

World Journal of *Cardiology*

World J Cardiol 2017 August 26; 9(8): 640-714





REVIEW

- 640 Diagnosis and management challenges of in-stent restenosis in coronary arteries

Alraies MC, Darmoch F, Tummala R, Waksman R

- 652 Cardiovascular involvement in celiac disease

Ciaccio EJ, Lewis SK, Biviano AB, Iyer V, Garan H, Green PH

MINIREVIEWS

- 667 Is there evidence for statins in the treatment of aortic valve stenosis?

Akin I, Nienaber CA

ORIGINAL ARTICLE

Basic Study

- 673 Interleukin-19 is cardioprotective in dominant negative cyclic adenosine monophosphate response-element binding protein-mediated heart failure in a sex-specific manner

Bruns DR, Ghincea AR, Ghincea CV, Azuma YT, Watson PA, Autieri MV, Walker LA

Case Control Study

- 685 Effects of hypertonic saline solution on body weight and serum creatinine in patients with acute decompensated heart failure

Lafrenière G, Béliveau P, Bégin JY, Simonyan D, Côté S, Gaudreault V, Israeli Z, Lavi S, Bagur R

Observational Study

- 693 Estimating pressure gradients by auscultation: How technology (echocardiography) can help improve clinical skills

Kadle RL, Phoon CKL

- 702 Coronary angiography findings in cardiac arrest patients with non-diagnostic post-resuscitation electrocardiogram: A comparison of shockable and non-shockable initial rhythms

Martínez-Losas P, Salinas P, Ferrera C, Nogales-Romo MT, Noriega F, Del Trigo M, Núñez-Gil JJ, Nombela-Franco L, Gonzalo N, Jiménez-Quevedo P, Escaned J, Fernández-Ortiz A, Macaya C, Viana-Tejedor A

CASE REPORT

- 710 Very late bioresorbable scaffold thrombosis and reoccurrence of dissection two years later chronic total occlusion recanalization of the left anterior descending artery

Di Serafino L, Cirillo P, Niglio T, Borgia F, Trimarco B, Esposito G, Stabile E

ABOUT COVER

Editorial Board Member of *World Journal of Cardiology*, Bahri Akdeniz, MD, Professor, Department of Cardiology, Dokuz Eylul University, 35340 Izmir, Turkey

AIM AND SCOPE

World Journal of Cardiology (*World J Cardiol*, *WJC*, online ISSN 1949-8462, DOI: 10.4330) is a peer-reviewed open access journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJC covers topics concerning arrhythmia, heart failure, vascular disease, stroke, hypertension, prevention and epidemiology, dyslipidemia and metabolic disorders, cardiac imaging, pediatrics, nursing, and health promotion. Priority publication will be given to articles concerning diagnosis and treatment of cardiology diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJC*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Cardiology is now indexed in Emerging Sources Citation Index (Web of Science), PubMed, and PubMed Central.

FLYLEAF

I-IV Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Ya-Jing Lu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Fang-Fang Ji*
Proofing Editorial Office Director: *Jin-Lei Wang*

NAME OF JOURNAL
World Journal of Cardiology

ISSN
ISSN 1949-8462 (online)

LAUNCH DATE
December 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Jian-Jun Li, MD, PhD, Professor, Center for Coronary Artery Disease, Fu Wai Cardiovascular Hospital, Chinese Academy of Medical Science, Beijing 100037, China

Giuseppe De Luca, PhD, Assistant Professor, Department of Cardiology, Piedmont University, Novara 28100, Italy

Nathan D Wong, FACC, FAHA, PhD, Director, Professor, Heart Disease Prevention Program, Division of Cardiology, Department of Medicine, University of California, Irvine, CA 92629, United States

sity of California, Irvine, CA 92629, United States

EDITORIAL BOARD MEMBERS
All editorial board members resources online at <http://www.wjgnet.com/1949-8462/editorialboard.htm>

EDITORIAL OFFICE
Xiu-Xia Song, Director
World Journal of Cardiology
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

PUBLICATION DATE
August 26, 2017

COPYRIGHT
© 2017 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.f6publishing.com>

Observational Study

Estimating pressure gradients by auscultation: How technology (echocardiography) can help improve clinical skills

Rohini L Kadle, Colin KL Phoon

Rohini L Kadle, Colin KL Phoon, Division of Pediatric Cardiology, Hassenfeld Children's Hospital of New York at NYU Langone, Fink Children's Center, New York, NY 10016, United States

Author contributions: Kadle RL assisted in data analysis and contributed extensively to the writing of the manuscript; Phoon CKL designed the research, performed the research, analyzed the data, and wrote and approved the final manuscript.

Institutional review board statement: This study was reviewed by the NYU School of Medicine's Institutional Review Board (IRB).

Informed consent statement: As per the Institutional Review Board-approved protocol, no informed consent was required (and therefore none was obtained), since all data were collected anonymously and de-identified.

Conflict-of-interest statement: We report no conflicts of interest, real or perceived, financial or otherwise.

Data sharing statement: Dataset is available from the corresponding author at colin.phoon@nyumc.org. No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Colin KL Phoon, MPhil, MD, Associate Professor of Pediatrics, Division of Pediatric Cardiology, Hassenfeld Children's Hospital of New York at NYU Langone, Fink Children's Center, 160 East 32nd Street, 2nd floor/L-3, New York, NY 10016, United States. colin.phoon@nyumc.org

Telephone: +1-212-2639990

Fax: +1-212-2639678

Received: November 7, 2016

Peer-review started: November 10, 2016

First decision: March 8, 2017

Revised: March 29, 2017

Accepted: May 3, 2017

Article in press: May 5, 2017

Published online: August 26, 2017

Abstract

AIM

To extend our previously-published experience in estimating pressure gradients (PG) *via* physical examination in a large patient cohort.

METHODS

From January 1, 1997 through December 31, 2009, an attending pediatric cardiologist compared clinical examination (EXAM) with Doppler-echo (ECHO), in 1193 patients with pulmonic stenosis (PS, including tetralogy of Fallot), aortic stenosis (AS), and ventricular septal defect (VSD). EXAM PG estimates were based primarily on a murmur's pitch, grade, and length. ECHO peak instantaneous PG was derived from the modified Bernoulli equation. Patients were 0-38.4 years old (median 4.8).

RESULTS

For all patients, EXAM correlated highly with ECHO: ECHO = 0.99 (EXAM) + 3.2 mmHg; $r = +0.89$; $P < 0.0001$. Agreement was excellent (mean difference = -2.9 ± 16.1 mmHg). In 78% of all patients, agreement between EXAM and ECHO was within 15 mmHg and within 5 mmHg in 45%. Clinical estimates of PS PG were more accurate than of AS and VSD. A palpable precordial thrill and increasing loudness of the murmur predicted higher

gradients ($P < 0.0001$). Weight did not influence accuracy. A learning curve was evident, such that the most recent quartile of patients showed $ECHO = 1.01 (EXAM) + 1.9$, $r = +0.92$, $P < 0.0001$; during this time, the attending pediatric cardiologist had been > 10 years in practice.

CONCLUSION

Clinical examination can accurately estimate PG in PS, AS, or VSD. Continual correlation of clinical findings with echocardiography can lead to highly accurate diagnostic skills.

Key words: Physical examination; Ventricular septal defect; Clinical skills; Echocardiography; Aortic stenosis; Pulmonary stenosis

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Knowing pressure gradients across valves, arteries, and ventricular septal defects is important to clinical management of patients. In a large cohort of patients, we have determined the high degree of accuracy of the physical examination against the benchmark Doppler echocardiography. We discuss this clinical approach in the context of clinical practice, technology, and healthcare costs.

Kadle RL, Phoon CKL. Estimating pressure gradients by auscultation: How technology (echocardiography) can help improve clinical skills. *World J Cardiol* 2017; 9(8): 693-701 Available from: URL: <http://www.wjgnet.com/1949-8462/full/v9/i8/693.htm> DOI: <http://dx.doi.org/10.4330/wjc.v9.i8.693>

INTRODUCTION

Strong clinical skills, including history-taking and physical diagnostic skills, remain an important part of patient evaluation - central to the practice of medicine. The clinical skills required for auscultation are especially important in childhood, when more than 50% of children have heart murmurs, most of which are benign^[1,2]. In recent years however, there have been a decline in clinical examination skills and an increasing reliance on diagnostic testing^[3-7].

The gradual loss of emphasis on physical exam skills has several implications^[8-11]. The physical exam is an integral part of the doctor-patient relationship, and can also garner otherwise unattainable observations and findings. Additionally, the information obtained from the physical exam can help delineate the need for further testing. Although there have been several initiatives to minimize wasteful testing by focus on clinical examination^[12-14], few groups have described specific and learnable techniques to do so.

In this follow-up to a small pilot study^[15], our objectives of this study were several-fold. We hoped

to further validate our technique of estimating peak pressure gradients through auscultation with a much larger cohort of patients. We also hoped to debunk the idea that the physical exam has a dwindling role in medicine; we believe its use in conjunction with technology can allow for a more accurate clinical assessment. We also hoped to determine the specific situations and characteristics associated with a more accurate physical exam, allowing others to learn this technique as well.

MATERIALS AND METHODS

The methods are essentially as detailed in our previous report^[15]. This study was approved by the Institutional Review Boards at NYU Langone Medical Center and Bellevue Hospital Center (both located in New York, NY, United States). Including our initial cohort of 151 patients^[15], a total of 1193 consecutive patients with pulmonary stenosis (PS, $n = 563$), aortic stenosis (AS, $n = 234$), or ventricular septal defect (VSD, $n = 396$) were studied by both auscultation and Doppler echocardiography over a 13-year period between February 1997 and December 2009. Not all patients were diagnosed with these lesions at the visits; some were "first" visits, but the physical examination was characteristic for valvar stenosis or VSD, and therefore a clinical estimate of the pressure gradient could be made even before a diagnosis was established by echocardiography. All levels of PS (including tetralogy of Fallot) and AS, all types of VSDs, and residual lesions after surgical or transcatheter interventions were included. In our patient population, the AS seen was congenital, rheumatic, or postoperative, not the fibrocalcific AS seen in older patients. "Complex" AS or PS (as opposed to valvar AS or PS) denotes non-valvar stenosis, or multi-level stenosis; examples include the PS in patients with tetralogy of Fallot, subvalvular AS and supravalvular AS. It has been standard clinical practice in our pediatric echocardiography laboratory for the author (CKLP), an attending echocardiographer, to examine every patient briefly as time permits; it is felt by at least some echocardiographers, including the author, that this preliminary examination (which may include palpation and auscultation, especially of the heart sounds and murmurs) improves the reliability of the echocardiographic study. This physical examination helps to assess the degree of clinical suspicion and to focus the requested echocardiogram. For lesions with pressure gradients, the author routinely estimates a pressure gradient (see below) before the echocardiographic study. It should be noted this study was started (1997) only 1.5 years following the completion of clinical fellowship training by CKLP; therefore, at the completion of data acquisition (2009), 13.5 years had elapsed since completion of training.

The auscultatory pressure gradient was estimated by an "auscultatory scale" based predominantly on

Table 1 Summary table of key findings for pulmonary stenosis, aortic stenosis, and ventricular septal defect

Lesion	<i>n</i>	Mean gradient (mmHg)	Agreement to: ≤ 15 mmHg	≤ 10 mmHg	≤ 5 mmHg	<i>r</i>
Pulmonary stenosis						
PS (all)	563	42 ± 28	82%	70%	49%	0.85
Valvar PS	313	36 ± 22	89%	77%	56%	0.85
Complex PS	250	49 ± 32	72%	61%	40%	0.84
PVR	81	48 ± 25	84%	65%	42%	0.86
Aortic stenosis						
AS (all)	234	38 ± 24	81%	71%	49%	0.8
Valvar AS	112	42 ± 24	77%	68%	46%	0.76
Complex AS	122	34 ± 23	85%	75%	52%	0.85
AVR	34	46 ± 22	71%	65%	38%	0.71
Ventricular septal defect						
VSD	396	83 ± 31	70%	60%	36%	0.82

"Complex" AS or PS denotes non-valvar stenosis or multi-level stenosis, such as the PS observed in patients with tetralogy of Fallot. AS: Aortic stenosis; AVR: Aortic valve replacement; CHD: Congenital heart defects; PS: Pulmonary stenosis; PVR: Pulmonary valve replacement; VSD: Ventricular septal defect.

a murmur's perceived predominant frequencies and frequency spread^[15,16]. A stethoscope is inched around the chest until the highest frequencies of a murmur are heard. These frequencies are then used to estimate the pressure gradient. As the examiner continued to gain clinical experience, other components of auscultation were incorporated into the clinical estimate of the pressure gradients, including murmur loudness and length. Short murmurs generally comprised < 50% of systole, medium-length 50% to < 100% of systole with a crescendo-decrescendo quality, and long/holosystolic 100% of systole. Gradients were estimated in 5 mmHg range increments (for example, 5-10 mmHg or 25-30 mmHg) and then recorded as a midpoint value [5-10 (= 8 mmHg), 25-30 (= 28 mmHg), *etc.*]. In the remainder of this article, the terms "auscultation" and "auscultatory gradient" will refer to this technique of assessing the frequency composition of a murmur unless otherwise specified.

To avoid bias, the auscultatory gradient was recorded before Doppler echocardiography, and the Doppler examination was performed by a pediatric cardiac sonographer who was unaware of the auscultatory estimate. Echocardiograms performed solely by the author were excluded. In standard fashion, the Doppler beam was aligned as parallel as possible with the blood flow jet, without angle correction, interrogating for the maximal flow velocity from multiple views. The peak instantaneous Doppler pressure gradient was calculated with the modified Bernoulli equation. Any perceived inconsistencies between the auscultatory gradient and the echocardiographic results were resolved with further imaging.

Ideally, patients should be in a calm resting state for both the auscultatory examination and the echocardiogram because changes in activity level will change the cardiac output and therefore flow characteristics, including gradients. Because we do not routinely use conscious sedation, we examined patients in as calm a state as possible, recognizing that

variability in the resting state will introduce variability into our assessments.

Age, weight, diagnoses, and history of interventions were obtained from the patient reports.

The relationship between the auscultatory and Doppler pressure gradients was assessed by simple linear regression. Agreement was assessed by Bland-Altman analysis^[17]. Results are expressed as mean ± SD. Differences were analyzed with a 2-tailed Student *t* test. Comparison of categorical variables was performed with chi-square analysis or Fisher's exact test. Statistical significance was set at *P* < 0.05.

RESULTS

Patient demographics

Patients were 0-38.4 years old (mean 6.8 years, median 4.8), weighing 0.83-129 kg (mean 26.8 kg, median 18.2). There were 339 patients between 0-1 years of age (infants); 270 patients > 1 year-5 years (toddlers and young children); 311 patients between > 5 years-12 years (school-age children); 200 patients between 12-18 years (adolescents); and 73 patients older than 18 years (adults).

Accuracy and correlations of various congenital cardiac conditions

For all patients, auscultation correlated highly with echocardiography: ECHO= 0.99 (AUSC) + 3.2 mmHg; *r* = +0.89 (*r*² = +0.79); *P* < 0.0001 (Figure 1A). Agreement was excellent [mean difference between clinical exam and echo = -2.9 ± 16.1 mmHg (SD), also as seen in the Bland-Altman analysis, Figure 1B]. In 78% of all patients, agreement between auscultation and echocardiography was within 15 mm Hg; in 67%, within 10 mmHg; and in 45%, within 5 mmHg (Figure 1C). Clinical estimates of PS pressure gradients were more accurate than of AS and VSD (Table 1). Valvar PS appeared to be more accurately estimated than other lesions, and VSD showed the worst agreement overall.

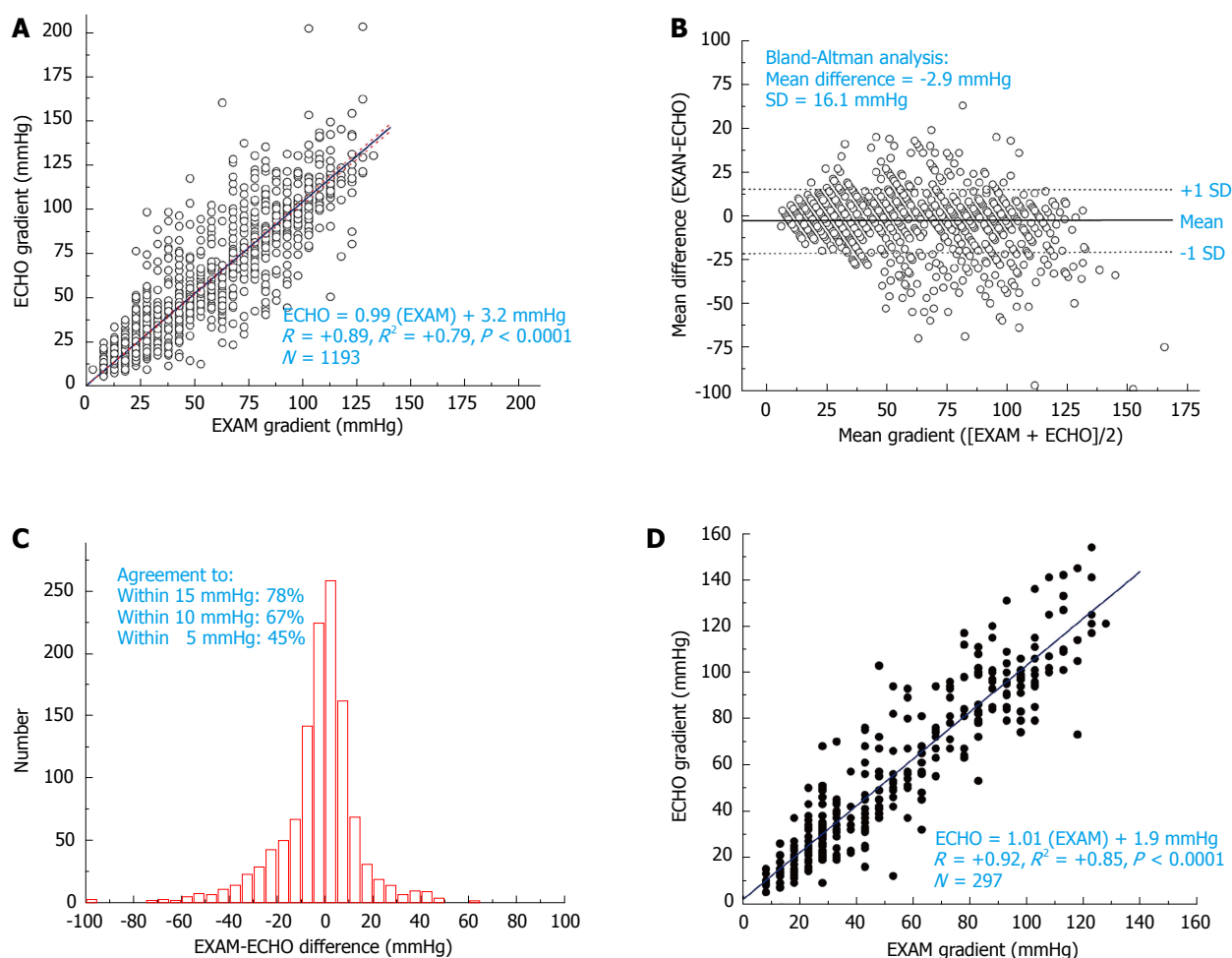


Figure 1 Accuracy and correlations of various congenital cardiac conditions. A: Regression plot of all patients; B: Bland-Altman plot; C: Histogram displaying spread between the Doppler and physical examination gradients, and the agreement between Doppler and physical examination to within 15, 10, and 5 mmHg; D: Regression plot of most recent quartile of patients.

A learning curve was evident. Overall agreement and correlation in the original published cohort of 151 patients [$ECHO = 0.99 (\text{AUSC}) + 7.12$, $r = +0.84$ ($r^2 = +0.71$)] were worse (Phoon 2001); the most recent quartile of patients showed $ECHO = 1.01 (\text{AUSC}) + 1.9$, $r = +0.92$ ($r^2 = +0.85$), $P < 0.0001$ ($n = 297$) (Figure 1D). The initial cohort^[15] corresponded to a time period from early 1997 through mid-1998, while the most recent quartile of data corresponded to a time period from mid-2007 through end of 2009; thus, there was a 10-year difference in clinical experience.

Correlates with patient factors affecting accuracy

Increasing loudness of the murmur (standard 1-6 grade scale) predicted higher gradients ($r = +0.54$, $P < 0.0001$), with the largest gap occurring between grades 2 (mean PG: $36 \pm 29 \text{ mmHg}$) and 3 (mean PG: $63 \pm 35 \text{ mmHg}$) (Figure 2A). Similarly and as expected, a palpable precordial thrill predicted significantly higher gradients [all $P < 0.0001$: PS: $32 \pm 22 \text{ mmHg}$ (no thrill) vs 67 ± 25 (+thrill); AS: 31 ± 20 vs 59 ± 29 ; VSD: 80 ± 31 vs 101 ± 28] (Figure 2B, C). Despite the highly significant differences in patients

with and without a palpable precordial thrill, there was considerable overlap in the pressure gradients. Possible influencing factors are shown in Table 2. Heavier weight and prior surgery did not appear to influence accuracy. Infants and young toddlers appeared to be less accurately assessed. Although a previous echocardiogram (and therefore possibly knowledge of the previous gradient) exhibited a better correlation, the correlation coefficient even during a “first” visit was very high (Table 2).

In several cases, the physical examination “trumped” the echocardiogram, although this represented a small percentage of all patients. Nearly all were VSD’s, for which Doppler echocardiography underestimated the predicted peak gradient due to a suboptimal Doppler incident angle (Table 3). In such cases, the VSD gradient alone would have predicted the presence of pulmonary hypertension.

DISCUSSION

This large dataset extends our previous observations and confirms that physical examination, relying mainly

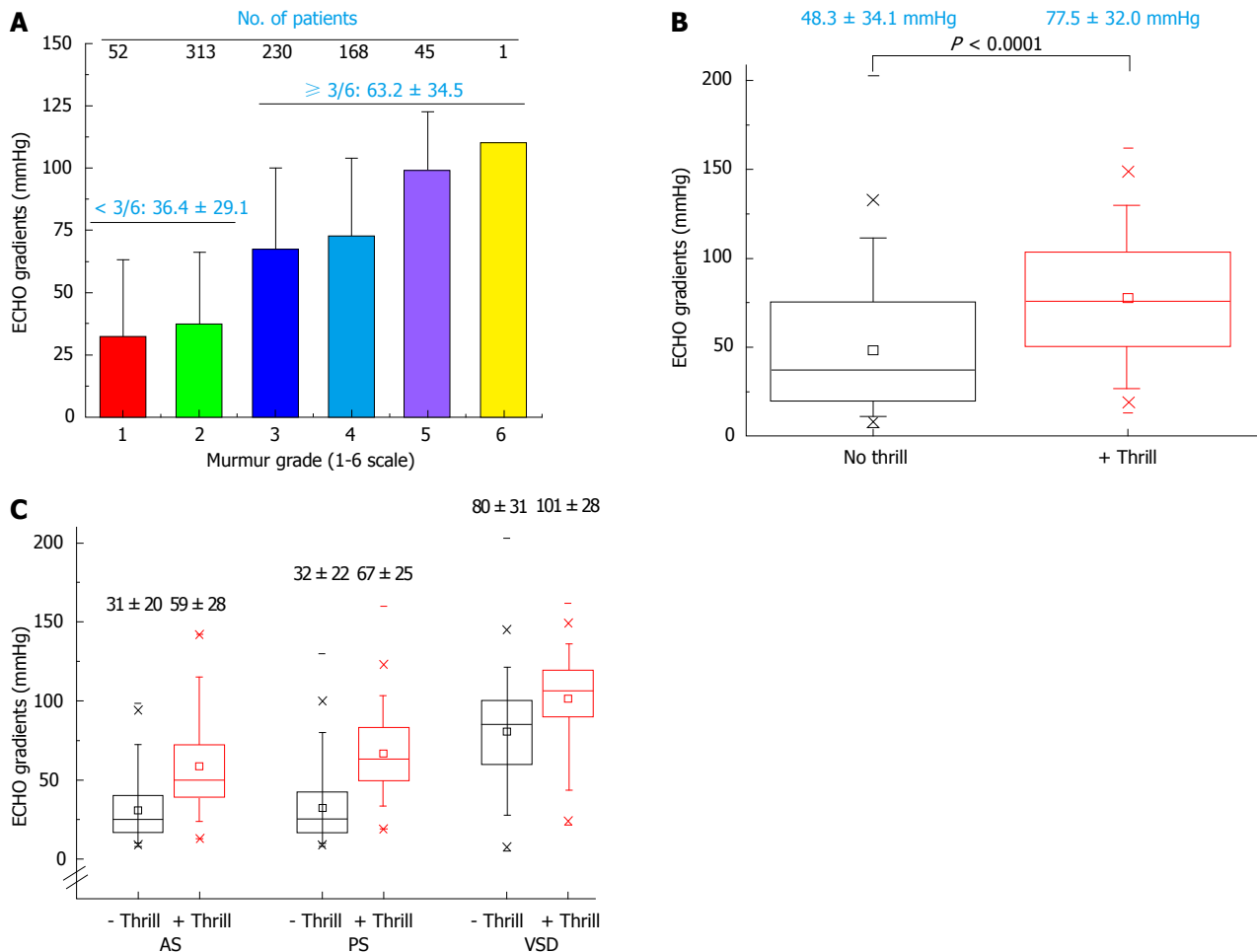


Figure 2 Correlates with patient factors affecting accuracy. A: Loudness of heart murmur (standard grade system, 1-6) plotted against peak Doppler ("ECHO") gradient; B: Box-and-whiskers plot of Doppler peak gradients in the absence and presence of a palpable thrill, all patients; C: Box-and-whiskers plots of specific congenital lesions (aortic stenosis, pulmonic stenosis, ventricular septal defect), thrill absent vs thrill present.

on auscultation, can be very accurate in determining pressure gradients. We emphasize that our purpose was not to diagnose specific conditions *de novo*, but to evaluate pressure gradients clinically. Other studies have previously demonstrated that the cardiac physical exam, specifically auscultation, can accurately distinguish benign from pathologic murmurs^[15,18-24]. Although these studies look at auscultation in general, they do not specifically analyze pressure gradients. We have now in more detail analyzed some of those aspects of clinical auscultation, as well as patient characteristics, which impact the accuracy of the physical examination. A key finding in this study is how technology - in this case, echocardiography - can help improve clinical skills, presumably by providing feedback to the examiner.

Comparison of different lesions: PS, AS, VSD

Pressure gradients have been examined in dogs, and have been found to both correlate with echocardiographic findings^[25-28] and be associated with severity of disease^[29]. These studies corroborate the validity of our findings, and we further show its applicability to human subjects. Several groups have

shown that examination can diagnose both AS and PS successfully^[30-36]. Diagnosis of VSDs by clinical exam is also accurate but can be imperfect for major VSDs^[37]. Our study takes these analyses further by laying out a specific auscultatory technique to assess heart murmurs, and by continually correlating clinical findings with echocardiographic data to improve accuracy. We demonstrate that auscultation has the greatest accuracy in predicting pressure gradients in PS, and is still accurate but less so in VSD. We speculate that the murmur of PS is consistently directed in a similar direction in nearly all patients, whereas VSD jets would exhibit far more variability that may change their auscultatory characteristics. We additionally experienced several cases in which echocardiography underestimated the severity of the murmur, or missed the etiology of a murmur completely, demonstrating the significance of auscultation in a clinical exam.

When to be careful: Accuracy is affected by certain patient variables

Several auscultatory characteristics have been identified to predict pathologic disease, such as holosystolic timing, harshness, grade 3 or more, or palpable

Table 2 Summary table of variables that might affect accuracy of clinical estimates of gradients

Variable	n	Mean gradient (mmHg)	Agreement to: ≤ 15 mmHg	≤ 10 mmHg	≤ 5 mmHg	r
Weight						
≤ 10 kg	367	61 ± 32	71%	61%	42%	+0.81
> 10 to 20 kg	270	57 ± 36	79%	69%	46%	+0.92
> 20 to 40 kg	236	53 ± 38	81%	71%	48%	+0.91
> 40 to 70 kg	237	49 ± 34	81%	67%	42%	+0.91
> 70 kg	82	45 ± 35	85%	74%	48%	+0.88
Age						
< 2 yr	414	60 ± 32	71%	62%	42%	+0.83
≥ 2 yr	779	52 ± 36	81%	70%	46%	+0.91
Prior echo?						
No prior	321	61 ± 36	72%	64%	43%	+0.85
+Prior	872	53 ± 35	79%	68%	45%	+0.90
Operative status (all CHD)						
No operative	688	65 ± 37	74%	64%	43%	+0.89
Post-operative	505	42 ± 27	82%	70%	46%	+0.87

CHD: Congenital heart defects.

Table 3 Examples of cases when physical examination “trumped” echocardiography or echocardiography presented misleading data

Case	Age (yr)	Lesion	Clinical Gradient	DOPP Gradient	Comment
1	6.7	Supravalvar PS s/p repair of TOF with homograft from RV to PA	63	24	Homograft poorly visualized; tricuspid regurgitation jet predicted a systolic RV pressure of 66 mmHg plus the right atrial v-wave, so the PS gradient was significantly underestimated by DOPP
2	6.9	VSD, s/p repair of TOF	70	66	Prior echocardiograms did not visualize VSD; exam led to finding of a tiny residual VSD
3	10.8	VSD	88	63	Poor DOPP incident angle predicted pulmonary hypertension
4	0.005	VSD	68	NA	VSD was so tiny and anterior, a jet could not be obtained for a DOPP gradient
5	4.3	VSD	73	61	BP 104/50; poor DOPP incident angle predicted pulmonary hypertension
6	0.01	VSD	88	48	Technician obtained initial VSD DOPP gradient of 28 mmHg; exam prompted a search for a better DOPP angle
7	2.8	VSD	83	55	Poor DOPP incident angle predicted pulmonary hypertension; tricuspid regurgitation jet predicted normal PA pressures
8	5.5	VSD, s/p repair	98	62	Poor DOPP incident angle predicted pulmonary hypertension; tricuspid and pulmonary regurgitation jets predicted normal PA pressures
9	3.8	VSD	73	53	Poor DOPP incident angle predicted pulmonary hypertension; tricuspid regurgitation jet predicted normal PA pressures
10	15.4	VSD, Shone's complex with minimal LV outflow tract obstruction	93	63	Poor DOPP incident angle predicted pulmonary hypertension
11	15.7	VSD	118	73	Poor DOPP incident angle predicted pulmonary hypertension, even though the VSD was 2.8 mm in diameter; tricuspid and pulmonary regurgitation jets predicted normal PA pressures

BP: Blood pressure; DOPP: Doppler echocardiography; LV: Left ventricular; PA: Pulmonary artery; PS: Pulmonary stenosis; RV: Right ventricular; TOF: Tetralogy of Fallot; VSD: Ventricular septal defect.

precordial thrill^[24,38]. We confirmed such factors can be used to estimate pressure gradients clinically, specifically the loudness of the murmur and the presence of a palpable thrill. Somewhat surprisingly, neither heavier weight nor prior surgery worsened clinical accuracy, even though we had wondered if adipose or scar tissue would impact the auscultated frequency spectrum of heart murmurs.

We believe several teaching points can be made from our data. Although the data exhibit much overlap, the presence of a precordial thrill may help differentiate higher gradients in PS and AS, although this appears to be much less useful with VSD's. For both PS and AS,

the presence of a thrill is likely to indicate a pressure gradient of > 40-45 mmHg. Infants and toddlers also are more difficult to assess clinically.

Philosophical and practical issues

Our study raises the question of whether clinical skills such as these are important in the current era of medical practice. It is debatable or even unlikely a study such as this will impact use of technology or healthcare costs significantly. Nevertheless, it is our impression that: (1) some cases were diagnosed based primarily on clinical findings, and echocardiography played a limited or initially misleading role; and (2)

our data exposes some strengths and weaknesses of the cardiac physical examination with regards to estimating pressure gradients. We and others continue to believe the gradual loss of emphasis on physical exam skills has several implications.

The physical exam is a central part of the doctor-patient relationship. The intimate contact of a physical exam not only gives the patient a sense of comfort and confidence in their physician, but can itself help the patient heal^[10,11,39,40]. Besides the desired dynamic bedside skills help to create, there is also a great deal of information obtained through the physical exam that might otherwise be lost^[11,41]. Many clinical signs and symptoms cannot be classified by technology alone, and can only be appreciated with a thorough physical exam. Fred discussed the implications of over-reliance on CT scans in the diagnosis of patients, including delays in treatment by waiting for a CT scan to confirm a diagnosis that can be made by physical examination alone^[9]. McGee described several instances where the physical exam bested technological testing, including reactive arthritis and pericarditis^[42].

However, as Verghese *et al.*^[39] argue, it is not a fight of physical exam skills vs technology, but the attempt to merge these two to produce the optimal comprehensive exam. Ippisch *et al.*^[43] demonstrated this with regards to cardiology specifically. Neither the physical exam nor a hand-carried echocardiography machine were as accurate as the two used together^[6]. We conclude that technology does not erode physical exam skills but in fact improves both bedside skills and clinical judgment. Technology and clinical examination can and should go hand-in-hand for optimal patient care. "It has to make sense"^[16].

Balancing exam with technology

Recently, several groups have discussed the development of technologies that can assist physicians in analyzing heart murmurs, including computer-assisted auscultation and artificial neural networks^[44,45]. Heart murmurs are complex sounds that can nevertheless be analyzed by a simple frequency analysis, which can be done either with advanced technologies or with a trained ear and a stethoscope.

It has been shown that physicians listening to recorded heart sounds can accurately distinguish innocent from pathologic murmurs^[46-48]. Therefore, telecardiology (tele-auscultation) may find potential use in areas where access to echocardiography is limited. Many rural areas, both in the United States and around the world, do not have either an echocardiography machine or a trained echocardiographer. Doctors trained to auscultate for peak pressures could feasibly receive digital heart sounds from remote areas, and improve remote diagnostic capabilities.

Cost considerations

As physicians move away from their stethoscopes,

they increasingly rely on diagnostic testing that may be unnecessary and is often uninformed, and certainly costly. Unfortunately in our study, it is impossible to know how many patients could have avoided an echocardiogram, based purely on auscultatory estimation of a pressure gradient; other clinical questions may also prompt an echocardiogram. Nevertheless, in response to the increasing impact of echocardiography on health care costs, the ACCF and the ASE prepared a 2011 revision on appropriate use criteria (AUC) for echocardiography^[14]. More recently AUC has also been described for pediatric echocardiography, specifically to determine the need for TTE as an initial diagnostic tool in the outpatient setting^[13]. The AUC are not absolute, but should be applied to clinical exams to determine when an echocardiogram is appropriate. We believe that an increased focus on auscultation would aid in this.

Limitations

This technique has been proven rigorously for one cardiologist only. The study period corresponded to this cardiologist's early and middle career. Of note, in our original study, we validated the auscultatory scale using a senior pediatric cardiology fellow. In our anecdotal experience, several other individuals have mastered this technique to some degree. Similar to our findings, others have shown that attention to clinical examination skills can allow residents and students to improve their physical exam skills and diagnoses^[1]. Moreover, similar findings in animal studies as cited above further validate our approach^[25-29].

This study was performed primarily in children but included heavier children as well as some adults. Still, this data may not be applicable to adults with calcific valve disease or other pathologies not addressed in this study. In addition, pressure gradients depend on flow, and the true severity of a valvar or arterial obstruction may not be reliably assessed when there is myocardial failure. For instance, severe AS in adults may present with only a short, unimpressive midsystolic murmur or even no murmur at all. Finally, we did not test this technique for diastolic gradients.

Conclusions and future directions

Physical examination can accurately estimate pressure gradients in most patients with PS, AS, or VSD. An accurate physical examination may provide data that may be missed by technology, contribute to the patient-doctor relationship, and has a role for the cost-conscious physician. And it may prove useful in areas with limited access to technological resources. We do not propose that the physical exam should replace echocardiography, but believe that the use of the two in conjunction allows for the optimal patient assessment. Contrary to the belief that technology erodes clinical skills, continual correlation of clinical findings with a technological "gold standard" such as echocardiography can lead to highly accurate

diagnostic skills and improved clinical judgment, thereby enhancing clinical skills training and further substantiating the value of clinical examination.

COMMENTS

Background

Strong clinical skills, including physical examination skills, remain central to the practice of medicine. In recent years, there has been a much-decried decline in clinical examination skills. The authors had performed a small pilot study over 15 years ago with 151 patients that indicated that physical examination can be very accurate in determining pressure gradients across stenosis or septal defects.

Research frontiers

Very little research is being performed to help clinicians improve clinical skills, or to determine the strengths and/or weaknesses of clinical examination. Moreover, very little is known about how technology such as imaging can help clinicians improve their physical examination skills.

Innovations and breakthroughs

In pediatric cardiology, physical examination is felt to be very accurate in determining normal from abnormal heart murmurs. What is not known, however, is whether the physical examination can accurately predict pressure gradients in aortic stenosis, pulmonary stenosis, and ventricular septal defect. Knowledge of such pressure gradients helps guide clinical management. Almost no work has been done on this area.

Applications

Honing physical examination skills such as being able to predict pressure gradients has two potential benefits: (1) The clinician may rely less on technology and therefore may reduce the use of expensive testing (imaging); and (2) The clinician may use the physical examination findings in conjunction with testing (imaging) to come to a better overall evaluation of the patient.

Terminology

Aortic stenosis (AS): Anatomical obstruction to blood flow at any level, including subaortic stenosis, valvar aortic stenosis, supra-aortic stenosis (narrowing of the ascending aorta). In this project, aortic stenosis did not include coarctation of the aorta; Pulmonary stenosis (PS): Anatomical obstruction to blood flow at any level, including subpulmonary or infundibular stenosis, valvar stenosis, and supra-aortic stenosis (narrowing of the main pulmonary artery). For the purposes of this project, the authors did not include stenoses of the peripheral branch pulmonary arteries; Ventricular septal defect (VSD): the authors included VSD's at any site, including perimembranous, muscular, and supracristal (subpulmonary) VSD's; Doppler echocardiography, peak instantaneous pressure gradient: For aortic or pulmonary stenosis, there will be a higher-pressure site (proximal to the obstruction) and a lower-pressure site (distal to the obstruction). For ventricular septal defects, the higher-pressure site is generally the left ventricle, while the lower-pressure site is the right ventricle. The difference in pressures (ΔP) between the two sites in the heart or arteries can be estimated using the Doppler principle on echocardiography systems; most commonly, one uses the modified Bernoulli equation, $\Delta P = 4V^2$, where V is the maximal velocity across the region of interest (stenosis or VSD) as acquired from the Doppler ultrasound transducer.

Peer-review

This is a well-written and interesting paper demonstrating how clinical auscultation in expert hands may approximate echo results. The results are important in an era of considerable expenses in technology and of looking down on clinical examination.

REFERENCES

- 1 Dhuper S, Vashist S, Shah N, Sokal M. Improvement of cardiac auscultation skills in pediatric residents with training. *Clin Pediatr*

- (Phila) 2007; **46**: 236-240 [PMID: 17416879 DOI: 10.1177/0009922806290028]
- 2 Noponen AL, Lukkariinen S, Angerla A, Sepponen R. Phonospectrographic analysis of heart murmur in children. *BMC Pediatr* 2007; **7**: 23 [PMID: 17559690 DOI: 10.1186/1471-2431-7-23]
- 3 Mangione S, Nieman LZ, Gracely E, Kaye D. The teaching and practice of cardiac auscultation during internal medicine and cardiology training. A nationwide survey. *Ann Intern Med* 1993; **119**: 47-54 [PMID: 8498764]
- 4 St Clair EW, Oddone EZ, Waugh RA, Corey GR, Feussner JR. Assessing housestaff diagnostic skills using a cardiology patient simulator. *Ann Intern Med* 1992; **117**: 751-756 [PMID: 1416578]
- 5 Gaskin PR, Owens SE, Talner NS, Sanders SP, Li JS. Clinical auscultation skills in pediatric residents. *Pediatrics* 2000; **105**: 1184-1187 [PMID: 10835055 DOI: 10.1542/peds.105.6.1184]
- 6 Roelandt JR. The decline of our physical examination skills: is echocardiography to blame? *Eur Heart J Cardiovasc Imaging* 2014; **15**: 249-252 [PMID: 24282219 DOI: 10.1093/ehjci/jet195]
- 7 Johnson JE, Carpenter JL. Medical house staff performance in physical examination. *Arch Intern Med* 1986; **146**: 937-941 [PMID: 3963985]
- 8 Fred HL. Hyposkillia: deficiency of clinical skills. *Tex Heart Inst J* 2005; **32**: 255-257 [PMID: 16392201 DOI: 10.1016/S0146-6453(05)00032-1]
- 9 Fred HL. The downside of medical progress: the mourning of a medical dinosaur. *Tex Heart Inst J* 2009; **36**: 4-7 [PMID: 19436778]
- 10 Phoon CK. Must doctors still examine patients? *Perspect Biol Med* 2000; **43**: 548-561 [PMID: 11058991 DOI: 10.1353/pbm.2000.0050]
- 11 Verghese A, Horwitz RI. In praise of the physical examination. *BMJ* 2009; **339**: b5448 [PMID: 20015910 DOI: 10.1136/bmj.b5448]
- 12 Levinson W, Kallewaard M, Bhatia RS, Wolfson D, Shortt S, Kerr EA; Choosing Wisely International Working Group. 'Choosing Wisely': a growing international campaign. *BMJ Qual Saf* 2015; **24**: 167-174 [PMID: 25552584 DOI: 10.1136/bmjqs-2014-003821]
- 13 Writing Group for Echocardiography in Outpatient Pediatric Cardiology, Campbell RM, Douglas PS, Eidem BW, Lai WW, Lopez L, Sachdeva R; American College of Cardiology Appropriate Use Criteria Task Force; American Academy of Pediatrics; American Heart Association; American Society of Echocardiography; Heart Rhythm Society; Society for Cardiovascular Angiography and Interventions; Society of Cardiovascular Computed Tomography; Society for Cardiovascular Magnetic Resonance; Society of Pediatric Echocardiography. ACC/AAP/AHA/ASE/HRS/SCAI/SCCT/SCMR/SOPE 2014 appropriate use criteria for initial transthoracic echocardiography in outpatient pediatric cardiology: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Academy of Pediatrics, American Heart Association, American Society of Echocardiography, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Pediatric Echocardiography. *J Am Soc Echocardiogr* 2014; **27**: 1247-1266 [PMID: 25479897 DOI: 10.1016/j.echo.2014.10.002]
- 14 American College of Cardiology Foundation Appropriate Use Criteria Task Force; American Society of Echocardiography; American Heart Association; American Society of Nuclear Cardiology; Heart Failure Society of America; Heart Rhythm Society; Society for Cardiovascular Angiography and Interventions; Society of Critical Care Medicine; Society of Cardiovascular Computed Tomography; Society for Cardiovascular Magnetic Resonance, Douglas PS, Garcia MJ, Haines DE, Lai WW, Manning WJ, Patel AR, Picard MH, Polk DM, Ragosta M, Ward RP, Weiner RB. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 Appropriate Use Criteria for Echocardiography. A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic

- Resonance Endorsed by the American College of Chest Physicians. *J Am Coll Cardiol* 2011; **57**: 1126-1166 [PMID: 21349406 DOI: 10.1016/j.jacc.2010.11.002]
- 15 **Phoon CK**. Estimation of pressure gradients by auscultation: an innovative and accurate physical examination technique. *Am Heart J* 2001; **141**: 500-506 [PMID: 11231450 DOI: 10.1067/mhj.2001.113222]
 - 16 **Phoon CKL**. A Guide to Pediatric Cardiovascular Physical Examination, Or, How to Survive in an Outreach Clinic. Philadelphia: Lippincott-Raven, 1998
 - 17 **Bland JM**, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307-310 [PMID: 2868172]
 - 18 **Bloch A**, Crittin J, Jaussi A. Should functional cardiac murmurs be diagnosed by auscultation or by Doppler echocardiography? *Clin Cardiol* 2001; **24**: 767-769 [PMID: 11768739]
 - 19 **Geva T**, Hegesh J, Frand M. Reappraisal of the approach to the child with heart murmurs: is echocardiography mandatory? *Int J Cardiol* 1988; **19**: 107-113 [PMID: 3372064 DOI: 10.1016/0167-5273(88)90196-9]
 - 20 **Klewer SE**, Samson RA, Donnerstein RL, Lax D, Zamora R, Goldberg SJ. Comparison of accuracy of diagnosis of congenital heart disease by history and physical examination versus echocardiography. *Am J Cardiol* 2002; **89**: 1329-1331 [PMID: 12031743]
 - 21 **Shub C**. Echocardiography or auscultation? How to evaluate systolic murmurs. *Can Fam Physician* 2003; **49**: 163-167 [PMID: 12619738]
 - 22 **Smythe JF**, Teixeira OH, Vlad P, Demers PP, Feldman W. Initial evaluation of heart murmurs: are laboratory tests necessary? *Pediatrics* 1990; **86**: 497-500 [PMID: 2216611]
 - 23 **Roldan CA**, Shively BK, Crawford MH. Value of the cardiovascular physical examination for detecting valvular heart disease in asymptomatic subjects. *Am J Cardiol* 1996; **77**: 1327-1331 [PMID: 8677874]
 - 24 **McCordle BW**, Shaffer KM, Kan JS, Zahka KG, Rowe SA, Kidd L. Cardinal clinical signs in the differentiation of heart murmurs in children. *Arch Pediatr Adolesc Med* 1996; **150**: 169-174 [PMID: 8556121]
 - 25 **Jenni S**, Gardelle O, Zini E, Glaus TM. Use of auscultation and Doppler echocardiography in Boxer puppies to predict development of subaortic or pulmonary stenosis. *J Vet Intern Med* 2009; **23**: 81-86 [PMID: 19175725 DOI: 10.1111/j.1939-1676.2008.0213.x]
 - 26 **Linde A**, Koch J. Screening for aortic stenosis in the Boxer: Auscultatory, ECG, blood pressure and Doppler echocardiographic findings. *J Vet Cardiol* 2006; **8**: 79-86 [PMID: 19083341 DOI: 10.1016/j.jvc.2006.02.002]
 - 27 **Kvart C**, French AT, Fuentes VL, Häggström J, McEwan JD, Schober KE. Analysis of murmur intensity, duration and frequency components in dogs with aortic stenosis. *J Small Anim Pract* 1998; **39**: 318-324 [PMID: 9693417]
 - 28 **Höglund K**, Ahlstrom CH, Häggström J, Ask PN, Hult PH, Kvart C. Time-frequency and complexity analyses for differentiation of physiologic murmurs from heart murmurs caused by aortic stenosis in Boxers. *Am J Vet Res* 2007; **68**: 962-969 [PMID: 17764410 DOI: 10.2460/ajvr.68.9.962]
 - 29 **Ahlstrom Ast C**, Höglund K, Hult P, Häggström J, Kvart C, Ask P. Assessing aortic stenosis using sample entropy of the phonocardiographic signal in dogs. *IEEE Trans Biomed Eng* 2008; **55**: 2107-2109 [PMID: 18632375 DOI: 10.1109/TBME.2008.923767]
 - 30 **Perloff JK**. The Clinical Recognition of Congenital Heart Disease. 6th ed. Philadelphia: Saunders, 2012
 - 31 **Perloff JK**, Lebauer EJ. Auscultatory and phonocardiographic manifestations of isolated stenosis of the pulmonary artery and its branches. *Br Heart J* 1969; **31**: 314-321 [PMID: 5401809]
 - 32 **Crawford MH**, O'Rourke RA. A systematic approach to the bedside differentiation of cardiac murmurs and abnormal sounds. *Curr Probl Cardiol* 1977; **1**: 1-42 [PMID: 67009]
 - 33 **Leatham A**, Weitzman D. Auscultatory and phonocardiographic signs of pulmonary stenosis. *Br Heart J* 1957; **19**: 303-317 [PMID: 13446314]
 - 34 **Lembo NJ**, Dell'Italia LJ, Crawford MH, O'Rourke RA. Bedside diagnosis of systolic murmurs. *N Engl J Med* 1988; **318**: 1572-1578 [PMID: 2897627]
 - 35 **Ellison RC**, Wagner HR, Weidman WH, Miettinen OS. Congenital valvular aortic stenosis: clinical detection of small pressure gradient. Prepared for the joint study on the joint study on the natural history of congenital heart defects. *Am J Cardiol* 1976; **37**: 757-761 [PMID: 1266742]
 - 36 **Danford DA**, Salaymeh KJ, Martin AB, Fletcher SE, Gumbiner CH. Pulmonary stenosis: defect-specific diagnostic accuracy of heart murmurs in children. *J Pediatr* 1999; **134**: 76-81 [PMID: 9880453]
 - 37 **Danford DA**, Martin AB, Fletcher SE, Gumbiner CH, Cheatham JP, Hofschire PJ, Kugler JD. Children with heart murmurs: can ventricular septal defect be diagnosed reliably without an echocardiogram? *J Am Coll Cardiol* 1997; **30**: 243-246 [PMID: 9207649 DOI: 10.1016/S0735-1097(97)00101-0]
 - 38 **Frommelt MA**. Differential diagnosis and approach to a heart murmur in term infants. *Pediatr Clin North Am* 2004; **51**: 1023-1032, x [PMID: 15275986 DOI: 10.1016/j.pcl.2004.03.003]
 - 39 **Verghese A**, Brady E, Kapur CC, Horwitz RI. The bedside evaluation: ritual and reason. *Ann Intern Med* 2011; **155**: 550-553 [PMID: 22007047 DOI: 10.7326/0003-4819-155-8-201110180-00013]
 - 40 **Elder A**, Chi J, Ozdalga E, Kugler J, Verghese A. A piece of my mind. The road back to the bedside. *JAMA* 2013; **310**: 799-800 [PMID: 23982364 DOI: 10.1001/jama.2013.227195]
 - 41 **Fred HL**, Grais IM. Bedside skills: an exchange between dinosaurs. *Tex Heart Inst J* 2010; **37**: 205-207 [PMID: 20401295]
 - 42 **McGee S**. A piece of my mind. Bedside teaching rounds reconsidered. *JAMA* 2014; **311**: 1971-1972 [PMID: 24846031 DOI: 10.1001/jama.2013.286201]
 - 43 **Ippisch HM**, Kimball TR. The impact of evolving hand-carried echocardiographic technology on outpatient physical examination accuracy in pediatric cardiology. *Congenit Heart Dis* 2007; **2**: 170-178 [PMID: 18377461 DOI: 10.1111/j.1747-0803.2007.00052.x]
 - 44 **Watrous RL**, Thompson WR, Ackerman SJ. The impact of computer-assisted auscultation on physician referrals of asymptomatic patients with heart murmurs. *Clin Cardiol* 2008; **31**: 79-83 [PMID: 18257026 DOI: 10.1002/clc.20185]
 - 45 **Bhatikar SR**, DeGroff C, Mahajan RL. A classifier based on the artificial neural network approach for cardiologic auscultation in pediatrics. *Artif Intell Med* 2005; **33**: 251-260 [PMID: 15811789 DOI: 10.1016/j.artmed.2004.07.008]
 - 46 **Belmont JM**, Mattioli LF. Accuracy of analog telephonic stethoscopy for pediatric telecardiology. *Pediatrics* 2003; **112**: 780-786 [PMID: 14523166 DOI: 10.1542/peds.112.4.780]
 - 47 **Mahnke CB**, Mulreany MP, Inafuku J, Abbas M, Feingold B, Paolillo JA. Utility of store-and-forward pediatric telecardiology evaluation in distinguishing normal from pathologic pediatric heart sounds. *Clin Pediatr (Phila)* 2008; **47**: 919-925 [PMID: 18626106 DOI: 10.1177/0009922808320596]
 - 48 **Dahl LB**, Hasvold P, Arild E, Hasvold T. Heart murmurs recorded by a sensor based electronic stethoscope and e-mailed for remote assessment. *Arch Dis Child* 2002; **87**: 297-301; discussion 297-301 [PMID: 12244000 DOI: 10.1136/adc.87.4.297]

P- Reviewer: Innasimuthu A, Peteiro J, Petretta M
S- Editor: Song XX L- Editor: A E- Editor: Lu YJ





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

