Correlation of Auscultatory Severity of Aortic Stenosis with Trans Thoraic Echocardiography (CASSETTE): Pilot Study for Tele-stethoscopy in Rural or Global Health Applications

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ABSTRACT

Objectives: This pilot study seeks to evaluate the utility of an electronic stethoscope in assessing the severity of isolated aortic stenosis.

Methods: Echocardiograms for 653 patients with aortic stenosis were screened. 50 patients with isolated aortic stenosis were enrolled in the study. Patients were excluded for more than mild non-aortic valvular disease. Participants received an updated echocardiogram and cardiac recordings in the supine position were performed at four standard sites utilizing the Littmann 3200 electronic stethoscope. Recordings were analyzed using the Zargis Cardioscan® Software and the correlation of the aortic valve mean gradient by echocardiography to the time of peak systolic murmur (ASAI) averaged over the auscultative points was obtained.

Results: Thirty-six enrolled subjects met the criteria for study inclusion. The ASAI was averaged across each site and compared to the mean aortic gradient. A receiver operator characteristic curve was calculated for an ASAI value, which reliably predicted a mean pressure gradient of >30mmHg. An ASAI of 33 gave a sensitivity of 1.0 and a specificity of 0.72 with a corresponding negative predictive value of 100% and a positive predictive value of 47%.

Conclusion: In patients with greater than mild aortic stenosis without other significant valve disease, the Littmann 3200 stethoscope and Cardioscan software package provides an easy to use screening tool for aortic valve stenosis severity. With continued validation, electronic stethoscope monitoring would provide cheap, reliable and instantaneous surveillance for aortic stenosis in remote areas with constrained medical assets or for patients without access to care.

INTRODUCTION

Aortic stenosis (AS) is a common valvular disease, affecting 2%- 4% of persons 65 years of age and older worldwide.[1-3] Calcific aortic stenosis is the most common cause of AS in industrialized nations, whereas rheumatic heart disease is the predominant cause of aortic valvulopathy in developing countries.[4,5] With the increasing age of the global population, the worldwide prevalence of AS is predicted to increase. In the United Kingdom the population-based estimate for AS is approximately 2.5%, but the documented observed echocardiographic incidence approaches 1.8%, suggesting a significant shortfall in diagnosis. This indicates that the focus of new efforts should be on improving access to echocardiography as a way to address this deficiency and diagnose patients earlier in the disease progression.[6] While little specific data is available for developing nations, a recent review of the worldwide burden of rheumatic heart disease suggests the prevalence of significant undiagnosed valvular heart disease is high.[7] Late recognition of cardiac disease limits treatment options and affects mortality.[8] The remote deployment of mobile health technologies such as hand-held ultrasound machines and stethoscopes has been studied to improve diagnosis of treatable conditions in remote areas with either constrained medical assets or in patients lacking the means to access care.[9-11] Tele-stethoscopy has been shown to be a unique and deployable auscultation tool that can aid in diagnosis in areas with limited resources.[12] Tele-stethoscopy is a technique that utilizes a stethoscope and a device which can transmit sound to an offsite provider in real time or for later review. In this pilot study, we sought to validate the utility of

an electronic stethoscope (Fig. 1) that can function without an active Internet or communication link and requires only minimal end user training for assessing the severity of aortic stenosis. These results, once validated, could be expanded in worldwide global health applications, such as military humanitarian missions and large-scale remote health screening events.[13]

METHODS

The study was approved by the Institutional Review Board at Naval Medical Center San Diego and registered on ClinicalTrials.gov (Identifier: NCT 01605669).

In 1963, Braunwald and colleagues evaluated the clinical and hemodynamic findings in 100 patients with aortic stenosis.[14] They found a weak correlation between the timing of the peak of the murmur and the severity of the stenosis. Forty years later, in 2003, Kim and Tavel used an electronic stethoscope to generate a spectral display of AS murmurs.[15] They found a significant correlation between the peak pressure gradient on the transthoracic echocardiogram (TTE) and the duration of the spectra at >300 Hz. The strength of this correlation was improved when the duration was adjusted for heart rate. Based on this earlier work, we developed a novel, easily obtained index, namely the final aortic stenosis auscultative index (ASAI), which we felt would correlate well with the severity of aortic stenosis. The ASAI measures the time to peak intensity of the murmur adjusted for the heart rate. It is represented by the equation

$$\frac{S_2 - X}{S_2 - S_1} = ASAI$$

where S1 and S2 represent the time of mitral and aortic valve closure respectively and X represents the time to peak intensity of the recorded murmur. The ASAI was derived using the correlation Braunwald documented concerning the time of peak murmur with the spectral analysis suggested by Kim and Tavel. This was then adjusted for heart rate (specifically ejection time as represented by S2-S1).

We searched our electronic medical records for patients with aortic stenosis (ICD9 424.1 and 395) and excluded associated mitral regurgitation (ICD9 codes 394.2 and 396.2). We identified 653 patients who met the initial inclusion criteria of having asymptomatic mild to severe aortic stenosis by TTE. Patients were excluded if they had more than mild non-aortic valvular disease by TTE. This decision was made to prevent potential interference from other non-aortic murmurs in the aortic sound analysis. A total of 50 patients with a history of mild to severe isolated aortic stenosis were enrolled in the study (Fig. 2). The total number of enrolled subjects was limited by funding and staff availability at the time the study was performed. Each study participant received an updated TTE by the same experienced echocardiographer. The aortic valve area as calculated using the continuity equation and the mean gradients were recorded as a measure of aortic stenosis severity. The severity of concomitant non-aortic valvular disease was also recorded using standard definitions based on the American Society of Echocardiography guidelines.[16] Three of the 50 patients were excluded after analysis of their TTEs demonstrated aortic sclerosis without stenosis. Eight patients were excluded when they were found to have greater than mild non-aortic valve disease that was not present on the prior echo.

Auscultative recordings were then obtained in the supine position utilizing the Littmann model 3200 electronic stethoscope (3M St. Paul, MN) (Fig. 1). The first three patients were recorded in a seated position but were excluded due to suboptimal recordings. All subsequent recordings were done in the supine, face up position as described previously. The recordings were performed at four separate auscultative sites representing the traditional auscultative positions for the aortic valve, pulmonic valve, tricuspid valve and mitral valve. The CardioScan software provided a voice-guided protocol prompting the end user with both audio and visual instructions on proper recording technique. Each site was recorded for 20 seconds. Instant feedback on the quality of the recordings was available via visual phonograph of the stethoscope recording and a quality check done by the software. If the CardioScan software informed the recorder that the signal

Figure 1. Littmann model 3200 electronic stethoscope

was unacceptable, a repeat recording was performed at the same auscultative site before advancing to the next site. A full recording of all sites was estimated to be completed in less than two minutes. The recordings were transmitted by Bluetooth to the study laptop and then analyzed using the 3M Cardioscan software. The software first determined the endpoints of systole and diastole through detection of S1 and S2 as well as the identification of the point of peak systolic murmur energy. The software next filtered the phonocardiogram signal, segmented the systolic and diastolic time-intervals and computed the central tendency of the time-aligned segments over multiple heartbeats. This allowedfor the creation of a murmur contour that was displayed by the CardioScan software for immediate analysis by the recorder. The recordings were then transmitted to the 3M core lab for further analysis of the ASAI. An average ASAI was computed for each detected systolic interval and averaged over the 15-20 recorded systolic intervals. A graphical representation of the recorded murmur was produced for each recording (Fig. 2) and returned to the primary investigators. The core lab was blinded to the patients' TTE results. The time to peak intensity of the systolic murmur was recorded and averaged over the four auscultative points. The primary endpoint was the correlation of the aortic valve mean gradient by TTE to the ASAI averaged over the four auscultative points.

3M provided all study stethoscopes as well as a grant to support data collection and reimbursement to the hospital for each echocardiogram performed. The 3M core lab calculated the average ASAI based on each recording but was blinded to all other patient data. They had no review or decision on submission of the final paper.

RESULTS

The ASAI was averaged across each recorded site and compared to the mean aortic gradient. A receiver operator characteristic (ROC) curve was calculated for an ASAI value which reliably predicted a mean pressure gradient of >30mmHg (threshold for moderate aortic stenosis) (Fig. 4). An ASAI of 33 resulted in a sensitivity of 100%, specificity of 72% corresponding to a negative predictive value of 100% and a positive predictive value of 47%.

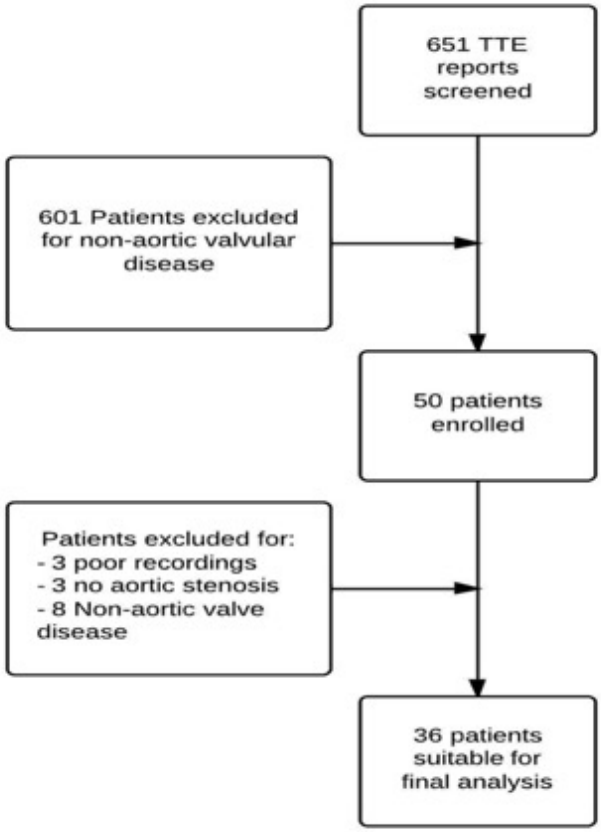

Figure 2. Enrollment

DISCUSSION

Our tele-stethoscopy method described employs a simple configuration consisting of an electronic stethoscope, a standard desktop or laptop computer, and off the shelf, inexpensive software. In addition to being user friendly, this method requires minimal set-up time and end user training. Furthermore, the method allows for the rapid analysis and/or transmission of murmurs during the physical exam for final assessment. The software directly guides the user where to place the stethoscope, how long to place it there, and if any re-recording is necessary. Three of our early recordings had significant artifact noise, but as we changed to a supine recording technique we were able to quickly optimize recording quality with this equipment. A sensitivity of 100% and corresponding 100% negative predictive value show that this technology is useful as a screening tool for significant (at least moderate) aortic stenosis. Once the ASAI threshold of 33 is met, the patient can be referred for a more thorough evaluation by TTE at a tertiary referral site.

This would avoid routine monitoring with echocardiography which can be expensive or difficult to obtain, particularly in remote or austere locations. Additionally, it may be useful in monitoring the enrolled subject between recommended annual or biannual TTE exams once the threshold of moderate AS is crossed.[17,18] Lastly, we are particularly interested in this technology for deployment on humanitarian missions or global outreach programs. The utility of such remote auscultation devices has not been previously tested. Based on the performance of these devices in the typical clinical setting, we hope further study in remote missions will prove beneficial for large population screening to guide future therapy.

There are several limitations to our study. First, patients with significant concomitant valvular disease were not evaluated. It is unclear how the sounds generated by other significant murmurs would affect the quality of the recording and subsequent analysis, or the timing or the peak intensity of the aortic stenosis murmur. Second, in its current iteration, the Cardioscan software package does not provide data on the timing of the ASAI, although this could be easily added in future updates if ultimately validated. Finally, the small sample size limits the broad applicability of the technology across a large population. Further validation in a larger population with more complex valvular disease is needed.

CONCLUSIONS

In patients with mild to severe aortic stenosis without significant concomitant non-aortic valvular disease, the Littmann 3200 electronic stethoscope demonstrated promise as an inexpensive and user-friendly screening tool for at least moderate aortic stenosis. Further study

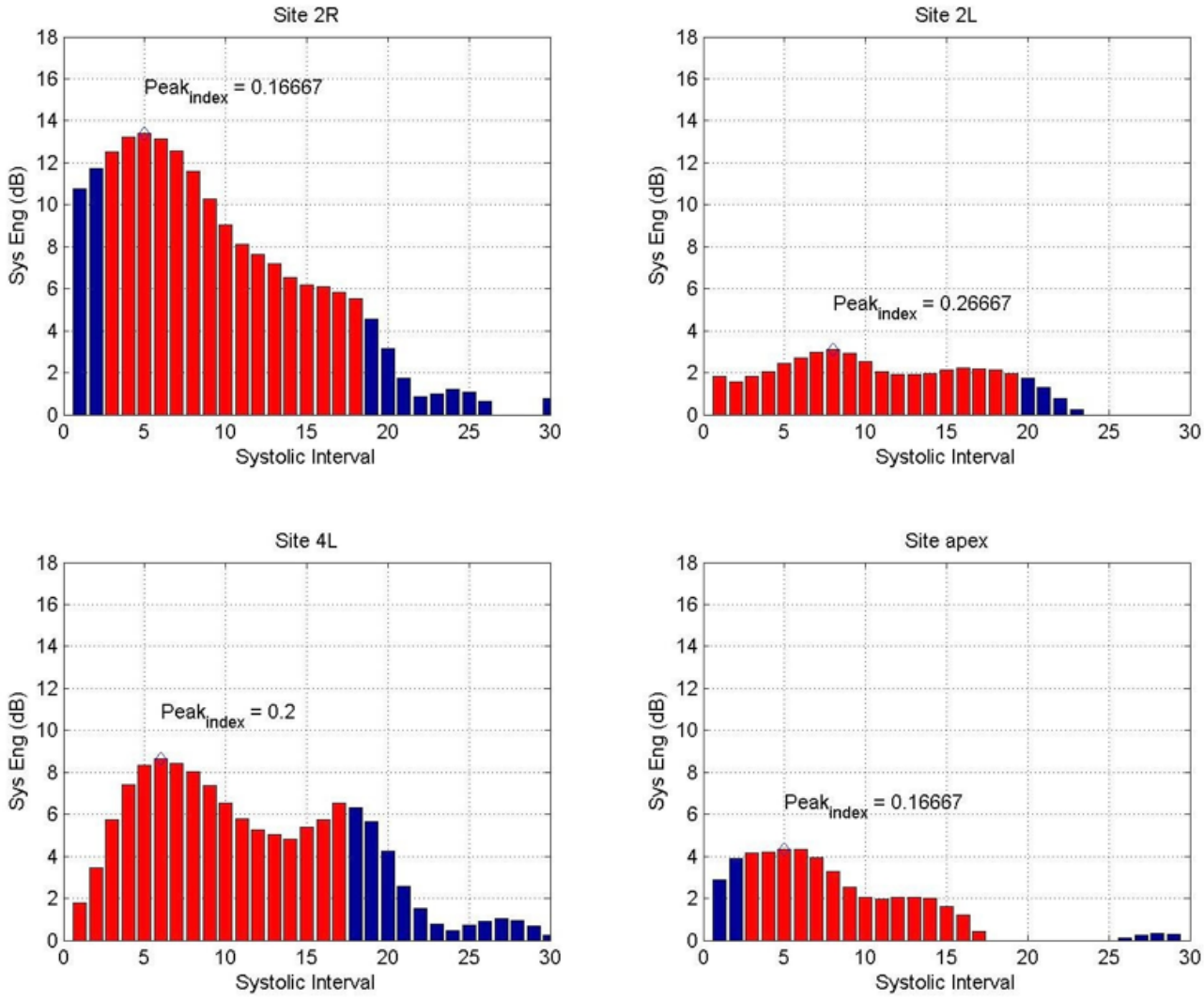

Figure 3. Graphical representation of the recorded murmur

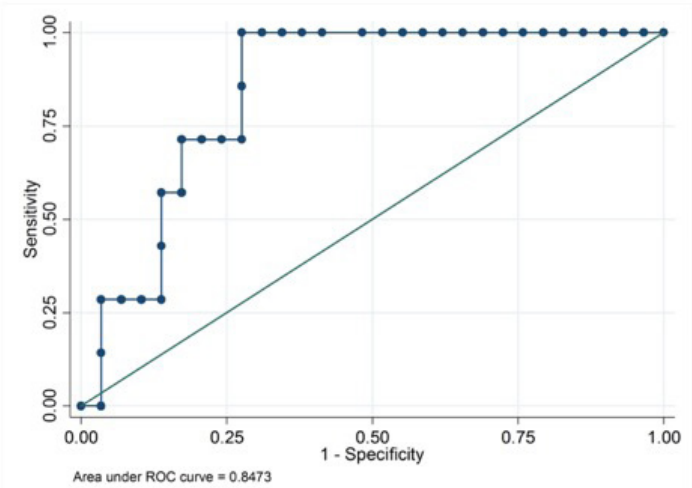

Figure 4. Receiver operator characteristic (ROC) curve for an ASAI of 33

is needed to show if this tool could reliably augment surveillance echocardiography for longitudinal evaluation of aortic stenosis. If ultimately validated, electronic stethoscope monitoring could provide low cost, reliable diagnosis and monitoring to a much larger population than echocardiography today. Such low-cost alternatives will improve quality and access to care to underserved populations in remote locations that do not have access to conventional echocardiography.

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DISCLAIMER

The views expressed herein are those of the authors' and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the U.S. Government.

DECLARATION OF INTERESTS

3M provided grant support to support a research assistant, study stethoscopes, and reimbursement to the hospital for each echocardiogram. There are no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; nor other relationships or activities that could appear to have influenced the submitted work.

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