The Rational Clinical Examination: Evidence-Based Clinical Diagnosis >

**Murmur, Diastolic**

**Make the Diagnosis: Murmur, Diastolic**

**Prior Probability**

One study of randomly selected elderly (75-86 years old) Finnish persons found a 29% prevalence of mild or greater AR. Evaluation of more than 3000 men and women (aged 54 ± 10 years) in the Framingham heart study detected AR of trace or greater severity in 13.0% of men and 8.5% of women. Increasing age was associated with higher prevalence of AR.

**Population for Whom the Signs Should Be Evaluated**

- Any patient undergoing cardiac auscultation

A variety of medical and traumatic conditions are associated with AR:

- Rheumatic fever
- Endocarditis
- Conditions associated with aortic valve leaflet abnormalities (eg, Marfan syndrome, rheumatoid arthritis, ankylosing spondylitis)
- Diseases that affect the aortic root (eg, hypertension, syphilis, inherited connective tissue disorders, aortic aneurysm)

**Physical Examination Signs Useful in the Diagnosis of Aortic Regurgitation**

The presence of a typical murmur of AR (an early diastolic, decrescendo murmur) should prompt echocardiographic evaluation (Table 32-5). Many eponymic peripheral pulse findings are associated with AR, but they are not useful for screening or for distinguishing the severity of regurgitation.

<table>
<thead>
<tr>
<th>Finding (Type of Clinician)</th>
<th>Severity by Echocardiogram or Cardiac Catheterization</th>
<th>LR+ (Range or Point Estimate With 95% CI)</th>
<th>LR− (Range or Point Estimate With 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical murmur<strong>2, 8</strong> (cardiologist)</td>
<td>Mild or greater</td>
<td>8.8-32</td>
<td>0.2-0.3</td>
</tr>
<tr>
<td>Moderate or greater</td>
<td>4.0-8.3</td>
<td>0-0.1</td>
<td></td>
</tr>
<tr>
<td>Murmur intensity<strong>2</strong> (generalist or <strong>Grade 3</strong>)</td>
<td></td>
<td>4.5 (1.6-14)</td>
<td></td>
</tr>
</tbody>
</table>
cardiologist)\(^a\)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Value (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1.1 (0.5-2.4)</td>
</tr>
<tr>
<td>1</td>
<td>0 (0 -0.9)</td>
</tr>
<tr>
<td>No murmur</td>
<td>0 (0 -1.1)</td>
</tr>
</tbody>
</table>

Third heart sound\(^4\) (cardiologist) Severe 5.9 (1.4-25) 0.83 (0.73-0.95)

Abbreviations: CI, *confidence interval*; LR+, *positive likelihood ratio*; LR–, *negative likelihood ratio*.

\(^a\)All patients had aortic regurgitation, so the likelihood ratios here are for severe aortic regurgitation associated with the murmur intensity.

Reference Standard Tests

Echocardiography and angiography.

**Original Article: Does This Patient Have Aortic Regurgitation?**

**Clinical Scenario**

You are asked to see a 59-year-old woman with liver *cirrhosis* and esophageal *varices*. When she was checked into the clinic, she had a pulse pressure of 70 mm Hg. Because of the wide pulse pressure, you wonder if she has aortic regurgitation (AR). You conduct a complete physical examination and hear no early-diastolic murmur in the third or fourth intercostal spaces at the left sternal border. You suspect that the wide pulse pressure is a peripheral hemodynamic consequence of *cirrhosis*, not AR. Do you need an echocardiogram to confirm your clinical impression that she does not have AR?

**Why Is the Clinical Examination Important in Evaluating for Aortic Regurgitation?**

Aortic regurgitation is a potentially serious cardiac abnormality that may be caused by important underlying disorders. Patients with AR require careful clinical monitoring to identify the optimal time for surgical intervention. Asymptomatic patients with severe AR may benefit from vasodilator therapy.\(^1\)

The use of noninvasive cardiac testing, such as echocardiography, has increased in recent years. It is estimated that 2% of the general population undergo noninvasive cardiac diagnostic evaluation annually.\(^2\) If a careful clinical examination can exclude the presence of AR, then there would be no need to proceed with further cardiac evaluation.

**Anatomic and Physiologic Origins of Diastolic Murmurs**

The cardinal manifestation of AR is a diastolic murmur. Diastolic murmurs are important indicators of structural cardiac abnormalities or pathologic states of increased flow (*Table 32-1*). As discussed in a previous article in this series,\(^3\) heart murmurs are produced when turbulent blood flow causes prolonged auditory vibrations of cardiac structures. The intensity of the murmur depends on many factors, including blood viscosity, blood flow velocity and turbulence, the distance between the vibrations and the stethoscope, the angle at which the vibrations meet the stethoscope, the transmission qualities of the tissue between the vibration and the stethoscope, and the auditory skills of the examiner.\(^4\)
Table 32-1  Selected Causes of Diastolic Murmurs

Abnormal cardiac structure
Aortic regurgitation
Mitral stenosis
Pulmonic regurgitation
Tricuspid stenosis
Atrial myxoma
Ventricular septal defect\(^a\)
Atrial septal defect\(^a\)
Mitral regurgitation\(^a\)
Normal cardiac structure, increased flow
Renal failure with volume overload
Thyrotoxicosis
Anemia
Sepsis

\(^a\)Diastolic murmurs are caused by abnormally increased diastolic flow across the mitral or tricuspid valves.

How to Examine for Aortic Regurgitation

A complete clinical history and physical examination are essential in the evaluation of a patient with a diastolic murmur. A diastolic murmur in a patient with renal failure and volume overload will have different significance than a diastolic murmur in a patient with a history of rheumatic fever and atrial fibrillation.

The examiner's ability to detect a diastolic murmur can be undermined by environmental factors such as noisy rooms, examiner factors such as fatigue or haste, and patient factors such as dyspnea or tachycardia. If examining conditions are not optimal, the examination should be repeated when conditions improve.

The precision and accuracy of many components of the examination for AR, including all of the cardiac history and most of the physical examination, have not been adequately evaluated. This article will focus on aspects of the cardiac physical examination that have been sufficiently assessed for precision or accuracy.

Cardiac Auscultation

During routine auscultation, the examiner attempts to detect a diastolic murmur. Diastole is the period that begins with the closure of the aortic and pulmonic valves (second heart sound [\(S_2\)]) and ends with the closure of the mitral and tricuspid valves (first heart sound [\(S_1\)]). A common maneuver used to identify diastole is to palpate the carotid artery pulse during auscultation; \(S_1\) is synchronous with the carotid artery pulsation, whereas \(S_2\) follows the pulse. A diastolic murmur is a diastolic sound longer than a heart sound. Examiners should describe the grade, location of maximal intensity (Figure 32-1), timing (Figure 32-2), duration, pitch, and radiation of the murmur.

Figure 32-1

Typical Location of Abnormal Diastolic Murmurs

There are 3 important areas to auscultate for diastolic murmurs. Area 1 is the second and third intercostal
spaces at the right sternal border. Area 2 is the second and fourth intercostal spaces at the left sternal border. Aortic regurgitation murmurs may be heard in both areas 1 and 2. If the murmur is loudest in area 1, then the underlying cause of aortic regurgitation may be an ascending aortic aneurysm or aortic dissection. Pulmonic regurgitation murmurs are loudest in the superior part of area 2 and may radiate downward. The murmur of mitral stenosis and the Flint murmur of aortic regurgitation are best heard at the apex (area 3).

Selected Features of Diastolic Murmurs

Diastolic murmurs are classified according to the time of onset of the murmur.\textsuperscript{14} An early diastolic murmur begins with the second heart sound (S\textsubscript{2}). Top, Early diastolic murmurs typically decrease in intensity (decrescendo) and disappear before the first heart sound (S\textsubscript{1}). In some cases, an early diastolic murmur can continue through diastole. Bottom, A mid-diastolic murmur begins clearly after S\textsubscript{2} (in mitral stenosis, classically after an opening snap [OS]). A late-diastolic (or presystolic) murmur begins in the interval immediately before S\textsubscript{1}. In mitral stenosis, the mid-diastolic murmur may merge with the late-diastolic (presystolic) murmur.
The Levine grading system, with slight modifications, was developed for systolic murmurs but may also be used to describe diastolic murmurs. A grade 1 murmur is not heard immediately on auscultation but is heard after the examiner focuses for a few seconds. Grade 2 murmurs are heard immediately on auscultation but are softer than the loud grade 3. Grade 4 murmurs are associated with a palpable precordial vibration called a thrill. Grades 5 and 6 murmurs are also associated with a thrill. A grade 5 murmur is audible when only one edge of the stethoscope is on the chest, and a grade 6 murmur is audible with the entire stethoscope lifted off the chest.

The typical AR murmur is an early-diastolic, decrescendo blowing sound (Figure 32-2) that may be accentuated with the patient sitting upright and leaning forward. In some cases, S₂ can be obscured by the murmur. Most AR murmurs are high pitched and are best heard with the diaphragm of the stethoscope placed firmly on the chest wall. Some AR murmurs are low pitched and are better heard with the bell of the stethoscope placed lightly on the chest wall. For example, the AR murmur associated with endocarditis and a fenestrated aortic valve can be low pitched.

The examiner should apply the stethoscope to the chest wall in the third or fourth intercostal space at the left sternal border and listen between normal breaths at the end of expiration. The patient should not voluntarily breath-hold because it may inadvertently create a Valsalva maneuver. If the murmur is louder at the second to third right intercostal space, the underlying cause of AR may be an ascending aortic aneurysm or aortic dissection.

Aortic regurgitation also may be associated with a systolic murmur, created by the flow of an abnormally large volume of blood through a nonstenotic aortic valve or a bicuspid aortic valve. The murmur is an early-peaking, crescendo-decrescendo systolic sound that is best heard with the diaphragm of the stethoscope applied to the second right intercostal space.

The Flint murmur is a low-pitched late-diastolic apical murmur, which is associated with AR. The murmur is likely produced when the regurgitant jet of blood collides with the left ventricular endocardium. The murmur may have a mid-diastolic component, but the original description by Flint referred only to “presystolic blubbing.” It is best heard with the patient in the left-lateral decubitus position, using the bell of the stethoscope. Differentiating the Flint murmur from the murmur of mitral stenosis can be difficult. The murmur of mitral stenosis is primarily mid-diastolic (possibly with a late-diastolic component) and may be associated with an opening snap (OS) and a loud S₁ (Figure 32-2).
The typical murmur of pulmonic regurgitation (PR) is an early-diastolic decrescendo murmur heard best in the second-left intercostal space at the sternal border. The murmur may radiate to the third and fourth left intercostal spaces and may increase during quiet inspiration. If there is splitting of S₂, the astute examiner may note that the murmur begins after the pulmonic valve component (P₂) of S₂ rather than the aortic component. The murmur of PR may be lower pitched than the murmur of AR, unless pulmonary hypertension is present. A right-sided Flint murmur can be heard, particularly in patients with pulmonary hypertension.

Mitral stenosis is associated with a mid-diastolic, decrescendo, low-frequency rumble, which, if the patient is in sinus rhythm, may be followed by late-diastolic (presystolic) crescendo that ends with the mitral component of S₁ (Figure 32-2). It is best heard using the bell of the stethoscope placed at the apex soon after moving the patient into the left lateral decubitus position. Rolling the patient onto the left side brings the left ventricle closer to the chest wall and serves as a form of exercise, increasing blood flow across the mitral valve and increasing the murmur's intensity. The murmur of mitral stenosis may be inaudible in patients with low cardiac output.

The S₁ may be increased in intensity in mitral stenosis. A normal S₁ is best appreciated near the apex, where it should be louder than S₂. The S₁ is normally softer than S₂ in the second right and second left intercostal spaces adjacent to the sternum. If S₁ is as loud as or louder than the S₂ in these areas, then the S₁ is increased in intensity.

An OS is a high-frequency, early-diastolic sound that is associated with the opening of a stenotic mitral valve. It occurs 50 to 100 ms after the aortic valve component (A₂) of S₂ and is best heard in the area from the left sternal border to the apex. Much like the murmur of mitral stenosis, it may be accentuated by auscultating while the patient is in the left lateral decubitus position shortly after the patient has performed exercise. The A₂-OS interval shortens with increasing severity of mitral stenosis. The OS may be absent in the case of a heavily calcified immobile mitral valve. It is often difficult to differentiate an OS from the P₂ of S₂. The OS usually decreases in intensity with inspiration and S₂-OS interval widens on standing. Conversely, P₂ becomes louder with inspiration, and the A₂-P₂ interval remains the same or narrows with standing. In addition, P₂ is not expected to be heard at the apex unless the patient has pulmonary hypertension.

Maneuvers

Selective use of maneuvers can enhance the detection and interpretation of diastolic murmurs. There is no point in doing maneuvers if a loud AR murmur has been detected during routine auscultation. However, if the clinician is unsure about the presence of a faint diastolic murmur, then a maneuver that increases murmur intensity may clarify the situation. If the clinician has a heightened suspicion for AR (eg, after hearing an aortic ejection sound), or if examining conditions are not optimal, then a maneuver to augment murmur intensity might bring out an otherwise inaudible murmur. Finally, the maneuvers may help distinguish PR from AR. In this latter situation, the clinician should listen where the murmur is just barely audible, so that it is easy to detect a decrease or increase in murmur intensity during the maneuver.

Quiet inspiration increases venous return and augments right-sided heart murmurs such as PR. To determine the effect of inspiration on the intensity of the murmur, the examiner should listen during quiet inspiration, rather than asking the patient to breathe deeply, because the murmur may be obscured by breath sounds.

Transient arterial occlusion primarily increases systemic arterial resistance that intensifies left-sided regurgitant lesions such as AR and may help distinguish the murmur from PR. To perform this maneuver, sphygmomanometers are placed around both of the patient's arms and are inflated to 20 to 40 mm Hg above the previously recorded systolic blood pressure. Any changes in murmur intensity are noted 20 seconds after cuff inflation.
Peripheral Hemodynamic Signs

There are a variety of peripheral hemodynamic signs traditionally associated with AR. Some of these signs have been adequately evaluated, including de Musset head-bobbing sign, a wide pulse pressure, the brachial-popliteal pulse gradient (Hill sign), Duroziez femoral murmur, the femoral pistol shot murmur, and Corrigan water hammer pulse. The de Musset head-bobbing sign consists of a forward shaking of the head with every heartbeat; it is best observed in patients who are sitting.

Pulse pressure refers to the difference between systolic and diastolic blood pressures. A widened pulse pressure may be defined as greater than 50 mm Hg. Other definitions include a pulse pressure greater than 50% of the systolic pressure. Determination of the blood pressure has been described in another article in this series.

The brachial-popliteal pulse gradient (Hill sign) can be defined as a systolic blood pressure in the lower extremities that is at least 20 mm Hg higher than that in the arms. To determine a popliteal blood pressure, an appropriately sized blood pressure cuff should be placed on the patient's thigh with the artery marker over the popliteal artery. The cuff should be inflated and the systolic pressure can then be determined in the popliteal fossa either by palpation, as judged by the point where the pulse reappears as the cuff is deflated, or by auscultation, listening for Korotkoff sounds to appear. Both the brachial and popliteal blood pressures should be measured while the patient is supine. The average of repeated readings should be used, especially in patients with irregular heart rates, such as atrial fibrillation.

Duroziez double intermittent femoral bruit is elicited by first gently compressing the femoral artery with the diaphragm of the stethoscope. This will yield a systolic bruit in all patients. As increasing pressure is applied to the diaphragm, an early-diastolic bruit will become audible in patients with AR. While listening to the diastolic bruit, the clinician should tilt the stethoscope so that the distal rim (closest to the patient's feet) is compressing the femoral artery. If the bruit becomes louder with this maneuver, then the diastolic bruit is due to the retrograde flow of blood toward the heart in AR. The stethoscope should then be tilted such that the proximal rim (closest to the patient's head) is compressing the femoral artery. If the diastolic bruit becomes softer, this can be taken as supportive evidence of the presence of retrograde blood flow. If, however, the bruit becomes louder with proximal pressure (and softer with distal pressure), then this sign should not be used as evidence of AR but may indicate the presence of a high-flow state such as renal failure with volume overload.

Femoral pistol shot sounds are elicited by auscultating with the diaphragm of the stethoscope over the femoral arteries. A high-pitched pistol shot sound may be heard in AR. Corrigan water hammer pulse refers to an increased volume and rate of increase of the radial pulse when the wrist is elevated perpendicular to the body of a supine patient. The radial pulse should first be assessed while the patient is lying supine with his or her arms resting at the sides. Sufficient pressure should be applied to obliterate the pulse. While this pressure is maintained, the patient's arm should be elevated so that it is perpendicular to the plane of the body. In AR, the pulse will become palpable despite applying an equivalent amount of pressure as when the arm was at the patient's side.

Other peripheral hemodynamic signs, such as Mayne sign (a decrease in diastolic blood pressure of 15 mm Hg when the arm is held above the head compared with when the arm is held at the level of the heart), Quinke capillary pulsation, Muller pulsatile uvula, and Rosenbach liver pulsation, have not been adequately evaluated for precision or accuracy.

Methods

To identify articles pertaining to the precision and accuracy of the physical examination for AR, we used...
standard methods for conducting research overviews.\textsuperscript{24} Our data collection strategy involved 3 steps and was deliberately broad to reduce the possibility of overlooking important articles. First, we searched MEDLINE for English-language articles published from 1966 through July 1997, using a structured search strategy (available on request from the authors). Second, we manually reviewed potentially relevant articles and their reference lists. Third, we contacted the authors of relevant studies for additional information. Studies were excluded if they were review articles, involved patients younger than 18 years, were small (ie, <20 participants), involved prosthetic heart valves, had no clinical examination performed or reported, or had no acceptable reference standard (Doppler echocardiography or cardiac catheterization).

\textbf{Table 1-7} for a summary of Evidence Grades and levels).\textsuperscript{25} \textbf{Grade A} studies involve the independent comparison of a sign or symptom with a reference standard of diagnosis among a large number of consecutive patients suspected of having the target condition. \textbf{Grade B} studies meet the criteria for grade A studies but have a small number of patients. \textbf{Grade C} studies involve nonconsecutive patients, who are known to have the target condition and healthy individuals, nonindependent comparisons between the sign or symptom and the reference standard, or nonindependent comparisons with a reference standard of uncertain validity. \textbf{Grade C} studies tend to overestimate the accuracy of the sign or symptom.

We created contingency tables for all studies and determined the likelihood ratios (LRs) for aortic regurgitation.\textsuperscript{26, 27} We also sought information on the examination for other causes of diastolic murmurs, such as mitral stenosis or PR. Unfortunately, we found few studies of sufficient methodologic quality for these conditions. This relative lack of information implies that methodologically sound studies are needed but does not imply that the clinical examination for these conditions is imprecise, inaccurate, or unimportant.

\textbf{Precision of the Examination Related to Diastolic Murmurs}

Precision refers to agreement regarding a particular clinical finding between different physicians (interobserver) or between multiple assessments by the same physician (intraobserver). The precision of the clinical examination for diastolic murmurs has been evaluated in usual clinical situations by auscultating patients\textsuperscript{28, 29} or in controlled nonclinical circumstances by listening to recorded audiotapes (\textbf{Table 32-2}).\textsuperscript{30}

\textbf{Table 32-2} \textbf{Interobserver Reliability (Precision) for Detecting Diastolic Murmurs}

<table>
<thead>
<tr>
<th>Finding</th>
<th>Type of Examiner</th>
<th>No. of Examiners</th>
<th>No. of Patients</th>
<th>$\kappa$</th>
<th>Simple Agreement, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murmur absent vs present</td>
<td>Cardiologists (tapes)\textsuperscript{30}</td>
<td>5</td>
<td>100</td>
<td>0.51</td>
<td>79</td>
</tr>
<tr>
<td>Cardiologists\textsuperscript{28}</td>
<td>2</td>
<td>32</td>
<td>…</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Noncardiologists\textsuperscript{28}</td>
<td>3</td>
<td>32</td>
<td>…</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Intensity of murmur</td>
<td>Not stated\textsuperscript{29, b}</td>
<td>5</td>
<td>25</td>
<td>…</td>
<td>92</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Ellipses indicate data not available.

\textsuperscript{b}Examiners used paper disks, 0.5 mm in thickness, that were progressively inserted between the chest wall and the stethoscope until the murmur became inaudible. The total thickness of the disks used was used as the measure of intensity. For example, if a murmur was inaudible after insertion of 3 disks, then this was a 1.5-mm murmur.

There have been 4 studies that address the interobserver precision of cardiac auscultation to detect diastolic murmurs (\textbf{Table 32-2}). Although simple agreement is high in these studies, the one study for which it was possible to calculate agreement adjusted for chance ($\kappa$) showed only moderate agreement. The experience of observers likely affects precision. The one study\textsuperscript{28} that compared cardiologists with noncardiologists found a
higher simple agreement for cardiologists.

The interobserver agreement between examiners on the intensity of heart sounds is excellent (92%). In this study, examiners progressively inserted 0.5-mm-thick paper disks between the patient's chest and the stethoscope. The total thickness of the disks was used as a measure of heart sound intensity. Murmur intensity was also assessed with this technique (Table 32-2).

The Bottom Line for Precision

The interobserver precision of cardiologists examining for any diastolic murmur is moderate with audiotapes (κ = 0.51) and good in the clinical setting (simple agreement, 94%). Noncardiologists may be less precise than cardiologists. The precision of examining for the intensity of murmurs and heart sounds with a standardized series of paper disks to assess intensity is good (simple agreement, 92%-96%).

Accuracy of the Examination for Aortic Regurgitation

We consider Doppler echocardiography and cardiac catheterization to be acceptable reference standards for AR (Table 32-3). In one study, the reference standard was open-heart surgery.

Table 32-3  Accuracy of the Physical Examination for Detecting Aortic Regurgitation

<table>
<thead>
<tr>
<th>Study, y</th>
<th>Patient Population</th>
<th>Reference Standard</th>
<th>No. of Patients With AR</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
<th>Quality Gradea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical Murmur With Severity of AR Specified</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aronow and Kronzon33 (1989)</td>
<td>Elderly patients</td>
<td>Echocardiography (n = 450)</td>
<td>131</td>
<td>32 (16-63)</td>
<td>0.2 (0.1-0.3)</td>
<td>A</td>
</tr>
<tr>
<td>Mild or greater AR</td>
<td>74</td>
<td>8.3 (6.2-11)</td>
<td>0.1 (0.0-0.2)</td>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grayburn et al34 (1986)</td>
<td>Referred for catheterization</td>
<td>Catheterization (n = 106)</td>
<td>82</td>
<td>8.8 (2.8-32)</td>
<td>0.3 (0.2-0.4)</td>
<td>A</td>
</tr>
<tr>
<td>Mild or greater AR</td>
<td>57</td>
<td>4.0 (2.5-6.9)</td>
<td>0.1 (0.1-0.3)</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roldan et al35 (1996)</td>
<td>Asymptomatic connective tissue disease and controls</td>
<td>Echocardiography (n = 143)</td>
<td>10</td>
<td>80 (14-470)</td>
<td>0.4 (0.2-0.7)</td>
<td>C</td>
</tr>
<tr>
<td>Mild or greater AR</td>
<td>82</td>
<td>12 (8.1-19)</td>
<td>0.2 (0.1-0.3)</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Procedure and Diagnosis</td>
<td>Method</td>
<td>Results</td>
<td>Control</td>
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<td></td>
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<tr>
<td><strong>Mild or greater AR</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cohn et al 37 (1967)</td>
<td>Mitral valve repair</td>
<td>Open-heart surgery (n = 156)</td>
<td>50</td>
<td>5.2 (3.3-8.4) 0.3 (0.2-0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meyers et al 38 (1982)</td>
<td>Referred for aortography</td>
<td>Catheterization (n = 75)</td>
<td>66</td>
<td>3.3 (1.3-12) 0.4 (0.2-0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meyers et al 40 (1985)</td>
<td>Valvular heart disease</td>
<td>Catheterization (n = 20)</td>
<td>42</td>
<td>16 (2.1-155) 0.4 (0.3-0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linhart 41 (1971)</td>
<td>Mitral stenosis</td>
<td>Catheterization (n = 28)</td>
<td>11</td>
<td>9.8 (1.3-96) 0.5 (0.2-0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate or greater AR</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohn et al 37 (1967)</td>
<td>Mitral valve repair</td>
<td>Open-heart surgery (n = 156)</td>
<td>37</td>
<td>3.9 (2.6-5.7) 0.2 (0.1-0.4)</td>
<td></td>
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<tr>
<td>Meyers et al 38 (1982)</td>
<td>Referred for aortography</td>
<td>Catheterization (n = 75)</td>
<td>39</td>
<td>1.6 (1.2-2.4) 0.4 (0.2-0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meyers et al 40 (1985)</td>
<td>Valvular heart disease</td>
<td>Catheterization (n = 20)</td>
<td>39</td>
<td>1.6 (1.2-2.4) 0.4 (0.2-0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dittmann et al 39 (1987)</td>
<td>Valvular heart disease</td>
<td>Catheterization (n = 55)</td>
<td>42</td>
<td>16 (2.1-155) 0.4 (0.3-0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meyers et al 40 (1985)</td>
<td>Valvular heart disease</td>
<td>Catheterization (n = 20)</td>
<td>19</td>
<td>3.6 (2.1-6.6) 0.1 (0.0-0.4)</td>
<td></td>
<td></td>
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<tr>
<td>Linhart 41 (1971)</td>
<td>Mitral stenosis</td>
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<td>19</td>
<td>3.6 (2.1-6.6) 0.1 (0.0-0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe AR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meyers et al 40 (1985)</td>
<td>Valvular heart disease</td>
<td>Catheterization (n = 20)</td>
<td>19</td>
<td>3.6 (2.1-6.6) 0.1 (0.0-0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linhart 41 (1971)</td>
<td>Mitral stenosis</td>
<td>Catheterization (n = 28)</td>
<td>19</td>
<td>3.6 (2.1-6.6) 0.1 (0.0-0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Typical Murmur Without AR Severity Specified (May Include Trivial AR)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Come et al 42 (1986)</td>
<td>Mitral valve prolapse, plus patients with systolic flow murmurs</td>
<td>Echocardiography (n = 165)</td>
<td>11</td>
<td>16 (2.1-155) 0.4 (0.3-0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linhart 41 (1971)</td>
<td>Mitral stenosis</td>
<td>Catheterization (n = 28)</td>
<td>11</td>
<td>6.2 (1.9-23) 0.3 (0.1-0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maneuver</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ward et al 44 (1977)</td>
<td>Clinically suspected aortic dissection</td>
<td>Catheterization (n = 65)</td>
<td>49</td>
<td>13 (2.9-75) 0.2 (0.1-0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esper 45 (1982)</td>
<td>AR and other heart disease</td>
<td>Echocardiography (n = 43)</td>
<td>24</td>
<td>12 (2.4-67) 0.4 (0.3-0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saal et al 46 (1985)</td>
<td>Mitral stenosis</td>
<td>Catheterization (n = 45)</td>
<td>35</td>
<td>8.0 (1.9-45) 0.2 (0.1-0.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Associated Physical Findings**

- With transient arterial occlusion murmur increases in intensity
- Associated with AR, mitral stenosis, and pulmonic regurgitation
<table>
<thead>
<tr>
<th>Physical Finding</th>
<th>Study Population</th>
<th>Procedure</th>
<th>Number</th>
<th>Mean Value (Range)</th>
<th>95% CI (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flinm murmur</td>
<td>Isolated AR and controls</td>
<td>Echocardiography (n = 36)</td>
<td>48</td>
<td>0.8 (0.6-1.3)</td>
<td></td>
</tr>
<tr>
<td>Mild or greater AR</td>
<td>28</td>
<td>4 (0.5-40)</td>
<td>0.5 (0.2-1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate or greater AR</td>
<td>13</td>
<td>25 (2.8-243)</td>
<td>0.5 (0.2-0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any systolic murmur</td>
<td>Isolated AR and controls</td>
<td>Echocardiography (n = 36)</td>
<td>48</td>
<td>0.8 (0.6-1.3)</td>
<td></td>
</tr>
<tr>
<td>Mild or greater AR</td>
<td>28</td>
<td>1.3 (0.9-2.7)</td>
<td>0.5 (0.2-1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate or greater AR</td>
<td>13</td>
<td>1.5 (1.0-2.1)</td>
<td>0.0 (0.0-1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Popliteal-brachial gradient &gt; 20 mm Hg</td>
<td>Mild to severe AR</td>
<td>Catheterization (n = 33)</td>
<td>20</td>
<td>8.2 (1.5-78)</td>
<td></td>
</tr>
<tr>
<td>Moderate or greater AR</td>
<td>28</td>
<td>8.2 (1.5-78)</td>
<td>0.2 (0.1-0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral hemodynamic signs</td>
<td>Mild to severe AR</td>
<td>Catheterization (n = 34)</td>
<td>20</td>
<td>2.1 (0.3-22)</td>
<td></td>
</tr>
<tr>
<td>Moderate or greater AR</td>
<td>28</td>
<td>2.1 (0.3-22)</td>
<td>0.8 (0.7-1.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse pressure &gt; 50 mm Hg</td>
<td>Mild to severe AR</td>
<td>Catheterization (n = 33)</td>
<td>20</td>
<td>1.0 (0.7-2.2)</td>
<td></td>
</tr>
<tr>
<td>Moderate or greater AR</td>
<td>28</td>
<td>1.0 (0.7-2.2)</td>
<td>0.9 (0.2-5.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AR, aortic regurgitation; CI, confidence interval; LR+, positive likelihood ratio; LR–, negative likelihood ratio.

aSee Table 1-7 for a summary of Evidence Grades and levels.

bGrade B study, except catheterization results were not interpreted independently of clinical findings.

cGrade B study, except echocardiograms were not interpreted independently of clinical findings.

dIncluded Duroziez bruit, femoral pistol shots, and Corrigan pulses.

Cardiologists conducted the clinical examinations in most studies. Too few studies, using few patients, allow for reasonable estimates of the accuracy of noncardiologists, although noncardiologists are likely less adept at detecting the diastolic murmur of AR. Approximately 20% of residents and medical students correctly identified the murmur of AR on high-fidelity digitized audiobases, whereas 46% of internal medicine residents correctly identified an AR murmur on a patient simulator.

The best-studied physical finding is the typical early-diastolic murmur of AR. If an examiner does not hear a typical AR murmur, then the likelihood that the patient has moderate or greater AR is significantly reduced (negative likelihood ratio [LR–], 0.1 for grade A studies); the likelihood of mild or greater AR is also significantly reduced (LR–, 0.2-0.3 for grade A studies). If an examiner hears the typical AR murmur, the likelihood that the patient has moderate or greater AR is increased (positive likelihood ratio [LR+], 4.0-8.3 for grade A studies); the likelihood of mild or greater AR is also significantly increased (LR+, 8.8-32 for grade A studies).
The intensity of the murmur correlates with the severity of echocardiographic AR. Desjardins et al\(^47\) studied 40 patients with echocardiographic AR, including 17 with severe AR. A grade 3 diastolic murmur had an LR of 4.5 (95% CI, 1.6-14) for distinguishing severe AR from less severe AR, whereas a grade 2 murmur had an LR of 1.1 (95% CI, 0.5-2.4), a grade 1 murmur had an LR of 0.0 (95% CI, 0.0-0.9), and absence of a diastolic murmur had an LR of 0.0 (95% CI, 0.0-1.1).\(^{47}\)

Two grade C studies of the Flint murmur and some peripheral hemodynamic findings are reported in Table 32-3. Grade C studies tend to overestimate diagnostic test accuracy. Despite this tendency, one study found that absence of a Flint murmur did not rule out AR (LR–, 0.5-0.8).\(^{48}\) Another study of patients with mild to severe AR found only that a wide pulse pressure or peripheral hemodynamic sign (Duroziez bruit, femoral pistol shots, and Corrigan pulses) was not helpful for distinguishing mild AR from moderate or severe AR.\(^{20}\) The de Musset head-bobbing sign was seen in only 1 of 20 patients (sensitivity, 5%), while Duroziez femoral bruit was observed in 8 of 12 patients (sensitivity, 67%),\(^{16}\) making them interesting but not particularly useful findings.

**The Bottom Line for Aortic Regurgitation**

When a cardiologist hears the typical murmur of AR, the likelihood of mild or greater AR is increased significantly (2 grade A studies). The absence of a typical diastolic murmur significantly reduces the likelihood of AR (2 grade A studies). Noncardiologists may be less proficient than cardiologists at detecting the murmur of AR.

**Mitral Stenosis and Pulmonic Regurgitation**

In one grade A study of 529 unselected nursing home residents (31 with mitral stenosis), a cardiologist detected a mid-diastolic murmur in all cases of mitral stenosis, with no false-positive or -negative examinations.\(^{49}\) Only 1 patient had an audible OS.

Noncardiologists may be less proficient at detecting the physical findings of mitral stenosis. Less than 10% of residents and medical students correctly identified a mid-diastolic murmur of mitral stenosis on a high-fidelity digitized audiotape,\(^{31}\) whereas 43% of medical residents identified a mid-diastolic murmur of mitral stenosis with a patient simulator. In the latter study, only 21% identified the OS of mitral stenosis.\(^{32}\)

The only evaluated element of the clinical examination for PR is the presence of a typical diastolic decrescendo murmur best audible in the second intercostal space at the left-upper sternal border, which may increase in intensity with quiet inspiration. All studies used cardiologists as examiners and were of poor methodologic quality (grade C).

When a cardiologist hears the murmur of PR, the likelihood of PR increases (LR+, 17 in both studies), but the absence of a PR murmur was not helpful for ruling out PR (LR, 0.9 in both studies).\(^{36},^{42}\)

**The Bottom Line for Mitral Stenosis and Pulmonic Regurgitation**

The presence of a mid-diastolic murmur significantly increases the likelihood of mitral stenosis, whereas the absence of a mid-diastolic murmur significantly reduces the likelihood of mitral stenosis (1 grade A study). When a cardiologist hears a typical PR murmur, the likelihood of PR increases significantly. The absence of a typical murmur does not alter the likelihood of PR (2 grade C studies). Noncardiologists may be less proficient at detecting the mid-diastolic murmur of mitral stenosis.

**Diastolic Murmurs in Patients With Renal Failure**

The presence of a mid-diastolic murmur significantly increases the likelihood of mitral stenosis, whereas the absence of a mid-diastolic murmur significantly reduces the likelihood of mitral stenosis (1 grade A study). When a cardiologist hears a typical PR murmur, the likelihood of PR increases significantly. The absence of a typical murmur does not alter the likelihood of PR (2 grade C studies). Noncardiologists may be less proficient at detecting the mid-diastolic murmur of mitral stenosis.
Diastolic murmurs caused by abnormal flow states, rather than abnormal cardiac structure, may be associated with a variety of conditions. Renal failure with volume overload is the only abnormal flow state associated with diastolic murmurs that has been evaluated.

Up to 9% of patients with end-stage renal disease have diastolic murmurs, particularly when these patients also have volume overload, anemia, and hypertension. These murmurs typically disappear after the treatment of volume overload, as was demonstrated in 2 small studies (grade C). These murmurs are probably due to transient pulmonary hypertension and dilatation of the pulmonary artery root, leading to PR.

The Bottom Line for Diastolic Murmurs in Patients With Renal Failure

Although there is an insufficient amount of data on which to make rigorous recommendations, if an early-diastolic murmur is heard in a dialysis patient with volume overload, the patient should be reexamined after treatment because the murmur may disappear.

When to Examine for Aortic Regurgitation

There are no evaluative data on which to base a recommendation regarding when to examine for AR. Undetected AR may be common in elderly persons: 13% (n = 552) of asymptomatic elderly Finnish persons had moderate or severe echocardiographic AR. Unfortunately, that study does not indicate how many of these patients had audible diastolic murmurs. Audible diastolic murmurs may be relatively uncommon findings in asymptomatic persons. In one study, only 1% (n = 103) of elderly asymptomatic nursing home residents had an audible diastolic murmur.

Despite the lack of evaluative data, we think that a prudent clinician will examine for AR in most clinical settings. AR is a serious cardiac abnormality, which may be caused by underlying disorders and may be asymptomatic. The clinician's suspicion for AR may be heightened by evidence of systemic disease, such as ankylosing spondylitis, a peripheral hemodynamic finding (although these are by no means indicative of underlying AR), or an abnormality detected during routine auscultation (such as an aortic ejection sound). Other findings may suggest different cardiac abnormalities associated with diastolic murmurs, such as evidence of pulmonary hypertension (for PR), a wide-fixed split S₂ (for atrial-septal defect), or a holosystolic apical murmur (for mitral regurgitation).

Recommendations for Further Research

Most studies used cardiologists to conduct clinical examinations. There are some data that suggest that noncardiologists may be less accurate than cardiologists, so studies evaluating techniques to improve the skills of noncardiologists are needed. There are also no studies defining the optimal examination technique for detecting the AR murmur.

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Clinical Scenario—Resolution

Your patient has a wide pulse pressure but no typical early-diastolic murmur. The likelihood of mild or moderate AR is significantly reduced by the absence of a typical early-diastolic murmur (LR–, 0.1-0.3; 2 grade A studies). You perform transient arterial occlusion, and no diastolic murmur appears, which enhances your confidence (LR–, 0.3). You are confident in your assessment because it was conducted in a quiet room with a comfortable and cooperative patient. Therefore, AR is unlikely and echocardiography is not necessary.

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References

8.


[JAMA and JAMA Network Journals Full Text]


[JAMA and JAMA Network Journals Full Text]


37.


Update

Clinical Scenario

A 58-year-old man presents for a routine physical examination, not having visited a physician in many years. He denies any cardiovascular symptoms. On auscultation, you are surprised to hear a loud (grade 3) early diastolic murmur. There is an audible S₃ and a collapsing radial pulse (Corrigan sign). After explaining to the patient that you heard a murmur, he asks, “How bad do you think it is?”

Original Review


Updated Literature Search

Our literature search combined the parent search strategy for The Rational Clinical Examination with the terms “diastolic and murmur, aortic valve insufficiency, mitral valve stenosis,” and “pulmonary valve insufficiency,” limited to English-language publications in the Ovid MEDLINE database from 1997 to July 2004. The titles and abstracts of the search results were screened, case reports were excluded, and 8 potentially relevant articles were retrieved and reviewed. We manually reviewed the reference list of each article for additional studies. Articles were retained if they were studies of adult participants, included sensitivity and specificity data of physical findings, and had a quality score of level 3 or greater. This yielded 1 new study, and we found 1 other study during the updated literature search for systolic murmurs.

New Findings

The presence of an S₃ in patients with isolated aortic regurgitation (AR) predicts severity.

Details of the Update

Were There Changes in the Original Publication?

In the original article, the need to identify patients at higher risk for endocarditis because of valvular abnormalities was suggested as a rationale for performing the clinical examination. The recommendations for endocarditis prophylaxis have changed. Patients with murmurs from structural abnormalities of a native valve
do not automatically require antibiotic prophylaxis to prevent infective endocarditis.¹

**Changes in the Reference Standard**

The *reference standard* is the echocardiogram or the results from a cardiac catheterization that assess valvular competency.

**Results of the Literature Review**

Diastolic murmurs are always important, requiring ascertainment of the underlying abnormality. Most studies of the detection of AR assess the performance of cardiologists or the ability to distinguish patients with serious AR from those with less significant impairment. The *sensitivity* and *specificity* of a variety of peripheral hemodynamic findings, popularized in many textbooks of physical diagnosis and cardiology, have not been adequately assessed.

Since the original review, 1 study² assessed the ability of cardiologists to identify the presence of AR (Table 32-4). In this study, 100 consecutive patients referred for evaluation of a systolic murmur of unknown cause underwent a standard cardiac examination by a cardiologist, who described the murmur and assigned a clinical diagnosis. Mild or greater AR was identified with high *specificity* but low *sensitivity*. Compared with studies cited in the original review, the lower *sensitivity* might reflect a challenging sample with a high *prevalence* of multiple valvular lesions and a predominance of mild regurgitation among those patients with AR.

Table 32-4  Likelihood Ratios of the Physical Examination for Detecting Aortic Regurgitation

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall cardiac examination²</td>
<td>5.1 (1.4-19)</td>
<td>0.82 (0.67-1.0)</td>
</tr>
<tr>
<td>Referred for evaluation of systolic murmur</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Third heart sound (to identify severe AR)³</td>
<td>5.9 (1.4-25)</td>
<td>0.83 (0.73-0.95)</td>
</tr>
<tr>
<td>Patients with isolated aortic insufficiency, referred for echocardiography</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AR, aortic regurgitation; CI, *confidence interval*; LR+, positive *likelihood ratio*; LR–, negative *likelihood ratio*.

One additional study³ evaluated the ability of the clinical examination to distinguish severe AR from less severe disease. The presence of an S₃, recorded by a physician referring a patient for cardiac ultrasonography, predicted severe AR (defined as a regurgitant fraction ≥ 40%), with a *likelihood ratio* of 5.9. The absence of an S₃ was not useful for ruling out severe AR (negative *likelihood ratio*, 0.83) (Table 32-4).³

**Evidence From Guidelines**

The American College of Cardiology and American Heart Association guidelines⁴ (2003) state that Doppler echocardiography to exclude valvular regurgitation in asymptomatic patients with normal physical examination results is not indicated.

**Clinical Scenario—Resolution**

Your patient has a typical diastolic murmur of AR. This finding alone warrants echocardiography because it is highly suggestive of an underlying abnormality. If the patient has AR, the *grade* 3 intensity of the murmur and the third heart sound increase the likelihood of severe AR. The collapsing radial pulse (Corrigan pulse) is of
uncertain usefulness. Putting together all of your findings, you advise your patient that you are concerned that he might have important valvular disease. You provide information regarding endocarditis prophylaxis and arrange for an echocardiogram.

References for the Update


aFor the Evidence to Support the Update for this topic, see Next.
Evidence to Support the Update

Evidence Summary and Review 1

Title Echocardiography in Evaluating Systolic Murmurs of Unknown Cause.

Authors Attenhofer Jost CH, Turina J, Mayer K, et al.


Question How well can cardiologists identify pathologic murmurs by auscultation and palpation alone?

Design Consecutive patients were prospectively identified at referral for evaluation of a systolic murmur of unknown cause. Each participant was independently examined by 2 cardiologists from a pool of 8 and blinded to supplementary data and echocardiography results. Two-dimensional/Doppler echocardiography was performed as the gold standard in all participants.

Setting Cardiology division in Switzerland.

Patients One hundred patients referred for evaluation of systolic murmur of unknown cause were enrolled. Patients were excluded if they had a previously documented echocardiographic examination. The mean age of the participants was 55 years, with SD 22, and 57% were women.

Description of Tests and Diagnostic Standard

Full cardiac examination, with or without dynamic auscultation, was performed by 1 staff cardiologist and 1 cardiology associate. Only the results of the staff cardiologist's examinations were used in the analysis, and no comparison with the associate's findings is presented in the article. Murmurs were classified by Levine grade according to predefined characteristics, and the murmurs were classified as functional or organic according to the examiner's clinical expertise. All patients underwent transthoracic 2-dimensional and Doppler echocardiography, and valvular stenosis and regurgitation were classified according to standard criteria.

Main Outcome Measures

Descriptive statistics, sensitivity, specificity.

Main Results

Twenty-eight of the patients referred for systolic murmurs had aortic regurgitation (AR). The degree of regurgitation was mild in 22 cases (79%) and associated with another echocardiographic lesion in 15 (54%) cases. The examiners made a clinical diagnosis of aortic insufficiency in 9 patients (Table 32-6).

Table 32-6 Likelihood Ratio for Aortic Regurgitation According to the Presence of a Diastolic Murmur in Patients Referred for Systolic Murmurs

<table>
<thead>
<tr>
<th>AR by Echocardiography</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+ (95% CI)</th>
<th>LR− (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR by clinical examination</td>
<td>0.21</td>
<td>0.96</td>
<td>5.1 (1.4-19)</td>
<td>0.82 (0.67-1.0)</td>
</tr>
</tbody>
</table>

Abbreviations: AR, aortic regurgitation; CI, confidence interval; LR+, positive likelihood ratio; LR−, negative likelihood ratio.
Conclusion

Level of Evidence

Level 3.

Strengths Prospective, consecutive patients.

Limitations

Small, referral population referred for evaluation of a murmur. The echocardiographers were not blinded to the clinical findings.

The clinical examination was useful for ruling in AR but not for ruling out regurgitation. The negative likelihood ratio obtained in this study is higher than in a number of previous studies performed in a variety of settings. The difficult population in this study might explain this finding: patients were referred for evaluation of systolic murmurs, and those with AR had predominantly mild disease and approximately half had additional lesions. The ability of the cardiologist to identify those with AR (likelihood ratio, 5.1) despite the referral indication of a systolic murmur is impressive. These data support the clinical suggestion that finding a diastolic murmur requires an echocardiogram to assess AR.

Evidence Summary and Review 2

Title Pathophysiologic Determinants of Third Heart Sounds: A Prospective Clinical and Doppler Echocardiographic Study.

Authors Tribouilloy CM, Enriquez-Sarano M, Mohty D, et al.


Question Does an audible S₃ predict severe hemodynamic alterations in cardiology patients?

Design Patients were identified at referral for echocardiography. Clinical data were obtained by noting the results of a clinical examination performed by the referring physician (a cardiologist or internist), who was unaware of the study. Transthoracic echocardiography was performed on all patients.

Setting Cardiology referral center in the United States.

Patients One hundred twenty-one patients with aortic regurgitation (AR) (mean age, 57 years; SD, 18 years; 66% men; 15% New York Heart Association classes III-IV) were included in the study. These patients were prospectively enrolled from among patients referred by their personal physician for echocardiography for any indication and found to have isolated mitral regurgitation or AR. Exclusion criteria included previous valve surgery, associated valvular stenosis, acute myocardial infarction, congenital or pericardial disease, or a change in cardiovascular status since clinical examination was performed.

Description of Tests and Diagnostic Standard

Documentation of the presence or absence of an S₃ was abstracted from each patient's chart as documented by the referring physician. Two-dimensional/Doppler echocardiography was performed on all patients by an echocardiographer. Severe regurgitation was defined as a regurgitant fraction of 40% or greater.

Main Outcome Measures
Main Results

Fourteen patients with AR had an $S_3$. Of the 121 patients with AR, 61 were classified as severe according to the echocardiogram (Table 32-7).

Table 32-7  Likelihood Ratio for the Presence of a Third Heart Sound to Predict Severe Aortic Regurgitation (AR) as Opposed to Less Severe AR

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_3$ to identify severe AR</td>
<td>0.20</td>
<td>0.97</td>
<td>5.9 (1.4-25)</td>
<td>0.83 (0.73-0.95)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR+, positive likelihood ratio; LR–, negative likelihood ratio.

Conclusion

Level of Evidence

Level 3.

Strengths Large sample size.

Limitations

The data were collected retrospectively, and it is not clear whether the echocardiographer was blinded to the clinical examination. The patients with an $S_3$ may have been selectively referred for echocardiograms, but this would have led to an inflated sensitivity and underestimated specificity, which is the opposite of what the investigators found.

The presence of an $S_3$ is highly specific for severe regurgitation in patients with isolated valvular regurgitation, and its presence reflects hemodynamically significant regurgitation reflected by left ventricular dysfunction. The detection of an $S_3$ should prompt further evaluation. However, the absence of an $S_3$ is not useful in ruling out significant AR.

Compiled Clinical Scenarios

Clinical Scenario

A 58-year-old man presents for a routine physical examination, not having visited a physician in many years. He denies any cardiovascular symptoms. On auscultation, you are surprised to hear a loud (grade 3) early diastolic murmur. There is an audible $S_3$ and a collapsing radial pulse (Corrigan sign). After explaining to the patient that you heard a murmur, he asks, “How bad do you think it is?”

Clinical Scenario—Resolution

Your patient has a typical diastolic murmur of AR. This finding alone warrants echocardiography because it is highly suggestive of an underlying abnormality. If the patient has AR, the grade 3 intensity of the murmur and the third heart sound increase the likelihood of severe AR. The collapsing radial pulse (Corrigan pulse) is of uncertain usefulness. Putting together all of your findings, you advise your patient that you are concerned that
he might have important valvular disease. You provide information regarding endocarditis prophylaxis and arrange for an echocardiogram.

undefined

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