Clinical Investigations

A Systolic Murmur Is a Common Presentation of Aortic Regurgitation Detected by Echocardiography

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Summary

Background: The finding of aortic regurgitation at a classical examination is a diastolic murmur.

Hypothesis: Aortic regurgitation is more likely to be associated with a systolic than with a diastolic murmur during routine screening by a noncardiologist physician.

Methods: In all, 243 asymptomatic patients (mean age 42 ± 10 years) with no known cardiac disease but at risk for aortic valve disease due to prior mediastinal irradiation (≥ 35 Gy) underwent auscultation by a noncardiologist followed by echocardiography. A systolic murmur was considered benign if it was grade $\leq$ II/VI, not holosystolic, was not heard at the apex, did not radiate to the carotids, and was not associated with a diastolic murmur.

Results: Of the patients included, 122 (49%) were male, and 86 (35%) had aortic regurgitation, which was trace in 20 (8%), mild in 52 (21%), and moderate in 14 (6%). A systolic murmur was common in patients with aortic regurgitation, occurring in 12 (86%) with moderate, 26 (50%) with mild, 6 (30%) with trace, and 27 (17%) with no aortic regurgitation ($p < 0.0001$). The systolic murmurs were classified as benign

in 21 (78%) patients with mild and 8 (67%) with moderate aortic regurgitation. Diastolic murmurs were rare, occurring in two (14%) with moderate, two (4%) with mild, and three (2%) with no aortic regurgitation ($p = 0.15$).

Conclusions: An isolated systolic murmur is a common auscultatory finding by a noncardiologist in patients with moderate or milder aortic regurgitation. A systolic murmur in patients at risk for aortic valve disease should prompt a more thorough physical examination for aortic regurgitation.

Key words: aortic valve insufficiency, heart murmurs, echocardiography, heart auscultation

Introduction

Aortic regurgitation is a common echocardiographic finding, occurring in 8–14% of unselected persons aged 50–60 years, and in 24–33% of those aged ≥ 70 years.^{1,2} Severe aortic regurgitation can lead to left ventricular dysfunction and heart failure, but even mild aortic regurgitation may put patients at risk for endocarditis.^{3,4} Thus, knowledge of aortic regurgitation is important for treatment (e.g., endocarditis prophylaxis) even if the patient is asymptomatic.

Cardiac auscultation is the most common screening test used to determine whether aortic regurgitation is present. The classical auscultatory finding of aortic regurgitation is a blowing decrescendo diastolic murmur heard best along the left sternal border.⁵ We hypothesized that the increased forward flow secondary to aortic regurgitation would produce a systolic murmur that would be more easily heard than a diastolic murmur during routine screening examination by a noncardiologist.

Materials and Methods

Patient Population

This study used data collected as part of an investigation of noninvasive cardiac testing in 294 asymptomatic patients with

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a history of irradiation treatment for Hodgkin's disease. Patients were recruited for the study if they had received at least 35 Gy of mantle irradiation for treatment for Hodgkin's disease, had no history of significant cardiac disease, and gave written consent to undergo noninvasive testing with echocardiography. We identified eligible subjects by attempting to contact all patients followed at Stanford University Medical Center, who were not known to have died or to have cardiac disease. Patients were enrolled from October 1994 through November 1998.

Study Protocol

Cardiac Auscultation

Of 294 patients enrolled in the primary study, 243 underwent cardiac auscultation by their attending medical or radiation oncologist. Cardiologists were not used because examination by them is not applicable to community practice where the majority of screening auscultation occurs. Patients were examined either at the time of enrollment ($n = 213$) or during the 30 days prior to enrollment ($n = 30$). There was no difference in age, gender, dose of irradiation, and prevalence of aortic regurgitation between patients enrolled and those not enrolled in the study. The extent of auscultation was at the discretion of the oncologist. The physician recorded the presence of a murmur, the timing, duration, location, grade, and any radiation to the carotids. A systolic murmur was considered pathologic if it had any of the following characteristics: grade three or higher, holosystolic, heard best at the apex, radiation to the carotids, and concomitant diastolic murmur. Systolic murmurs with none of these characteristics were considered benign. The physician performing auscultation was blinded to the echocardiography results and to this study's intent (to compare auscultation and transthoracic echocardiography).

Echocardiography

Each subject underwent two-dimensional and Doppler (color, pulse, and continuous-wave) echocardiography of the aortic, mitral, tricuspid, and pulmonary valves. All studies were performed using commercially available ultrasound scanners (HP Sonos 1500, 2500, Hewlett Packard, Mountain View, Calif., USA). All echocardiography studies were evaluated by a single experienced echocardiographer who was blinded to the results of auscultation.

Aortic regurgitation was evaluated using the parasternal long- and short-axis cross-sectional views.^{6,7} Mitral and tricuspid regurgitation were graded using standard criteria.^{6,7} Aortic thickening was defined as any calcification or valve thickening with or without stenosis. Aortic stenosis was considered present if the motion of the aortic valve leaflets was restricted and the peak aortic velocity was > 2.0 m/s. The study protocol was approved by the Human Research Committee at Stanford University Medical Center.

Statistics

Comparisons of means were performed using the Student's *t*-test and analysis of variance. Differences in proportions were performed using the chi-square test or Fisher's exact test (for cells with ≤ 5 counts). A two-tailed p value < 0.05 was considered statistically significant. Multivariate analyses were performed using logistic regression to determine if murmur type (systolic, diastolic) was independently associated with mild or greater aortic regurgitation, controlling for age, gender, height, weight, hypertension (yes/no), diabetes (yes/no), and radiation dose.⁸ Covariates were removed from the models stepwise, until only those variables that remained associated ($p < 0.10$) with the dependent variable remained. All analyses were performed using JMP (SAS Institute, Cary, N.C.) statistical software.

Results

Auscultation

A total of 243 patients (mean age 42 ± 10 years) underwent auscultation followed by echocardiography. Of these, 122 (49%) were male and 86 (35%) had Doppler evidence of aortic regurgitation: trace 20 (8%), mild 52 (21%), moderate 14 (6%), severe 0 (0%). Systolic murmurs were present in 71 (29%), and diastolic murmurs in 7 (2.9%) patients. Compared with those without systolic murmurs, patients with systolic murmurs were of similar age, more likely to be female, and had received more mediastinal irradiation (Table I).

Valvular Disease and Systolic Murmurs

The prevalence of a systolic murmur for different types and severity of valvular regurgitation is shown in Figure 1. Prevalence increased markedly with increasing severity of aortic regurgitation and, for a given level of severity of regurgitation (e.g., mild, moderate), was as high if not higher in patients with aortic regurgitation than in those with mitral or tricuspid regurgitation. The systolic murmur was considered benign in 78%

TABLE I Characteristics of patients with and without systolic murmurs

Characteristic	Systolic murmur $n = 71$	No systolic murmur $n = 172$	p Value
Age (years)	43.2 ± 8	41.5 ± 10	0.21
Males (%)	25 (35)	93 (54)	0.008
Height (cm)	171 ± 10	173 ± 10	0.11
Weight (kg)	74 ± 18	78 ± 17	0.20
Hypertension (%)	9 (13)	15 (9)	0.37
Diabetes (%)	0 (0)	3 (2)	0.56
Mean biological equivalent dose (units) ^a	74.0 ± 6	70.0 ± 7	< 0.0001

^a For calculation of the biological equivalent dose see Ref. No. 8.

FIG. 1 The systolic murmur prevalence is displayed for different types and severity of valvular regurgitation. The association between systolic murmurs and severity of valvular disease was highest for aortic regurgitation. No patient had moderate pulmonic regurgitation. □ = None, □ = trace, ■ = mild, ■ = moderate.

FIG. 2 The prevalence of a systolic murmur is displayed for different grades of aortic regurgitation and valvular thickening. It increases with increasing severity of aortic regurgitation (AR) regardless of valvular thickening. □ = No AR, □ = trace AR, ■ = mild AR, ■ = moderate AR.

(21/26) of patients with mild and 67% (8/12) of patients with moderate aortic regurgitation.

Regurgitant aortic valves were frequently thickened or calcified. Valves with moderate aortic regurgitation were thickened in 81% compared with 17% in patients with no regurgitation. To separate the effect of aortic regurgitation from valvular thickening, we compared systolic murmur prevalence in patients grouped by severity of regurgitation and presence of aortic valve thickening (Fig. 2). Aortic regurgitation was frequently associated with systolic murmurs for both thickened and nonthickened valves.

Diastolic versus Systolic Murmur

Diastolic murmurs were rare, occurring in 2 (14%) patients with moderate, 2 (4%) with mild, and 3 (2%) with no aortic regurgitation ($p = 0.15$). A diastolic murmur had a sensitivity of only 6% (4/66) and specificity of 98% (174/177) for mild or moderate aortic regurgitation as determined by the noncardiologists' examination. In contrast, a systolic murmur had a sensitivity of 58% (38/66) and a specificity of 81% (144/177) and a similar positive predictive value (54 vs. 57%), but a higher negative predictive value (84 vs. 74%) than a diastolic murmur for mild or moderate aortic regurgitation. A multivariate logistic model of aortic regurgitation found that a systolic ($p < 0.0001$) but not a diastolic murmur ($p = 0.55$) was associated with mild or greater aortic regurgitation (Table II).

Predictive Value of a Systolic Murmur for Aortic Regurgitation in Different Populations

The prevalence of aortic regurgitation was greater in women than in men (34 [44/125] vs. 19% [22/118], $p = 0.003$). However, a systolic murmur was a more accurate test for regurgitation in men (sensitivity 65% [17/26], specificity 88%

[101/115]) than in women (sensitivity 53% [26/49], specificity 75% [73/97]).

To estimate the predictive value of a systolic murmur for aortic regurgitation for different patient populations, we used our gender-specific test characteristics with the age- and gender-specific prevalence of aortic regurgitation from the Framingham Heart Study¹ (Table III). This analysis indicates that among elderly men (age ≥ 70 years), aortic regurgitation may be present in up to 50% of those with a systolic murmur.

Discussion

This study found that the most common auscultatory finding in patients with mild to moderate aortic regurgitation was a benign systolic murmur when examination was performed by a noncardiologist. The association between a systolic murmur and the severity of aortic regurgitation increased with increasing severity of regurgitation and persisted after controlling for

TABLE II Independent predictors of aortic regurgitation^a

Characteristic	Odds ratio (95% confidence interval)	p Value
Female	1.62 (1.12–2.33)	0.008
Age (per 10-year increase)	2.97 (1.86–4.76)	<0.0001
Radiation dose (per 10 unit increase) ^b	1.97 (1.06–3.65)	0.03
Systolic murmur	2.28 (1.58–3.28)	<0.0001
Diastolic murmur	1.32 (0.57–3.03)	0.55

^a For mild or greater regurgitation. R^2 for model = 0.28.

^b For calculation of the biological equivalent dose see Ref. No. 8.

TABLE III Predictive value of a systolic murmur for aortic regurgitation for different age groups based on the Framingham Heart Study

Patient population	Estimated prevalence of mild or moderate aortic regurgitation			
	All patients ^a		Those with systolic murmur ^b	
	Men	Women	Men	Women
Age < 50 (%)	1.4	0.2	7	< 1
Age 50–59 (%)	4	2	19	5
Age 60–69 (%)	13	7	44	14
Age 70–83 (%)	14	17	47	30
Past mediastinal irradiation (current study) (%)	19	35	55	53

^a Age- and gender-specific prevalence of aortic regurgitation from the Framingham Heart Study.¹

^b Assumes a sensitivity of 65% for men, 53% for women, and a specificity of 88% for men, 75% for women.

valvular calcification, suggesting that it is the regurgitation itself, likely through increased forward flow during systole, that leads to the systolic murmur. Diastolic murmurs were rarely audible on routine examination by the noncardiologist, even in patients with moderate aortic regurgitation.

A possible mechanism for the systolic murmur of aortic regurgitation is an increase in stroke volume resulting in turbulence in the outflow tract or aorta. Concomitant aortic valve thickening or calcification is also likely to contribute to turbulence and the generation of a murmur. This systolic murmur would have the same origin as other flow murmurs such as pregnancy or anemia and would sound benign or “innocent” as was the case in over 70% of the systolic murmurs associated with mild or greater aortic regurgitation in our study. This hypothesis is consistent with a prior study that noted that increased flow across the aortic valve during systole was the primary determinant of a systolic murmur in patients with aortic regurgitation.⁹

Although the association of a systolic murmur and aortic regurgitation is recognized,⁹ clinicians rarely consider aortic regurgitation as a cause for an isolated systolic murmur. Studies describing sensitivity and specificity of a systolic murmur to detect valvular disease rarely discuss aortic regurgitation.^{10–12} Similarly, a systolic murmur is rarely described as a physical finding in aortic regurgitation.^{5, 13}

Diastolic murmurs were remarkably rare in patients with moderate or milder aortic regurgitation. Past studies have found a sensitivity of 0–38% of a diastolic murmur for mild and 60–80% for mild or greater aortic regurgitation.^{14–19} There are two important reasons for the lower accuracy of diastolic murmurs in our study. First, unlike most prior studies, we used noncardiologists to perform auscultation. Second, the examiners were not aware that their examination would be compared with echocardiography. Thus, they were unlikely to perform special maneuvers (leaning forward in end-expiration) that would improve the chance of detecting a diastolic murmur.

Clinical Implications

A diastolic murmur may be inaudible or easily missed by the noncardiologist during a routine screening examination. However, a systolic murmur can be a clue to the presence of aortic regurgitation and should prompt a more careful search for a diastolic murmur, particularly in patients at risk for aortic valve disease, including the elderly and those with a history of mediastinal irradiation.

Knowledge of mild or greater aortic regurgitation is of value because these patients may benefit from endocarditis prophylaxis, based on current guidelines recommending prophylaxis for patients with “acquired” valvular disease.³ Although the risk of endocarditis in patients with mild or moderate aortic regurgitation has not been formally evaluated, the Food and Drug Administration includes mild or greater aortic regurgitation in its definition of valvular heart disease.⁴

Limitations

This study has several potential limitations. We examined a patient cohort with a higher than normal prevalence of systolic murmurs and valvular disease. The prevalence of aortic regurgitation in our study (34%) was comparable with that found in patients aged > 70 years.^{2, 19} Although the high prevalence of aortic regurgitation in our study was due to irradiation, prior anatomic studies have found that valvular lesions in irradiated patients are similar to age-related valve changes observed in nonirradiated patients.²⁰ Thus, the prevalence of a systolic murmur conditional on the presence of aortic regurgitation observed in our study is likely to be similar to the prevalence in nonirradiated patients.

Although the physicians in this study did not have specialized training in auscultation or cardiology, their detection of a systolic murmur correlated highly with aortic regurgitation. This correlation should only increase with the use of more accurate examiners. In addition, the prevalence of a systolic murmur increased with severity of regurgitation for mitral and tricuspid at levels similar to those in a previous study comparing echocardiography to auscultation by a single cardiologist.²¹ A more accurate measure of the potential of the physical examination as a diagnostic test would be achieved if we had used cardiologists.^{13, 22} However, noncardiologists provide the majority of primary care and are first to evaluate the patient with a systolic murmur. For screening purposes, the relevant diagnostic accuracy is that of the noncardiologist. Although the relative auscultation skill for primary care providers and noncardiology specialists is unknown, studies comparing medical students and internal medicine residents found no improvement in auscultation skill following the third year of medical school.^{23, 24} Thus, we believe the accuracy of auscultation we observed is likely to be typical of community primary care practice.

Conclusion

In summary, our study found a high prevalence of a systolic murmur in patients with moderate or milder aortic regurgita-

tion when undergoing routine physical examination by a non-cardiologist. The systolic murmur was usually considered "benign" and was likely due to increased flow across the aortic valve leading to turbulence. Aortic regurgitation should be included in the differential diagnosis of a systolic murmur and should prompt a more detailed physical examination aimed at detecting the diastolic murmur.

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