Murmur, Systolic

Figure 33-1

Make the Diagnosis: Murmur, Systolic

Systolic murmurs are common, and echocardiography is normal in the majority of asymptomatic individuals with murmurs. Clinical evaluation offers the potential to identify those patients with increased likelihood of underlying structural disease and to avoid costly echocardiographic evaluation in all patients with systolic murmurs.

Prior Probability

One study of randomly selected elderly Finnish persons (aged 75-86 years) found a prevalence of moderate to severe AS of 8.8% in women and 3.6% in men. The prevalence in younger patients ought to be less. The Framingham Heart Study showed that echocardiographic evidence of MR is common and a function of both age and sex. A useful approximation for the prevalence of mild to moderate MR is 15% from age 40 to 60 years for both men and women. After age 60, women have a prevalence of about 25% compared with men, who have an increasing frequency of MR that approximates 40% by age 80 years. The prevalence of MVP is about 2.5%.

Population for Whom a Systolic Murmur Should Be Assessed

- It is sensible to listen for a systolic murmur in every patient for whom a complete cardiac database is necessary.

- Once a patient with a systolic murmur is identified, the clinical examination helps identify those more likely to have significant underlying cardiac lesions. However, a cardiac echocardiogram is required to determine whether the finding represents a significant or less significant cardiac lesion.

- The presence of a murmur can be heard with a variety of underlying lesions such as myocardial ischemia, endocarditis, and disturbances that cause a high flow rate.

Identifying Normal (Innocent) Murmurs

Cardiologists and emergency physicians are accurate at distinguishing abnormal from innocent murmurs (Tables 33-13 and 33-14).

Table 33-13 Likelihood Ratio for the Overall Examination for Detecting Valvular Disease

LR for Valvular Disease
LR+ (95% CI) | LR– (95% CI)
---|---
Cardiologists | 38 (9.5-154) | 0.31 (0.18-0.52)
Emergency department physicians | 14 (10-19) | 0.21 (0.13-0.34)
Summary | 15 (11-20) | 0.25 (0.17-0.36)

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

Table 33-14 Likelihood Ratios of Individual Findings for Identifying Murmurs That Are Significant

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic thrill (n = 8)</td>
<td>12 (0.76-205)</td>
<td>0.73 (0.58-0.93)</td>
</tr>
<tr>
<td>Holosystolic murmur (n = 26)</td>
<td>8.7 (2.3-33)</td>
<td>0.19 (0.08-0.43)</td>
</tr>
<tr>
<td>Loud murmur (n = 29)</td>
<td>6.5 (2.3-19)</td>
<td>0.08 (0.02-0.31)</td>
</tr>
<tr>
<td>Plateau-shaped murmur (n = 20)</td>
<td>4.1 (1.4-12)</td>
<td>0.48 (0.30-0.77)</td>
</tr>
<tr>
<td>Loudest at the apex (n = 30)</td>
<td>2.5 (0.58-11)</td>
<td>0.84 (0.65-1.1)</td>
</tr>
<tr>
<td>Radiation to the carotid (n = 9)</td>
<td>0.91 (0.28-3.0)</td>
<td>1.0 (0.78-1.3)</td>
</tr>
</tbody>
</table>

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

*aModerate to severe aortic stenosis or mitral regurgitation, congenital shunt, or intraventricular pressure gradient.

Because the overall performance of generalist physicians has not been described, attention to individual findings may be even more useful than the overall clinical impression when a murmur is auscultated.

Aortic Stenosis

The presence of AS requires detection of a systolic murmur, generally radiating to the right clavicle. For such patients, evaluate the $S_2$ to determine whether it is reduced in intensity, feel the carotid artery to assess whether the volume is reduced and the upstroke slower than normal, and assess whether the murmur is loudest in the second right intercostal space (Table 33-15).

Table 33-15 Likelihood Ratios of Combinations of Findings for Aortic Stenosis

<table>
<thead>
<tr>
<th>Clinical Findings$^a$</th>
<th>LR (95% CI) for Moderate or Greater Aortic Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic murmur over right clavicle + 3-4 associated findings</td>
<td>40 (6.6-239)</td>
</tr>
<tr>
<td>Systolic murmur over right clavicle + 0-2 associated findings</td>
<td>1.8 (0.93-2.9)</td>
</tr>
<tr>
<td>No systolic murmur over right clavicle</td>
<td>0.1 (0.02-0.44)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR, likelihood ratio.

*aReduced or absent second heart sound, reduced carotid volume, slow rate of increase of carotid pulse, and maximal murmur intensity in second right intercostal space.
Mitral Regurgitation and Mitral Valve Prolapse

Although cardiologists are accurate at identifying echocardiographic MR (Table 33-16), the performance of generalist physicians has not been evaluated as well. Once MR is identified, the intensity of the murmur helps to identify the severity of the regurgitation.6

Table 33-16  Likelihood Ratio for the Murmur Intensity to Identify Severe Mitral Regurgitation

<table>
<thead>
<tr>
<th>Finding</th>
<th>LR+ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murmur grades 4-5</td>
<td>14 (3.3-56)</td>
</tr>
<tr>
<td>Murmur grade 3</td>
<td>3.5 (2.1-5.7)</td>
</tr>
<tr>
<td>Murmur grade 0-2</td>
<td>0.19 (0.11-0.33)</td>
</tr>
</tbody>
</table>

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

The absence of a murmur and click rules out MVP (LR, 0.04), whereas the presence of a systolic click, with or without a murmur, slightly increases the likelihood of echocardiographic MVP (LR, 3.8).

Reference Standard Test

Echocardiography or cardiac angiography.

Original Article: Does This Patient Have an Abnormal Systolic Murmur?

Clinical Scenarios

Case 1

You are asked to see a 64-year-old man who has been admitted to the orthopedic service after a packing crate tipped over on his leg, producing an unstable fracture of his distal tibia and fibula. You see him as he is being prepared for surgery. The patient previously had a normal exercise tolerance and no cardiac symptoms. You conduct a complete cardiac examination, observing a grade 2 systolic murmur, loudest at the lower left sternal border, which does not radiate to the right carotid artery. The $S_2$ has normal intensity, and you do not hear a fourth heart sound ($S_4$). The carotid artery pulsation has a normal rate of increase and normal volume. The orthopedic surgeon is concerned about the murmur because a recent patient had a postoperative myocardial infarction (MI) and was subsequently diagnosed with aortic stenosis. The surgeon wonders whether surgery should be delayed until an echocardiogram is obtained to rule out aortic stenosis.

Case 2

Your next patient is a 34-year-old woman without cardiovascular symptoms who has normal exercise tolerance. She has a grade 2 systolic murmur that begins late in systole and is loudest at the lower left sternal border. When the patient is examined in a standing position, the murmur increases in intensity, and you detect a loud systolic click just before the onset of the murmur. The rest of the cardiovascular examination result is normal. You suspect mitral valve prolapse (MVP), but you wonder how confident you should feel about the diagnosis.

Why Is the Clinical Examination Important in Evaluating Systolic Murmurs?
Systolic murmurs can be an important clue to a structural cardiac abnormality (Table 33-1). The use of noninvasive cardiac testing, such as echocardiography, has increased dramatically. It is estimated that 2% of the general population undergoes noninvasive cardiac diagnostic evaluation. In lieu of performing routine echocardiography on patients with systolic murmurs, a careful clinical examination may eliminate the need for additional tests in selected patients.

Table 33-1 Selected Causes of Systolic Murmurs
Abnormal cardiac structure
Aortic stenosis
Hypertrophic cardiomyopathy
Mitral regurgitation
Mitral valve prolapse
Ventricular septal defect
Pulmonic stenosis
Tricuspid regurgitation
Atrial septal defect
Normal cardiac structure, increased flow
Anemia
Thyrotoxicosis
Sepsis
Renal failure with volume overload

The Anatomic and Physiologic Origins of Systolic Murmurs

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 and blood flow velocity and turbulence. In addition, the distance between the vibrations and the stethoscope, the angle at which the vibrations meet the stethoscope, and the transmission qualities of the tissue between the vibration and the stethoscope affect murmur intensity.2

In this article, we will arbitrarily define an abnormal systolic murmur as one associated with abnormal cardiac structure. We will not consider the diagnosis of systolic murmurs caused by abnormally increased blood flow across normal cardiac structures, such as in anemia or thyrotoxicosis. However, clinicians must consider the diagnosis of abnormally increased blood flow in patients with systolic murmurs.

How to Examine for Systolic Murmurs

Most clinicians agree that a complete clinical history and physical examination, including a detailed cardiac examination, is an essential step in the assessment of systolic murmurs. Clinicians will interpret a systolic murmur in an asymptomatic 24-year-old woman with iron deficiency anemia differently from a systolic murmur in a 76-year-old woman with fever, weight loss, and digital infarctions after recent dental surgery.

Although a complete cardiac examination is important, the reliability and accuracy of many components of the cardiac examination for systolic murmurs have not been adequately evaluated. For example, the only adequately evaluated individual element of the cardiac history related to murmurs is effort syncope, which refers to a transient loss of consciousness during effort or exertion. This article focuses on features of the cardiac physical examination for systolic murmurs that have been adequately evaluated for precision and accuracy. A complete description of the cardiac physical examination of systolic murmurs is beyond the scope of this article but can be found in many textbooks.
The cardiac physical examination includes nonauscultatory and auscultatory components. Adequately evaluated nonauscultatory components include carotid artery palpation, apical-carotid delay, and brachioradial delay. To assess the carotid pulse, the clinician applies both light and firm pressure over the artery and assesses both the rate of increase and the pulse volume. Experts suggest that examiners pay special attention to the peak of pulsation. A normal rate of increase feels like a sharp tap, whereas an abnormal rate of increase feels like a nudge. An abnormal rate of increase can also feel like a weak tap, followed by a nudge or push. Surprisingly, no clear guidelines exist for interpreting carotid volume. Suggested methods include palpating the artery with both hands and all fingers, or palpating with the thumb only. We can only offer that a normal carotid volume is easily felt with light palpation, whereas a reduced carotid volume is difficult to feel even with firm palpation.

Brachioradial delay and apical-carotid delay may be important findings for detecting aortic stenosis. For brachioradial delay, the examiner palpates simultaneously the right brachial artery of the patient with the right thumb and the right radial artery of the patient with the left index and middle finger. The examiner should use only light pressure on the brachial artery to avoid dampening the pulse waveform. The examiner attempts to detect a delay between the brachial artery and the radial artery pulsations; any palpable delay is considered abnormal. For apical-carotid delay, the examiner simultaneously palpates the precordial apex pulsation and the right carotid artery. The examiner attempts to detect a delay between the apical and the carotid artery pulsation; any palpable delay is abnormal.

In contrast to the cardiac history and nonauscultatory examination, many components of routine cardiac auscultation have been adequately evaluated. During routine auscultation, the examiner attempts to detect a systolic murmur, which can be defined as a systolic noise with a duration longer than a heart sound. Examiners describe the grade, radiation (Table 33-2), onset, duration, and timing of peak murmur intensity (Figure 33-1). The Levine grading system facilitates description of intensity: a grade 1 murmur is not heard immediately on auscultation but only after the examiner has focused on systole for a few seconds, a grade 2 murmur is heard immediately on auscultation but is not loud, a grade 3 murmur is heard immediately on auscultation and is loud, and a palpable precordial vibration, called a thrill, signifies a grade 4 murmur. Other murmur characteristics, such as pitch and tonal quality, have not been adequately evaluated.

Table 33-2  Typical Location of Maximal Intensity and Radiation for Various Types of Abnormal Systolic Murmurs

<table>
<thead>
<tr>
<th>Location of Maximal Intensity</th>
<th>Radiation</th>
<th>Typical for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second right intercostal space</td>
<td>Right carotid artery</td>
<td>Aortic stenosis</td>
</tr>
<tr>
<td>Right clavicle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fifth or sixth left intercostal space mid left thorax</td>
<td>Left anterior axillary line</td>
<td>Mitral regurgitation (including mitral regurgitation caused by mitral valve prolapse)</td>
</tr>
<tr>
<td>Left axilla</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower left sternal border</td>
<td>Lower right sternal border</td>
<td>Tricuspid regurgitation</td>
</tr>
<tr>
<td>Epigastrium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fifth intercostal space, mid left thorax</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fifth left intercostal space mid left thorax</td>
<td>Lower left sternal border</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
</tbody>
</table>

Figure 33-1
Select Features of Systolic Murmurs
In the holosystolic murmur, the murmur begins just after the first heart sound ($S_1$) and continues throughout the systole. In the late systolic murmur, the murmur begins at the middle of the systole or later and ends at the second heart sound ($S_2$). In an early peaking murmur, peak intensity is before the middle of the systole. In a mid- or late-peaking murmur, peak intensity is at the middle of the systole or later.

**Murmur onset and duration**

- Holosystolic murmur
- Late systolic murmur

**Timing of peak murmur intensity**

- Early peaking murmur
- Mid or late peaking murmur

Other evaluated relevant features on routine auscultation include the intensity of the $S_2$, the $S_4$, and systolic clicks. The intensity of $S_2$ can be graded as normal, decreased, or absent. A normal $S_2$ should be easily heard in the second right and left intercostal spaces next to the sternum and should be louder than the first heart sound ($S_1$) in these areas. Abnormal splitting of the $S_2$ in relation to cardiac murmurs has not been adequately evaluated.

An $S_4$ is a low-pitched sound occurring just before systole, sometimes described as a presystolic sound. The $S_4$ from the left ventricle is best heard with the bell of the stethoscope lightly applied to the patient in the left lateral decubitus position.

Systolic clicks are high-pitched sounds with a duration similar to that of heart sounds. Systolic clicks (previously termed nonejection clicks) are associated with MVP. They generally occur later than 40 to 60 ms after the $S_1$, and patient position greatly affects their timing. When a patient stands, a systolic click moves closer to the $S_1$. Ejection sounds (previously termed *ejection clicks*) come from aortic or pulmonary valves opening in early systole, approximately 40 to 60 ms after the $S_1$. The $S_1$ and an ejection sound together have roughly the cadence of saying “pa-da” or “pa-ta” quickly. Patient position causes no appreciable change in the timing of ejection sounds.
After routine auscultation, the clinician may wish to further assess a systolic murmur using special maneuvers. If the maneuver is intended to increase the intensity of the murmur, then the clinician should listen at the edge of the murmur's radiation, where the murmur is barely audible. This will make it easier to detect an increase in murmur intensity. Similarly, if the maneuver is intended to decrease the intensity of the murmur, then the clinician should listen at the point of maximal intensity.

Maneuvers that primarily increase the venous return include quiet inspiration and sustained abdominal pressure. These maneuvers are intended to increase the intensity of right-sided heart murmurs, such as tricuspid regurgitation (TR) or pulmonic stenosis. For the quiet inspiration maneuver, the examiner determines the effect of quiet inspiration on the intensity of the murmur. The examiner should not ask the patient to breathe deeply, because the murmur will be obscured by the breath sounds. For the sustained abdominal pressure maneuver, the examiner exerts firm, sustained pressure inward and cephalad below the right costal margin. The intensity of the murmur is observed during several cardiac cycles.

Transient arterial occlusion primarily increases systemic arterial resistance. This maneuver increases the intensity of left-sided regurgitant murmurs, such as mitral regurgitation (MR) or ventricular septal defect. The examiner inflates simultaneously 2 sphygmomanometers placed around each of the patient's upper arms to approximately 20 to 40 mm above the previously recorded systolic blood pressure of the patient. Twenty seconds after cuff inflation, any changes in murmur intensity are observed.

Maneuvers that increase both venous return and systemic arterial resistance include standing to squatting and passive leg elevation. These maneuvers are intended to decrease the intensity of the murmur of hypertrophic cardiomyopathy and MVP. For the standing to squatting maneuver, the clinician sits to the side of the patient and instructs him or her to rapidly squat from the standing position. Changes in murmur intensity are noted immediately after squatting. For the passive leg elevation maneuver, an assistant passively elevates both of the patient's legs to approximately 45 degrees while the patient is supine. Changes in murmur intensity are observed 15 to 20 seconds after leg elevation.

The Valsalva maneuver decreases venous return and increases systemic arterial resistance. The Valsalva maneuver decreases the intensity of aortic stenosis murmurs. The patient strains against a closed glottis for 20 seconds, and changes in murmur intensity are observed just before the end of the 20-second period. Patients may inadvertently do a Valsalva during other maneuvers, such as sustained abdominal pressure or standing to squatting, so clinicians should ensure that patients breathe normally during these latter maneuvers.

**Precision of the Examination Related to Systolic Murmurs**

*Precision* refers to agreement among clinicians regarding a particular clinical finding. The precision of the clinical examination for systolic murmurs has been evaluated in usual clinical circumstances by auscultating patients, or in controlled nonclinical circumstances by listening to prerecorded audiotapes. Studies using audiotapes will yield higher estimates of precision, as will studies consisting of only normal patients or very abnormal patients. Most of the available precision studies include patients with various causes of abnormal systolic murmurs, although one study included only patients with mild or moderate aortic stenosis. The experience of observers likely affects precision; all but one study used cardiologists as the examiners.

The only evaluated historical variable for diagnosing murmurs is effort syncope, which had a κ of 1.0 (simple agreement, 100) in one small study (n = 22). This study excluded patients with other types of syncope that could be confused with effort syncope, so it was relatively easy for the cardiologists to agree on the presence or absence of effort syncope.

One study found that the agreement between cardiology trainees on the carotid upstroke was poor, but data to
calculate simple agreement or κ values were not provided. The precision of physical findings is summarized in Table 33-3.

Table 33-3 Precision of the Clinical Examination of Systolic Murmurs

<table>
<thead>
<tr>
<th>Finding</th>
<th>Examiner</th>
<th>No.</th>
<th>κa</th>
<th>Simple Agreement, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No murmur vs grades 1-4</td>
<td>Cardiologists (tapes)18</td>
<td>100</td>
<td>0.48</td>
<td>70</td>
</tr>
<tr>
<td>Cardiologists14</td>
<td>100</td>
<td>0.30</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Cardiologists15</td>
<td>80</td>
<td>...</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Cardiologists16</td>
<td>32</td>
<td>...</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Noncardiologists16</td>
<td>32</td>
<td>...</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>No murmur/grade 1 vs grades 2-4</td>
<td>Cardiologists (tapes)18</td>
<td>100</td>
<td>0.74</td>
<td>87</td>
</tr>
<tr>
<td>Cardiologists14</td>
<td>100</td>
<td>0.29</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>Acoustic shape (late peaking vs not late peaking)</td>
<td>Cardiologists17</td>
<td>22</td>
<td>0.74</td>
<td>95</td>
</tr>
<tr>
<td>Midsystolic click</td>
<td>Cardiologists15</td>
<td>80</td>
<td>...</td>
<td>85</td>
</tr>
</tbody>
</table>

aEllipses indicate data not available.

The Bottom Line for Precision

- The precision of examining for any systolic murmur is moderate using audiotapes (κ, 0.48) but only fair in the clinical setting (κ, 0.30). The precision of examining for a loud (grade 2 or louder) systolic murmur is good using audiotapes (κ, 0.74) but only fair in the clinical setting (κ, 0.29).

- The precision of examining for a late-peaking systolic murmur is excellent (κ, 0.74).

- The precision of examining for a systolic click is good (simple agreement, 85%).

Accuracy of the Examination Related to Systolic Murmurs

To develop a structured search strategy, we used pertinent articles already in our files. Our strategy was deliberately broad to minimize the possibility of overlooking important articles. We then searched MEDLINE (English language) from 1966 through January 1996, using our structured search strategy (available on request). We manually reviewed potentially relevant articles that we identified; we also reviewed the reference lists of these articles. We contacted authors of relevant studies for additional information.

Table 1-7 for a summary of Evidence Grades and levels).20 Grade A studies involve the independent, blind comparison of sign or symptom with a gold standard of diagnosis among a large number of consecutive patients suspected of having the target condition. Grade B studies involve the independent, blind comparison of sign or symptom with a gold standard of diagnosis among a small number of consecutive patients suspected of having the target condition. Grade C studies involve the independent, blind comparison of sign or symptom with a gold standard of diagnosis among nonconsecutive patients suspected of having the target condition; nonindependent comparison of sign or symptom with a gold standard of diagnosis among a sample of patients who obviously had the target condition plus, perhaps, normal individuals; or nonindependent comparison of a sign or symptom with a standard of uncertain validity.

Many of the studies were conducted in cardiology clinics, so the prevalence of abnormalities in these studies will be higher than in usual practice. For example, a study of patients undergoing cardiac catheterization for
suspected aortic stenosis found a prevalence of aortic stenosis of 73%, so a positive clinical examination result virtually ruled in aortic stenosis. In usual practice, the prevalence of aortic stenosis would be much lower, so a positive clinical examination result would not rule in aortic stenosis, but rather indicate the need for further testing with echocardiography.

Is This an Abnormal Murmur?

Clinicians are primarily concerned whether a systolic murmur indicates a cardiac abnormality. In this context, the goal of the clinical examination is not an exact diagnosis, but rather identification of patients needing further testing to confirm or quantify an abnormality.

Several studies evaluated the accuracy of the entire clinical examination, including the medical history, physical examination, electrocardiogram, and chest radiograph; none has evaluated the history and physical examination alone. In each study, cardiologists used the clinical examination to classify a systolic murmur as normal, possibly abnormal, or abnormal. Patients then underwent an echocardiogram or cardiac catheterization as the reference standard test. The most common abnormalities detected were valvular stenosis or regurgitation, atrial or ventricular septal defects, MVP, and cardiac hypertrophy. The study results, which are summarized in Table 33-4, indicate that cardiologists are efficient at identifying abnormal and normal murmurs.

Table 33-4  Accuracy of Clinical Examination for Detecting Abnormal Systolic Murmur

<table>
<thead>
<tr>
<th>Overall Clinical Assessment</th>
<th>LR (95% CI)</th>
<th>Quality Grade^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal Murmur</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 121^b</td>
<td>∞ (14-∞)</td>
<td>A</td>
</tr>
<tr>
<td>Study 223^c</td>
<td>∞ (2.8-∞)</td>
<td>C</td>
</tr>
<tr>
<td>Study 322^d</td>
<td>3.8 (2.8-5.4)</td>
<td>C</td>
</tr>
<tr>
<td>Possibly Abnormal Murmur</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 121^b</td>
<td>2.3 (0.7-5.9)</td>
<td>A</td>
</tr>
<tr>
<td>Study 224^e</td>
<td>1.3 (1.2-1.4)</td>
<td>C</td>
</tr>
<tr>
<td>Normal Murmur</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 121^b</td>
<td>0 (0-0.4)</td>
<td>A</td>
</tr>
<tr>
<td>Study 222^c</td>
<td>0.01 (0-0.02)</td>
<td>C</td>
</tr>
<tr>
<td>Study 324^e</td>
<td>0.05 (0.01-0.20)</td>
<td>C</td>
</tr>
<tr>
<td>Study 423^c</td>
<td>0.3 (0.1-0.6)</td>
<td>C</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR, likelihood ratio.

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

^bOf 103 patients, 93 had normal murmurs. The study was conducted among pregnant patients. Reference standard: echocardiogram.

^cOf 30 patients, 16 had normal murmurs. Reference standard: echocardiogram.

^dOf 1059 patients, 100 had normal murmurs. Reference standard: cardiac catheterization.

^eOf 532 patients, 378 had normal murmurs. Reference standard: echocardiogram.
The Bottom Line for Abnormal Murmur

- A clinical assessment of “normal murmur” by a cardiologist significantly reduces the likelihood of a cardiac abnormality.

- A clinical assessment of “abnormal murmur” by a cardiologist significantly increases the likelihood of a cardiac abnormality.

Aortic Stenosis

Effort _syncope_ is the only adequately studied individual historical variable. Presence of effort _syncope_ in patients with a systolic murmur effectively rules in aortic stenosis (positive _likelihood ratio_ [LR+], ∞; 95% _confidence interval_ [CI], 1.3–∞) but absence of effort _syncope_ is not helpful (negative _likelihood ratio_ [LR–], 0.76; 95% CI, 0.67-0.86) (grade C study).17

Several studies have examined the accuracy of the physical examination for detecting aortic stenosis. In these studies, echocardiography or cardiac catheterization confirmed aortic stenosis. Definitions of aortic stenosis varied, with peak instantaneous gradients ranging from as low as 25 mm Hg to as high as 50 mm Hg or aortic valve areas ranging from as low as 0.7 cm² to as high as 1.1 cm².

Many physical findings may increase or decrease the likelihood of aortic stenosis.17, 25, 26 Table 33-5 lists the findings beginning with the highest positive LRs from the largest studies with the best methodologic quality. All of the studies used cardiologist examiners.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Reference Standard (No. of Patients)</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
<th>Quality Gradea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow rate of increase of carotid pulse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 125</td>
<td>Cardiac catheterization (781)</td>
<td>130 (33-560)</td>
<td>0.62 (0.51-0.75)</td>
<td>A</td>
</tr>
<tr>
<td>Study 226</td>
<td>Cardiac catheterization (231)</td>
<td>2.8 (2.1-3.7)</td>
<td>0.18 (0.11-0.30)</td>
<td>Cb</td>
</tr>
<tr>
<td>Study 317</td>
<td>Cardiac catheterization (106)</td>
<td>6.4 (0.8-45)</td>
<td>0.73 (0.59-0.90)</td>
<td>C</td>
</tr>
</tbody>
</table>

Timing of peak murmur intensity

| Late peaking25                        | Cardiac catheterization (781)        | 101 (25-410)               | 0.31 (0.22-0.44)           | A              |
| Midpeaking17                          | Cardiac catheterization (106)        | 8.0 (2.7-23)               | 0.13 (0.07-0.24)           | C              |

Decreased intensity or absent second heart sound

| Study 125                             | Cardiac catheterization (781)        | 50 (24-100)                | 0.45 (0.34-0.58)           | A              |
| Study 226                             | Cardiac catheterization (231)        | 3.1 (2.1-4.3)              | 0.36 (0.26-0.49)           | Cb             |
| Apical carotid delay6                  | Cardiac catheterization (44)         | ∞ (2.4-∞)                  | 0.05 (0.01-0.31)           | C              |
| Brachioradial delay5                   | Echocardiogram (58)                  | 6.8 (3.2-14)               | 0.0 (0.0-0.3)              | C              |
| Fourth heart sound25                   | Cardiac catheterization (781)        | 2.5 (2.1-3.0)              | 0.26 (0.14-0.49)           | A              |
Presence of any murmur\textsuperscript{25} & Cardiac catheterization (781) & 2.4 (2.2-2.7) & 0 (0-0.13) & A \\
Reduced carotid volume & Study \textsuperscript{26} & Cardiac catheterization (231) & 2.3 (1.7-3.0) & 0.31 (0.21-0.46) & C \textsuperscript{b} \\
Study \textsuperscript{217} & Cardiac catheterization (106) & 2.2 (1.2-4.2) & 0.39 (0.22-0.69) & C \\
Radiation to right carotid & Study \textsuperscript{25} & Cardiac catheterization (781) & 1.4 (1.3-1.5) & 0.10 (0.13-0.40) & A \\
Study \textsuperscript{26} & Cardiac catheterization (231) & 1.5 (1.3-1.7) & 0.05 (0.01-0.20) & C\textsuperscript{b} \\
With Valsalva maneuver intensity is decreased\textsuperscript{27} & Cardiac catheterization (50) & 1.2 (0.8-1.6) & 0 (0-1.6) & C \\

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

\textsuperscript{a}See Table 1-7 for a summary of Evidence Grades and levels.

\textsuperscript{b}Grade A study except cardiac catheterization interpreted with knowledge of clinical findings.

Two studies are notable for their high methodologic quality and large sample sizes. The first study\textsuperscript{25} involved 781 consecutive, unreferred elderly patients who were nursing home residents. Each study participant received an examination by a single senior cardiologist, followed by an echocardiogram. Overall, 68 patients (9\%) had aortic stenosis defined as a peak instantaneous Doppler gradient of 25 mm Hg or greater. This study provides a reasonable estimate of the accuracy of the clinical examination in an elderly population. Many of the patients had no symptoms and no audible murmur, which may have elevated the estimates of specificity and the positive LR for some of the findings.

The second study\textsuperscript{26} evaluated 231 consecutive patients referred for cardiac catheterization for various reasons, including suspected aortic stenosis. Cardiology fellows or cardiologists examined patients before cardiac catheterization. Overall, 113 patients (49\%) had aortic stenosis, defined as a valve area of 0.8 cm\textsuperscript{2} or less or a peak gradient of 50 mm Hg or greater, at cardiac catheterization. This study population was highly selected, so the prevalence of aortic stenosis was much higher than would be expected in usual clinical practice.

The accuracy of special maneuvers was evaluated by 2 trained cardiologists, who examined 50 nonconsecutive participants with a variety of heart diseases, including aortic stenosis, MR, ventricular septal defect, hypertrophic cardiomyopathy, pulmonic stenosis, and TR.\textsuperscript{27} No maneuver was useful for ruling in aortic stenosis (data not shown), but certain findings from the Valsalva maneuver reduced the likelihood of aortic stenosis (Table 33-5).

A potentially useful multivariate decisional aid for diagnosing aortic stenosis was developed using split-sample validation (Table 33-6).\textsuperscript{26} The study showed an excellent positive LR for patients with point scores higher than 10. One of the variables in this model was aortic valve calcification on the lateral chest radiograph.

Table 33-6 Multivariable Decision Rule for Suspected Aortic Stenosis\textsuperscript{26}

<table>
<thead>
<tr>
<th>Point Score</th>
<th>Aortic Stenosis\textsuperscript{a} LR (95% CI)\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>(\infty (0.6-\infty))</td>
</tr>
</tbody>
</table>
Although the preceding results are encouraging, 2 small studies had less impressive results. The first study included 75 patients with severe multivalvular disease who were undergoing cardiac catheterization and found that a cardiologist's clinical diagnosis of aortic stenosis was only reasonably accurate (LR+, 3.7; 95% CI, 2.2-7.0; LR–, 0.23; 95% CI, 0.11-0.44). Many of these patients had severe multivalvular disease, which may have made an exact diagnosis more difficult. A study on 35 elderly patients with systolic murmurs who were examined by a geriatrician found that a clinical diagnosis of neither “aortic stenosis present” (LR+, 2.4; 95% CI, 0.72-6.9) nor “aortic stenosis absent” (LR, 0.7; 95% CI, 0.30-1.1) was accurate. This study suggests that assessments by cardiologists may be better than assessments by noncardiologists.

The Bottom Line for Aortic Stenosis

- The presence of any of the following clinical findings significantly increases the likelihood of aortic stenosis: effort syncope, slow rate of increase of the carotid pulse, timing of peak murmur intensity in late or midsystole, decreased intensity or absent S₂, apical-carotid delay, or brachioradial delay.

- The absence of any of the following clinical findings significantly reduces the likelihood of aortic stenosis: any systolic murmur or murmur radiation to the right carotid artery.

- Combinations of the following clinical variables can be useful to rule in or rule out aortic stenosis: decreased carotid volume, delayed carotid upstroke, decreased or absent S₂, murmur loudest at second right intercostal space, and valve calcification on chest radiograph.

Mitral Regurgitation

We report the accuracy of the clinical examination for detecting moderate to severe regurgitation confirmed through echocardiography or cardiac catheterization (Table 33-7). Detection of moderate to severe MR, even in asymptomatic patients, may influence recommendations for echocardiographic monitoring or medical treatment.

Table 33-7  Accuracy of the Clinical Examination for Detecting Mitral Regurgitation
<table>
<thead>
<tr>
<th>Finding</th>
<th>Reference Standard (No. of Patients)</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
<th>Quality Gradea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murmur in mitral area</td>
<td>Study 133 Echocardiogram: moderate to severe MR (394)</td>
<td>3.9 (3.0-5.1)</td>
<td>0.34 (0.23-0.47)</td>
<td>C</td>
</tr>
<tr>
<td>Study 232 Cardiac catheterization: moderate to severe MR (35)</td>
<td></td>
<td>3.6 (1.9-7.7)</td>
<td>0.12 (0.02-0.50)</td>
<td>C</td>
</tr>
<tr>
<td>Late or holosystolic murmur15</td>
<td>Echocardiogram: moderate to severe MR (80)</td>
<td>1.8 (1.2-2.5)</td>
<td>0 (0-0.8)</td>
<td>C</td>
</tr>
<tr>
<td>Any murmur during acute MI34</td>
<td>Cardiac catheterization: moderate to severe MR (206)</td>
<td>4.7 (1.3-11)</td>
<td>0.66 (0.25-1.0)</td>
<td>C</td>
</tr>
<tr>
<td>With transient arterial occlusion, murmur increases in intensity27</td>
<td>Cardiac catheterization: severity not statedb</td>
<td>7.5 (2.5-23)</td>
<td>0.28 (0.13-0.60)</td>
<td>C</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR+, positive likelihood ratio; LR–, negative likelihood ratio; MI, myocardial infarction; MR, mitral regurgitation.

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

bOutcome of interest was left-sided regurgitant lesions, including MR or ventricular septal defect.

If a cardiologist hears a murmur in the mitral area (mid left thorax, fifth intercostal space), then the likelihood of MR is increased slightly, but absence of a murmur significantly reduces the likelihood of MR.15, 32, 33 Similarly, a late systolic or holosystolic murmur slightly increases the likelihood of MR, but absence of such a murmur significantly reduces the likelihood of MR. In the setting of acute MI, absence of a murmur is less useful for ruling out acute MR (LR–, 0.66; 95% CI, 0.25-1.0).34 Transient arterial occlusion was accurate for ruling in and ruling out left-sided regurgitant murmurs, such as MR and ventricular septal defect.27

Internal medicine house staff are less accurate than cardiologists for detecting the murmur of MR, with positive LRs ranging from 1.1 (for interns) to 4.6 (for medical students) and negative LRs ranging from 0.7 (for junior residents) to 1.0 (for interns and senior residents)35 (grade A study).

The Bottom Line for Mitral Regurgitation

- For cardiologists, absence of a mitral area murmur or a late systolic/holosystolic murmur significantly reduces the likelihood of MR, except in the setting of acute MI.

- Cardiologists can accurately distinguish left-sided regurgitant murmurs, such as MR and ventricular septal defect, using transient arterial occlusion.

- Noncardiologists’ assessments for MR are considerably less accurate.

Tricuspid Regurgitation

Cardiologists are reasonably accurate for diagnosing the murmur of moderately severe to severe TR in patients (n = 21, with TR; n = 295, without TR) referred for echocardiography (LR+, 10.1; 95% CI, 5.8-18; LR–, 0.41;
95% CI, 0.24-0.70) (grade C). Special maneuvers may also be helpful for diagnosing TR and other right-sided lesions such as pulmonic stenosis. One study (n = 10, with TR or pulmonic stenosis; n = 40, without TR or pulmonic stenosis) using cardiologist examiners found that an increase in murmur intensity with inspiration significantly increased the likelihood of a right-sided valvular lesion, whereas the absence of increased intensity made these conditions less likely (LR+, 8.0; 95% CI, 3.5-18; LR–, 0.0; 95% CI, 0-0.43) (grade C).

In another study, patients with severe MR (n = 15) or TR (n = 15) were examined by experienced cardiologists before cardiac catheterization. To distinguish TR from MR, increased murmur intensity on inspiration had a positive LR of ∞ (95% CI, 3.1-∞) and a negative LR of 0.20 (95% CI, 0.07-0.45). For the finding of increased murmur intensity with sustained abdominal pressure, the positive LR was ∞ (95% CI, 2.5-∞) and the negative LR was 0.33 (95% CI, 0.15-0.58) (grade C).

The Bottom Line for Tricuspid Regurgitation

- Cardiologists can accurately detect the murmur of TR.
- Cardiologists can accurately rule in and rule out TR with the quiet inspiration and sustained abdominal pressure maneuvers.

Hypertrophic Cardiomyopathy

There are limited data on the accuracy of clinical examination for hypertrophic cardiomyopathy (also termed idiopathic hypertrophic subaortic stenosis). Many studies evaluate phonocardiography or intracardiac tracings rather than auscultation, whereas others include fewer than 15 patients. One study evaluated carotid sinus pressure, which is not routinely recommended for the clinical examination.

Special maneuvers may help distinguish the murmur of hypertrophic cardiomyopathy. Using cardiologist examiners, if a murmur decreased in intensity with passive leg elevation, then hypertrophic cardiomyopathy was significantly more likely (LR+, 8.0; 95% CI, 3.0-21), whereas if the murmur did not decrease in intensity, the likelihood was significantly reduced (LR–, 0.22; 95% CI, 0.06-0.77). If murmur intensity was decreased or unchanged with standing to squatting, then hypertrophic cardiomyopathy was significantly more likely (LR+, 4.5; 95% CI, 2.3-8.6), whereas if the murmur increased in intensity, the likelihood of hypertrophic cardiomyopathy was significantly reduced (LR–, 0.13; 95% CI, 0.02-0.81) (grade C).

The Bottom Line for Hypertrophic Cardiomyopathy

Cardiologists can rule in or rule out hypertrophic cardiomyopathy by evaluating for decreased murmur intensity with passive leg elevation or increased murmur intensity when the patient goes from a squatting to standing position.

Mitral Valve Prolapse

The accuracy of the clinical examination for diagnosing MVP cannot be defined, because clinical findings alone are sufficient for the diagnosis of MVP. A patient with a systolic click and a systolic murmur meets the diagnostic criteria for MVP even if the patient has a normal echocardiogram result.

However, we can examine the relationship between clinical findings and echocardiographic findings (Table). With cardiologist examiners, a systolic click accompanied by a systolic murmur helped to rule in echocardiographic MVP. The accuracy of an isolated systolic click is variable, possibly because of unreliability of the clinical examination and differences between studies regarding the definition of
echocardiographic MVP. An isolated systolic murmur has little effect on the likelihood of echocardiographic MVP, whereas absence of both a systolic click and a murmur appears to reduce the likelihood of echocardiographic MVP. Noncardiologists are less accurate than cardiologists for all of these findings.

Table 33-8  Accuracy of the Clinical Examination for Detecting Echocardiographic Mitral Valve Prolapse

<table>
<thead>
<tr>
<th>Finding</th>
<th>Clinician (No. of Patients)</th>
<th>LR (95% CI)</th>
<th>Quality Grade (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic click and murmur</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1 49 Cardiologists (401)</td>
<td>19 (4.6-80)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Study 2 50 Noncardiologists (104)</td>
<td>2.4 (1.0-5.7)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Systolic click</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1 49 Cardiologists (401)</td>
<td>12 (5.4-25)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Study 2 50 Noncardiologists (104)</td>
<td>1.3 (0.7-2.2)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Nonejection click, with or without a murmur</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1 51 Cardiologists (155)</td>
<td>3.8 (2.3-6.8)</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Study 2 52 Cardiologists (140)</td>
<td>1.7 (1.3-2.1)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Murmur, with or without a systolic click</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1 52 Cardiologists (140)</td>
<td>1.9 (1.3-3.0)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Study 2 53 Noncardiologists (259)</td>
<td>1.2 (0.9-1.5)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Murmur only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1 50 Cardiologists (401)</td>
<td>2.4 (1.0-5.7)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Study 2 51 Noncardiologists (104)</td>
<td>0.7 (0.3-1.3)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>No murmur, no systolic click</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1 51 Cardiologists (155)</td>
<td>0.04 (0.02-0.11)</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Study 2 52 Cardiologists (140)</td>
<td>0.26 (0.12-0.54)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Study 3 49 Cardiologists (401)</td>
<td>0.21 (0.15-0.29)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Study 4 50 Noncardiologists (104)</td>
<td>0.53 (0.23-1.20)</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR, likelihood ratio.

\(^a\)See Table 1-7 for a summary of Evidence Grades and levels.

Mitral valve leaflet redundancy or thickening is the echocardiographic variable most strongly associated with adverse clinical outcomes.\(^{54, 55}\) In one study, neither a systolic click (LR+, 2.8; 95% CI, 1.8-4.6; LR–, 0.76; 95% CI, 0.69-0.84) nor a systolic murmur (LR+, 1.3; 95% CI, 1.1-1.5; LR–, 0.57; 95% CI, 0.43-0.76) affected the likelihood of echocardiographic mitral valve leaflet thickening or redundancy (grade C study).\(^{56}\)

Several longitudinal studies of patients with echocardiographic MVP have related baseline clinical findings to the development of adverse clinical events, including cardiac death, progressive MR requiring surgery, endocarditis, and systemic embolism.\(^{57, 58}\) A holosystolic murmur without a systolic click significantly increased the likelihood of an adverse event, whereas absence of both a systolic click and murmur was associated with no adverse events. Other clinical findings had little effect on the likelihood of adverse events (Table 33-9).

Table 33-9  Accuracy of the Clinical Examination for Predicting Adverse Clinical Outcomes Related to Mitral Valve Prolapse\(^a\)
### Finding

<table>
<thead>
<tr>
<th>Finding</th>
<th>Clinician (No. of Patients)</th>
<th>LR (95% CI)</th>
<th>Quality Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holosystolic murmur</td>
<td>Cardiologists (316)</td>
<td>18 (6.6-51)</td>
<td>C</td>
</tr>
<tr>
<td>Study 1</td>
<td>Cardiologists (321)</td>
<td>5.1 (2.2-9.9)</td>
<td>C</td>
</tr>
<tr>
<td>Late systolic murmur or click and murmur</td>
<td>Cardiologists (316)</td>
<td>1.2 (0.7-1.7)</td>
<td>C</td>
</tr>
<tr>
<td>Study 2</td>
<td>Cardiologists (321)</td>
<td>0.8 (0.3-1.5)</td>
<td>C</td>
</tr>
<tr>
<td>Click and holosytolic murmur</td>
<td>Cardiologists (321)</td>
<td>0.8 (0.2-2.4)</td>
<td>C</td>
</tr>
<tr>
<td>Any click or isolated click</td>
<td>Cardiologists (316)</td>
<td>0.4 (0.2-0.8)</td>
<td>C</td>
</tr>
<tr>
<td>No click/no murmur</td>
<td>Cardiologists (321)</td>
<td>0.26 (0.05-1.1)</td>
<td>C</td>
</tr>
<tr>
<td>Study 1</td>
<td>Cardiologists (237)</td>
<td>0 (0-4.1)</td>
<td>C</td>
</tr>
<tr>
<td>Study 2</td>
<td>Cardiologists (316)</td>
<td>0 (0-1.4)</td>
<td>C</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR, likelihood ratio.

---

**The Bottom Line for Mitral Valve Prolapse**

- A systolic click, with or without systolic murmur, is sufficient for the diagnosis of MVP.
- If a cardiologist hears a systolic click, with or without a murmur, then the likelihood of echocardiographic MVP is significantly increased. The absence of both a systolic click and murmur significantly reduces the likelihood of echocardiographic MVP.
- In patients with echocardiographic MVP, a holosystolic murmur without a systolic click significantly increases the likelihood of long-term complications, whereas absence of both a systolic click and murmur significantly reduces the likelihood of long-term complications.

---

**When to Examine for Systolic Murmurs**

We are unaware of data by which one might give an evidence-based recommendation regarding the examination for systolic murmurs. Auscultation for systolic murmurs should probably be carried out in any patient for whom a complete cardiovascular database is necessary.

---

**Are Systolic Murmurs Ever Normal?**

In unreferred young adults, the prevalence of systolic murmurs ranges from 5% to 52%\(^8, 59, 60, 61\); echocardiography result is normal in 86% to 100%\(^62, 63, 64\). Echocardiography result is normal in 90% to 94% of pregnant women with systolic murmurs who are referred for testing\(^21, 24, 65\). In elderly medical outpatients or residents of long-term care facilities, the prevalence of systolic murmurs ranges from 29% to 60%\(^66, 67, 68\).
Echocardiography is normal in 44% to 100%. This wide range of normal in the elderly can be partially explained by various study definitions of normal echocardiograms. Commonly detected abnormalities in the elderly were left ventricular systolic dysfunction, aortic stenosis, and MR. Other studies include aortic valve sclerosis as an abnormality, although the clinical importance of aortic valve sclerosis is uncertain.

A venous hum and a mammary souffle are both normal conditions that present either as systolic murmurs or, more commonly, as continuous murmurs.

**How to Improve Skills in Examining This Area**

The characteristics of murmurs can be learned using cardiovascular auscultatory tapes or cardiac patient simulators, although the effectiveness of these aids is uncertain. Most audiotapes are accompanied by phonocardiographic and expert cardiologist analyses, so these tapes can help clinicians to calibrate their ears to those of experts.

Most commercially available stethoscopes have similar acoustic properties, although some have poor performance at low frequencies. Good stethoscope maintenance is essential because dirt or cracked tubing will significantly reduce accuracy. Large earpieces are better because small earpieces can be occluded by the sharp bony angle at the external auditory meatus.

At the bedside, eliminate background noise whenever possible. If background noise is unavoidable, try to repeat your examination in a quieter setting.

Finally, relate your clinical findings to the results of assessments by a colleague, a cardiologist, or an echocardiogram whenever possible. Resolving disagreements between your assessments and those of others is an excellent way of upgrading your clinical skills.

**Recommendations for Further Research**

Most studies used cardiologists or senior cardiology fellows to conduct the clinical examinations. There are few data on the precision and accuracy of the clinical examination conducted by noncardiologists. Some studies include inappropriately narrow spectrums of patients, such as only patients with moderate and severe aortic stenosis. Further studies should focus on a broad spectrum of patients from primary or secondary care settings, particularly patients older than 40 years when the prevalence of abnormal murmurs is significantly increased.

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**Clinical Scenarios—Resolutions**

Case 1
Your first patient, who is awaiting urgent surgery for an open fracture, had a systolic murmur that did not radiate to the right carotid artery. The likelihood of aortic stenosis is significantly reduced by this finding. In addition, the carotid artery pulsation had normal volume, the $S_2$ intensity was normal, and there was no $S_4$. These findings also help to reduce the likelihood of aortic stenosis. You are confident in your assessment because it was conducted in a quiet room with a comfortable and cooperative patient. You can advise the surgeon that aortic stenosis is unlikely.

**Case 2**

Your second patient has a systolic click and a systolic murmur, strongly suggesting MVP. If you are an experienced auscultator, then these findings significantly increase the likelihood that the echocardiogram will show evidence of MVP. However, even if the echocardiogram result is normal, you already have enough evidence to diagnose MVP. You may wish to obtain an echocardiogram at a later date to determine the severity of the valvular abnormality.

**References**

   [CrossRef] [PubMed: 10292970]
   [CrossRef] [PubMed: 1971044]
   [CrossRef] [PubMed: 6216867] [Archives of Internal Medicine Full Text]
   [CrossRef] [JAMA and JAMA Network Journals Full Text]
   [CrossRef]
CrossRef [PubMed: 6497192]

CrossRef [PubMed: 2874761]

CrossRef


CrossRef [PubMed: 3958380]


CrossRef [PubMed: 4083081]


CrossRef [PubMed: 7053601]

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[JAMA and JAMA Network Journals Full Text]

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Aronow WS, Kronzon I. Correlation of prevalence and severity of valvular aortic stenosis determined by continuous-wave Doppler echocardiography with physical signs of aortic stenosis in patients aged 62 to 100 years with aortic systolic ejection murmurs. *Am J Cardiol.* 1987;60(4):399–401. [CrossRef] [PubMed: 3497570]


Update

Clinical Scenario

A 62-year-old man scheduled for elective total knee replacement has been referred to you for preoperative assessment of a systolic murmur. The orthopedic surgeon detected a systolic murmur and wants to rule out aortic stenosis (AS) before surgery. The patient has no cardiovascular symptoms. On auscultation, you hear normal first and second heart sounds ($S_1$ and $S_2$). There is a grade 3 early systolic murmur, loudest at the lower left sternal border, which does not radiate to either the right clavicle or carotids. You detect a normal volume and normal rate of increase of the carotid pulse. The rest of the clinical examination results, including
those for the electrocardiogram (ECG) and chest radiograph, are normal.

Original Review

Etchells EE, Bell C, Robb K. Does this patient have an abnormal systolic murmur? JAMA. 1997;277(7):564–571.

Updated Literature Search

Our literature search combined the parent search strategy for The Rational Clinical Examination with the following terms: “systolic and murmur,” “heart valve diseases,” “aortic valve stenosis,” “pulmonary valve stenosis,” “mitral valve prolapse,” “mitral valve insufficiency,” “tricuspid valve insufficiency,” “hypertrophic cardiomyopathy,” and “heart murmurs.” Results were limited to English-language publications in the MEDLINE database from 1996 to July 2004. The titles and abstracts of the search results were screened, case reports were excluded, and 28 potentially relevant primary studies and review articles were retrieved. We scanned the reference list of each article for additional studies. For accuracy studies, we retained those of adult subjects that included sensitivity and specificity data of physical findings and had a quality score of level 3 or greater. We excluded level 3 studies with fewer than 100 patients. Five new studies were ultimately included in this update.

New Findings

1. Cardiologists are able to distinguish normal (“innocent”) murmurs from abnormal murmurs by the physical examination alone.

2. Emergency department physicians are able to detect normal murmurs by clinical evaluation (including physical examination; medical history; ECG, chest radiograph, and laboratory test results; and previously recorded chart data).

3. The presence of a holosystolic murmur, loud murmur, decreased carotid upstroke, or systolic thrill makes it much more likely that a systolic murmur represents an underlying cardiac abnormality rather than a functional murmur.

4. In patients for whom examiners did not know whether a murmur was present before examination, emergency department physicians and cardiologists identified valvular heart disease with good accuracy.

5. Absence of murmur radiation to the right clavicle makes moderate to severe AS much less likely.

6. The presence of any 3 of the following findings makes moderate to severe AS much more likely: maximal murmur intensity in second right intercostal space, reduced carotid pulse volume, slow rate of increase of carotid pulse, and reduced or absent second heart sounds (S₂).

7. When mitral regurgitation (MR) is identified, murmur intensity equal to or more than grade 3 makes severe regurgitation more likely.

Improvements in Data Presented in the Original Publication

The newer studies do not alter the results reported in the original publication but do provide new information on the role of individual auscultatory findings.
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 an echocardiogram or a cardiac catheterization that assesses valvular competency.

Results of the Literature Review

Precision

Since the original review, 2 published studies involving noncardiologist examiners have evaluated the precision of various physical examination maneuvers in actual patients.2-3 In a large study of medical patients presenting to the emergency department, there was substantial agreement on the presence of systolic murmurs (κ = 0.8). The precision of examining for a loud murmur (κ = 0.59) and for an S₂ in the clinical setting is moderate (κ = 0.54), whereas the precision of other findings is only fair. In both of these studies, the various findings were not evaluated independently, so the examiners’ opinions may have been influenced by the presence or absence of related findings.

Accuracy

Distinguishing Abnormal From Normal (Innocent) Murmurs

Two new studies evaluated examiners’ ability to distinguish murmurs caused by an underlying cardiac abnormality from those generated by structurally normal hearts (innocent murmurs). One of these studies evaluated the accuracy of the entire clinical evaluation (including physical examination, medical history, echocardiogram, chest radiograph, laboratory tests, and data from old charts) by noncardiologist emergency department physicians, and one evaluated the accuracy of the cardiologist's physical examination alone.4

In a study of high methodologic quality, Reichlin et al2 evaluated the performance of emergency department physicians’ clinical assessments of patients with systolic murmurs. Although these noncardiologists are somewhat less accurate at distinguishing normal from innocent murmurs than cardiologists, a normal clinical assessment significantly reduces the likelihood of a cardiac abnormality (negative likelihood ratio [LR–], 0.29; 95% confidence interval [CI], 0.17-0.45).

The second study assessed the ability of cardiologists to distinguish innocent from pathologic murmurs by physical examination alone in patients referred for evaluation of a systolic murmur. The cardiologists’ overall assessments of significant heart disease (defined as moderate to severe valvular heart disease, congenital shunt, or an intraventricular gradient identified by echocardiography) performed with a positive likelihood ratio (LR+) of 11 (95% CI, 5.0-26) and LR– of 0.22 (95% CI, 0.10-0.41). In addition, several clinical signs were assessed to appraise their performance in categorizing significant systolic murmurs confirmed by echocardiography. The most frequently detected findings, and those that were most useful, are shown in Table 33-10.

Table 33-10  Ability of Findings to Identify Patients With Significant Cardiac Lesions vs Functional Systolic Murmur

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>LR for a Significant Systolic Murmura</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR+ (95% CI)</td>
<td>LR– (95% CI)</td>
</tr>
</tbody>
</table>
Holosystolic murmur (n = 26) 8.7 (2.3-33) 0.19 (0.08-0.43)
Loud murmur (n = 29) 6.5 (2.3-19) 0.08 (0.02-0.31)
Plateau-shaped murmur (n = 20) 4.1 (1.4-12) 0.48 (0.30-0.77)
Loudest at the apex (n = 30) 2.5 (0.58-11) 0.84 (0.65-1.1)

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

*The LR+ is the likelihood ratio when the finding is present and indicates an increased likelihood that the systolic murmur is associated with moderate to severe aortic stenosis or mitral regurgitation, congenital shunt, or intraventricular pressure gradients. The LR– is the likelihood ratio when the finding is absent and shows the likelihood that a significant lesion will be present when the finding is absent.

Patients with mild AS or regurgitation are not included in the calculation of these LRs. Patients with a loud, plateau-shaped, or holosystolic murmur are more likely to have significant lesions than functional murmurs or mild valvular heart disease. Similarly, the absence of holosystolic or loud murmur suggests that there are no significant lesions. However, an echocardiogram must be obtained when the clinician wants to determine whether the murmur represents moderate to severe AS or regurgitation, a congenital shunt, or an intraventricular pressure gradient.

Identifying Valvular Heart Disease by Physical Examination

The ability to distinguish innocent from pathologic murmurs is important in stratifying patients for referral for echocardiography. However, the ability to make this distinction does not reflect examiners’ true ability to determine the presence of valvular heart disease: by excluding patients with no audible murmur, the specificity of the physical examination for valvular disease is underestimated.

In the study by Reichlin et al., the inclusion criteria required that at least 2 of 3 screening physicians agree that a subject had a murmur: 203 patients were enrolled from 852 screened, whereas 582 were excluded because no systolic murmur was heard. There was excellent agreement among examiners about the presence of a murmur, with disagreement in only 18 patients (2%). The exclusion of those patients with no murmur is an example of verification bias. Verification bias occurs when the gold standard test is not applied to all the potentially eligible patients to confirm their disease status. In this case, patients without systolic murmurs were excluded from the analysis and had no echocardiogram to confirm the absence of structural heart disease. Typically, selective inclusion creates an overestimate of the sensitivity and an underestimate of the specificity of the clinical assessment. However, because the study provides complete information on all patients, we are able to correct for verification bias, with the assumption that patients with no murmur truly had no valvular disease. Recalculation yields an LR+ of 14 (95% CI, 10-19) and a LR– of 0.21 (95% CI, 0.13-0.34) when either no murmur was heard or the murmur was deemed normal. Because some patients without systolic murmurs can still have AS or MR, these corrected LRs represent the best possible clinical performance.

Another study using cardiologist examiners addressed the performance of a complete cardiovascular physical examination without additional information in a population of asymptomatic individuals. The patients were not selected because of an auscultated abnormality. A murmur was heard in 63 patients, with 17 murmurs classified as abnormal; transesophageal echocardiography identified valvular abnormalities in 33 patients. In this population, the cardiovascular physical examination alone performed with an LR+ of 38 (95% CI, 9.5-154) and a LR– of 0.31 (95% CI, 0.18-0.52).

Thus, these 2 studies provide information on the clinician's ability to identify valvular heart disease irrespective of the presence of a murmur, which better reflects an initial assessment in clinical practice. Although the populations of patients studied are different and the emergency department assessment includes supplementary information, the examiners’ overall performance in these studies is similar. When an abnormal
murmur is identified, the pooled LR+ for echocardiographic valvular disease is 15 (95% CI, 11-20; results homogenous with \( P = .11; \hat{I}^2 = 48\%; 95\% CI, 0\%-86\%\); when no murmur is heard or the murmur is determined to be “normal,” the pooled LR– is 0.25 (95% CI, 0.17-0.36; results homogenous with \( P = .29; \hat{I}^2 = 16\%; 95\% CI, 0\%-55\%\)).

Aortic Stenosis

One new grade 2 study \((n = 123)\), performed by noncardiologists, prospectively evaluated individual findings and combinations of findings for the detection of moderate or severe AS (defined as an aortic valve area less than 1.2 cm\(^2\) or peak transvalvular gradient of 25 mm Hg or more). A slow carotid upstroke was the most important individual finding for ruling in AS (LR+, 9.2; 95% CI, 3.4-24) (Table 33-11). The 2-step process for using combinations of findings begins with examination for the presence of a murmur over the right clavicle. If this murmur is absent, AS is considerably less likely (LR–, 0.1; 95% CI, 0.02-0.44). When a murmur radiates to the right clavicle, 4 associated findings are sought: highest intensity of murmur at second right intercostal space, reduced intensity of \(S_2\), reduced carotid volume, and slow carotid upstroke. When zero to 2 of these associated findings are present, the result is indeterminate (LR, 1.8; 95% CI, 0.93-2.9), whereas if 3 to 4 of these findings are present, the likelihood of AS is significantly increased (LR, 40; 95% CI, 6.6-239).

Table 33-11 Accuracy of the Physical Examination for Detecting Aortic Stenosis

<table>
<thead>
<tr>
<th>Finding</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow carotid upstroke</td>
<td>9.2 (3.4-24)</td>
<td>0.56 (0.32-0.8)</td>
</tr>
<tr>
<td>Murmur radiating to right carotid</td>
<td>8.1 (4-16)</td>
<td>0.29 (0.12-0.57)</td>
</tr>
<tr>
<td>Reduced or absent (S_2)</td>
<td>7.5 (3.2-17)</td>
<td>0.50 (0.27-0.76)</td>
</tr>
<tr>
<td>Murmur over right clavicle</td>
<td>3.0 (2-4.1)</td>
<td>0.10 (0.02-0.44)</td>
</tr>
<tr>
<td>Any systolic murmur</td>
<td>2.6 (1.8-3.5)</td>
<td>0 (0-0.45)</td>
</tr>
<tr>
<td>Reduced carotid volume</td>
<td>2.0 (1-3.2)</td>
<td>0.64 (0.34-0.99)</td>
</tr>
</tbody>
</table>

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

Mitral Regurgitation

One study evaluated the accuracy of isolated findings in predicting severe MR, defined as a regurgitant fraction of 40% or more detected by echocardiography (Table 33-12). The clinical findings of interest were abstracted from the patients’ personal charts, as recorded by the patients’ own physicians (cardiologists and internists), who were unaware of the study. The study evaluated the relationship between the intensity of the murmur and the severity of regurgitation, and demonstrated a significant correlation.

Table 33-12 Accuracy of the Physical Examination for Detecting Severe Mitral Regurgitation

<table>
<thead>
<tr>
<th>Finding</th>
<th>LR+ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murmur grades 4-5</td>
<td>14 (3.3-56)</td>
</tr>
<tr>
<td>Murmur grade 3</td>
<td>3.5 (2.1-5.7)</td>
</tr>
<tr>
<td>Murmur grades 0-2</td>
<td>0.19 (0.11-0.33)</td>
</tr>
</tbody>
</table>

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

Mitral Valve Prolapse

No new high-quality studies added to the information in the original review. The absence of a murmur and...
click rules out mitral valve prolapse (MVP) (LR, 0.04). The presence of a nonejection click (a high-pitched sound of short duration in mid or late systole) with or without a murmur slightly increases the likelihood of echocardiographic MVP (LR 3.8).\textsuperscript{8}

**Evidence From Guidelines**

The American College of Cardiology/American Heart Association guidelines (2003)\textsuperscript{9} recommend echocardiography to evaluate heart murmurs in patients with cardiovascular symptoms or in asymptomatic patients with clinical features that suggest a moderate or greater probability that the murmur is reflective of underlying structural heart disease. Echocardiography is not recommended in asymptomatic adults whose murmur has been identified as functional or innocent by an experienced observer.\textsuperscript{9}

**Clinical Scenario—Resolution**

Your patient's murmur did not radiate to the right clavicle. This finding makes AS much less likely (LR, 0.1). There are no other concerning features that raise the possibility of other serious structural heart disease, including the ECG and chest radiograph. If you are an experienced clinician, this reduces the likelihood of important structural heart disease (LR, 0-0.1). If you are less experienced and not certain of your overall assessment that the murmur is “functional,” concentrating on whether the murmur is holosystolic or “loud” and whether the patient has a decreased carotid upstroke or systolic thrill may yield more useful information than your clinical gestalt. Conditions that can cause increased blood flow through a structurally normal heart should be excluded, such as anemia, renal failure, and thyrotoxicosis.

**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 A Bedside Clinical Prediction Rule for Detecting Moderate or Severe Aortic Stenosis.

Authors Etchells E, Glenns V, Shadowitz S, Bell C, Siu S.


Question Can a clinical prediction rule using simple physical examination findings accurately detect aortic stenosis (AS) in a broad spectrum of patients?

Design Consecutive patients were prospectively enrolled when they were referred for echocardiography. Two examiners (a third-year medical resident and a staff general internist) performed the maneuvers on all enrolled patients. An echocardiographer, blinded to the findings, identified all patients with moderate or greater AS.

Setting General medical/cardiology wards in an urban university hospital in Toronto.
Patients One hundred twenty-three patients admitted to the general medicine and cardiology wards. The majority had some history of congestive heart failure, angina, or myocardial infarction. The median age was 68 years, 58% were men, and 56% had Canadian Cardiovascular Society class I symptoms at the study. Exclusion criteria were age younger than 50 years, cardiac care unit/intensive care unit admission, unstable angina within 48 hours, history of cardiovascular surgery or valve replacement, severe dyspnea at rest, or inability to consent.

Description of Tests and Diagnostic Standard

Two examiners, blinded to echocardiographic findings, independently performed a structured physical examination and focused medical history on all enrolled patients. Transthoracic echocardiography was performed on all patients by an echocardiographer blinded to the clinical findings, who identified moderate to severe AS, defined as aortic valve area of 1.2 cm$^2$ or smaller or peak transvalvular gradient of 25 mm Hg or higher.

Main Outcome Measures

Main Results

Seventeen patients (14%) were found to have AS, with complete physical examination data available for 15.

Conclusion

Level of Evidence

Level 2.

Strengths Prospective data collection with valid reference standard and confirmed independence of clinical examination.

Limitations

This study included only 17 patients with the condition of interest.

This study validates several physical examination maneuvers as performed by generalist physicians in a broad spectrum of older general medical inpatients (Table 33-17). These patients are typical of those admitted into hospitals or referred for cardiovascular evaluation. The use of moderate to severe AS as the finding of interest is a clinically significant endpoint. The study confirms that the absence of any murmur or the absence of a murmur over the right clavicle is the best finding for ruling out AS. A reduced carotid upstroke by palpation, a murmur radiating to the right carotid, or S$_2$ that is reduced in intensity increases the likelihood the most. In contrast to previous studies, a murmur radiating to the right carotid is useful for identifying patients with AS if detected, but AS can still exist without the presence of a murmur radiating to the carotid.

<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>Slow carotid upstroke (n = 12)</td>
<td>0.47</td>
<td>0.95</td>
<td>9.2 (3.4-24)</td>
<td>0.56 (0.32-0.8)</td>
</tr>
<tr>
<td>Murmur radiating to right carotid (n = 20)</td>
<td>0.73</td>
<td>0.91</td>
<td>8.1 (4-16)</td>
<td>0.29 (0.12-0.57)</td>
</tr>
<tr>
<td>Reduced S$_2$ (n = 15)</td>
<td>0.53</td>
<td>0.93</td>
<td>7.5 (3.2-17)</td>
<td>0.50 (0.27-0.76)</td>
</tr>
<tr>
<td>Murmur over right clavicle (n = 45)</td>
<td>0.93</td>
<td>0.69</td>
<td>3.0 (2-4.1)</td>
<td>0.10 (0.02-0.44)</td>
</tr>
<tr>
<td>Any systolic murmur (n = 52)</td>
<td>1.0</td>
<td>0.64</td>
<td>2.6 (1.8-3.5)</td>
<td>0 (0-0.45)</td>
</tr>
</tbody>
</table>
Reduced carotid volume (n = 35) 0.53 0.73 2.0 (1.0-3.2) 0.64 (0.34-0.99)

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

The examiners participating in the study underwent a brief training period (30 minutes) and performed a standardized physical examination. As a result, the performance of the examination might be lower among examiners without the training, although the brief training period could be easily replicated. In addition, because the findings are assessed as part of a standardized physical examination, it is impossible to evaluate their independence. In other words, an examiner who observes that one of the findings is present might be more influenced and likely to describe other abnormal findings.

The authors also created and prospectively evaluated combinations of findings (Table 33-18), which performed with excellent accuracy: a lack of a murmur radiating to the right clavicle effectively rules out AS of moderate or greater severity, whereas the presence of such a murmur in association with 3 or more other findings rules in the diagnosis.

Table 33-18 Combination of Findings for Predicting Aortic Stenosis

<table>
<thead>
<tr>
<th>Finding</th>
<th>LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murmur over clavicle + 3-4 associated findings(a) (n = 7)</td>
<td>40 (6.6-239)</td>
</tr>
<tr>
<td>Murmur over clavicle + 0-2 associated findings (n = 38)</td>
<td>1.8 (0.93-2.9)</td>
</tr>
<tr>
<td>No murmur over right clavicle (n = 69)</td>
<td>0.1 (0.02-0.44)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR, likelihood ratio.

\(a\)Associated findings include reduced second heart sound (\(S_2\)), reduced carotid volume, slow carotid upstroke, and murmur loudest at second right intercostal space.

The reliability assessment of individual maneuvers is useful and demonstrates that individual findings have reliabilities that vary from slight to moderate (Table 33-19).

Table 33-19 Reliability of Findings for Aortic Stenosis

<table>
<thead>
<tr>
<th>Finding</th>
<th>Generalized (\kappa) (Lower 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S_2) (normal vs decreased)</td>
<td>0.54 (0.46)</td>
</tr>
<tr>
<td>Loud murmur (&gt;II/VI) second RICS</td>
<td>0.45 (0.37)</td>
</tr>
<tr>
<td>Radiation to right clavicle</td>
<td>0.36 (0.28)</td>
</tr>
<tr>
<td>Radiation to right carotid</td>
<td>0.33 (0.25)</td>
</tr>
<tr>
<td>Delayed carotid upstroke</td>
<td>0.26 (0.18)</td>
</tr>
<tr>
<td>Reduced carotid volume</td>
<td>0.24 (0.16)</td>
</tr>
<tr>
<td>Presence of any systolic murmur</td>
<td>0.19 (0.11)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; RICS, right intercostal space.

Evidence Summary and Review 2

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 or palpation alone?

**Design** Consecutive patients were prospectively identified at referral for evaluation of a systolic murmur of unknown cause. Each subject was independently examined by 2 cardiologists from a pool of 8, blinded to supplementary data and echocardiography results. Two-dimensional (2D)/Doppler echocardiography was performed as the gold standard in all participants. It is not clear whether the ultrasonographers were blinded to the clinical examination.

**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 subjects was 55 ± 22 years, and 57% were women.

**Description of Tests and Diagnostic Standard**

Full cardiac examination with or without dynamic auscultation as deemed appropriate by 2 blinded cardiologist examiners. Murmurs were classified by Levine grade and described and characterized as functional or organic according to the examiners’ clinical expertise. All patients underwent transthoracic 2D/Doppler echocardiography; valvular stenosis and regurgitation were classified according to standard criteria.

**Main Outcome Measures**

Raw data, sensitivity, specificity.

**Main Results**

Twenty-one patients had a “functional” murmur and were considered normal. Of the 79 patients with “organic” murmurs, 29 patients had aortic stenosis (AS) of various severity and 30 patients had mitral regurgitation (MR). Although the patients were referred for evaluation of systolic murmurs, echocardiography revealed aortic regurgitation in 28. The data in Table 33-20 indicate the likelihood of the finding when the cardiologists’ overall assessment results were positive.

**Table 33-20** Likelihood Ratios for Overall Assessment of a Valvular Lesion of Any Severity

<table>
<thead>
<tr>
<th>Lesion</th>
<th>LR+ (95% CI)</th>
<th>LR– (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic stenosis (n = 33)</td>
<td>2.1 (1.1-3.9)</td>
<td>0.78 (0.61-0.95)</td>
</tr>
<tr>
<td>Mitral regurgitation (n = 33)</td>
<td>2.3 (1.5-3.6)</td>
<td>0.43 (0.23-0.71)</td>
</tr>
<tr>
<td>Aortic regurgitation (n = 9)</td>
<td>5.1 (1.5-3.9)</td>
<td>0.82 (0.63-0.95)</td>
</tr>
</tbody>
</table>

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

The cardiologists’ overall clinical assessments of significant heart disease (defined as moderate to severe valvular heart disease, congenital shunt, or an intraventricular gradient) performed with a positive likelihood ratio (LR+) of 11 (95% confidence interval [CI], 5.0-26) and negative likelihood ratio (LR–) of 0.22 (95% CI, 0.10-0.41). The characteristics of the murmur and response to a few maneuvers were assessed to identify their performance in categorizing significant systolic murmurs confirmed by echocardiography (Table 33-21).

**Table 33-21** Likelihood Ratio of Signs for a Significant Systolic Murmur

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>LR for a Significant Systolic Murmur vs a Functional Murmur</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR+ (95% CI)</td>
<td>LR– (95% CI)</td>
</tr>
</tbody>
</table>
A loud (diagnostic odds ratio, 81) or holosystolic murmur (diagnostic odds ratio, 46) was the most accurate finding for identifying those patients with a significant murmur vs those with a functional murmur.

No patient had a diminished carotid upstroke, so this finding cannot be assessed from the data. A diminished second heart sound ($S_2$) was assessed, but the finding was heard in 5 patients only. One maneuver, the response to Valsalva, was assessed. Typically, patients with AS or MR would have a decreased intensity with the initiation of the maneuver, whereas patients with hypertrophic cardiomyopathy would have an increase. The maneuver in this study did not help identify patients with significant lesions (LR+, 1.2; 95% CI, 0.66-2.2; and LR-, 0.84; 95% CI, 0.50-1.4), but no patients with hypertrophic cardiomyopathy were found.

**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 CIs around some of these findings are large.

For the individual clinical signs, we could calculate the LR comparing patients with a significant murmur vs those with a functional murmur. This analysis ignores the patients who had less significant cardiac lesions as the explanation for their systolic murmur (eg, mild AS or MR). Thus, clinicians must understand that although these findings might identify patients more likely to have a significant vs a functional murmur, an echocardiogram must be done to determine whether the findings are associated with a significant or less-significant cardiac lesion.

The results suggest that a cardiologist's examination is useful even when the referring clinician is uncertain that a murmur is innocent. Because these patients are likely the most difficult to examine, the results for the cardiologist might be a “worst-case” scenario for the LRs. We can anticipate that for all patients with systolic murmurs, the LRs would suggest greater accuracy.

The presence of a variety of findings increases the likelihood that a systolic murmur will be significant. Loud, plateau-shaped, holosystolic murmurs with a thrill will have a high likelihood of emanating from significant cardiac abnormalities. These individual findings might work better than the clinician's overall clinical assessment for assessing systolic murmurs for patients in whom the diagnosis might not be readily apparent from the physical examination findings. An important caveat is that this analysis suggests only the presence of a significant lesion as defined by the authors as opposed to a functional murmur. Thus, the presence of
findings with a high LR+ means that the clinician must request an echocardiogram to determine whether the underlying cardiac lesions are significant or less significant. Similarly, the absence of a loud or holosystolic murmur makes a significant lesion less likely, but an echocardiogram would be required to identify patients with less significant lesions.

The results of this study should be interpreted in light of the clinical population—patients referred for evaluation of systolic murmurs that likely included those for whom the referring clinician was uncertain of the diagnosis. The data in the table do not represent the LRs for a specific diagnosis (eg, AS), but for any significant lesion associated with a systolic murmur.

The response to Valsalva does not help identify significant AS or mitral regurgitant murmurs, but this maneuver could still be important for identifying significant hypertrophic cardiomyopathy.

Evidence Summary and Review 3

Title Intensity of Murmurs Correlates With Severity of Valvular Regurgitation.

Authors Desjardins VA, Enriquez-Sarano M, Tajik AJ, Bailey KR, Seward JB.

Citation Am J Med. 1996;100(2):149-156.

Question Does the intensity of regurgitant murmurs on clinical examination correlate with the degree of echocardiographic regurgitation?

Design Investigators prospectively enrolled 210 consecutive patients undergoing Doppler echocardiography who were found to have chronic isolated mitral or aortic regurgitation. Results of a physical examination performed within 2 weeks of echocardiography by the patient's own physician (179 cardiologists, 31 general internists), who was unaware of the study, were abstracted from chart data.

Setting Echocardiography laboratory in a major US center.

Patients Two hundred ten consecutive patients prospectively identified with chronic, isolated mitral regurgitation (MR) or aortic insufficiency (AI) of mild or greater severity. Exclusion criteria included previous valve repair or replacement, associated valvular stenosis or acute regurgitation, and lack of physical examination performed by the referring physician within 2 weeks of echocardiography. For the 40 patients with isolated AI, the mean age was 58 ± 16 years, 65% were men, 8% were in atrial fibrillation, and the mean regurgitant fraction was 36% ± 16%. For the 170 patients with MR, the mean age was 64 ± 13 years, 54% were men, 21% were in atrial fibrillation, and the mean regurgitant fraction was 36% ± 18% by Doppler echocardiography.

Description of Tests and Diagnostic Standard

Quantitative Doppler and 2-dimensional echocardiography were performed on all patients before enrollment. It is not clear whether the echocardiographers were blinded to clinical data. Severe regurgitation was defined as a regurgitant fraction of 40% or higher. The clinical examination documenting murmur severity was performed independently by each patient's personal physician, who was not aware of the study and did not receive any special training or instruction regarding standardization of murmur grading.

Main Outcome Measures

Raw data, correlation coefficients ($r$). Likelihood ratios were calculated from the data provided.

Main Results
The intensity of the murmur predicts the severity of MR (Table 33-22).

Table 33-22  Likelihood Ratios for the Presence of Severe Mitral Regurgitation as a Function of the Murmur Intensity

<table>
<thead>
<tr>
<th>Murmur Grade</th>
<th>LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Or 5</td>
<td>14 (3.3-56)</td>
</tr>
<tr>
<td>3</td>
<td>3.5 (2.1-5.7)</td>
</tr>
<tr>
<td>0-2</td>
<td>0.19 (0.11-0.33)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR, likelihood ratio.

Conclusion

Level of Evidence

**Level 2.**

**Strengths** The population included in this study represents a difficult sample because all had some degree of regurgitation. The study examines a relevant clinical question because the ability to correlate the intensity of a regurgitant murmur with the degree of regurgitation is a useful clinical tool.

Limitations

Only patients with isolated lesions were included. The results demonstrate that the evaluation of murmur intensity of isolated MR by internists and cardiologists is a useful diagnostic test: a loud murmur (grade 4 or greater) is a good predictor of severe MR, whereas a murmur of grade 2 or less effectively rules out the presence of severe MR.

This study simulated normal clinical conditions without special training or standardized instructions to the examiner. These results are valid only in chronic, isolated MR and cannot be applied to the acute setting or to patients with complex murmurs.

Evidence Summary and Review 4

**Title** Initial Clinical Evaluation of Cardiac Systolic Murmurs in the Emergency Department by Noncardiologists.

**Authors** Reichlin S, Dieterle T, Camli C, Leimenstoll B, Schoenenberger RA, Martina B.

**Citation** *Am J Emerg Med*. 2004;22(2):71-75.

**Question** How well do noncardiologists distinguish innocent systolic murmurs from those produced by valvular heart disease in a typical emergency department evaluation?

**Design** Medical patients presenting to the emergency department were prospectively identified and evaluated for the presence of a systolic murmur. If 2 of 3 physicians, including 1 study physician, agreed on the presence of a murmur, the patient was enrolled in the study.

**Setting** Emergency department of a university teaching hospital in Switzerland.

**Patients** Two hundred three patients were enrolled from 852 medical patients screened in the emergency department. The patients were typical medical patients, with mean age of 64.7 (± 22.3) years, and 58% were
women. A significant percentage of the enrolled patients, had chest pain at presentation, and the majority had a pathologic electrocardiogram (ECG) (61%) or chest radiograph (53%) in the emergency department.

Description of Tests and Diagnostic Standard

The emergency department attending physician's clinical evaluation (including medical history, physical examination, ECG, chest radiograph, and laboratory tests) sought to distinguish normal from abnormal murmurs in all enrolled patients. Transthoracic echocardiography was performed to identify valvular heart disease in all enrolled subjects within 24 hours by 2 cardiologists blinded to the results of the clinical evaluation.

Main Outcome Measures

Main Results

Seventy-one of 203 patients had structural heart disease evident on echocardiography. Twenty-one patients were excluded because there was no informed consent (17) or the echocardiography was not performed (4), leaving 582 patients with no systolic murmur. Of the entire sample size, there was disagreement for only 18 patients, for whom a third examiner settled the discordance.

The $k$ statistic for the presence of a murmur was 0.8; the $k$ statistic for murmur grades 0 to 2 vs those greater than grade 2 was 0.59.

Conclusion

Level of Evidence

Level 1.

Strengths Prospective, consecutive patients with independent application of the reference standard in a population typical for those in whom distinguishing a normal from an abnormal systolic murmur by clinical examination is an important clinical question. Because the patients provided information on all potentially eligible patients, we can correct for verification bias.

Limitations

Entrance criteria required that 2 of 3 examiners agree that a murmur was present. Although this may decrease generalizability, it improves our confidence that a murmur was present.

This large, high-quality study evaluated the utility of the clinical evaluation by noncardiologists. The examiners in this study had access to all available clinical information, including patient charts that documented previously identified valvular heart disease in 10% of patients; however, this represents a realistic clinical scenario.

The level of agreement among examiners in identifying the presence of a systolic murmur of intensity greater than grade II/VI documented in this study compares favorably to that of previous studies involving cardiologists examining patients.

This study provides complete information on all patients, allowing us to correct for verification bias by making certain assumptions about the patients for whom both clinicians did not hear a murmur or for whom there was a disagreement about the presence of a murmur. The majority of patients who did not undergo echocardiography did not have a systolic murmur, as judged by 2 examiners. If we assume that none of these
patients truly had valvular heart disease, the LRs are as shown in Table 33-23. These LRs estimate the **efficiency** of the clinicians to identifying aortic or mitral valvular disease among all patients. Because most patients do not have valvular heart disease, the **specificity** of the examination is excellent.

Table 33-23  **Likelihood Ratio** of the Overall Examination for an Abnormal Murmur

<table>
<thead>
<tr>
<th>Clinical Evaluation</th>
<th>Patients</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+ (95% CI)</th>
<th>LR− (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall examination suggests abnormal murmur, corrected for verification bias</td>
<td>All patients</td>
<td>14 (10-19)</td>
<td>0.21 (0.13-0.34)</td>
<td>0.21 (0.13-0.34)</td>
<td></td>
</tr>
<tr>
<td>Overall examination, uncorrected for verification bias Only patients with systolic murmurs</td>
<td>0.80 (2.0-3.4)</td>
<td>0.69 (0.17-0.45)</td>
<td>0.29 (0.17-0.45)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

The LRs reported by the investigators, uncorrected for verification bias, show the performance of the clinical examination among patients known to have a systolic murmur. In clinical practice, these patients would be more reflective of those referred for echocardiography to determine the presence of a systolic murmur.

**Evidence Summary and Review 5**

**Title** Value of the Cardiovascular Physical Examination for Detecting Valvular Heart Disease in Asymptomatic Subjects.

**Authors** Roldan CA, Shively BK, Crawford MH.

**Citation** Am J Cardiol. 1996;77(15):1327-1331.

**Question** How useful is the physical examination in detecting the presence or absence of valvular heart disease in asymptomatic individuals?

**Design** Nonconsecutive patients were prospectively identified for inclusion and were examined by a cardiologist blinded to other data. An echocardiographer, blinded to clinical findings, identified valvular heart disease.

**Setting** Outpatient clinic in the United States.

**Patients** The population consisted of 75 patients with connective tissue diseases and 68 healthy volunteers. The patients with connective tissue diseases had systemic disease without cardiac symptoms and constituted a group of patients for whom most physicians would auscultate the heart to detect asymptomatic cardiac disease associated with their underlying disorder (systemic lupus erythematosus, ankylosing spondylitis, rheumatoid arthritis, antiphospholipid antibody syndrome).

The mean age of participants was 38 ± 11 years, 56 were men, and none had cardiovascular symptoms. Only 5% of subjects were known to have murmur or valvular heart disease.

**Description of Tests and Diagnostic Standard**

Subjects were randomly sequenced for a complete physical examination, including dynamic auscultation by a cardiologist blinded to other data. The cardiologist recorded the findings for jugular venous pulse; the palpated carotid pulse; the palpated precordial maximal impulse; the presence of a right ventricular lift; abnormalities of
the second, third, and fourth heart sounds; clicks; and ejection sounds. The dynamic auscultation included evaluation of murmur change with respiration, Valsalva maneuver, handgrip, and changes in body position.

Transesophageal echocardiography was performed on all subjects by an echocardiographer blinded to the clinical examination and other data. Diagnosis of valvular disease was based on established criteria.

**Main Outcome Measures**

**Main Results**

Thirty-three patients had echocardiographic evidence of valvular abnormalities, the majority (24 of 33) of which were mitral valve regurgitant lesions or prolapse. The predictive value of the individual findings is reported, but none occurred in more than 8% of patients, providing broad confidence intervals. It is difficult to disentangle the individual findings from the overall assessment because the individual components and categorization of individual murmurs were based on the total evaluation (Table 33-24).

**Table 33-24 Likelihood Ratio for the Overall Clinical Examination to Identify Patients With Abnormal Cardiac Valves**

<table>
<thead>
<tr>
<th>Test</th>
<th>Valvular Heart Disease by Echocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Overall clinical assessment for a valvular abnormality</td>
<td>0.70</td>
</tr>
</tbody>
</table>

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

**Conclusion**

**Level of Evidence**

*Level 3.*

**Strengths** Prospective, blinding of examination, and gold standard test.

**Limitations**

Cardiologist examiner may limit generalizability to generalist physicians. Nonconsecutive patients.

The study population is unique in that these patients were not selected according to an auscultated abnormality. They represent a combination of healthy patients and patients with noncardiac disease, all of whom might undergo auscultation in the course of “routine” medical care. By including healthy patients, a high specificity for the examination could be expected because most patients would not have abnormal findings and would not have cardiac abnormalities shown by echocardiogram.

This study evaluated physical examination by a cardiologist alone, without supplementary information or investigations in a healthy population at risk for valvular heart disease. It is useful that the report includes the actual individual components used by the cardiologists to determine their overall clinical assessment. The cardiologists heard a surprising number of murmurs, but when they described a murmur as abnormal, the likelihood of an echocardiograph abnormality increased greatly.

**Compiled Clinical Scenarios**
Clinical Scenario

A 62-year-old man scheduled for elective total knee replacement has been referred to you for preoperative assessment of a systolic murmur. The orthopedic surgeon detected a systolic murmur and wants to rule out aortic stenosis (AS) before surgery. The patient has no cardiovascular symptoms. On auscultation, you hear normal first and second heart sounds (S₁ and S₂). There is a grade 3 early systolic murmur, loudest at the lower left sternal border, which does not radiate to either the right clavicle or carotids. You detect a normal volume and normal rate of increase of the carotid pulse. The rest of the clinical examination results, including those for the electrocardiogram (ECG) and chest radiograph, are normal.

Clinical Scenario—Resolution

Your patient's murmur did not radiate to the right clavicle. This finding makes AS much less likely (LR, 0.1). There are no other concerning features that raise the possibility of other serious structural heart disease, including the ECG and chest radiograph. If you are an experienced clinician, this reduces the likelihood of important structural heart disease (LR, 0-0.1). If you are less experienced and not certain of your overall assessment that the murmur is “functional,” concentrating on whether the murmur is holosystolic or “loud” and whether the patient has a decreased carotid upstroke or systolic thrill may yield more useful information than your clinical gestalt. Conditions that can cause increased blood flow through a structurally normal heart should be excluded, such as anemia, renal failure, and thyrotoxicosis.