shown dramatic progress over the past several years, and many more options are currently available than was the case as recently as the early 1990s. With the discovery and clinical application of new biomarkers, such as B-type natriuretic peptide (BNP) and the rapidly expanding field of implantable devices, HF care has become an emergent subspecialty within the field of cardiology. However, despite the progress made within the HF arena, there remains significant unmet clinical need. Because HF occurs most frequently in the elderly, a population with many simultaneous comorbidities, it can be a challenging diagnosis in the emergency department (ED). Moreover, since its most common presentation is dyspnea, a symptom that is common to many diseases, misdiagnosis is routine. Even in the BNP era, accurate diagnosis of acute decompensated HF (ADHF) at ED presentation remains difficult. BNP has aided in "ruling out" ADHF with its high negative predictive value, but due to the limited positive predictive value and specificity of abnormal BNP values, problems with accurately "ruling in" ADHF persist. Results from a large prospective blinded study have shown that 18.5% of ED HF diagnoses are inaccurate.[2]

Medical therapies, such as angiotensin-converting enzyme inhibitors, β blockers, and spironolactone, have led to marked improvements in both symptom control and overall survival in patients with HF.[3–5] The addition of devices such as implantable cardioverter-defibrillators and pacemakers have also proven beneficial.[6] Some HF

W. Frank Peacock, MD;[1] Alex Harrison, MD;[2] Alan S. Maisel, MD[3]
From the Department of Emergency Medicine, Cleveland Clinic, Cleveland, OH;[1] the Division of Cardiology, Department of Medicine, University of California, Irvine Medical Center, Orange, CA;[2] and the Department of Medicine, Veterans Affairs San Diego Healthcare System and University of California, San Diego, San Diego, CA[3]
Address for correspondence: Alex Harrison, MD, Division of Cardiology, Department of Medicine, University of California, Irvine, 101 The City Drive, Building 53, Route 81, Room 100, Orange, CA 92868-4080
E-mail: alexharrisonmd@hotmail.com

patients benefit from simultaneous pacing of both ventricles (biventricular, or BiV, pacing) or of one ventricle in patients with bundle branch block. This approach is referred to as cardiac resynchronization therapy (CRT) and is recommended in advanced HF (usually New York Heart Association class III or IV), severe systolic dysfunction (e.g., ejection fraction ≤35%), and intraventricular conduction delay (e.g., QRS >120 milliseconds).[7–11] The rationale behind CRT is that it improves pump performance and reverses ventricular remodeling. Importantly, when BiV pacing is used, the delay between atrial and ventricular stimulation (the AV delay) should be adjusted to achieve the maximum attainable cardiac output. Studies have suggested that the optimal AV delay can be defined by Doppler echocardiography[12]; however, this is a limited resource in many environments.

Unfortunately, expensive and highly programmable CRT devices have been shown in real-world practice to have a 30% nonresponder rate.[13] This may be largely attributable to the fact that only 10% of CRT devices are optimized and is in stark contrast to the randomized controlled clinical trials that led to the approval of CRT devices.[7–11] There continues to be a tremendous need for robust, inexpensive, widely accessible, and easy-to-use technology that is highly specific for proactive HF diagnosis and management.

Heart sounds and systolic time intervals recorded in an acoustic cardiogram may improve the areas of weakness in the current HF era and have proven valuable in assisting clinical diagnostic and management challenges encountered during HF care.

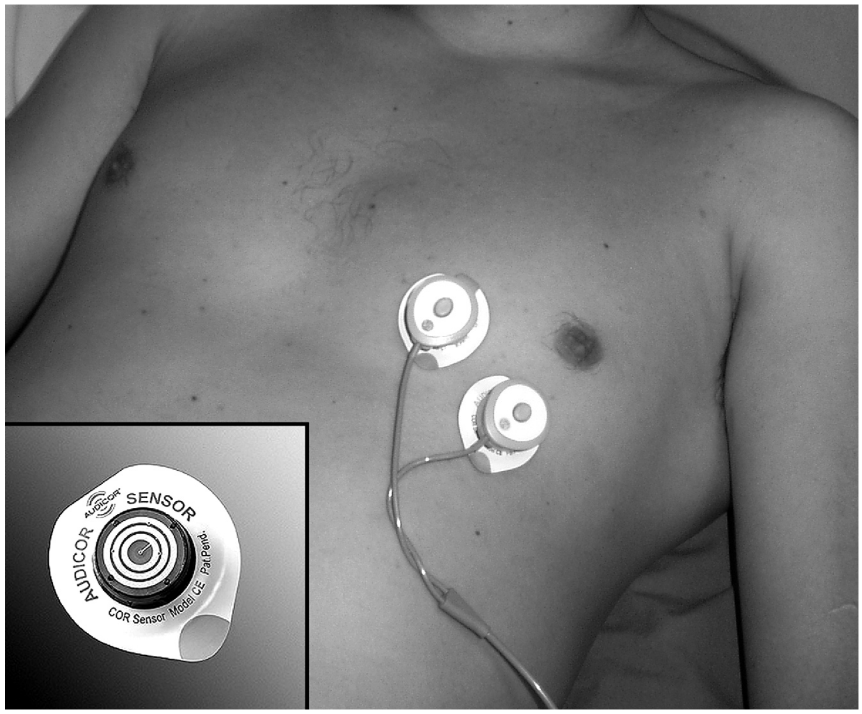

Figure 1. Placement of the AUDICOR sensors (Inovise Medical, Inc., Portland, OR)

Heart Sounds and Systolic Time Intervals

Auscultation of heart sounds has been a diagnostic tool employed by clinicians to detect abnormalities associated with cardiac dysfunction for centuries. Potain[14] first described abnormal diastolic cardiac sounds in the literature in 1880. With relatively normal heart rates, S_3, also known as a ventricular gallop, occurs 0.12–0.16 sec after the S_2 in early diastole.[15] The most likely explanation for the extra sound producing the S_3 is that vigorous and excessively rapid filling of blood into a stiff ventricle is suddenly halted, causing vibrations audible as the S_3.[16] The S_4, also known as an atrial gallop, occurs after P-wave onset and before the S_1 in the cardiac cycle. The S_4 occurs as blood enters a relatively noncompliant ventricle late in diastole because of atrial contraction and causes vibrations of the left ventricular (LV) muscle, mitral valve apparatus, and LV blood mass.[17]

The auscultated S_3 and S_4 have long been used as clinical signs of heart disease with both diagnostic and prognostic importance.[18–23] However, the value of these physical findings has been diminished by reports of poor accuracy and a large degree of interobserver variability.[24,25] In addition, it has been well documented that physician physical examination skills have deteriorated and are not emphasized during training as much as they once were.[26] The phonocardiogram has traditionally been the gold standard tool for the detection of extra heart sounds because it produces objective data that is reproducible and quantifiable. Phonocardiography has been used to understand the mechanisms and associated clinical characteristics of diastolic sounds,[27–30] and results of phonocardiography have been used to determine the accuracy of physician auscultation.[25] In addition to providing objective measures of heart sounds, phonocardiography used in conjunction with a carotid pulse tracing allows for the collection of valuable data about systolic time intervals.[31,32] While phonocardiography provides reliable and objective information, obtaining the data has proven difficult, timely, and cumbersome and requires a technician with specialized skill to operate the device. Consequently, its use has been supplanted by echocardiography.

With the invention of new technology, the phonocardiogram has recently been reincarnated as a newer modern version of the older proven technique. This newly renovated phonocardiogram is called an acoustic cardiogram. By replacing the standard V_3 and V_4

Table. Definitions of Diastolic Time Intervals		
ABBREVIATION	CARDIAC CYCLE TERMINOLOGY	DEFINITION
EMAT	Electromechanical activation time	Time from the Q-wave onset to mitral valve closure (S_1)
LVST	Left ventricular systolic time	Time from mitral valve closure (S_1) to aortic valve closure (S_2); includes the IVCT
PEP	Pre-ejection period	Time from Q-wave onset to aortic valve opening; includes the IVCT
LVET	Left ventricular ejection time	Time when the left ventricle is actively ejecting blood into the aorta (time from aortic valve opening to aortic valve closure)
IVRT	Isovolumic relaxation time	Time when the left ventricle relaxes during early diastole before any filling occurs (time after the aortic valve closes and before the mitral valve opens)
IVCT	Isovolumic contraction time	Time during contraction of the ventricle after the mitral valve closes and before the aortic valve opens

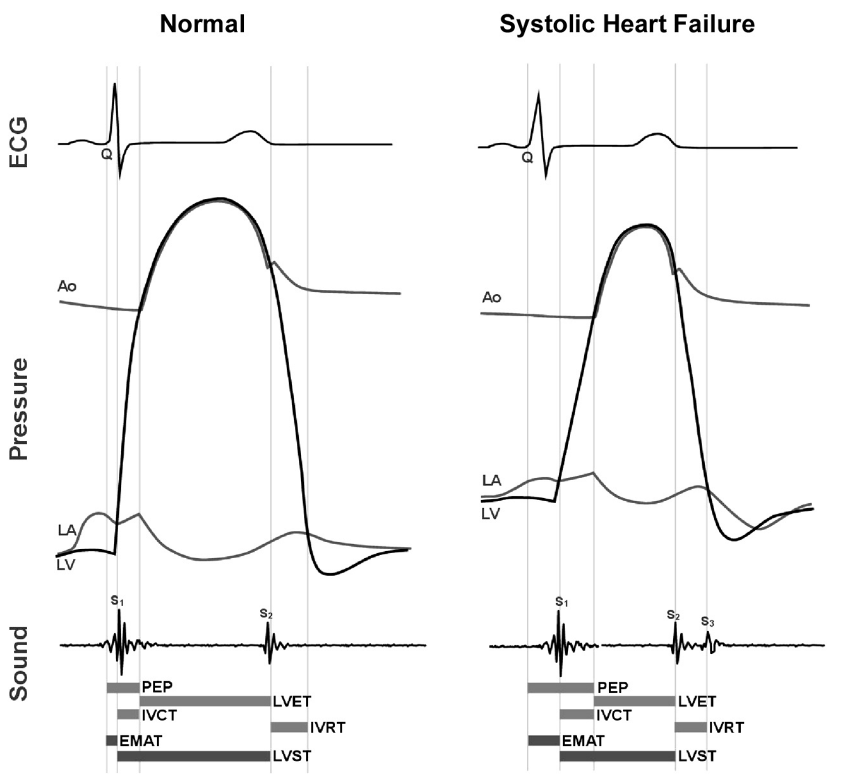

Figure 2. Heart sounds and systolic time interval data provided by the AUDICOR device (Inovise Medical, Inc., Portland, OR). (Pressure waveforms are provided here for convenience of reference and are not part of the AUDICOR data.) ECG=electrocardiogram; Ao=aorta; LA=left atrium; LV=left ventricle; PEP=pre-ejection period; LVET=left ventricular ejection time; IVCT=isovolumic contraction time; IVRT=isovolumic relaxation time; EMAT=electromechanical activation time; LVST=left ventricular systolic time

leads with newly designed sensors, both sound and electrical information can be gathered. To process the acoustic cardiogram data, Inovise Medical, Inc. (Portland, OR) has developed the AUDICOR technology. This is a system that records, stores, displays, and algorithmically interprets the simultaneous digital electrocardiographic (ECG) and acoustical data (Figure 1). The strengths of this system are that it does not require a pulse sensor, works in noisy environments (e.g., in an ED where accurate auscultation may be difficult), and has relatively forgiving sensor placement. Computer algorithms allow for rapid, reproducible, and objective data to be generated and analyzed for prompt clinical use. Acoustic cardiography can provide objective measurements of heart sounds as well as valuable information about systolic time intervals that have proven useful in a variety of clinical settings (Figure 2, Table). A detailed investigation and discussion of the hemodynamic correlates of the S_3 and systolic time interval follows in this supplement.[33]

Acoustic Cardiography and Its Correlation to Gold Standards

Acoustic cardiography is a validated, rapid, and noninvasive means to assess cardiac hemodynamics. It has been compared with cardiac catheterization, an invasive procedure that represents the gold standard of cardiac hemodynamics. Acoustic cardiography has also been compared with echocardiography, a similarly noninvasive method to assess cardiac hemodynamics. However, both cardiac catheterization and echocardiography are much more costly, time-consuming, and highly limited resources.

Recent studies demonstrated the relationship between various measurements of cardiac hemodynamics. In one report, 100 subjects each underwent acoustic cardiography, echocardiography, BNP measurement, and left heart catheterization within a 4-hour period. These studies demonstrated that there was a strong association between the presence of an S_3 and a number of parameters, including the incidence of HF diagnosis, depressed LV ejection fraction, elevated LV end-diastolic pressure, abnormal ventricular relaxation, and tissue Doppler imaging assessments indicative of ventricular dysfunction (e.g., increased deceleration rate of early mitral valve inflow patterns).[34,35] While BNP values performed well in predicting the absence of HF, they fared poorly in predicting depressed LV ejection fraction and elevated LV end-diastolic pressure. Therefore, acoustic cardiography can help "rule in" certain diagnoses with its high specificity for ventricular dysfunction and abnormal cardiac hemodynamics,[35] thus supplementing the clinical impression in precisely the range where BNP performs poorly. In addition, systolic time interval data have proven to correlate well with hemodynamic measures: the LV systolic time correlates well with the LV ejection fraction, and the electromechanical activation time correlates with measures of cardiac contractility (dP/dt).[35,36] This easily and rapidly obtainable information has been proven to assist clinicians in assessing dyspneic patients in the ED and in other areas of HF management and could be widely implemented to help proactive HF diagnosis and management.

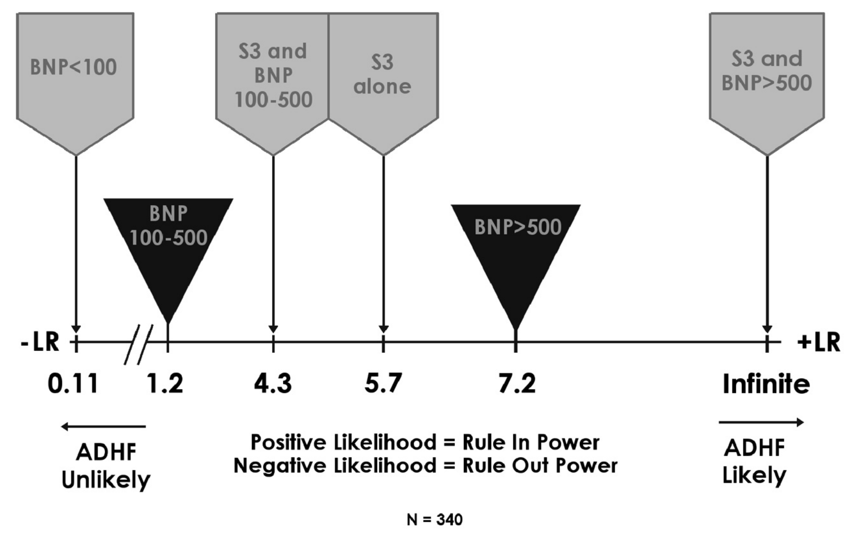

Figure 3. Synergy between acoustic cardiography–detected S_3 and B-type natriuretic peptide (BNP) (pg/mL). ADHF=acute decompensated heart failure; LR=likelihood ratio

Clinical Applications of Acoustic Cardiography

Emergency Department. Although HF may be readily diagnosed in its advanced stages, it can be difficult to diagnose clinically in its earlier stages.[37] HF has many nonspecific signs and symptoms that can present diagnostic and management ambiguities. Also, the ED can be a challenging environment for detecting an S_3 by routine auscultation. Even in the BNP era, an accurate diagnosis of ADHF within the ED remains poor, with 18.5% of cases of ADHF being undiagnosed.[2] Recent studies evaluating the clinical utility of acoustic cardiography in the ED setting have found that the detection of S_3 is significant and aids physicians in accurate diagnosis. While not sensitive enough to be used as a screening tool, the detection of an S_3 is highly specific for abnormal cardiac function.[22] Studies have demonstrated the additive information garnered by S_3 heart sounds detected by acoustic cardiograms and the combined utility it serves with BNP values when evaluating dyspneic patients in the ED.[38,39] These studies illustrate that an S_3 detected by acoustic cardiography is highly specific for ADHF and is ideally suited for use in combination with BNP to improve diagnostic accuracy in ED patients with dyspnea of unclear etiology (Figure 3).

The implementation of BNP testing has improved the diagnostic accuracy of detecting ADHF;[2] however, the nondiagnostic values of BNP between 100–500 pg/mL, the range referred to as the "gray zone," are found in an important portion of dyspneic patients. Acoustic cardiography has been shown to help resolve a significant amount of these indeterminate BNP values and can substantially improve the diagnostic evaluation of patients with gray-zone BNP values. In doing so, acoustic cardiography can increase the confidence with which physicians initiate treatment for clinically significant ADHF, as recently corroborated by M. Zuber, MD (unpublished data, May 2006). Moreover, the presence of an S_3 in combination with a BNP value >500 pg/mL virtually assures the presence of ADHF as depicted by the infinite positive likelihood ratio in Figure 3.[39]

The clinical advantages of an early accurate diagnosis of ADHF are apparent. Interestingly, there appears to be a significant fiscal penalty for an inaccurate initial ED diagnosis missing HF when it is present. According to a study appearing later in this supplement, patients who were misdiagnosed as non-ADHF (most often chronic obstructive pulmonary disease and pneumonia) at ED presentation accrued hospital charges that were significantly higher than those correctly diagnosed: $10,508 vs. $7977, respectively. The difference of more than $2500 represented a 32% increase in charges and resulted in a near doubling of the financial loss experienced by the hospital.[39]

Because acoustic cardiography can be performed at the time of the ECG (a test routinely obtained within minutes in the ED as compared with central laboratory testing, which can take hours), it can help solve some of the unmet clinical need for more rapid and accurate diagnosis. As a result, fewer missed diagnoses, more rapid and accurate initial diagnoses, and valuable risk assessment should allow prompt initiation of appropriate treatment and early risk stratification. This translates to better clinical outcomes and more economically sound delivery of health care. The Acute Decompensated Heart Failure National Registry (ADHERE) database[40,41] has collected data on over 100,000 patient cases and has taught us that earlier diagnosis and initiation of appropriate treatment renders better outcomes and more cost-efficient care. A review and analysis of the existing literature surrounding acoustic cardiography and its role in assisting ED diagnosis of ADHF appears in this supplement, along with original articles and case studies demonstrating the powerful utility of this application.

Inpatient Hospital Setting. The appearance, disappearance, or change in the S_3 intensity in response to maneuvers or therapies, e.g., vasodilators or diuretics, has been well studied. Dynamic changes may reveal significant information about clinical status regarding treatment response.[42] The baseline data obtained in the ED may then be utilized to assist in determining therapeutic efficacy throughout a patient's hospital stay. As well, while few data currently exist for diagnosing ADHF that occurs as a secondary event during a hospitalization, one could speculate that having a baseline or BNP and acoustic cardiogram on admission could significantly aide in this diagnosis. Should an elevation in BNP occur and/or an S_3 appear that was not initially present, the diagnosis of a new, or exacerbation of an existing, cardiac dysfunction should be considered and investigated. Similarly, knowledge of the dry weight acoustic status at discharge could help at follow-up and subsequent outpatient assessments.

Outpatient Cardiology Offices and HF Clinics. The utility of acoustic cardiograms in outpatient settings for monitoring has been hypothesized as a means to detect early signs of ADHF, because an S_3 occurs before the onset of symptoms. This may potentially help to identify patients who require prompt medical intervention, as opposed to the more stable patient for whom a routine check-up with an HF nurse practitioner or physician's assistant could be scheduled. In doing so, early adjustments in medications and/or further evaluation may help prevent an episode of ADHF requiring hospitalization. This rapidly and easily obtainable information can be gathered at the time of arrival at the clinician's office when baseline vital signs and ECG are recorded. This information is much easier and faster to obtain than any laboratory test, including the BNP value, which requires phlebotomy and laboratory analysis.

CRT and Outpatient Optimization. One of the most exciting and promising new uses of acoustic cardiography is its rapid and easy use in CRT optimization. Expensive and highly programmable CRT devices have been shown in real-world practice to have a 30% nonresponder rate, which may be largely attributable to the fact that only 10% of CRT devices are optimized.[13] This is in stark contrast to the randomized controlled clinical trials that led to the approval of CRT devices for treating HF. All of these trials implemented optimization strategies.[7–11]

The paucity of CRT optimization in clinical practice stems from the labor- and time-intensive echocardiography protocols. These procedures are costly and require an expensive echocardiogram machine and a skilled echocardiographer. Acoustic cardiography offers a cost-efficient, easy-to-use method to optimize CRT patients. Acoustic cardiography has been compared with other optimization techniques employing echocardiographic protocols and has proven comparable.[43] In this study, 22 CRT patients had independently obtained recommendations for best AV delays through echocardiography and acoustic cardiography, revealing that both technologies yield equivalent clinical results. Echocardiographic optimization strategies attempt to achieve optimal AV delay by coordinating the end of the A wave (indicating the end of the atrial contribution of LV filling) with the onset of systolic mitral regurgitant flow (indicating the onset of ventricular contraction).[12] Acoustic cardiography can optimize the settings of the CRT device by creating the shortest electromechanical activation time, defined as the time from the onset of the QRS complex (ventricular depolarization), to the S_1, indicating ventricular systole and closure of the mitral valve. In doing so, the LV systolic time—the interval from S_1 to S_2—can be maximized, which has been shown to correlate well with maximizing ejection fraction.[33] In addition, the strength of the S_3, as measured by AUDICOR, can be minimized, thereby lowering LV end-diastolic pressure if initially above the detection threshold. All of this can be performed easily, rapidly, at the point of care, and without the need for expensive devices and skilled technicians. A detailed analysis of benefits of acoustic cardiography in CRT optimization appears later in this supplement, along with the echocardiography equivalency study[43] and case studies demonstrating the applicability of this technique in CRT optimization.

The easy-to-use and rapidly obtainable information gathered by acoustic cardiography should foster more widespread CRT optimization. This could allow for real-world experience with CRT to approach the success rates seen in the large randomized controlled trials.

Summary and Conclusions

Acoustic cardiography is an exciting new modernized technology implementing the already proven techniques of phonocardiography and systolic time intervals. When applied to clinical practice, acoustic cardiography can improve diagnosis and management of HF patients. Its clinical use should help address some of the need for robust, inexpensive, widely accessible, and easy-to-use technology for proactive HF diagnosis and management. Heart sounds and systolic time intervals captured by acoustic cardiograms have proven valuable in assisting clinical diagnostic and management challenges encountered in HF care.

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