CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Artificial Intelligence-Based Stethoscope for the Diagnosis of Aortic Stenosis

Tamer Ghanayim, MD,[a,1] Lior Lupu, MD, MBA,[b,1] Sivan Naveh, MD,[b] Noa Bachner-Hinenzon, PhD,[c] Doron Adler, PhD,[c] Salim Adawi, MD,[a,d] Shmuel Banai, MD,[b] Avinoam Shiran, MD[a,d]

[a]Department of Cardiology, Lady Davis Carmel Medical Center, Haifa, Israel; [b]Department of Cardiology, Tel Aviv Medical Center, affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Israel; [c]Sanolla, Nesher, Israel; [d]The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa.

ABSTRACT

BACKGROUND: The diagnostic accuracy of the stethoscope is limited and highly dependent on clinical expertise. Our purpose was to develop an electronic stethoscope, based on artificial intelligence (AI) and infrasound, for the diagnosis of aortic stenosis (AS).

METHODS: We used an electronic stethoscope (VoqX; Sanolla, Nesher, Israel) with subsonic capabilities and acoustic range of 3-2000 Hz. The study had 2 stages. In the first stage, using the VoqX, we recorded heart sounds from 100 patients referred for echocardiography (derivation group), 50 with moderate or severe AS and 50 without valvular disease. An AI-based supervised learning model was applied to the auscultation data from the first 100 patients used for training, to construct a diagnostic algorithm that was then tested on a validation group (50 other patients, 25 with AS and 25 without AS). In the second stage, conducted at a different medical center, we tested the device on 106 additional patients referred for echocardiography, which included patients with other valvular diseases.

RESULTS: Using data collected at the aortic and pulmonic auscultation points from the derivation group, the AI-based algorithm identified moderate or severe AS with 86% sensitivity and 100% specificity. When applied to the validation group, the sensitivity was 84% and specificity 92%; and in the additional testing group, 90% and 84%, respectively. The sensitivity was 55% for mild, 76% for moderate, and 93% for severe AS.

CONCLUSION: Our initial findings show that an AI-based stethoscope with infrasound capabilities can accurately diagnose AS. AI-based electronic auscultation is a promising new tool for automatic screening and diagnosis of valvular heart disease.

 • The American Journal of Medicine (2022) 135:1124–1133

KEYWORDS: Algorithm; Aortic stenosis; Artificial intelligence; Infrasound; Stethoscope

INTRODUCTION

The stethoscope has been used for auscultation for the diagnosis of valvular heart disease for more than 200 years, since it was invented in 1816 by the French physician René Théophile Hyacinthe Laënnec.[1] However, its diagnostic accuracy is limited by the presence of obesity, emphysema, and ambient noise, and is highly dependent on clinical expertise and on the acoustic hearing range of the human ear.[2,3] Low-frequency sound waves (infrasound; 3-40 Hz), which are not heard by the human ear, contain pertinent diagnostic information that is currently unavailable.[4] Until recently, efforts to develop electronic stethoscopes did not significantly improve clinical auscultation performance and did not replace the traditional stethoscope.[5]

Aortic stenosis (AS) is the most common valvular disease requiring surgical or transcatheter intervention in

Funding: The study was supported by Sanolla, Nesher, Israel.

Conflicts of Interest: The study was supported by Sanolla. NBH and DA are employees of Sanolla. AS is a consultant for Sanolla and holds stock options in Sanolla. SB is the medical director of Sanolla.

Authorship: All authors had access to the data and a role in writing the manuscript.

Requests for reprints should be addressed to Avinoam Shiran, MD, Department of Cardiology, Lady Davis Carmel Medical Center, 7 Michal Street, Haifa 3436212, Israel.

E-mail address: av.shiran@gmail.com

[1] These authors contributed equally to this work.

0002-9343/
https://doi.org/10.1016/j.amjmed.2022.04.032

Europe and North America, and its prevalence has increased with the aging of the population.[6-8] Timely diagnosis of AS and its severity by general practitioners and community physicians is paramount for optimal patient outcome. Reliance on the acoustic stethoscope alone may not always be sufficient, especially in the setting of busy primary care practice.[9,10] Reliance on echocardiography over the past decades has led to a decrease in the utility of auscultation by primary care physicians, which together with low public awareness of AS and its related symptoms has led to significant underdiagnosis and undertreatment of AS.[11] A point-of-care ultrasound has been shown to be superior to auscultation for the diagnosis of valvular heart disease, but it is not always available for primary and community care physicians, it is time consuming, and it is limited by availability and by physician expertise.[9,12] As such, it may be of limited use for initial screening. Artificial intelligence (AI) algorithms using deep neural networks are increasingly used in medicine, and recently have been applied for automatic interpretations of echocardiograms and for the prediction of atrial fibrillation from baseline electrocardiogram.[13,14]

CLINICAL SIGNIFICANCE

- The clinical utility of the stethoscope, invented by Laënnec 200 years ago, is limited, leading to underdiagnosis of valvular heart disease.
- We have developed an electronic stethoscope with infrasound capabilities, which can accurately diagnose aortic stenosis using artificial intelligence.
- The stethoscope diagnosed severe aortic stenosis with 93% sensitivity and 84%-92% specificity.
- The artificial intelligence-based stethoscope can be used for wide screening of patients for the presence of significant aortic stenosis.

The purpose of our study was to develop an AI algorithm for a smart stethoscope that can also record a wide acoustic range, including infrasound, and has an integrated artificial intelligence capability, for accurate and instantaneous diagnosis of moderate or severe AS in outpatients or in the emergency department.

METHODS

The study had 2 stages and was conducted at 2 separate medical centers in Israel. During the first stage of training and validation, recording of heart sound samples using the smart VoqX stethoscope (Sanolla, Nesher, Israel), from patients undergoing echocardiography, was performed at Carmel Medical Center (a 477-bed general hospital). Subsequently, the AI-based stethoscope was tested in patients with and without AS at Tel Aviv Medical Center (a 1500-bed tertiary hospital). The study was approved by the local institutional review board of both medical centers, and all patients signed an informed consent

Stage One – Training and Validation Phase

Study population. Heart sounds were recorded from 100 patients referred for echocardiography (training group), 50 with moderate or severe AS (defined as aortic valve area $\leq$1.5 cm^2), and 50 without valvular heart disease by echocardiography (Figure 1). The following patients were excluded from the study: age younger than 18 years; pregnant women; patients who had a nondiagnostic echocardiogram, prosthetic heart valves, or congenital heart disease (other than a bicuspid aortic valve); patients with more than mild aortic regurgitation; pulmonic valve disease; more than mild mitral or tricuspid valve disease; or hypertrophic cardiomyopathy. Next, heart sounds were recorded in 50 more patients (validation group), 25 with moderate or severe AS and 25 without valvular heart disease.

Clinical data and laboratory tests were collected from patients' electronic records. Each patient underwent a complete physical examination, and the occurrence of heart murmurs, point of maximal intensity, and the intensity and character of the murmur were recorded.

Heart sounds data acquisition and analysis. Real-time heart sounds recordings were performed in the sitting position using an electronic stethoscope (VoqX, Sanolla). For each patient, 5 auscultation points on the anterior chest wall (A-E) were sampled for at least 10 seconds using direct skin contact (Figure 2). At the end of each examination the data were stored for offline analysis. The VoqX stethoscope captures acoustic waves between 3 and 2000 Hz, which can then be both amplified and presented graphically as a sound signature (Figure 3). Each heart sounds recording was processed as follows:

1. Background noise was eliminated by using a second microphone recording the ambient noise, thus enabling dynamic noise reduction from the heart sound data.
2. The beginning and end of each recording were trimmed to eliminate noise generated by placing and removing the stethoscope on the chest.
3. Click noises generated from movements of the stethoscope on the chest during the recording were eliminated.

Several features, differentiating AS from non-AS recordings, were identified:

1. Ejection time corrected for heart rate, derived from the spectrogram in frequency ranges of 90-300 Hz.
2. Ejection time corrected for heart rate, derived from the spectrogram in frequency ranges of 100-200 Hz.
3. Heart sound signal entropy.

Next, multiple machine learning methods were tested to identify the best algorithm, which was then used to construct a classifier. Data for building the first classifier were derived from all of the 5 auscultation points (A-E) from the

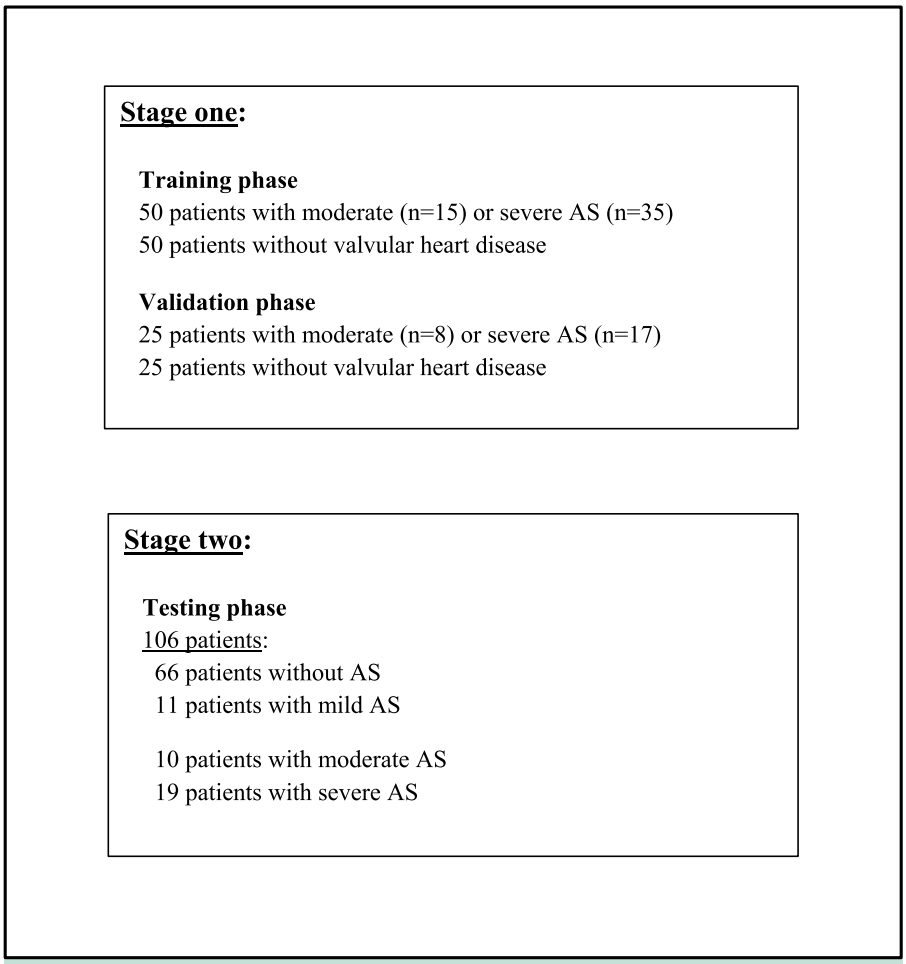

Figure 1 Study flow chart. Stage one included only patients with or without aortic stenosis (AS). Stage two, performed at a different medical center, included also patients with valvular heart disease other than AS.

100 subjects in the derivation group. A second classifier was constructed from the combined scores of the auscultation points showing the best results (A and B). Receiver operating characteristic (ROC) curves were used to determine the optimal cutoff point for diagnosing AS, which was then tested on the 50 patients in the validation group by an operator blinded to the clinical data and the echocardiographic diagnosis.

Stage Two – Testing Phase

Study population. In the study's second (testing) phase, we used the VoqX stethoscope with the built-in automatic classifier to examine 106 subjects (Figure 1). We recorded heart sounds from hospitalized patients who were referred for echocardiography. We included patients without valvular heart disease as well as patients with a different degree of aortic valve stenosis. In order to examine the acoustic effect of other valve pathologies, in this second confirmatory stage we did not exclude patients with other valve pathologies. We excluded subjects younger than 18 years, pregnant women, and subjects who had non-diagnostic echocardiography, prosthetic heart valves, or congenital heart disease (other than a bicuspid aortic valve).

The recordings were made at points A and B (Figure 2), which were found to have optimal diagnostic accuracy in the first stage. Each point was recorded until the recording time indicator signaled a satisfactory recording length (16 seconds). We aimed to distinguish between moderate or severe AS and non-significant AS. For each auscultation point, the smart stethoscope (Figure 4) indicated within a few seconds whether AS was diagnosed, questionable, or excluded, based on the AI algorithm developed using the training data (stage one). For each subject, AS was diagnosed if the smart stethoscope diagnosed AS in at least one of the auscultation points (A or B), or if both showed questionable AS (borderline classifier values).

Echocardiography. A complete transthoracic echocardiographic study was available for all subjects using standard views and techniques according to established guidelines.[15] The diagnosis and severity of AS was based on 2-dimensional

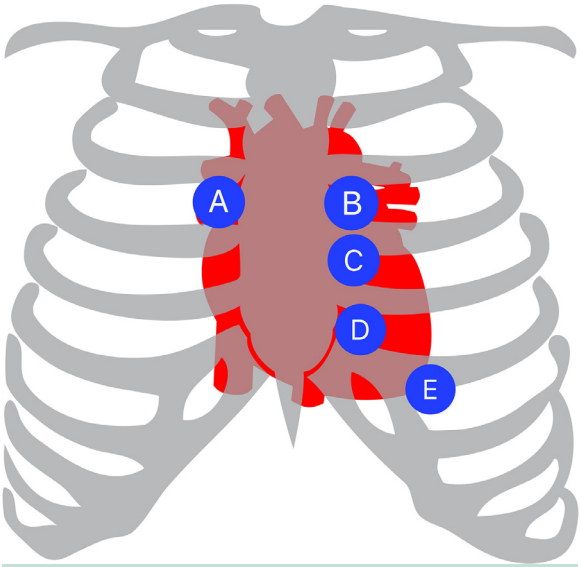

Figure 2 Auscultation points. **(A)** Aortic point, right sternal border, second intercostal space; **(B)** Pulmonic point, left sternal border, second intercostal space; **(C)** Erb's point, left sternal border, third intercostal space; **(D)** Tricuspid point, left sternal border, fourth intercostal space; **(E)** Mitral point, mid-clavicular line, fifth intercostal space.

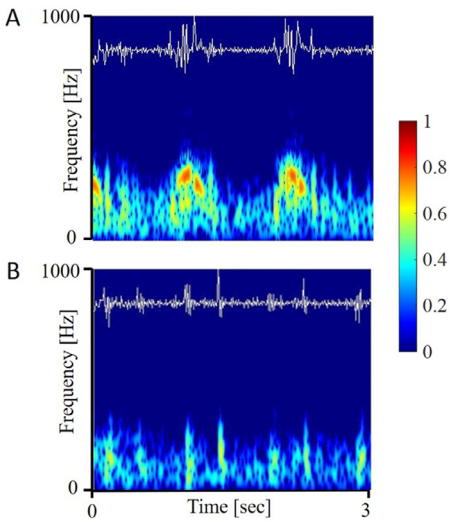

Figure 3 Heart sound signature. A graphical representation of the acquired heart sound: **(A)** Aortic stenosis; **(B)** No valvular heart disease. Sound waves frequency is presented as a function of time. Signal intensity is color-coded (blue minimal, red maximal). Top, a seismocardiogram (SCG) of the recorded heart sounds.
The classical "diamond shape" of the sound waves in aortic stenosis (AS) is characterized by midsystolic peaking of both intensity and pitch.

echocardiographic aortic valve anatomy, transaortic Doppler gradients, and aortic valve area.[16] Aortic valve area was calculated using the continuity equation.

Statistical methods. Statistical analyses were performed using SAS version 9.4 software (SAS Institute Inc., Cary, NC). For all analyses, $P < .05$ for the 2-tailed tests was considered statistically significant. Continuous variables are presented with mean ± SD (median, range), and categorical variables as numbers and proportions. Comparisons of patient characteristics and echocardiography data were performed using the chi-squared test (or Fisher's exact test) for categorical variables and Student's t test (or Wilcoxon rank-sum test) for continuous variables. ROC curves were constructed from classifier values created by the AI algorithm and used to select optimal cutoff points for the diagnosis of AS. Sensitivity, specificity, and total accuracy, based on a prespecified cutoff, were reported with 95% confidence intervals.

RESULTS

Stage One — Training and Validation Phase

Clinical characteristics of the training and validation groups are listed in Table 1. Subjects with AS were older than those without AS, and about half of them were male. All subjects with AS had an audible murmur, most often maximal at auscultation point A (Figure 2). The echocardiographic findings are listed in Table 2. Severe AS was present in 35 of the patients in the training group and moderate AS in 15. In the validation group, severe AS was present in 17 patients and moderate in 8. Most patients had preserved left ventricular ejection fraction. ROC curves constructed using the classifier created from the training group data are shown in Figure 5. Using the ROC curves, AS was defined for each auscultation point if the classifier value was ≤−0.3. For the combined data from A-B auscultation points, we defined AS if at least one point had a classifier value ≤−0.3, or both were <0.3 (−0.3 to 0.3: borderline zone). The sensitivity, specificity, and total accuracy of the AI algorithm are presented in Table 3. The algorithm developed using the training data was applied to the validation group using the combined A-B auscultation points data.

Stage Two — Testing Phase

In the testing phase of the study, the subject's population comprised 106 patients. Of them, there were 66 patients with a normal aortic valve, 11 with mild AS, 10 with moderate AS, and 19 patients with severe AS. Patients with moderate or severe AS were older as compared with patients with mild or no AS (Table 4). Similarly, the prevalence of atrial fibrillation was higher in the moderate or severe AS group. All patients in the moderate or severe AS

Table 1 Patient Characteristics: Stage 1 — Training and Validation Phase

	Derivation Group			Validation Group		
	No AS n = 50	AS n = 50	*P* Value	No AS n = 25	AS n = 25	*P* Value
Age (years)	58 ± 16 [60, 46-70]	78 ± 8.8 [78, 73-86]	< .0001	59 ± 18 [64, 41-72]	76 ± 9.1 [78, 70-83]	.0003
Male sex	39 (78%)	28 (56%)	.02	17 (68%)	12 (48%)	.15
BMI Kg/m^2	27.7 ± 5.5 [27, 17-47]	26.9 ± 5 [27, 14-41]	.45	27 ± 5.2 [26, 18-37]	27.2 ± 4.4 [28, 19-34]	.79
NYHA class III or IV	1 (2%)	23 (46%)	< .0001	0 (0%)	13 (52%)	< .0001
Smoking*	23 (46%)	22 (44%)	.8	8 (32%)	9 (36%)	.8
Symptoms						
Dyspnea	8 (16%)	26 (52%)	.0001	5 (20%)	16 (64%)	.002
Syncope	1 (2%)	4 (8%)	.36	4 (16%)	2 (8%)	.67
Angina pectoris	14 (28%)	13 (26%)	.8	5 (20%)	11 (44%)	.069
Coronary artery disease						
Coronary artery disease	11 (22%)	22 (44%)	.02	5 (20%)	10 (40%)	.12
Prior myocardial infarction	10 (20%)	17 (34%)	.1	5 (20%)	10 (40%)	.12
Prior CABG	2 (4%)	3 (6%)	> .99	3 (12%)	2 (8%)	> .99
Medical history						
Atrial fibrillation	5 (10%)	6 (12%)	.74	1 (4%)	4 (16%)	.35
Rheumatic heart disease	0 (0%)	1 (2%)	> .99	0 (0%)	0 (0%)	
Chronic lung disease	3 (6%)	4 (8%)	> .99	1 (4%)	3 (12%)	.61
Physical examination						
Heart rate, beats per minute	75 ± 15 [72, 52-115]	70 ± 11 [67, 51-97]	.038	75 ± 15 [70, 48-107]	68 ± 12 [64, 52-90]	.058
Systolic BP (mm Hg)	129 ± 22 [126, 88-182]	139 ± 18 [141, 105-180]	.015	134 ± 12 [134, 108-152]	133 ± 18 [130, 93-170]	.79
Diastolic BP (mm Hg)	77 ± 12 [78, 35-100]	68 ± 12 [68.5, 32-87]	.0008	76 ± 10 [77, 56-97]	66 ± 12 [70, 45-87]	.004
Systolic murmur	0 (0%)	50 (100%)		0 (0%)	25 (100%)	
Systolic murmur intensity (3-6/6)		2.6 ± 0.5 [3, 2-3]			3 ± 0.6 [3, 2-4]	
Max intensity at aortic point (A)		47 (94%)			23 (92%)	
Diminished A2 sound	0 (0%)	32 (64%)		0 (0%)	14 (56%)	
Diastolic murmur	0 (0%)	1 (2%)		0 (0%)	0 (0%)	
Abnormal lungs examination	1 (2%)	1 (2%)	> .99	0 (0%)	0 (0%)	
Laboratory findings						
Hemoglobin, gr%	13.7 ± 1.9 [13.9, 9.4-17.3]	12.3 ± 1.7 [12.2, 7.5-15]	.0002	13.5 ± 1.8 [13.9, 8.9-16.5]	12.2 ± 1.4 [12.4, 9.5-14.3]	.002
Creatinine, mg%	1 ± 0.3 [0.9, 0.5-1.9]	1.1 ± 0.3 [1, 0.5-2.1]	.03	1.3 ± 1.6 [1, 0.5-8.7]	1.3 ± 1.8 [0.93, 0.56-9.7]	.8
TSH, mU/L	2.1 ± 1 [1.7, 0.6-5.2]	2.4 ± 1.4 [2.3, 0-6.4]	.2	1.8 ± 1.1 [1.7, 0.36-5.4]	2.4 ± 1.95 [1.75, 0.96-10.2]	.3

Continuous variables are presented with mean ± SD [median, range].

*Active or former smoker.

A2 = second heart sound; AS = aortic stenosis; BMI = body mass index; BP = blood pressure; CABG = coronary artery bypass graft; CAD = coronary artery disease; NYHA = New York Heart Association; SM = systolic murmur; TSH = thyroid-stimulating hormone.

group had audible classic ejection-type murmur, and one patient also had an apical holosystolic murmur. In the mild or no AS group, most patients had no audible murmur (74%), while few had ejection-type murmur (13%) and apical holosystolic murmur (13%).

Left ventricular ejection fraction was higher in the moderate or severe AS group, while stroke volume was similar between the groups (Table 4). Diastolic dysfunction grade was higher with significant AS. Moderate or severe mitral regurgitation was present in 1 patient with moderate or severe AS and in 7 patients with mild or no AS. None of the patients had pulmonic stenosis or left ventricular outflow tract obstruction.

The sensitivity, specificity, and total accuracy in the testing phase are presented in Table 3. We also examined the sensitivity of the AI-based stethoscope for the diagnosis of AS according to AS severity in the combined study group (Table 5). The sensitivity of the AI stethoscope for AS increased with AS severity, and was 93% in patients with severe AS. The results were similar after exclusion of the

Table 2 Echocardiographic Findings: Stage 1 — Training and Validation Phase

	Derivation Group			Validation Group		
	No AS n = 50	AS n = 50	*P* Value	No AS n = 25	AS n = 25	*P* Value
Max aortic velocity, cm/s	132 ± 21 [131, 95-193]	415 ± 72 [419, 255-586]	< .0001	129 ± 14.8 [130, 98-152]	405 ± 64.9 [406, 298-573]	< .0001
Mean aortic gradient, mm Hg	—	43.6 ± 15.8 [42, 15-83]		—	41.2 ± 14.9 [39, 22-85]	
Aortic valve area, cm^2	—	0.9 ± 0.2 [0.9, 0.5-1.4]		—	0.88 ± 0.2 [0.89, 0.54-1.3]	
Aortic root, cm	3.2 ± 0.3 [3.1, 2.4-4.2]	3.1 ± 0.3 [3.1, 2.5-3.9]	.14	3.1 ± 0.34 [3.1, 2.5-3.7]	2.95 ± 0.36 [2.8, 2.4-3.7]	.12
Bicuspid aortic valve	0 (0%)	2 (4%)	.49	0 (0%)	1 (4%)	> .99
LV end-diastolic diameter, cm	4.6 ± 0.5 [4.7, 3.6-5.4]	4.6 ± 0.6 [4.4, 3.6-5.8]	.64	4.6 ± 0.4 [4.6, 3.8-5.3]	4.7 ± 0.6 [4.6, 3.8-5.9]	.71
LV end-systolic diameter, cm	2.9 ± 0.4 [2.9, 2-3.8]	3.1 ± 0.6 [2.9, 1.8-4.4]	.29	2.86 ± 0.38 [2.9, 2.3-4.1]	3.25 ± 0.63 [3.1, 2.4-4.9]	.017
LV ejection fraction, %	60.2 ± 4.3 [60, 45-65]	58.2 ± 6.6 [60, 40-75]	.06	61.2 ± 4.4 [60, 45-65]	58.2 ± 6.3 [60, 36-70]	.01
Interventricular septum, cm	1 ± 0.2 [1, 0.7-1.6]	1.3 ± 0.1 [1.3, 1-1.5]	< .0001	1.06 ± 0.13 [1.1, 0.8-1.3]	1.32 ± 0.17 [1.3, 1.1-1.8]	< .0001
Posterior wall thickness, cm	1 ± 0.1 [1, 0.6-1.4]	1.1 ± 0.1 [1.1, 0.9-1.3]	< .0001	0.97 ± 0.1 [1, 0.8-1.2]	1.03 ± 0.14 [1, 0.7-1.3]	.048
LAVI, cm^3/m^2	32.8 ± 15.2 [27.5, 13-80]	40.5 ± 19.8 [38, 4-118]	.028	25.8 ± 7.8 [27.5, 16-32]	40.7 ± 11 [42, 23-57]	.03
LV mass index, gr/m^2	83.8 ± 23.8 [83, 39-201]	107.4 ± 22.8 [100.5, 74-161]	< .0001	83.16 ± 11.9 [84, 61-119]	112.7 ± 27.6 [113, 64-168]	< .0001
A wave, cm/s	69.8 ± 19.9 [67, 37-114]	111 ± 28.6 [111, 46-168]	< .0001	74.2 ± 18.7 [78, 36-110]	89.9 ± 33.5 [87, 33-156]	.01
E wave, cm/s	73.1 ± 19.9 [73, 38-126]	95.6 ± 29.3 [97, 48-167]	< .0001	67 ± 14 [67, 48-94]	95.7 ± 32.8 [90.5, 46-168]	.0013
E/A ratio	1.1 ± 0.4 [1.1, 0.4-2.7]	0.9 ± 0.3 [0.8, 0.4-2.1]	.012	0.97 ± 0.32 [0.86, 0.56-1.7]	1.28 ± 0.78 [0.84, 0.53-2.82]	.52

Continuous variables are presented with mean ± SD [median, range].
AS = aortic stenosis; LAVI = Left Atrial Volume Index; LV = left ventricle,

first 50 patients from the derivation group (severe AS: sensitivity 92% [confidence interval 77-98], moderate AS: sensitivity 76% [confidence interval 50-92]).

DISCUSSION

We have developed an AI-based algorithm integrated into a smart stethoscope capable of accurately diagnosing AS within seconds. The AI-based algorithm was constructed using data from 50 patients with moderate or severe AS, based on echocardiography, and 50 patients without valvular heart disease. Although the control group was significantly younger than the AS group, they did not represent normal healthy subjects, and included patients with various disease states such as coronary disease, routinely referred for echocardiography. In this group, using data from the aortic and pulmonic auscultation points (A-B), the algorithm identified AS with a sensitivity of 86% and specificity of 100%. This algorithm was then blindly tested in 50 additional patients (25 with moderate or severe AS), yielding a sensitivity of 84% and specificity of 92%. Based on these data, an AI algorithm for a smart stethoscope was constructed (Figure 4), which was then tested on a third group of patients from a different medical center, which included patients with mild AS and other valvular diseases. The smart stethoscope identified moderate or severe AS (using auscultation points A-B) with a sensitivity of 90%, and specificity of 84%. The sensitivity of the AI stethoscope increased with AS severity, and was 93% in patients with severe AS.

In order to classify heart sounds using automated algorithms, public heart sound databases, such as the PhysioNet/Computing in Cardiology Challenge 2016, consisting of data from patients with heart valve disease and coronary artery disease, were constructed.[17] The development of robust AI-based algorithms for the diagnosis of valvular disease has been limited by the availability of high-quality heart sound recordings, which are essential for machine learning.[18] In the present study, we used a well-defined study population, prospectively enrolled specifically for the construction, validation, and testing of the AI-based stethoscope.

Thompson et al[19] used the Johns Hopkins Cardiac Auscultatory Recording Database to virtually test an AI algorithm, which identified pathological cases in a pediatric population with a sensitivity of 93% and specificity of 81%.

Figure 4 The artificial intelligence-based smart stethoscope.

The database included 70 patients with AS (severity unknown) in which the murmur was identified as pathological with a sensitivity of 96%. In that study, the algorithm was applied to 603 of 1200 patients in the Cardiac Auscultatory Recording Database, and was able to analyze 89% of the recordings. Recently, Chorba et al[20] developed a deep learning algorithm for the detection of cardiac murmurs, which was tested using recordings from electronic stethoscopes uploaded to a cloud. The algorithm detected cardiac murmurs with a sensitivity of 76% and specificity of 91%. When softer murmurs were omitted, the sensitivity increased to 90%. The study included 73 cases with AS, and all of them were severe AS. In these patients, the algorithm detected a murmur in the aortic or pulmonic auscultation points with a sensitivity of 93% and specificity of 86%, similar to our AI stethoscope. In the study of Chorba et al,[20] 13% of the recordings were excluded from analysis due to poor quality, and the control group consisted of healthy normal subjects, which probably increased both sensitivity and specificity. In our study we did not exclude patients with suboptimal heart sounds recordings, and we used mostly inpatients without valvular disease as controls, instead of normal healthy controls. Moreover, the fact that machine learning systems performance tends to improve as more information is collected raises the possibility that the performance of the algorithm and stethoscope will further improve as more recordings are collected.

The AI-based smart stethoscope may prove most useful for screening patients in the setting of a busy primary practice or in the emergency department. In the current era of echocardiography and sophisticated imaging, when physicians are required to spend more time in front of computers and have less time with patients, physical examination skills and, in particular, cardiac auscultation skills, deteriorate.[21] Sztajzel et al[22] reported the accuracy of cardiac auscultation by senior cardiologists and internists in the echocardiography era. Cardiologists and internists correctly identified 76% and 65% of all murmurs, respectively. They correctly identified 90% of patients with moderate or severe AS, but the study was limited by the small number of patients with significant AS. In our study, ejection-type murmur was identified in all patients with moderate or severe AS and in 77% of the patients with mild AS, but this part of the study was not blinded and the physician was aware of the echocardiographic findings. Cardiac examination skills do not improve after the third year in medical school, except for cardiology fellows, and may decline thereafter, even in faculty members.[23]

The smart stethoscope has proved useful for lung examination as well, in diagnosing pneumonia, bronchospasm, and COVID-19-associated lung infection (unpublished data). A home version of the smart stethoscope, consisting of a small, low-cost digital recorder that uploads lung and cardiac sound recordings to a cloud, may prove useful for mass screening and home monitoring of patients. The market price of the smart stethoscope is expected to be under $1000 (under $300 for a home version), which will make it cost effective for screening purposes, compared with

Table 3 Accuracy of AI Algorithm for the Diagnosis of AS

Auscultation Point	Sensitivity (95% CI)	Specificity (95% CI)	Total Accuracy (95% CI)
	Stage One — Training and Validation Phase		
	Derivation group (n = 100)		
A	86% (73-94)	96% (86-100)	91% (84-96)
B	78% (64-89)	96% (86-100)	87% (79-93)
A-B	86% (73-94)	100% (93-100)	93% (86-97)
	Validation group (n = 50)		
A-B	84% (64-96)	92% (74-99)	88% (76-96)
	Stage Two — Testing Phase (n = 106)		
A-B	90% (72-97)	84% (74-91)	86% (73-93)

AI = artificial intelligence; AS = aortic stenosis; CI = confidence interval.

Table 4 Patient Characteristics and Echocardiographic Findings: Stage Two — Testing Phase

	No AS/mild AS n = 77	Moderate or Severe AS n = 29	*P* Value
Age (years)	63 ± 19 [68, 53-76]	79 ± 13 [81, 73-87]	< .0001
Male sex	54 (70%)	16 (55%)	.17
BMI (Kg/m^2)	27 ± 6 [27, 24-30]	29 ± 4 [28, 27-31]	.068
Smoking*	31 (40%)	11 (38%)	.83
Symptoms			
Dyspnea	18 (23%)	22 (76%)	< .0001
Syncope	9 (12%)	3 (10%)	.84
Angina pectoris	29 (38%)	1 (3%)	< .0001
Coronary artery disease			
Coronary artery disease	25 (32%)	3 (10%)	.0063
Prior myocardial infarction	15 (19%)	4 (14%)	.48
Medical history			
Atrial fibrillation	15 (19%)	12 (41%)	.040
Chronic lung disease	3 (4%)	5 (17%)	.083
Chronic kidney disease	7 (9%)	7 (24%)	.093
Physical examination			
Heart rate, beats per minute	69 ± 19 [64, 56-78]	66 ± 15 [66, 58-72]	.31
Systolic ejection murmur	10 (13%)	29 (100%)	< .0001
Holosystolic murmur	10 (13%)	1 (3%)	.068
Echocardiography findings			
Max aortic velocity, cm/s†	2.5 ± 0.4 [2.6, 2.3-2.8]	4.0 ± 0.8 [4.2, 3.4-4.5]	< .0001
Max aortic gradient, mm Hg†	27 ± 5 [27, 23-30]	67±24 [70, 41-80]	< .0001
Mean aortic gradient, mm Hg†	15 ± 3 [16, 14-17]	40 ± 16 [40, 25-52]	< .0001
Aortic valve area, cm^2†	1.6 ± 0.4 [1.6, 1.4-1.6]	0.9 ± 0.3 [0.8, 0.7-1.1]	< .0001
Aortic root diameter, cm	3.4 ± 0.4 [3.2, 3.0-3.8]	3.2 ± 0.4 [3.2, 3.0-3.4]	.22
LV end-diastolic diameter, cm	4.8 ± 0.7 [4.9, 4.4-5.2]	4.6 ± 0.5 [4.7, 4.4-4.9]	.69
LV end-systolic diameter, cm	3.2 ± 0.8 [3.1, 2.7-3.5]	2.9 ± 0.5 [2.8, 2.5-3.2]	.028
LV ejection fraction, %	54 ± 9 [60, 50-60]	57 ± 6 [60, 60-60]	.010
Stroke volume, cm^3	73 ± 21 [72, 60-81]	81 ± 21 [79, 67-93]	.091
AS (n) mild, moderate, severe	11 (14%), 0, 0	0, 10 (34%), 19 (66%)	< .0001
AR (n) mild, moderate, severe	14 (18%), 0, 0	14 (48%), 1 (3%), 0	.0009
MS (n) mild, moderate, severe	2 (3%), 0, 0	2 (7%), 0, 0	.34
MR (n) mild, moderate, severe	23 (30%), 5 (6%), 2 (3%)	14 (48%), 1 (3%), 0	.78
TR (n) mild, moderate, severe	23 (30%), 3 (4%), 0	16 (55%), 0, 2 (7%)	.035
PR (n) mild, moderate, severe	3 (4%), 1 (1%), 0	1 (3%), 0,0	.63
PA systolic pressure (mm Hg)	34 ± 14 [30, 25-41]	43 ± 19 [38, 30-53]	.054
Diastolic dysfunction grade	0.8 ± 0.9 [1, 0-1]	1.6 ± 0.5 [2, 1-2]	< .0001

Continuous variables are presented with mean ± SD [median, interquartile range].

*Active or former smoker.AR = aortic regurgitation; AS = aortic stenosis; BMI = body mass index; LV = left ventricular; MR = mitral regurgitation, MS = mitral stenosis; PA = pulmonary artery; PR = pulmonary regurgitation; TR = tricuspid regurgitation.

†For patients with AS.

Table 5 Sensitivity of the AI Algorithm for the Diagnosis of AS by AS Severity

AS Severity	Sensitivity (95% CI)
Mild AS (n = 11)	55% (25-82)
Moderate AS (n = 33)	76% (57-88)
Severe AS (n = 71)	93% (84-97)

AI = artificial intelligence; AS = aortic stenosis; CI = confidence interval.

echocardiography. We are currently in the process of developing algorithms for the diagnosis of other valve pathologies, such as mitral regurgitation.

Limitations

Our study represents the initial construction, validation, and testing of an AI-based stethoscope for the diagnosis of AS, but is limited in its population size. In the present study we have not compared the performance of the AI-based stethoscope with that of clinicians in such settings. Further study is needed to test the smart stethoscope in the setting of a busy primary practice and the noisy emergency department, and in a more diverse patient population, and to compare it with the performance of clinicians. The sensitivity and specificity of the stethoscope may be lower in patients with low-flow, low-gradient AS and in patients with inaudible murmurs due to severe obesity or severe emphysema. It should not, therefore, replace clinical judgment, and symptomatic patients with a high likelihood of cardiac disease should be referred for echocardiography. Patients with pulmonic stenosis and hypertrophic cardiomyopathy were not included in this study, and there were only a few patients with mitral regurgitation. Because the smart stethoscope is intended for screening, misclassification of other cardiac pathologies such as AS will not be an issue, and will be resolved using echocardiography. AS severity also will be determined by echocardiography, because the smart stethoscope only indicates whether or not AS is present. Screening requires high sensitivity (in our study 76% for moderate and 93% for severe AS). Further work, including a quality-check algorithm for suboptimal sound recording that will prompt the user for additional recordings, may further increase sensitivity and accuracy.

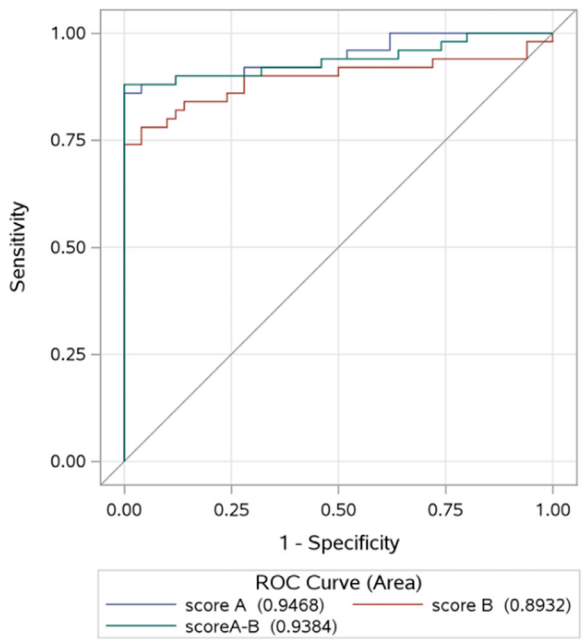

Figure 5 Receiver operating characteristics (ROC) curves. ROC curves of classifier values used for the diagnosis of aortic stenosis (AS), constructed using derivation group data (n = 100) from auscultation points A, B, and A-B combination.

CONCLUSION

We have developed and tested an AI algorithm for a smart stethoscope, which can rapidly and accurately diagnose moderate or severe AS. This device may be used to screen patients for AS at the primary care setting, the emergency department, or at home, independent of the clinical proficiency of the examiner.

References

1. Laënnec R. *De l'auscultation médiate ou Traité du Diagnostic des Maladies des Poumons et du Coeur [A treatise on the diseases of the chest and on mediate auscultation]*. Paris: Chaude; 1819 [[in French].
2. Montinari MR, Minelli S. The first 200 years of cardiac auscultation and future perspectives. *J Multidiscip Healthc* 2019;12:183–9.
3. Mangione S, Nieman LZ. Cardiac auscultatory skills of internal medicine and family practice trainees. A comparison of diagnostic proficiency. *JAMA* 1997;278(9):717–22.
4. Møller H, Pedersen CS. Hearing at low and infrasonic frequencies. *Noise Health* 2004;6(23):37–57.
5. Grenier MC, Gagnon K, Genest J, Durand J, Durand LG. Clinical comparison of acoustic and electronic stethoscopes and design of a new electronic stethoscope. *Am J Cardiol* 1998;81(5):653–6.
6. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2022;43(7):561–632.
7. Iung B, Delgado V, Rosenhek R, et al. Contemporary presentation and management of valvular heart disease: the EUrobservational research programme valvular heart disease II survey. *Circulation* 2019;140(14):1156–69.
8. Yadgir S, CO Johnson, Aboyans V, et al. Global, regional, and national burden of calcific aortic valve and degenerative mitral valve diseases, 1990-2017. *Circulation* 2020;141(21):1670–80.
9. Otto CM. Heartbeat: improving diagnosis and management of aortic valve disease. *Heart* 2018;104(22):1807–9.
10. Gardezi SKM, Myerson SG, Chambers J, et al. Cardiac auscultation poorly predicts the presence of valvular heart disease in asymptomatic primary care patients. *Heart* 2018;104(22):1832–5.
11. Thoenes M, Bramlage P, Zamorano P, et al. Patient screening for early detection of aortic stenosis (AS) - Review of current practice and future perspectives. *J Thorac Dis* 2018;10(9):5584–94.
12. Thomas F, Flint N, Setareh-Shenas S, Rader F, Kobal SL, Siegel RJ. Accuracy and efficacy of hand-held echocardiography in diagnosing valve disease: a systematic review. *Am J Med* 2018;131(10):1155–60.
13. Ghorbani A, Ouyang D, Abid A, et al. Deep learning interpretation of echocardiograms. *NPJ Digit Med* 2020;3(1):1–10.
14. Raghunath S, Pfeifer JM, Ulloa-Cerna AE, et al. Deep neural networks can predict new onset atrial fibrillation from the 12-lead ECG and help identify those at risk of atrial fibrillation-related stroke. *Circulation* 2021;143(13):1287–98.

15. Mitchell C, Rahko PS, Blauwet LA, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2019;32(1):1–64.
16. Baumgartner H, Hung J, Bermejo J, et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr* 2017;30(4):372–92.
17. Clifford GD, Liu C, Moody B, et al. Classification of normal/abnormal heart sound recordings: the PhysioNet/Computing in Cardiology Challenge 2016. *Comput Cardiol (2010)* 2016:(43):609–12.
18. Thoenes M, Agarwal A, Grundmann D, et al. Narrative review of the role of artificial intelligence to improve aortic valve disease management. *J Thorac Dis* 2021;13(1):396–404.
19. Thompson WR, Reinisch AJ, Unterberger MJ, Schriefl AJ. Artificial intelligence-assisted auscultation of heart murmurs: validation by virtual clinical trial. *Pediatr Cardiol* 2019;40(3):623–9.
20. Chorba JS, Shapiro AM, Le L, et al. Deep learning algorithm for automated cardiac murmur detection via a digital stethoscope platform. *J Am Heart Assoc* 2021;10(9):e019905.
21. Barrett MJ, Mackie AS, Finley JP. Cardiac auscultation in the modern era: premature requiem or Phoenix rising? *Cardiol Rev* 2017;25(5):205–10.
22. Sztajzel JM, Picard-Kossovsky M, Lerch R, Vuille C, Sarasin FP. Accuracy of cardiac auscultation in the era of Doppler-echocardiography: a comparison between cardiologists and internists. *Int J Cardiol* 2010;138(3):308–10.
23. Vukanovic-Criley JM, Criley S, Warde CM, et al. Competency in cardiac examination skills in medical students, trainees, physicians, and faculty: a multicenter study. *Arch Intern Med* 2006;166(6):610–6.