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Association of cardiac ausculatory findings with coronary heart disease mortality

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Abstract

Background: Relationships between cardiac murmurs detected during physical examination and coronary heart disease mortality among the general population are not well described. **Aims**: To assess the relationship between cardiac murmurs detected during physical examination and coronary heart disease mortality. **Methods and Results:** This relationship was examined with Cox regression analyses of data from 7990 adults, aged 30–75 years, from the Second National Health and Nutrition Examination Survey Mortality Study (1976–1992). Covariates included age, race, sex, history of CVD, diabetes, probable left ventricular hypertrophy, serum cholesterol, body mass index, blood pressure, and smoking status. During 16.8 follow-up years, there were 457 deaths from coronary heart disease (CHD) (ICD-9 410–414) and 661 deaths from diseases of the heart (ICD-9 390–398, 402, 404, 410–414, 415–417, 420–429). A systolic murmur was present in 420 persons and a diastolic murmur was present in 56 persons at baseline. Persons with a heart murmur were at increased risk of death from CHD (relative risk=1.7, 95% confidence interval=1.2, 2.5) and from diseases of the heart (RR=2.2, 95% CI=1.6, 2.9) after multivariate adjustment for cardiovascular disease risk factors. Similar results were observed when murmur intensity (i.e., murmur grade) was accounted for. **Conclusions:** These results suggest that the presence of a heart murmur may be associated with an increased risk for mortality from both CHD and diseases of the heart.

Keywords: Cardiac murmur, valvular disease, coronary heart disease, mortality, survival analysis.

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Introduction

An independent association between valvular disease and increased cardiovascular mortality and morbidity has been observed [1–5]. Severe aortic valve stenosis has been associated with a 4-fold increased risk of cardiovascular mortality within 4 years of diagnosis [6]. Estimates of 5-year survival from aortic regurgitation range from less than 20% to more than 60% [1]. However, the extent to which the results from these studies apply to the general population is unclear due to small sample sizes and lack of control for potential confounding cardiovascular disease (CVD) risk factors.

A heart murmur, or abnormal sound in the heartbeat, may result from an irregular flow of blood through one or more of the heart's four valves and may be due to underlying valvular defects or valvular disease. Cardiovascular physical examination and cardiac auscultation are useful for the detection of murmurs [7]. In addition, cardiac auscultation has been found useful in the detection of valvular disease in asymptomatic patients [8]. Data from the NHANES II Mortality Study were used to examine the independent association between the presence of a heart murmur and coronary heart disease (CHD) mortality among a nationally representative sample of adults.

Analyses were repeated for mortality from diseases of the heart.

Materials and Methods

The National Center for Health Statistics of the Centers for Disease Control and Prevention conducted NHANES II between February 1976 and February 1980.NHANES II, a nationwide probability sample of approximately 28000 persons, was designed to be representative of the civilian, noninstitutionalized population of the United States aged 6 months to 74 years. A detailed description of the NHANES II survey and sampling procedures has been provided elsewhere [9].

Briefly, data were collected through responses to questions on individual medical history, food-consumption, and health-related behavior [9]. In addition, persons underwent a physical examination by a licensed physician who followed a standardized procedure to complete the exam and to record exam results. An electrocardiogram was performed, and serum cholesterol (mg/dL), height (cm), weight (kg), systolic blood pressure and diastolic blood pressure (mmHg) were measured. To obtain a more accurate measure of blood pressure, three blood pressure readings were recorded. The blood pressure used in this analysis was the mean value of the second and third readings. Ausculatory examination results described the presence of heart murmurs and included timing (i.e., systolic or diastolic), type (i.e., organic or functional), and intensity of the murmur (i.e., grades 1–6).

Baseline data from NHANES II was merged with follow-up data from the NHANES II Mortality Study. As part of the NHANES II Mortality Study, data from the National Death Index, which has been shown to capture 93% to 98% of all mortality [10–12], and from the Social Security Administration Death Master File were used to ascertain the vital status of each cohort member through December 31, 1992 (approximately 16.8 years of follow-up). Information obtained from the Mortality Study data includes the month and year in which an individual was last known to be alive and the ICD-9 code for the underlying cause of death. Since only month and year of the date of death were ascertained, the 15th day of the month was analyzed as the day of the date last known to be alive for decedents. For all others, December 31, 1992, was assigned as the last known date alive. Follow-up (i.e., survival) time was calculated as the difference between the NHANES II baseline examination date for each subject and the last known date alive obtained from the NHANES II Mortality Study. As a result of the last known day alive assignment, one subject who was examined after the 15th of the month and who died within days of the baseline examination had a calculated negative value for follow-up time. This individual was assigned a follow-up time value of zero.

Our analysis was limited to 7849 white and black adults aged 30 to 75 years who received a baseline electrocardiogram, were matched to the NHANES II Mortality Study, and who had complete information for height, weight, systolic and diastolic blood pressures, total serum cholesterol, history of prior CVD, physical activity, and education.

Statistical methods

Cox proportional hazards regression was used to assess the independent relationship between the presence of a heart murmur and mortality from CHD and diseases of the heart in age- and multivariate-adjusted analyses. The multivariate-adjusted analysis took into account age, race, gender, hypertensive status, probable left ventricular hypertrophy, total cholesterol level, body mass index, smoking status, and history of CVD, stroke, and diabetes mellitus. Age, cholesterol level, and body mass index were entered into the model as continuous variables. Hypertension was defined as a baseline systolic blood pressure greater than or equal to 140 mmHg or baseline diastolic blood pressure greater than or equal to 90 mmHg or the current use of antihypertensive medication. Probable left ventricular hypertrophy was determined by coding electrocardiogram data according to the Minnesota code [13]. CHD mortality was defined by ICD-9 codes 410–414 and diseases of the heart mortality by ICD-9 codes 390–398, 402, 404, 410–414, 415–417, 420–429.

Differences in survival among persons with and without heart murmurs by severity were assessed for each cause of mortality. Using a Cox proportional hazards model, we obtained the effect on survival time for age and for each of the following groups: high intensity or very audible (i.e., Grade 5 or 6 murmur), moderate intensity or audible (i.e., Grade 3 or 4 murmur), low intensity or faint (i.e., Grade 1 or 2 murmur), and no murmur. The reference group was no murmur.

To make the NHANES representative of the United States population, sample weights were used in all analyses unless specified otherwise. A Cochran-Mantel-Haenszel χ^2 test was used to compare differences in categorical variables across groups, and a 2-sided t-test was used for continuous variables. Ordinal trend tests used logistic regression with either CHD mortality or diseases of the heart mortality as the dependent variable and an ordinal independent variable. To account for the complex sampling design and to achieve accurate variance estimates, we used SUDAAN 7.0 (Research Triangle Institute, 1996) to complete all analyses.

Results

At baseline, 420 persons had a systolic murmur and 56 persons had a diastolic murmur. Thirty-three persons were identified with both a systolic and a diastolic murmur. Persons with a heart murmur were more likely than those without a heart murmur to be black, less educated, older and physically inactive (Table 1). They also had a higher mean baseline systolic blood pressure (143.2 vs. 130.2 mmHg) and a greater mean serum cholesterol level (229.0 vs. 223.3 mg/dL). Left ventricular hypertrophy was more prevalent among those with a murmur (6.5% vs. 1.1%). Prior history of CVD differed between the two groups (Table 1). A greater proportion of those with a heart

murmur than without reported a prior myocardial infarction (9.3% vs. 3.9%), hardening of the arteries (6.2% vs. 3.3%), stroke (4.0% vs. 1.9%), and heart failure (2.6% vs. 1.0%). Persons with a murmur were also more likely to report a history of hypertension (42.0% vs. 29.0%) and diabetes (6.8% vs. 4.1%).

Eighty-eight percent (N=393) of murmurs were classified as organic. The gradation of murmurs was comprised of six levels. Among persons with systolic murmurs, 44.6% had a low intensity (i.e., grade 1 or 2), 51.3% had a moderate intensity murmur (i.e., grade 3 or 4), and 3.0% had a high intensity murmur (i.e., grade 5 or 6). Among those with diastolic murmurs, the proportion of persons with low, moderate, and high intensity murmurs was 26.7%, 67.3%, and 4.1%, respectively.

During a maximum of 16.8 years of follow-up, there were 661 deaths due to diseases of the heart. Of these deaths, coronary (or ischemic) heart disease (ICD–9 410–414), other forms of heart disease (420–429), and hypertensive heart disease (402) accounted for 70%, 26%, and 2%, respectively. Rheumatic heart disease (390–398), hypertensive and renal heart disease (404), and pulmonary heart disease (415–417) each accounted for less than 1% of the deaths classified as diseases of the heart. As expected, gender, increasing age, smoking status, education, physical activity, body mass index, cholesterol level, and history of myocardial infarction, hardening of the arteries, stroke, heart failure, hypertension, and diabetes were associated with mortality from CHD and diseases of the heart (data not shown). Race was only associated with CHD mortality. Among the 457 persons whose underlying cause of death was CHD, 10.4% had a heart murmur. Similarly, 17.8% of those who died from diseases of the heart had a baseline heart murmur.

The crude CHD mortality rate among persons with a heart murmur was more than three times greater than that for persons without (82.5 vs. 25.2 per 10 000 person-years) (Table 2). After adjustment for CVD risk factors, persons with a heart murmur remained at increased risk of death from CHD [Relative Risk (RR) =1.7, 95% confidence interval (CI) =1.2, 2.5]. For mortality from diseases of the heart, the crude mortality rate for persons with a heart murmur was 140.4 per 10000 person-years compared to a rate of 34.9 per 10000 person-years for persons without a murmur. After adjustment for CVD risk factors, those with heart murmurs were still at increased risk of death from diseases of the heart (RR=2.2, 95% CI=1.6, 2.9).

For both causes of death (CHD and diseases of the heart) and after adjustment for CVD risk factors, persons with diastolic murmurs were more than 4 times as likely as those without this condition at baseline to die (CHD: RR=4.4, 95% CI=1.9, 10.0; diseases of the heart: RR=4.6, 95% CI=2.4, 8.7) (Table 3). Among persons with a systolic murmur, the relative risk of death from CHD was 1.6 (95% CI=1.1, 2.4). The association between a systolic murmur and mortality was slightly stronger for diseases of the heart (RR=2.1, 95% CI=1.6, 2.9).

Table 1 Baseline characteristics of persons with and without a heart murmur, NHANES II Mortality Study

	Heart Murmur	
	Yes (N=443)	**No (N=7406)**
Male (%)	41.8	47.8
Black (%)*	14.4	9.3
Age, yrs (%)*†		
<40	15.3	29.2
40–49	15.2	23.7
50–59	23.5	23.5
60–69	29.8	17.8
≥70	16.2	5.8
Education (%)*†		
< High school	45.7	33.6
High school	32.1	36.4
> High school	22.2	30.0
Physical activity (%) †		
Inactive	14.9	9.9
Moderately active	74.4	80.0
Very Active	10.7	10.1
Smoking status (%) †		
Current smoker	33.5	36.0
Former smoker	23.8	25.8
Cholesterol, mg/dL (%)*†	42.7	38.2
<220	45.3	49.9
220–239	14.5	16.5
240–259	16.9	13.4
260–279	9.6	8.5
≥280	13.7	11.7
BMI, kg/m² (%) †		
<18.5	3.0	2.3
18.5–24.9	47.6	45.7
25.0–29.9	31.7	35.4
≥30.0	17.7	16.6
Hypertensive (%)*	63.0	46.9
History		
Myocardial infarction (%)*	9.3	3.9
Hardening of arteries (%)*	6.2	3.3
Stroke (%)*	4.0	1.9
Heart failure (%)*	2.6	1.0
Diabetes (%)*	6.8	4.1
Probable LVH (%)*	6.5	1.1
Cause of death (%)		
Coronary heart disease*‡	10.4	3.4
Diseases of the heart*‖	17.8	4.7

* Statistically significant difference between Murmur and No Murmur groups, p≤0.05, † Ordinal trend test used, ‡ Coronary heart disease defined by ICD-9 codes 410–414, ‖ Diseases of the heart defined by ICD-9 codes 390–398, 402, 404, 410–414, 415–417, 420–429. BMI: Body mass index.

Table 2 Association between presence of a heart murmur and mortality. NHANES II Mortality Study

Heart Murmur		Coronary Heart Disease*			Diseases of the Heart†		
		Crude Mortality Rate‡	Age-adjusted RR (95% CI)	Multivariable-adjusted RR‖ (95% CI)	Crude Mortality Rate	Age-adjusted RR (95% CI)	Multivariable-adjusted RR‖ (95% CI)
Yes	(N=443)	82.5	1.9 (1.3, 2.9)	1.7 (1.2, 2.5)	140.4	2.4 (1.8, 3.3)	2.2 (1.6, 2.9)
No	(N=7406)	25.2	1.0	1.0	34.9	1.0	1.0

* Coronary heart disease defined by ICD-9 codes 410–414, † Diseases of the heart defined by ICD-9 codes 390–398, 402, 404, 410–414, 415–417, 420–429, ‡ Rate per 10000 person-years, ‖ Adjusted for age, race, sex, education, hypertensive status, left ventricular hypertrophy, prior CVD (heart failure, hardening of the arteries, myocardial infarction, stroke), history of diabetes, cholesterol, body mass index, smoking status.

Table 3 Association between presence of a heart murmur and mortality. NHANES II Mortality Study

Type of Murmur		Coronary Heart Disease		Diseases of the Heart	
		Age-adjusted RR (95% CI)	Multivariable-adjusted RR‖ (95% CI)	Age-adjusted RR (95% CI)	Multivariable-adjusted RR‖ (95% CI)
Diastolic	Yes (N=55)	4.0 (1.8,8.7)	4.4 (1.9,10.0)	4.4 (2.5,7.7)	4.6 (2.4,8.7)
	No (N=7935)	1.0	1.0	1.0	1.0
Systolic	Yes (N=382)	1.8 (1.2,2.8)	1.6 (1.1,2.4)	2.4 (1.7,3.3)	2.1 (1.6,2.9)
	No (N=7608)	1.0	1.0	1.0	1.0

‖Adjusted for age, race, sex, education, hypertensive status, left ventricular hypertrophy, prior CVD (heart failure, hardening of the arteries, myocardial infarction, stroke), history of diabetes, cholesterol, body mass index, smoking status

Similar results were observed after accounting for murmur intensity. Moderate-to-high intensity (i.e., grades 3–6) murmurs were independent predictors of future CHD mortality. The multivariate-adjusted relative risks of death among persons with moderate-to-high intensity systolic and diastolic murmurs were 1.6 (95% CI=0.9, 2.7) and 4.4 (95% CI=1.9, 10.3), respectively. For mortality from diseases of the heart, a moderate-to-high intensity systolic murmur was associated with a more than 2-fold increased risk of death (RR=2.3, 95% CI=1.6, 3.3). Persons with a moderate-to-high intensity diastolic murmur were more than 4 times as likely to die from diseases of the heart (RR=4.8, 95% CI=2.4, 9.6).

Discussion

The value of using cardiac auscultation or cardiovascular physical examination to detect valvular heart disease in asymptomatic persons has been demonstrated [8]. In this retrospective cohort study, our results suggest an independent association between the presence of a heart murmur, which may reflect possible underlying valvular disease, and mortality from CHD and diseases of the heart among a nationally representative sample of black and white adults.

To the extent that cardiac murmurs are associated with valvular disease, our results are in agreement with the findings of other studies in which valvular disease is more directly determined. For example, in a study of 448 patients admitted to an emergency department for acute chest pain, Fleischmann and colleagues [2] observed a cardiovascular mortality rate ratio of 3.1 (95% CI=1.4, 7.0) among persons with moderate or severe regurgitation of the mitral, aortic, or tricuspid valve. In the Helsinki Aging Study, the 4-year mortality among 476 elderly men and women was greater among those with aortic stenosis than among those without this condition (32.8% vs. 12.9%, p<0.001) [6]. Consistent with these findings, the present study demonstrates that the risk of death among persons with a diastolic murmur, which may reflect aortic regurgitation or mitral stenosis, is more than 4 times that of persons without the condition; however, this result should be viewed with come caution because the number of persons with diastolic-related valvular disease was small (n=56).

In addition, murmur intensity has been shown to correlate well with the degree of aortic and mitral valve regurgitation [14, 15]. Severity is an important factor in the clinical management and prognosis of valvular heart disease [16, 17]. Iivanainen and colleagues [6] observed a 4-fold age- and sex-adjusted increased risk of all-cause and CVD mortality among persons with severe aortic valve stenosis within 4 years of diagnosis compared with those without aortic stenosis. In a prospective study of 1797 elderly men and women, severe and moderate-to-severe aortic stenoses were associated with an increased incidence of coronary events compared with elderly persons with mild aortic stenosis or without aortic stenosis [18]. Consistent with these findings, the present study demonstrates that moderate-to-high intensity murmurs are associated with a slight increase in risk of death compared with estimates that do not differentiate between severity.

Although severe aortic valve stenosis is associated with a poor prognosis, a review of the literature suggests that the same may not be true for mild-to-moderate aortic valve stenosis [4, 18]. To the extent that murmur intensity correlates with severity of valvular heart disease, our

results suggest that mild-to-moderate valvular disease, as reflected by a mild-to-moderate intensity murmur, may be associated with a lower survival probability compared with persons without valvular heart disease (i.e., no murmur) for mortality from CHD and diseases of the heart.

There are at least two possible explanations for the increased risk of CHD and diseases of the heart mortality observed among persons with a heart murmur. Excess post-operative mortality has been observed following valve replacement surgery due to thromboembolic events, infection, and other complications [16]. It is possible that persons in this study population may have undergone valve replacement surgery, which may partly explain why persons with a murmur had poor survival compared with those without this condition. In addition, there may be potential confounders of the association between heart murmurs and CHD for which we did not control. For example, persons with heart murmurs may also have had a chronic infection such as *Chlamydia pneumoniae*, which has been associated with both valvular heart disease (i.e., the possible underlying cause of the murmur) and CHD [19–21].

There are several possible limitations to the findings of this study. First, presence of a heart murmur was used as a surrogate for evidence of valvular heart disease. Although the clinical usefulness of cardiac auscultation for the detection of valvular heart disease has been described [8, 15, 22], auscultation may not be sufficient for the diagnosis of some forms of valvular disease because of the relatively low sensitivity [7, 23]. It is important to note that echocardiograms were not performed as part of NHANES II. Because echocardiographic findings may provide important prognostic data beyond physical examination, the cardiac ausculatory examination findings may be associated with a misclassification of patients with valvular disease; therefore, any observed association between the presence of a heart murmur and mortality is probably a conservative estimate.

Second, murmurs associated with some forms of valvular disease (e.g., mitral stenosis) may be silent and thus may not be detected by the physician during an examination, although ausculatory examination has been found to be a sensitive and highly specific method of screening for VHD in subjects without cardiac symptoms [24]. It is also possible that persons who were asymptomatic at baseline may have developed symptomatic valvular disease during follow-up. Thus, we may be underestimating the association between a heart murmur and mortality. Third, a large proportion of murmurs were classified as organic or pathological (87.9%, systolic murmurs; 96.0% diastolic murmurs). One might expect to observe more benign or functional murmurs in a sample such the NHANES. As a result of such misclassification, we may have overestimated the association between presence of a heart murmur and mortality. Finally, the increased risk of mortality observed among persons with moderate-to-high intensity murmurs may be the result of a misclassification associated with the assignment of ausculatory grade. Although the process of ausculatory grading maintains a degree of subjectivity, the process has been deemed reproducible [15]. Also, Desjardins and colleagues [15] note that functional mitral regurgitation and murmur intensity are not well correlated although this may not be an issue since such a large proportion of murmurs were classified as organic.

Despite these limitations, our results suggest that the presence of a heart murmur, which may reflect underlying valvular disease, greatly increases the risk for mortality from CHD and diseases of the heart. In addition, persons with a heart murmur are substantially more likely to have other CHD risk factors including diabetes, hypertension, and left ventricular hypertrophy. Thus, the presence of a heart murmur is clinically important and should not be dismissed. These findings are also important in light of suggestions that clinical auscultation skills are suboptimal among medical students and medical residents [25–27]. The physicians conducting the physical examinations for NHANES participated in a training session prior to the exams and followed a standardized procedure to complete the exam. These results suggest that physicians trained in auscultation techniques can identify a subset of patients at markedly increased risk, supporting the need to improve the teaching and assessment of cardiac auscultation as noted by others [26].

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References

1. Dujardin KS, Enriquez-Sarano M, Schaff HV. Mortality and morbidity of aortic regurgitation in clinical practice: a long-term follow-up study. Circulation 1999; 99:1851–1857.
2. Fleischmann KE, Lee RT, Come PC. Impact of valvular regurgitation and ventricular dysfunction on long-term survival in patients with chest pain. Am J Cardiol 1997; 80:1266–1272.
3. Kupari M, Lindroos M, Iivanainen AM. Congestive heart failure in old age: prevalence, mechanisms and 4-year prognosis in the Helsinki Aging Study. J Intern Med 1997; 241:387–394.
4. Turina J, Hess O, Sepulcri F. Spontaneous course of aortic valve disease. Eur Heart J 1987; 8:471–483.
5. Talbot S. Valvular heart disease: a study of mortality in the Sheffield population. Thorax 1973; 28:622–626.
6. Iivanainen AM, Lindroos M, Tilvis R. Natural history of aortic valve stenosis of varying severity in the elderly. Am J Cardiol 1996; 78:97–101.
7. Munt B, Legget ME, Kraft CD. Physical examination in valvular aortic stenosis: correlation with stenosis

severity and prediction of clinical outcome. Am Heart J 1999; 137:298–306.
8. 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.
9. Plan and Operation of the Second Health and Nutrition Examination Survey, 1976–1980, DHHS Pub No. (PHS) 81-1317 Series 1, No. 15, Public Health Service, US Government Printing Office, Washington, DC.
10. Stampfer MJ, Willett WC, Speizer FE, et al. Test of the National Death Index. Am J Epidemiol 1984; 119:837–839.
11. Edlavitch SA, Baxter J. Comparability of mortality follow-up before and after the National Death Index. Am J Epidemiol 1988; 127:1164–1178.
12. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. Am J Epidemiol 1993; 137:235–2341.
13. Rautaharju PM, MacInnis PJ, Warren JW, Wolf HK, Rykers PM, Calhoun HP. Methodology of ECG interpretation in the Dalhousie Program: NOVACODE ECG classification procedures for clinical trials and population health surveys. Methods of Inf Med 1990; 29:362–374.
14. Etchells E, Glenns V, Shadowitz S. A bedside clinical prediction rule for detecting moderate or severe aortic stenosis. J Gen Intern Med 1998; 13:699–704.
15. Desjardins VA, Enriquez-Sarano M, Tajik J. Intensity of murmurs correlates with severity of valvular regurgitation. Am J Med 1996; 100:149–56.
16. Lester SJ, Heilbron B, Gin K. The natural history and rate of progression of aortic stenosis. Chest 1998; 113:1109–1114.
17. Kitchiner D, Jackson M, Walsh K, Peart I, Arnold R. Prognosis of supravalve aortic stenosis in 81 patients in Liverpool (1960–1993). Heart 1996; 75:396–402.
18. Aronow WS, Ahn C, Shirani J, Kronzon I. Comparison of frequency of new coronary events in older persons with mild, moderate, and sever valvular aortic stenosis with those without aortic stenosis. Am J Cardiol 1998; 81:647–649.
19. Nieto FJ, Folsom AR, Sorlie PD, Grayston JT, Wang SP, Chambless LE. Chlamydia pneumoniae infection and incident coronary heart disease: the Atherosclerosis Risk in Communities Study. Am J Epidemiol 1999; 150:149–156.
20. Juvonen J, Juvonen T, Laurila A, et al. Can degenerative aortic valve stenosis be related to persistent Chlamydia pneumoniae infection? Ann Intern Med 1998; 128:741–744.
21. Ellis RW. Infection and coronary heart disease. J Med Microbiol 1997; 46:535–539.
22. Grayburn PA, Smith MD, Handshoe R. Detection of aortic insufficiency by standard echocardiography, pulsed Doppler echocardiography, and auscultation. A comparison of accuracies. Ann Intern Med 1986; 104:599–605.
23. Meyers DG, Sagar KB, Ingram RF. Diagnosis of aortic insufficiency: comparison of auscultation and M-mode echocardiography to angiography. South Med J 1982; 75:1192–1194.
24. 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.
25. 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.
26. Mangione S, Nieman LZ. Cardiac ausculatory skills of internal medicine and family practice trainees. A comparison of diagnostic proficiency. JAMA 1997; 278:717–722.
27. Gaskin PR, Owens SE, Talner NS, Sanders SP, Li JS. Clinical auscultation skills in pediatric residents. Pediatrics 2000; 105:1184–1187.