Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:		
	 Date	

By

Natalie Hoeting Master of Public Health

Epidemiology

Matthew Oster, MD, MPH Committee Chair

By

Natalie Hoeting

B.A., Hofstra University, 2012 B.S., Hofstra University, 2012

Thesis Committee Chair: Matthew Oster M.D., M.P.H.

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2017

Abstract

Title of Systolic Ejection Click vs. Split First Heart Sound: Are Our Ears Deceiving Us?

By Natalie Hoeting

Objective

Bicuspid aortic valve disease is associated with lifetime complications, but auscultation of this subtle pathology is commonly missed or mistaken for a benign split first heart sound. The authors sought to determine whether pediatric cardiologists could distinguish between bicuspid aortic valves and split first heart sounds.

Design

Quality evaluation project using de-identified recordings from Sibley Heart Center clinic patients, Atlanta, GA.

Outcome Measures

21 cardiologists listened to 5 recordings of pediatric heart sounds and indicated whether each recording was a bicuspid valve or split heart sound. 3 had the systolic ejection click of bicuspid aortic valves, and 2 contained mitral components of split first heart sounds. We determined accuracy of diagnoses using percent agreement and calculated kappa coefficients for the cohort and subgroups based on those with <10 years of experience vs. those with ≥10 years. To access precision, we used a Kappa extension for multiple raters to assess interrater agreement among the 21 cardiologists.

Results

Among participants, diagnostic accuracy of bicuspid aortic valves was 38%, while accuracy of split first heart sound was 41%. No participant correctly diagnosed all sounds. No difference in agreement was observed when stratifying by experience. Kappa was -0.11 (CI 95% -0.31-0.08) for all raters, -0.03 (CI 95% -0.39-0.33) for those with <10 years' experience, and -0.15 (CI 95% -0.38-0.08) for those with >10 years' experience. The Kappa statistic among the 21 raters was 0.01 (95% CI -0.03 - 0.04), indicating poor precision among the raters.

Conclusions

In this sample of pediatric cardiologists, the diagnostic accuracy of bicuspid atrial valves vs split first heart sounds was worse than chance. There was no association between years of experience and diagnostic accuracy. While further study is needed, these data suggest that an echocardiogram may be valuable when either a systolic ejection click or split first heart sound is heard.

Title of Systolic Ejection Click vs. Split First Heart Sound: Are Our Ears Deceiving Us?

By

Natalie Hoeting

B.A., Hofstra University, 2012 B.S., Hofstra University, 2012

Thesis Committee Chair: Matthew Oster M.D., M.P.H.

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Epidemiology 2017

Author Acknowledgements

The author is grateful to Michael McConnell, MD, for the original concept and design of the below study. Courtney McCracken, PhD, was instrumental in assisting with data analysis and interpretation. McConnell, McCracken, and Matthew Oster, MD, MPH all assisted with article revision and article approval prior to publication. Thank you to everyone for your guidance and support.

Introduction

Biscuspid aortic valve (BAV) disease in children is an often subtle pathology associated with potential lifetime complications. The heterogeneous presentation of BAV makes clinical diagnosis difficult, since at first presentation the patient may be asymptomatic (1). Of the 1-2% of the population in the United States born with BAV, over a third will develop serious complications including aortic valvular stenosis, aortic regurgitation, bacterial endocarditis, aortic aneurysm, and aortic dissection (2, 3, 4, 5). Some of those complications may occur during adolescence, but many of them may not occur until adulthood (6, 7).

Early correction by surgery prevents these complications, yet many BAV go undiscovered due to failure to diagnose (8, 9). The gold standard for diagnosis is echocardiography, but astute auscultation may detect the click from the delayed opening of the stiff BAV shortly following the closure sound of the mitral and tricuspid valves. When BAV disease is severe, there may be an accompanying systolic ejection murmur, but this is only found if the patient also has aortic valve stenosis. The click of the BAV alone often goes unheard or may be mistaken for the asynchronous closure of the mitral and tricuspid valves (10). This asynchronous closure causes a split first heart sound (S1), and can be physiologic in children (11).

The purpose of the study was to examine a sample of pediatric cardiologists and test if they could differentiate between BAV click and split S1. We hypothesized that the older physicians with longer experience would outperform physicians with fewer years of training, but that the overall cohort would be able to distinguish the lesion with greater than 50% accuracy.

Methods

We performed a quality evaluation project to determine the accuracy of BAV auscultation among cardiology fellows and faculty at Children's Healthcare of Atlanta and Emory University in 2012.

A Littman recording stethoscope was used to record heart sounds of pediatric patients with image confirmed bicuspid aortic valves. For control, we recorded the heart sounds of pediatric patients with a split first heart sound whose echocardiogram showed a structurally normal heart without any abnormalities of the mitral or aortic valves. All recordings were performed at the location where the sound was best heard, either the lower left sternal border or the apex. From these patients, we recorded a total of five sound files: three clicks from bicuspid aortic valves, and two split first heart sounds. All recordings were de-identified.

Each physician listened to the five sound files and were asked by the interviewer if the sound was a bicuspid aortic valve click or asynchronous closure of the mitral and tricuspid valves. Participants were allowed to decline to guess if they were uncertain. No participants or answers were excluded.

We determined the overall accuracy of diagnosis of pathological clicks versus physiological heart sounds for the overall cohort and sub-groups based on those with less than ten years of experience against those with ten or more years of experience. Each sub-group was roughly equal in size. A Wilcoxon rank sum test was used to compare the individual physician accuracy percentages in each of the two experience groups. To examine overall agreement between the physicians and the gold-standard echo, we calculated Cohen's kappa coefficient for both the overall physician cohort and sub-

groups stratified by experience. In this case, each physician's diagnoses of the 5 sounds were treated as independent observations, resulting in a total of 94 physician-echo scoring pairs. Cohen's kappa is a statistic measures agreement between two raters and is based on the difference between the observed agreement and the expected agreement based on chance alone. In this case, the physician was considered a single rater and the gold-standard echo was considered the other rater. A Kappa coefficient < 0 indicates worse than chance agreement, a Kappa of 0.2 indicates slight agreement, while a Kappa of 0.8 indicates substantial agreement. To assess precision in ratings among physicians across the 5 sounds, we used an extension to Kappa, proposed by Fleiss (1981), to allow for the calculation of the agreement statistic when there are more than 2 raters. The generalized kappa for more than two raters was calculated using the *MAGREE* macro in SAS (12). Statistical analyses were performed using SAS 9.4 (Cary, NC).

Results

The study population consisted of 21 pediatric cardiologists, divided into subgroups by years of experience. The average for those with less than 10 years' experience was 3 years, and the average for those with 10 or more years was 28 years' experience. Among the entire cohort, diagnostic accuracy of the BAV click was 38% (95% CI 28-48), and accuracy of identifying the split S1 was 41% (95% CI 26-55). Both subgroups performed poorly, with diagnostic accuracies between 37-44% for all sounds (Table 1). No participants correctly identified all sounds (Fig 1). Only 2 of 21 physicians accurately diagnosed 4 of the 5 sounds. Kappa, or percent agreement by chance, was -0.11 (CI 95%) -0.31-0.08), with no difference observed when stratifying by experience. Participants with < 10 years of experience had kappa of -0.03 (CI 95% -0.39-0.33), and those with >=10 years had kappa of -0.15 (CI 95% -0.38–0.08). There were no patterns observed among the raters, and no sound file had a consistently higher rate of accuracy. In addition to poor accuracy, the overall agreement among physicians, regardless of the gold standard, showed poor precision. The generalized Kappa comparing the 21 raters was 0.01 (95% CI -0.03 – 0.04).

Discussion

In this study, we found that our sample of pediatric cardiologists was unable to distinguish the physiologic sounds of the mitral and tricuspid valves closing from the ejection click of a bicuspid atrial valve. They performed worse than random guessing, with accuracy consistently below 50% for all subgroups for both heart sounds. Our study has important ramifications for clinical practice. In the most recent guidelines from the American College of Cardiology/American Heart Association regarding appropriate use of echocardiography, there was no mention of the appropriateness of echocardiography utilization for a click or S1 (13). However, in a 2015 pediatric multicenter trial on appropriate use of echocardiography, 5% of all transthoracic ultrasounds ordered were for auscultation of a click, and 2 of the 25 were discovered to have a bicuspid aortic valve (14). It is likely that the patient population with clicks is underreported due to the inability of physicians to detect this physical exam finding, as demonstrated in our study. Given the results of this study in which physicians poorly differentiate between a BAV click or a benign S1, it would be reasonable for physicians to order an echocardiogram when they hear what they perceive to be either of these findings.

It was surprising in our study that cardiologists with more experience did not perform better than those with less experience. This finding is in contrast to a study by Vukanovic-Criley et al which showed that expertise with cardiac examination skills improved with time since completion of training (15). However, that study included heart sounds from adults, and results specifically for a BAV click vs split S1 were not reported.

Nevertheless, the overall poor performance warrants efforts to improve clinician performance. Electronic stethoscopes, such as the one used to record sounds for this study, have been marketed as improving performance, but physician use of these devices has not been shown to meet those claims (16). However, a recent study by Lai et al. suggests that computer-aided interpretation of the phonocardiograms recorded by such electronic stethoscopes may indeed improve performance, with a sensitivity of 87% and specificity of 100% compared to echocardiogram for the evaluation of murmurs in children (17). Although this study did not evaluate the performance of distinguishing a BAV click vs. benign split S1, its findings hold the promise of potentially needing fewer echocardiograms in such instances.

This study does have some limitations, most notably that this was a simulation exercise and does not reflect real world experience. First, physicians had to rely solely on auscultation and did not have the benefit of having further history, physical exam, or electrocardiographic findings. Such information can be useful in determining the presence of disease. Second, the prevalence of BAV in our study was 60%, which is much higher than that of the general population. In real world experience, the vast majority of abnormal S1 sounds will be benign as evidenced in a recent study, but the consequences of missing a BAV can be severe (18).

With a current absence of a system in place to evaluate a physician's auscultation abilities, particularly for subtle findings, it is likely that auscultation skills vary widely between physicians. Our study suggests that, in general, depending on even a specialist's auscultation may be unreliable for the finding of bicuspid aortic valve disease, a disease with important lifelong clinical implications. Given the importance of this disease and the

results of this study, the authors encourage physicians to strongly consider an echocardiogram for an abnormal S1.

References

- Fedak PWM, Verma S, David TE, Leask RL, Weisel RD, Butany J. Clinical and Pathophysiological Implications of a Bicuspid Aortic Valve. *Circulation*. 2002;106:900-904
- 2. Braverman AC, Guven H, Beardslee MA, Makan M, Kates AM, Moon MR. The bicuspid aortic valve. *Curr Probl Cardiol*. 2005;**30**:470–522.
- 3. Michelena HI, Khanna AD, Mahoney D, et al. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA*. 2011 Sept 14;306(10):1104-12. doi: 10.1001/jama.2011.1286.
- 4. Michelena HI, Prakash WK, Della Corte A, et al. Bicuspid Aortic Valve. *Circulation*. 2014;**129**:2691-704.
- 5. Ohnemus D, Oster ME, Gatlin S, Jokhadar M, Mahle WT. The effect of angiotensin-converting enzyme inhibitors on the rate of ascending aorta dilation in patients with bicuspid aortic valve. *Congenit Heart Dis.* 2015;**10**:E1-5.
- 6. Mahle WT, Sutherland JL, Frias PA. Outcome of isolated bicuspid aortic valve in childhood. *J Pediatr*. 2010;**157**:445-9.
- 7. Tzemos N, Therrien J, Yip H, et al. Outcomes in Adults with Bicuspid Aortic Valves. *JAMA*. 2008;**300**:1317-1325.
- 8. Saha S, Bastiaenen R, Hayward M, McEwan JR. An undiagnosed bicuspid aortic valve can result in severe left ventricular failure. *BMJ*. 2007;**334**:420-422.
- 9. Steinberger J, Moller JH, Berry JM, Sinaiko AR. Echocardiographic diagnosis of heart disease in apparently healthy adolescents. *Pediatrics* 2000;**105**:815-8

- Jacobs WR. Ejection Clicks. In: Walker HK, Hall WD, Hurst JW, ed. *Clinical Methods: The History*, Physical, and Laboratory Examinations. 3rd edition.
 Boston: Butterworths; 1990: Chapter 28.
- 11. Jacobs WR. The First Heart Sound. In: Walker HK, Hall WD, Hurst JW, ed. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; 1990: Chapter 22.
- 12. Chen B, Zaebst D, Seel L. A Macro to Calculate Kappa Statistics for Categorizations by Mulitple Raters. Poster presented at: SAS Users Group International (SUGI) 30; April 10-13, 2005; Philidelphia, PA.
- 13. Nishimura RA, Otto CM, Bonow RO et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary. *J Am Coll Cardiol*. 2014:**63**:2438-88.
- 14. Sachdeva et al. "Pediatric Appropriate Use Criteria Implementation Project". *J Am Coll Cardiol.* 2015;**66**:1132-1140.
- 15. Vukanovic-Criley JM, Hovanesyan A, Criley SR, Ryan TJ, Plotnick G, Mankowitz K, Conti CR, Criley JM. Confidential testing of cardiac examination competency in cardiology and noncardiology faculty and trainees: a multicenter study. *Clin Cardiol*. 2010;33:738-45.
- 16. Iversen K, Søgaard Teisner A, Dalsgaard M, Greibe R, Timm HB, Skovgaard LT, Hróbjartsson A, Copenhagen O, Copenhagen S, Copenhagen K. Effect of teaching and type of stethoscope on cardiac auscultatory performance. *Am Heart J.* 2006;152:85.e1-7.

- 17. Lai LS, Redington AN, Reinisch AJ, Unterberger MJ, Schriefl AJ. Computerized Automatic Diagnosis of Innocent and Pathologic Murmurs in Pediatrics: A Pilot Study. Congen Heart Dis. 2016;11:386-395.
- 18. Sachdeva et al. "Pediatric Appropriate Use Criteria Implementation Project". *J Am Coll Cardiol.* 2015;**66**:1132-1140.

Tables

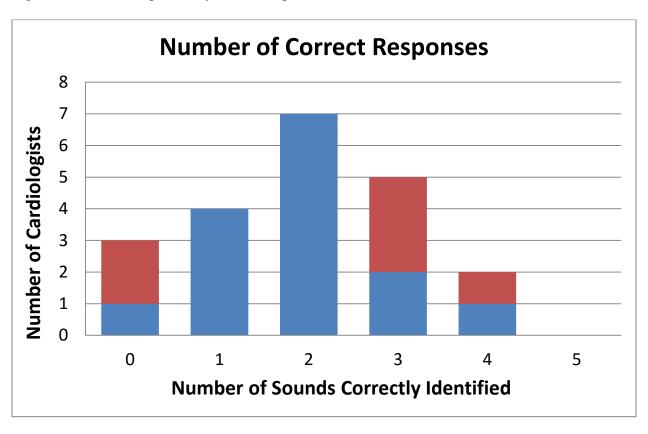
Table 1. Overall Diagnostic Accuracy and Cohen's Kappa for Detecting Bicuspid Aortic

Valve and Split S1

	Diagnostic Accuracy % (CI)			Kappa (CI)
	All	BAV	S1	
<10 years (n=6)	43 (16-71)	44 (36-53)	42 (27-56)	-0.11 (-0.31-0.08)
≥10 years (n=15)	37 (27-47)	36 (21-50)	40 (24-56)	-0.03 (-0.39-0.33)
Overall (n=21)	39 (29-49)	38 (28-48)	41 (26-55)	-0.15 (-0.38-0.08)

Figures

Figure 1. Correct Responses by the Participants.



- <10 years experience</p>
- ≥10 years experience