# Learning Cardiac Auscultation

## From Essentials to Expert Clinical Interpretation

Allen J. Taylor
*Editor*

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*Listen well, and you will see more deeply into the hearts of your patients.*
*To the patients and to the profession which I am privileged to serve as a true love. Thank you for teaching me every day.*

# Foreword

Since 1851, Georgetown University School of Medicine has focused on education with the Jesuit perspective of *cura personalis*, or care of the whole person. Here in your hand you have a powerful tool, written by Georgetown's finest under the guidance of one of its master clinicians, Dr. Allen J. Taylor. In the 162 years since the first graduating class from this school and in the 60 years since a Georgetown faculty member inserted the first artificial heart valve, Georgetown's educational focus has been consistent: to create a thoughtful and caring clinician with a solid base of clinical skills, an evidence-based intellectual curiosity about each patient encounter, and a clinical confidence in the nuance of the physical exam.

As Dr. Taylor will remind you, another Georgetown hero, Dr. W. Proctor Harvey, a kind and compassionate Virginia gentleman who listened graciously to patients' histories as he listened carefully to their hearts, fortunately digitally recorded over 30,000 heart murmurs from those patients. He developed a science and an art of auscultation that have only become more valuable as imaging and therapeutic technologies have advanced. This is nowhere more apparent than in the headlines of professional sports last year, when a routine physical exam of a professional basketball player could potentially detect the right-sided diastolic murmur, confirmed by imaging to be a dissection of the aortic arch; it was repaired successfully with a return to the sport.[1]

Keep in mind that excess use of high-technology imaging is not the clinical answer, and it certainly is not the economic answer. A senior medical executive at one of the nation's largest health insurers agrees that it is not defensive medicine driving unnecessary procedures, as much as lack of clinician confidence in his/her own clinical exam.[2] Sadly, it is occasionally the absence of careful clinical exam. Confidence in your clinical exam comes from practice, and confidence in the normal auscultation of the heart can discover the nuance of S3 gallop in the early failing heart or find the physiologic split and musical quality of the normal "Still's"

[1] http://t.co/vH79FxqxAm

[2] Michael Alexander, MD, personal communication.

murmur. Keep this precious book in your pocket next to that stethoscope. Successful growth of your "clinically informed platform" starts with the acquisition of auscultation skills that allow you to develop the confidence of a skilled clinician, providing the cost-conscious, personalized approach that this book empowers.

Take that careful history, and you will be 80 % there. This little book will stress those basics to create the clinical opportunities in your own "prepared mind." Next, create and develop your discipline in the cardiac exam until it is systematic and reproducible. Your reward will be the incredible gift of clinical discernment, what Dr. Taylor and Dr. Harvey would have called the nuances of cardiac diagnosis. Those findings, available to you at the bedside, are often not available through high technology.

This must begin with a good stethoscope with binaural fidelity and good acoustics. Pull it repeatedly out of your pocket until the metal develops a burnished patina of its own. Dr. Harvey's treasured original scope had worn the chrome plating through to the brass in several places. Develop the discipline of a systematic, consistent exam and apply it to every patient so that your repertoire of "benign" is equally deep as your experience with cardiac pathology. Follow each abnormal finding for which confirmatory studies are available with your own correlation. Be critical of what you missed, and by all means go back and listen again.

Use this precious little textbook, parsimoniously written to give you a quick, accurate, and evidence-based background of each condition. We hope it will become equally worn, dog-eared, and treasured as your stethoscope. Get started now and avidly seek out those findings that will make you the clinician Dr. Harvey and Dr. Taylor would respect.

(If you would like to pursue listening to more murmurs in humans, Dr. Harvey's book featuring the 2788 "greatest hits" of digital murmurs is available inexpensively on I-Tunes for any IOS system. [3])

Washington, DC, USA Stephen Ray Mitchell, MD, MBA, MACP, FAAP

[3] Cardiac Auscultation by Harvey, Canfield, Bednyk http://itunes.apple.com/us/book/clinical-heart-disease/id529684046?mt=11

# Preface

A recent declaration from a medical pundit lauded the era of technology entering the arena of the cardiac physical exam. "I haven't used a stethoscope in 2 years," he asserted, assuring us of a "momentous moment in medicine" in which a pocket ultrasound device will replace the stethoscope so long carried by physicians. "This isn't crazy," he concluded. "It's the future. Old medicine is about to change." Despite my healthy affinity for medical technology and progress, on the subject of auscultation, I respectfully disagree!

The foundation of this handbook on clinical auscultation of the heart lies in the supremacy of careful, clinical observation in medicine. The science and application of auscultation, developed over hundreds of years and not without its imperfections, represent a learnable, tangible, personal approach to assessment of the heart and remains crucial in medical practice. Today's medicine all too often focuses on the high tech, discarding simple approaches that at the least can and should steer clinicians towards when to utilize expensive testing, and at the most can, potentially, outperform technology for accurate cardiovascular diagnosis. Can an echocardiogram detect an S3? The answer is no, and an S3 has important diagnostic and prognostic implications. Can an electrocardiogram diagnose the fixed split S2 of an atrial septal defect? The answer is no, and people live under frequent medical care with atrial septal defects undetected until adult life, leading to unnecessary morbidity. Within a *cost conscious, personalized approach* to medicine, the art of clinical examination of the heart could never be more alive, or more important. Technology needs a *clinically informed platform* upon which to provide benefits to patients. Does every patient with a murmur need an echocardiogram? The answer is clearly "no." Careful clinical observation should properly identify patients in need of additional testing, leading to appropriate avoidance of expensive testing in patients at low risk of having important cardiovascular lesions.

This handbook provides a *clinically-oriented approach to the astute observation of heart sounds and other aspects of the cardiovascular examination*. Each chapter describes a case scenario, followed by a description of key clinical and auscultation features, and clinical clues to the diagnosis. *More importantly, auscultation of the heart should not just end with a simple diagnosis, but an unearthing of nuances of*

*the diagnosis, for example, describing the possible severity or diagnostic implications of the auscultation findings*. And linking physical examination with prognostic implications to ensure therapeutic interventions are properly calibrated to the risk of the patient represents the ultimate goal. The chapters in this handbook cover all major valvular abnormalities, with detailed descriptions of classical exam findings aiding the diagnosis and treatment of cardiovascular disease. Audiovisual links richly enhance the text presentation in the chapters.

*Auscultation is a learned art*. Data on auscultation suggest that the current status of our skills, as a clinical community, should be better. But data on auscultation also show us that auscultation can be learned and honed as a skill, so this is reason for hope. As Sherlock Holmes stated, "*The world is full of obvious things which nobody by any chance ever observes*." How does one remove "chance" from their examination skills? Knowledge provides the first step. What are the typical findings? What are the subtle findings? What are the important findings? And what do they mean for the care of the patient? Next, improved skills through practice must be attained such that, armed with *what* to look for, one can find it. As Holmes said, obvious things can be observed, but not by chance alone. *Chance favors the prepared mind*. This book compiles the skills necessary to become a more astute bedside observer. To my way of thinking, in that lies the fun of medicine: Of "figuring it out," of using your ears, eyes, and mind to take better care of your patients.

I am thankful to the talented men and women of the Georgetown University School of Medicine Class of 2015 for so ably and enthusiastically assisting in this project. Georgetown has a rich history and tradition of cardiac examination excellence, embodied by the late W. Proctor Harvey, M.D. Dr. Harvey maintained a "focus on the *patient* who, unfortunately, at present is too often relegated to the back burner," as echo reports and CT scans accumulate in the electronic medical record. *So, for me, my stethoscope remains with me at all times. It's the link to my patients. It engages my clinical thinking. It guides me to better patient care. It puts the fun in medicine. It is what drove me to be a doctor and a cardiologist*. I encourage you to not always just carry your stethoscope, but to actually take it out of your pocket from time to time and use it! Value it as a tool, and learn how to wield it well! In the words of Sherlock Holmes, it's "elementary"!

Washington, DC, USA Allen J. Taylor, MD, FACC, FAHA

# Acknowledgments

I would like to thank and acknowledge the following individuals for the audio links in the chapters that follow:

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These video links vastly enrich and enhance the text presentation.

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**Part VI Congenital Heart Disease**

# List of Videos

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# Part I
# Auscultation Principles

# Chapter 1
# Introduction to Cardiac Auscultation

**Meghan C. Kusko and Kathryn Maselli**

## Key Teaching Points

- Cardiac auscultation has a high predictive value for identification of many serious heart diseases. In some cases, it may be possible to obtain a definitive diagnosis from auscultation.
- Auscultation is quick and cost effective.
- Many heart sounds fall below frequency-threshold limit, so careful auscultation is needed for detection. In general, the diaphragm is used to hear higher frequency sounds (e.g., normal heart sounds, most murmurs), whereas the bell is used to detect lower frequency sounds (e.g., third and fourth heart sounds).
- Training and practice can improve auscultation skills.

## Physical Exam

### *Inspection*

- The first component of the physical exam should be inspection of the patient.
  - Note the patient's general appearance.
  - The frequency, regularity, depth, and effort of respiration can provide insight into the patient's cardiovascular health.
  - Shortness of breath can indicate a pulmonary pathology but may also be associated with cardiac disease such as congestive heart failure.

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- The patient's chest should also be inspected for any chest deformities.
  - Patients with long standing kyphoscoliosis are at risk of developing pulmonary hypertension and cor pulmonale.
  - Patients with pectus carinatus, or protrusion of the sternum, may have suboptimal heart and lung function.
    - This deformity is associated with Marfan's syndrome that can have cardiovascular manifestations such as mitral valve prolapse, aortic regurgitation, and aortic aneurysm or dissection.
  - Pectus excavatum is the most common chest wall deformity where the sternum and several ribs grow abnormally, giving the chest a sunken appearance.
    - Associated with Marfan's syndrome and Ehler Danlos syndrome.
    - May also have deformities of the heart that can impair cardiovascular function.
- The skin should be inspected for any scars, which can indicate surgical history, or other lesions.
- The chest should be inspected for abnormal pulsations.
  - A parasternal pulsation can indicate aortic or pulmonic enlargement.
  - Apical retraction during systole can indicate constrictive pericarditis.
  - The apical impulse should be within the midclavicular line.
  - Deflection of the apical impulse lateral to the midclavicular line is an indication of cardiomegaly.
- The patient's neck should be examined for jugular venous pressure and pulsations.
- The cheeks should be examined for the malar flush of mitral stenosis.
- The eyelids should be inspected for xanthelasmata that may indicate high cholesterol.
- Clubbing of the digits indicates chronic hypoxemia and poor perfusion of distal tissues. Additionally, cyanosis or bluish coloring of the skin can indicate hypoxemia.
- Edema, especially in the lower limbs, can be associated with volume overload and decreased cardiac function as in congestive heart failure.

## *Palpation*

- Palpation is an important part of the cardiac exam that is often overlooked.
- The setting should be controlled and the same approach and method used for every exam.
- The patient should be palpated in the supine position with the skin exposed.

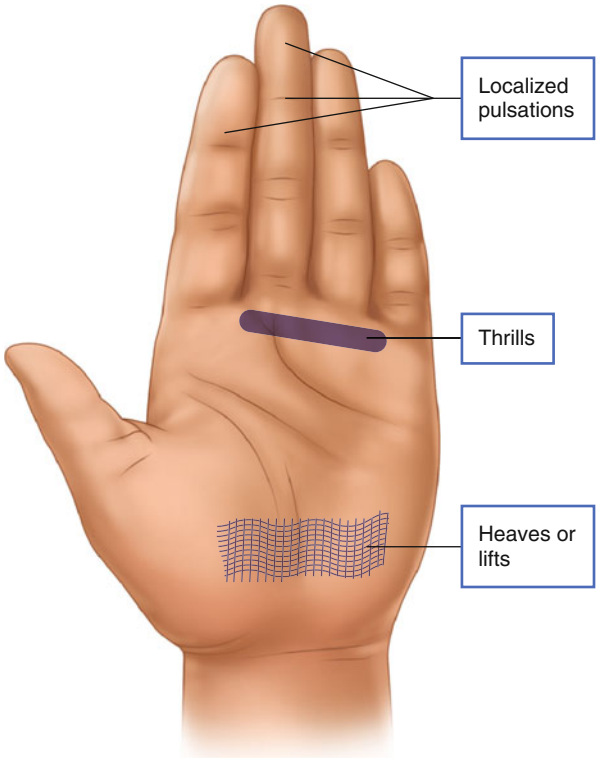


**Fig. 1.1** Areas of the hand used to palpate localized pulsations, thrills, and heaves or lifts. The patient should be palpated in the supine position and the fingertips used to palpate localized pulsations. The flat of the hand should be used to feel thrills and the heel of the hand should be used to feel heaves or lifts

  - Localized pulsations should be felt with the pads of the fingers (Fig. 1.1).
  - Thrills with the flat of the hand (Fig. 1.1).

- Heaves or lifts with the heel of the hand (Fig. 1.1).
  The apical impulse or point of maximal impact should be palpated first.
  - It should be located slightly medial and superior to the midclavicular line and the 5th intercostal space (Fig. 1.2).
  - It should be the lowest and most lateral impulse felt.
  - The left lateral decubitus position may make it easier to palpate the apical impulse.
  - In 50 % of normal patients, the apical impulse may not be palpable in the supine position.
  - The diameter of the impulse should be palpated and should be less than 2.5 cm in diameter, occupying only one intercostal space.
  - The amplitude should be small and the impulse should feel brisk and tapping.
  - If the apical impulse is displaced laterally or >3 cm in diameter, this indicates left ventricular enlargement.

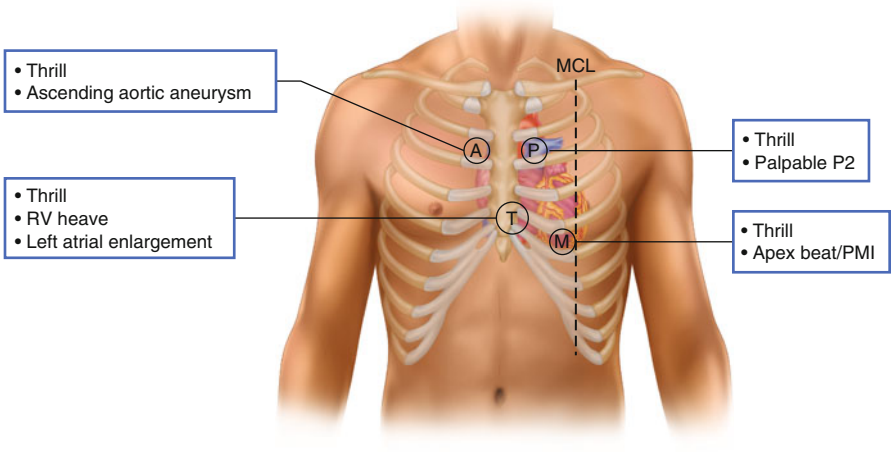


**Fig. 1.2** The aortic, pulmonary, mitral, and tricuspid areas should all be palpated as different pathologies can be felt at each location. *MCL* midcalvular line, *A* aortic, P pulmonary, M mitral, T tricuspid

- Diastolic palpitation may be used to detect ventricular motion associated with a pathologic third or fourth heart sound.
  - A brief mid-diastolic impulse at the apex indicates an S3 gallop.
  - An impulse felt just before the systolic apical beat indicates an S4 gallop.
- The right ventricle should not normally be palpable.
  - Right ventricle can be palpated at the left sternal border in the 3rd, 4th, and 5th intercostal spaces with the patient in the supine position (Fig. 1.2).
  - A palpable anterior systolic motion in the left parasternal area indicates right ventricular enlargement or hypertrophy.
  - In some patients, this may be easier to feel in the subxiphoid area.
  - It is important to distinguish between diffuse precordial action as seen with augmented stroke volume (which may be normal) and the sustained left parasternal outward thrust seen in right ventricular enlargement (always abnormal).
  - A prominent pulsation in the left second intercostal space indicates increased flow in the pulmonary artery and a palpable S2 indicates pulmonary hypertension (Fig. 1.2).
  - A palpable S2 at the right 2nd intercostal space (aortic area) suggests systemic hypertension and a pulsation here may indicate an aortic aneurysm (Fig. 1.2).
  - The pulmonic closure may be palpable in individuals with thin chest walls or in pulmonary hypertension.

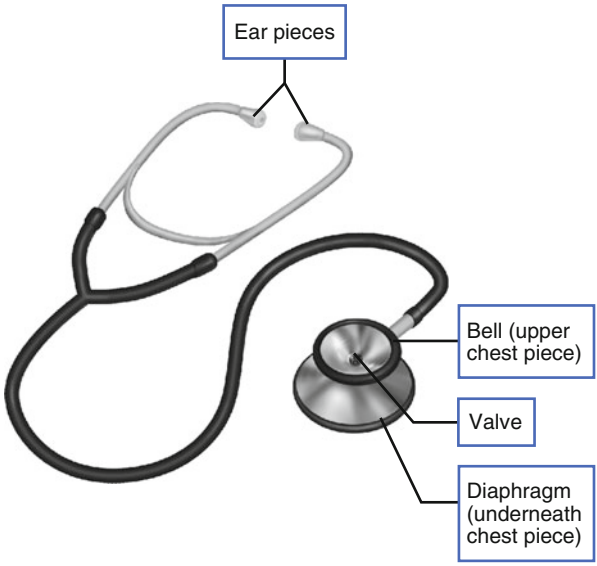


**Fig. 1.3** Schematic of a standard stethoscope, identifying the bell (low frequency sounds) and diaphragm (high frequency sounds) components

## *Auscultation*

### Auscultation Technique

- Auscultation is the act of listening to sounds arising from the internal organs for evaluation purposes. It is most often performed on fully exposed skin using a standard stethoscope (Fig. 1.3), though some physicians opt for more technologically advanced tools (e.g., electronic stethophones, fetoscope, Doppler stethoscope).
- Proper use of the stethoscope is crucial for accurate assessment of heart sounds and murmurs. In general, the diaphragm is used for high frequency sounds, while the bell is used for low frequency sounds; adjusting the bell pressure allows for a broader range of sounds to be heard.
- Auscultation is classically performed parasternally at individual interspaces of the thoracic wall. In some patients, it is helpful to listen at routine non-precordial sites, including the axillae, back, lower right sternal border, and clavicles.
- Proper auscultation technique is imperative for effective patient assessment. Once the stethoscope is placed on the patient, slowly inch the head along the body to listen for variation in sound. It is most productive to begin at the apex of the heart in the left lateral decubitis position and work toward the sternum.

## Cardiac Auscultation

### Normal Heart Sounds

- Heart sounds heard on auscultation reflect turbulent blood flow through the heart as the heart valves snap shut. The "lub dub" beating of the heart is directly related to the normal heart sounds, S1 and S2. More specifically, S1 is produced upon closure of the atria-ventricular valves, and S2 is produced upon closure of the semilunar valves.
- During inspiration, the S1 sound may be audibly split into two components. As the chest wall expands and intrathoracic pressure increases, venous return to the right atrium is also increased. This normal physiologic mechanism allows the pulmonic valve to remain open slightly longer than normal, thereby increasing the time between aortic and pulmonic valve closure.
- Two additional heart sounds, S3 and S4, may be heard during routine auscultation. In children and trained athletes, S3 is associated with rapid ventricular filling during early diastole; it is benign. However, its re-emergence later in life may be an indication of left ventricular systolic dysfunction and congestive heart failure. Thus an S3 heart sound in older populations requires additional work-up. The presence of S4 in an adult is associated with turbulent blood flow being forced into a hypertrophic ventricle. S4 is sometimes referred to as a presystolic gallop; it is always an abnormal finding, indicative of reduced ventricular compliance.

### Murmurs

- Heart murmurs refer to abnormal heart sounds with an underlying physiologic pathology. They are typically caused by turbulent blood flow due to a diseased/abnormal valve or an abnormal blood flow pathway.
  - Stenotic valves are thickened, fused or calcified, narrowing the effective orifice for forward blood flow.
  - Regurgitant/incompetent valves do not close completely so blood can easily leak back into the previous chamber even when the valve is "closed". This may occur secondary to structural valve changes caused by infection, inflammatory or degenerative changes, or nonvalvular abnormalities from chamber enlargement or wall motion abnormalities.
  - Abnormal blood flow resulting from an anatomic abnormality represents an error in development or persistence of fetal circulation. Some examples include atrial or ventricular septal defects, atria-ventricular canal, and patent ductus arteriosis.
- Murmurs are characterized by:
  - Intensity – Intensity is graded on a 1–6 scale, related to the amount of blood flow.
    - Grade 1: Murmur is faintly heard with a stethoscope. It requires special effort to hear.
    - Grade 2: Murmur is soft but readily detectable.

    - Grade 3: Murmur is prominent by not loud.
    - Grade 4: Murmur is loud with a palpable thrill.
    - Grade 5: Murmur is very loud.
    - Grade 6: Murmur is extremely loud and even audible without use of the stethoscope.
  - Frequency – Frequency, or pitch, is related to the amount of blood flow.
    - Lower and slower flow relates to a lower pitch.
    - Higher and faster flow relates to a higher pitch.
  - Configuration – Configuration refers to the shape of the murmur with respect to its audibility. Murmurs may exhibit crescendo, decrescendo, flat, or crescendo-decrescendo configurations.
  - Duration – Described in terms of the length of systole or diastole in which the murmur occurs, for example mid-systolic, or holo-diastolic.
  - Quality – Quality may be described as musical, humming, coarse, etc.
  - Timing – Murmur timing is described in relation to systole and diastole of the heart.
    - Systolic murmurs begin with or just after S1 and end before or at S2.
    - Diastolic murmurs begin with or just after S2 and end before or at S1.
    - Continuous murmurs are heard without interruption through systole and into all parts of diastole.

Performance of Cardiac Auscultation

Cardiac auscultation is performed at five discrete areas of the precordium, each reflecting a particular heart valve (Fig. 1.4). Take note that not all pathology associated with a valve may be heard at its named anatomical location.

- The aortic valve is auscultated at the second right intercostal space. Murmurs here indicate pathology of the atria ventricular or left ventricular outflow tracts. Common murmurs heard include aortic stenosis and hypertrophic cardiomyopathy, and aortic regurgitation. Interestingly, aortic murmurs and left ventricular sounds are more appreciated at the apex.
- The pulmonic valve is auscultated at the second left intercostal space. Although murmurs in this region tend to be quiet, an audible abnormality indicates pathology of the pulmonic valve, such as a patent ductus arteriosus. Pathology is further supported if the murmur's intensity varies with respiration.
- The third left intercostal space, often referred to as Erb's Point, is close to both semilunar valves. Murmurs in this region are sometimes more audible if the patient leans forward, bringing the heart closer to the chest wall. Common murmurs heard at Erb's Point include various aortic and pulmonic pathologies, as well as diastolic murmurs of the right atrium.
- The tricuspid valve is associated with the fourth left intercostal space. Systolic murmurs heard in this area indicate pulmonic stenosis or tricuspid regurgitation, whereas diastolic murmurs indicate tricuspid stenosis or pulmonic regurgitation.

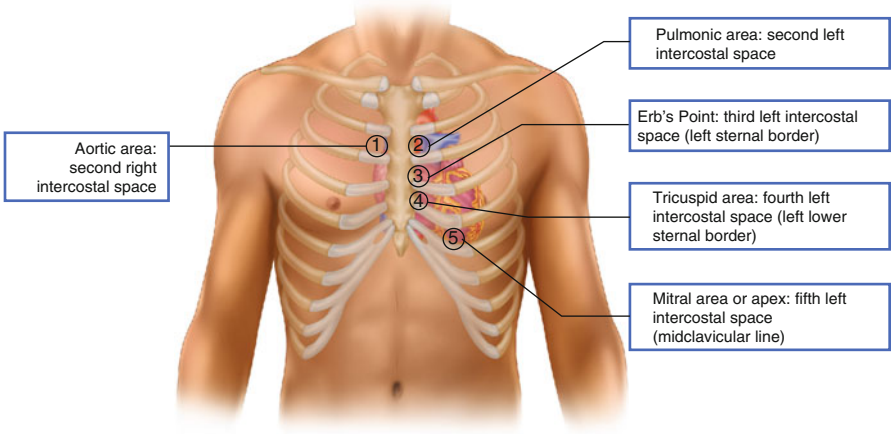


**Fig. 1.4** Schematic of the five discrete areas for cardiac auscultation: (1) aortic valve at the second left intercostal space, (2) pulmonic valve at the second right intercostal space, (3) both semilunar valves at the third left intercostal space, (4) tricuspid valve at the fourth left intercostal space, and (5) mitral valve at the heart's apex

- The mitral valve and the heart's apex are associated with the fifth left intercostal space. Since the right ventricle occludes the left ventricle in normal cardiac anatomy, having the patient roll to their side in the left lateral decubitus position may enhance auscultation.
  - Systolic murmurs heard at the heart's apex indicate mitral regurgitation, aortic outflow obstruction, or ventricular septal defect. To delineate between these three murmurs, further examination is required. In aortic outflow obstruction, the murmur radiates to the carotids and/or has an associated thrill; in mitral regurgitation, the murmur radiates to the left axilla; in ventricular septal defect, the murmur projects along the left sternal border.
  - Diastolic murmurs heard at the heart's apex indicate mitral stenosis or aortic regurgitation. Mitral stenosis is only audible at the apex, and is often accompanied by an opening snap sound. In contrast, aortic regurgitation murmurs can be heard at the apex, aortic area, and Erb's Point.

## Auscultation Maneuvers

Different maneuvers can be used to accentuate or decrease murmurs and can be used to aid in the diagnostic process. These maneuvers include respiration, Muller maneuver, Valsalva maneuver, standing to squat, passive leg elevation, isometric hand grip, and amyl nitrate inhalation.

**Table 1.1** The sensitivity, specificity, and diagnostic accuracy of the cardiac examination for various causes of systolic murmurs as determined from evaluation based solely on auscultation by two expert cardiologists and confirmed by echocardiogram

| Cause of murmur | Number of patients | Sensitivity | Specificity percent | Diagnostic accuracy |
|---|---|---|---|---|
| Functional murmur | 21 | 67 | 91 | 83 |
| Significant heart disease | 29 | 79 | 93 | 75 |
| Any aortic stenosis | 29 | 71 | 83 | 80 |
| Isolated ≥mild aortic stenosis | 15 | 73 | 90[a] | 86[a] |
| Combined ≥mild aortic stenosis | 14 | 69 | 51 | 63 |
| Any aortic regurgitation | 28 | 21 | 96 | 75 |
| Isolated ≥mild aortic regurgitation | 13 | 23 | 97 | 84[a] |
| Combined ≥mild aortic regurgitation | 15 | 20 | 92 | 52 |
| Any mitral regurgitation | 30 | 70 | 70 | 70 |
| Isolated ≥mild mitral regurgitation | 8 | 88 | 71 | 73 |
| Combined ≥mild mitral regurgitation | 22 | 64 | 60 | 63 |
| Mitral valve prolapsed | 11 | 55 | 96 | 91 |
| Combined aortic and mitral valve disease | 22 | 55 | 88 | 81 |
| Ventricular septal defect | 4 | 100 | 97 | 97 |
| Intraventricular pressure gradient | 11 | 18 | 98 | 89 |

Used with permission from Jost et al. [1]

[a]Indicates $P<0.05$ for comparison of results in patients who had isolated valvular lesions with those who had combined lesions

## Diagnostic Implications of the Auscultation Features

- The accuracy of auscultation has been systematically studied [1]:
  - 100 patients referred for a systolic murmur were examined by two cardiologists and then examined by echocardiography and the results of the two methods compared (Table 1.1).
  - Overall sensitivity of auscultation for detecting significant heart disease was 79 %.
  - Functional murmur could be detected with a sensitivity of 67 %.
  - The diagnostic accuracy for specific lesions ranged from 70 to 90 %, except for lesions of the aortic or mitral valves when combined with other heart disease.

  - The lowest accuracy was 52 % for combined aortic and mitral lesions.
  - Sensitivity was lowest detecting intraventricular pressure gradients followed by aortic regurgitation.
  - This study indicates the value of auscultation for detecting lesions and indicates the operating range of the accuracy of auscultation.
  - The clinicians taking part in the study were proficient at discriminating functional murmurs and only one in every five patients referred for echocardiogram had a normal echocardiogram.
  - However, the study did have several limitations as it was artificially limited to just auscultation and not the entire clinical exam.

- A second study looked at the accuracy of the cardiac physical exam in asymptomatic patients [2]:

  - 143 patients total, 68 presumed normal and 75 with known valvular disease.
  - An experienced cardiologist blinded to the clinical data except for auscultation examined the patients.
  - Results were compared with the patient's transesophageal echocardiogram.
  - Cardiac exam was found to have a sensitivity of 70 %, specificity of 90 %, a positive predictive value of 92 %, and a negative predictive value of 92 %.

- A study looking at the accuracy of auscultation in cardiac fellows, medical residents, and medical students showed that practice and effective teaching are needed for medical trainees to learn effective auscultation (Fig. 1.5) [3]:

  - Nationwide study of internal medicine and cardiology programs and cross-sectional analysis of students' and staff's auscultatory proficiency.
  - Program directors completed a 23 question survey and all students and trainees were tested using 12 prerecorded cardiac sounds including murmurs and extra sounds (rubs, gallops, etc.).
  - Accuracy ranged from 0 to 56.2 % for cardiology fellows and from 2 to 36.8 % for medical residents.
  - For the majority of sounds and murmurs, the participants were accurate less than half the time; only for aortic stenosis or aortic insufficiency, PDA, and pericardial friction rub did performance appear to improve with training, suggesting that there is ample room for improvement in training.
  - Only 27.1 % of internal medicine and 37.1 % of cardiology programs offered structured teaching of auscultation.
  - The study found a low identification rate for these 12 common cardiac events indicating a lack of effective teaching.

- A second study showed that medical students had significant improvement in proficiency after listening to 500 repetitions of 4 basic cardiac murmurs (Fig. 1.6) [4]:

  - 51 students were divided into a control, monitored, and unmonitored groups and each group was assessed with a pre and posttest which consisted of ten heart sounds.

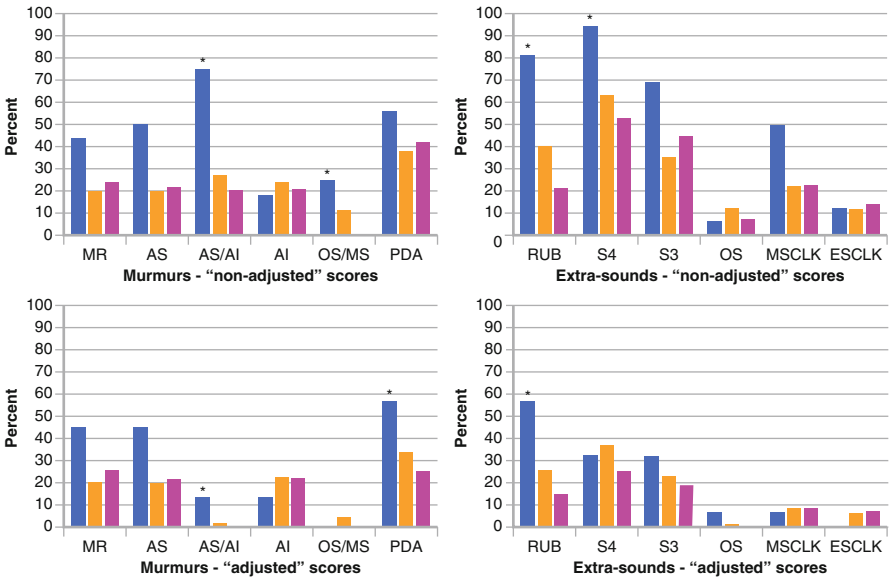


**Fig. 1.5** Auscultatory accuracy rates, according to type of training. Accuracy in identifying six cardiac murmurs (*left upper* and *lower panels*) and six extra sounds (*right upper* and *lower panels*) is shown. *AI* aortic insufficiency, *ESCLK* early systolic click, *MS* mitral stenosis rumble, *MSCLK* midsystolic click, *OS* opening snap of mitral stenosis, *PDA* patent ductus arteriosus, *RUB* pericardial friction rub, *S3* S3 gallop, *S4* S4 gallop. Accuracy is reported as a percentage of correct answers. Adjusted scores (*bottom panels*) were calculated whenever the respondents selected not only the correct finding but also findings acoustically similar but absent. The adjusted score considered these types of answers to be invalid. Significance is reported for improvement in each of the three participating groups when compared with each other (*asterisks* indicate P values <.02). *Blue bars*, cardiology fellows; *orange bars*, medical students; *purple bars*, medical residents. For the majority of sounds and murmurs, the participants were accurate less than half the time; only for aortic stenosis or aortic insufficiency, PDA, and pericardial friction rub did performance appear to improve with training, suggesting that there is ample room for improvement in training (Used with permission from Mangione et al. [3])

  - Students were tested on normal heart sounds, four pathologic murmurs, and an innocent murmur. Both listened to 500 repetitions of each murmur but the monitored group had six monitored sessions for listening.
  - Both the monitored and unmonitored groups showed significant improvement after 500 repetitions.
  - This suggests that although proficiency is poor among trainees, cardiac auscultation is a technical skill which can be improved with proper teaching methods and repeated exposure.

- Although students and trainees had poor auscultatory skills, the sensitivity and specificity of the cardiac exam when carried out by an expert cardiologist indicates that auscultation is an important diagnostic skill and with proper teaching and exposure, students can significantly improve their auscultatory skills.

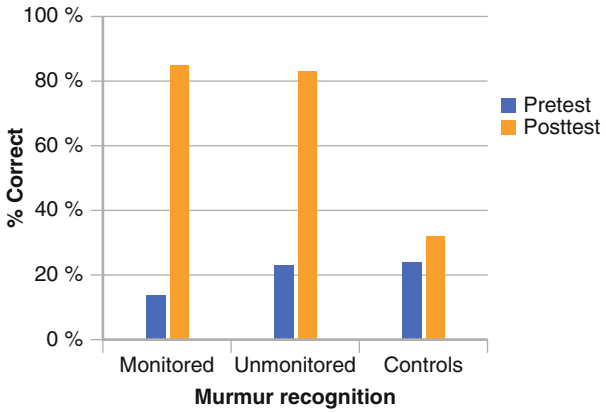


**Fig. 1.6** Improvement in murmur recognition in medical students. Students were divided into control, monitored, and unmonitored groups. The monitored group listened to 500 repetitions of 4 common murmurs (mitral regurgitation, aortic stenosis, aortic regurgitation, and mitral stenosis) in monitored sessions. The unmonitored group listened to 500 repetitions of the same four murmurs on their own and the control group received no intervention. The monitored and unmonitored groups both showed significant improvement in their proficiency after 500 repetitions (Used with permission from Barret et al. [4])

## General Statement on Management

Echocardiogram is not a replacement for history, physical exam, auscultation, etc.; should only be used after obtaining a complete history and exam.

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# Chapter 2
# Dynamic Auscultation

**Michael C. Mariorenzi, Amy Matson, and Christopher Sonne**

## Introduction

For many trained physicians, even novice cardiologists, the art of cardiac auscultation can be difficult to master. Being able to distinguish a murmur and determine the specific etiology can be challenging; however it is an indispensable skill for a cardiologist. One simple way to improve cardiac auscultation skills and more accurately determine the etiology of a murmur is to use dynamic auscultation maneuvers. The maneuvers alter the physiology and hemodynamics of the cardiovascular system and will accentuate or diminish in intensity specific murmurs, thereby guiding you to a more accurate differential diagnosis. All of these maneuvers can be easily performed in the examination room with minimal effort and with equipment that is readily available in any office setting.

## Respiration: S2 Splitting During Deep Inspiration

- The second heart sound represents the closure of the aortic and pulmonic valves. During deep inspiration, the two components of S2 become more distinct and can accentuate differentiation between right-sided vs. left-sided murmurs.
- A normal P2 sounds later during deep inspiration due to the increased blood flow through the pulmonic valve as a result of lowered intrathoracic pressure and increased venous return (Fig. 2.1).

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_2) contains supplementary material, which is available to authorized users.

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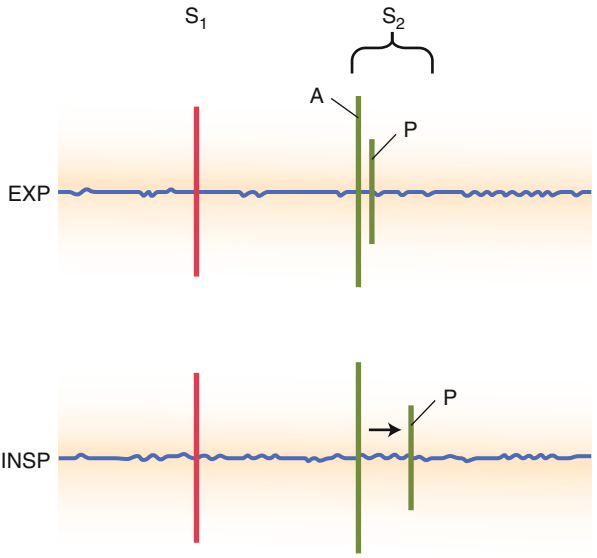


**Fig. 2.1** Normal splitting of S2 during inspiration. P2 sounds later during inspiration due to increased venous return and blood flow through the pulmonic valve (Used with permission of Texas Heart Institute)

- Accordingly, systolic murmurs that increase in intensity during deep inspiration are indicative of being right sided in origin.
- Pooled data from Rothman and Goldberger suggest that the sensitivity of the deep inspiration in diagnosis of tricuspid regurgitation is 61 % [1].

## The Valsalva Maneuver

- The Valsalva maneuver is performed by forcibly exhaling against closed glottis.
- Physiological response (Fig. 2.2): Venous return is reduced due to increased intrathoracic pressure and stroke volume is reduced due to increased mean arterial pressure during the strain phase of the Valsalva maneuver.
- The Valsalva maneuver diminishes nearly all systolic murmurs (Fig. 2.3), with the exception hypertrophic cardiomyopathy (HOCM) [2]. In a patient with HOCM, decreased left ventricular volume during the maneuver increases subaortic muscular obstruction increasing murmur intensity of HOCM.
- Diagnostic Value of Valsalva Maneuver for HOCM: Sensitivity: 65 %, Specificity: 96 %, Positive Predictive Value: 81 %, Negative Predictive Value: 92 % [3].
- The Valsalva maneuver can also help differentiate right vs. left heart murmurs. After release of the Valsalva maneuver, right-sided murmurs have been shown to return to baseline after two cardiac cycles while left-sided murmurs require 4–11 cycles to return to baseline intensity [4].

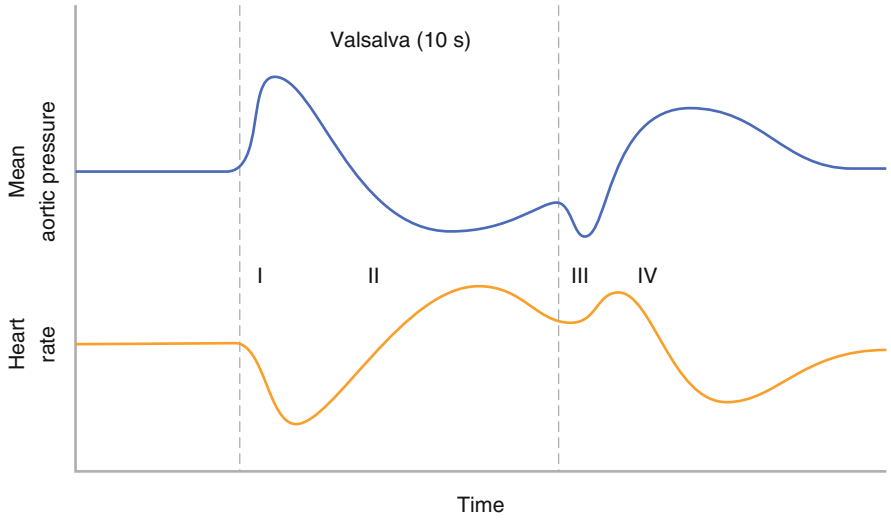


**Fig. 2.2** Physiological tracing of mean aortic pressure and heart rate during a valsalva maneuver

## Squatting and Standing

- To perform the maneuver: From a standing position, have patient squat down bringing knees to the axilla region. Auscultate as the patient remains squatting for approximately 30 s. This is most easily done while the physician sits beside the patient, so as to reduce movement and allow for better concentration. These maneuvers are best used to distinguish HOCM and Mitral valve prolapse.
- Physiological response: Squatting increases the venous return to the heart and additionally increases total peripheral resistance intensifying most systolic murmurs. The increased venous return allows for increased blood flow through a stenotic pulmonary and aortic valve, accentuating associated murmurs. Meanwhile, elevated peripheral resistance brought on by the maneuver increases murmurs of mitral and tricuspid regurgitant valves. See Fig. 2.4 [2].
- Importantly, squatting *diminishes* the HOCM murmur. During a squat, increased preload stretches the LV, reducing sub-aortic muscular obstruction.
- The decreased murmur intensity associated with HOCM during the squatting maneuver has been shown to have 95 % Sensitivity, 85 % Specificity, 61 % Positive Predictive Value, and a 99 % Negative Predictive Value [3].
  - Click here to listen to an example of the effect of squatting on HOCM as described by Dr. W. Proctor Harvey (Video 2.1).
- Squatting helps distinguish the origin of the systolic click of mitral valve prolapse. The Mitral Valve Prolapse Systolic "Click" moves away from S1 during the maneuver (Fig. 2.5).

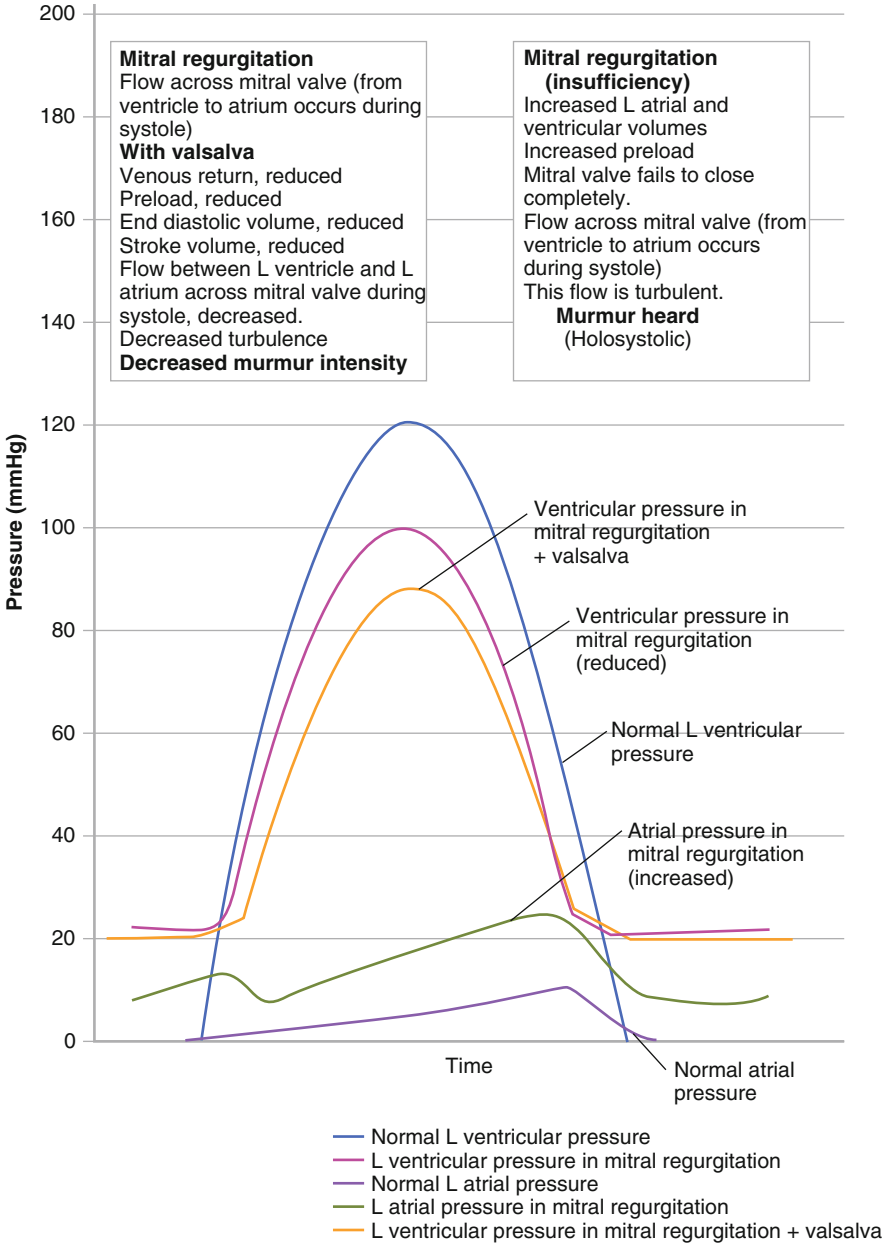


**Fig. 2.3** Atrial and Ventricular pressure tracings of a normal heart; resting heart with the common systolic murmur, mitral regurgitation (MR); and a heart with MR during a Valsalva maneuver. Note how the Valsalva maneuver reduces pressure in the ventricle due to decreasing venous return to the heart. The effect is a diminished intensity of the common systolic MR murmur (Used with permission from Salazar et al. [2])

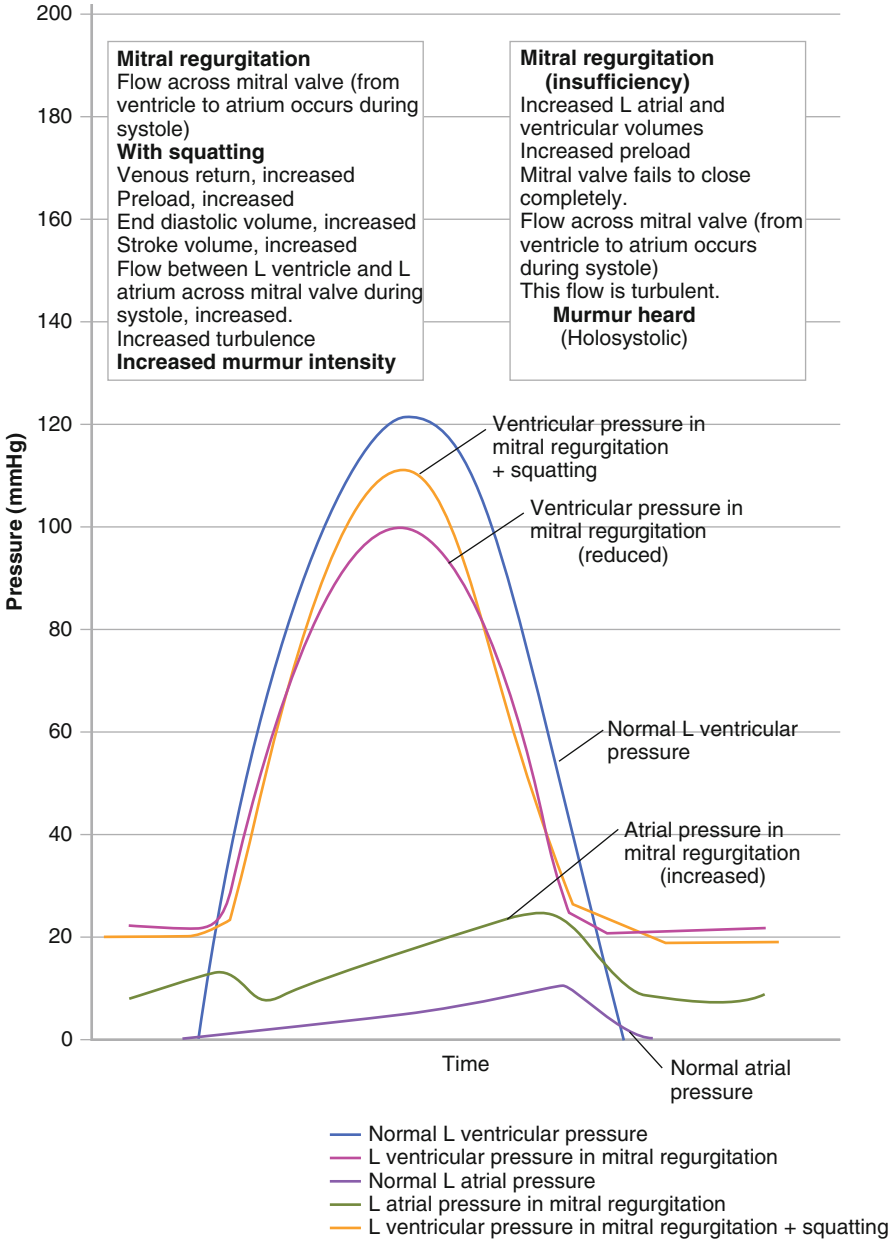


**Fig. 2.4** Atrial and Ventricular pressure tracings of a normal heart; resting heart with the common systolic murmur, mitral regurgitation (MR); and a heart with MR during a squatting maneuver. Note how the squatting maneuver increases pressure in the ventricle. This is due to increased venous return to the heart. Therefore, the effect of the maneuver is to increase the intensity of the common systolic MR murmur (Used with permission from Salazar et al. [2])

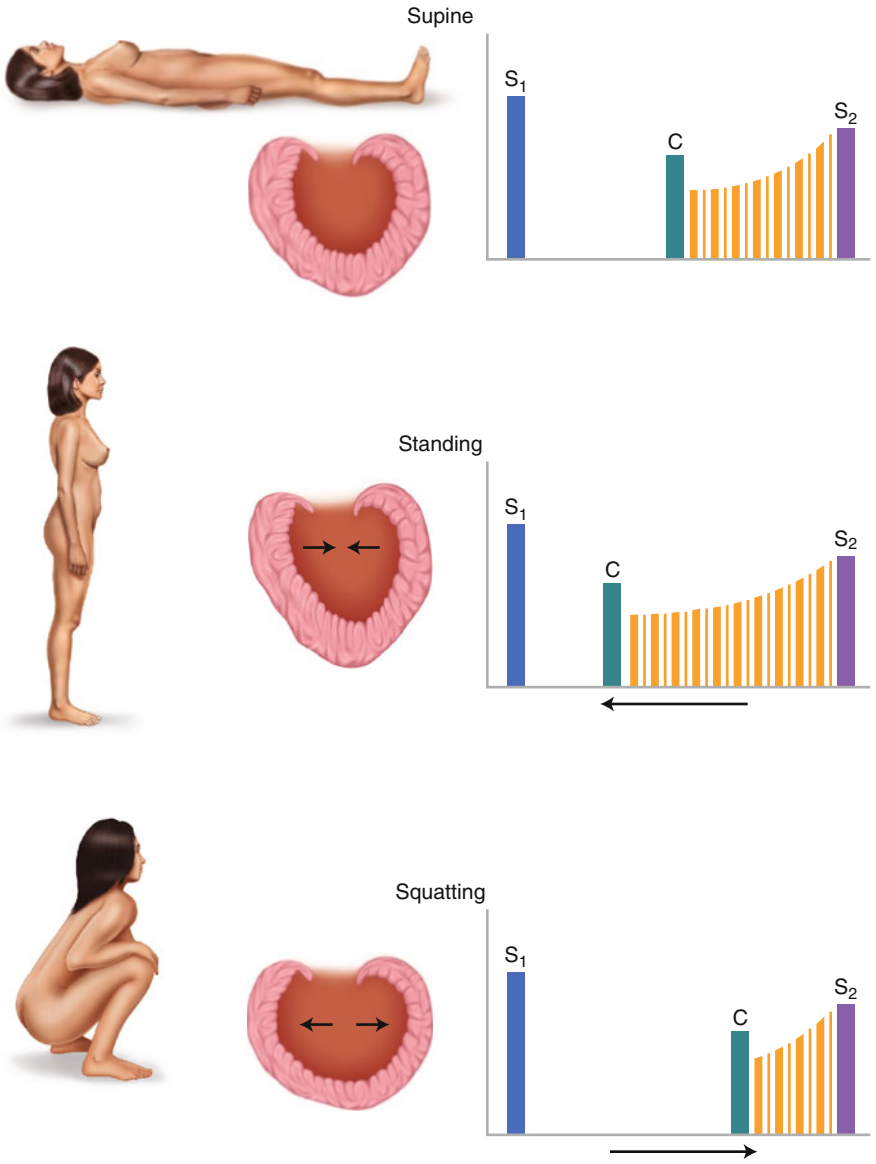


**Fig. 2.5** Dynamic auscultatory changes of the mitral valve prolapse click during standing and squatting compared to supine position. Standing decreases venous return moving the click closer to S1. Squatting increases venous return moving the click closer to S2 (Based on figure in the following source: Shaver et al. [6])

- Prompt standing from a squatting or supine position has also been shown specifically to accentuate the murmur of mitral valve prolapse in 74 % by at least 1 grade (Fig. 2.5) [4].

- In addition, standing quickly from a sustained squatted position or from a supine position will decrease venous return to the heart having the opposite effect of squatting; standing decreases most systolic murmurs while increasing the murmur of HOCM.
- Increased murmur intensity associated with HOCM: Sensitivity, 95 %; Specificity, 84 %; Positive Predictive Value, 59 %; Negative Predictive Value, 98 % [3].

## Passive Leg Elevation

- To perform the maneuver: While laying in the supine position, the patient holds their leg straight while it is passively raised to 45°. After 15–20 s, auscultation is performed again to listen for changes in murmur intensity.
- Physiologic response: Due to gravity, passive elevation of the leg displaces blood volume from the legs into the central compartment resulting in increased cardiac preload.
- Because the murmur of hypertrophic cardiomyopathy is caused by obstruction of the left ventricular outflow tract by the anterior leaflet of the mitral valve, the degree of obstruction is lessened when there is increased left ventricular volume.
- Passive leg elevation also *decreases* the intensity of the murmur of HOCM because increased preload stretches the LV lessening the obstruction of the left ventricular outflow tract. A decrease in intensity during passive leg elevation distinguished hypertrophic cardiomyopathy from other systolic murmurs with 85 % sensitivity and 91 % specificity. The majority of all other murmurs showed no change or slight increase in intensity [3].
- Passive leg elevation is very useful for distinguishing the murmur of hypertrophic cardiomyopathy in patients who are elderly or have musculoskeletal disease and cannot easily get out of bed because it requires no active participation.

## Isometric Hand Grip

- To perform the maneuver: Have the patient perform a sustained isometric handgrip exercise either using dynamometer or by making a fist and squeezing at maximal strength for 1 min. After 1 min, auscultation should be performed to detect changes in murmur intensity. The circulatory response can be induced in the supine or left lateral decubitus position and is related to intensity of contraction independent of muscle mass involvement.
- Physiologic response: Isometric handgrip increases HR that has been shown to be mediated by the release of vagal tone accompanied by an increase in sympathetic nervous system activity.

- An increase in blood pressure is also observed resulting from both an increase in heart rate, and thus cardiac output, as well as an increase in total peripheral resistance mediated by sympathetic nervous system activity.
  - The increase in total peripheral resistance results in an increase in afterload and therefore increases the intensity of murmurs related to conditions associated with backwards flow (e.g., mitral and aortic regurgitation, patent ductus arteriosus, and ventral septal defects). Murmurs that are related to conditions associated with forward flow (e.g., aortic stenosis and hypertrophic cardiomyopathy) will decrease. Click here to listen to an example of the effect of handgrip on a patent ductus arteriosus murmur as described by Dr. W. Proctor Harvey (Video 2.2).
- The murmurs of aortic and mitral regurgitation and ventricular septal defects increase in intensity due to elevation of aortic diastolic and left ventricular systolic pressure that accompanies isometric handgrip. Detecting an increase in intensity of these murmurs using isometric hand grip has a sensitivity of 68 %, specificity of 92 %, negative predictive value of 81 %. and positive predictive value of 84 % [3].
- Aortic stenosis murmurs decrease in intensity due to decrease in systolic gradient that results from increased total peripheral resistance.
- Changes of a HOCM murmur depend on the volume of blood in the left ventricle. Performing an isometric handgrip increases peripheral resistance (i.e., afterload) and increases the left ventricular volume. Consequently, the murmur observed in HOCM due to outflow tract obstruction will decrease with the increase in left ventricular volume. Detecting a decrease in intensity of this murmur using isometric hand grip has a sensitivity of 85 %, specificity of 75 %, negative predictive value of 95 %, and positive predictive value of 46 % [3].

## Transient Arterial Occlusion

- To perform the maneuver: Sphygmomanometer cuffs are placed on both of the patient's upper arms and they are inflated to 20–40 mmHg above the patient's known systolic blood pressure. After twenty seconds, auscultation is performed again to listen for changes in murmurs.
- Physiologic response: Occlusion of brachial arteries bilaterally causes increased left ventricular afterload. Transient arterial occlusion increases the intensity of left-sided regurgitant murmurs by decreasing compliance (increasing stiffness) of arterial vessels proximal to the cuff occlusion. Transient arterial occlusion has no effect on arterial pressures, heart rate, cardiac output, right atrial pressure, or systemic vascular resistance.

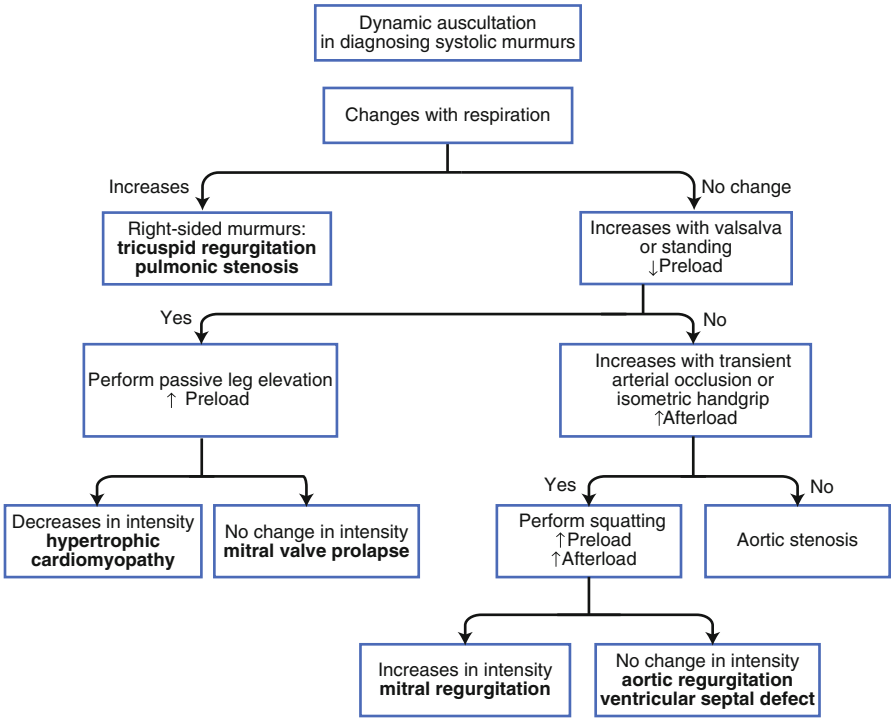


**Fig. 2.6** Dynamic auscultation algorithm. An example of how dynamic cardiac auscultation maneuvers can be used to differentiate murmur types

- Transient arterial occlusion intensifies the left-sided murmurs of mitral regurgitation, ventricular septal defect, and aortic regurgitation.
- The majority of other murmurs have not been shown to change or increase with transient arterial occlusion. There is no augmentation of murmurs that were not left-sided, therefore likelihood of false positives is decreased when compared with handgrip exercise and squatting. In a study by Lembo et al., transient arterial occlusion augmented murmurs of mitral regurgitation and ventricular septal defect with 78 % sensitivity and 100 % specificity [3, 5].

## Summary

See Fig. 2.6 for an algorithm that demonstrates how dynamic cardiac auscultation maneuvers can be used to differentiate murmur types.

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# Chapter 3
# Stethoscope Performance

**Maria Braileanu and Neelam Khan**

## Key Teaching Points

- No gold standard or guideline exists for selecting a stethoscope based on acoustic properties.
- Acoustic stethoscopes transmit low and high physiological frequencies and are portable and ergonomic.
- Electronic stethoscopes have a visual display and are capable of volume controlled frequency amplification.
- Scientific literature of stethoscope sound performance is limited and should be interpreted with caution.
- In general, the scientific literature suggests there is no statistically significant difference between acoustic stethoscopes.
- Albeit controversial, most studies have shown no significant difference between electronic or acoustic stethoscopes.

## Acoustic Stethoscopes

### *Basic Structure of Acoustic Stethoscopes (Fig. 3.1)*

- The chest piece.
  - The bell is used for low frequency sounds.

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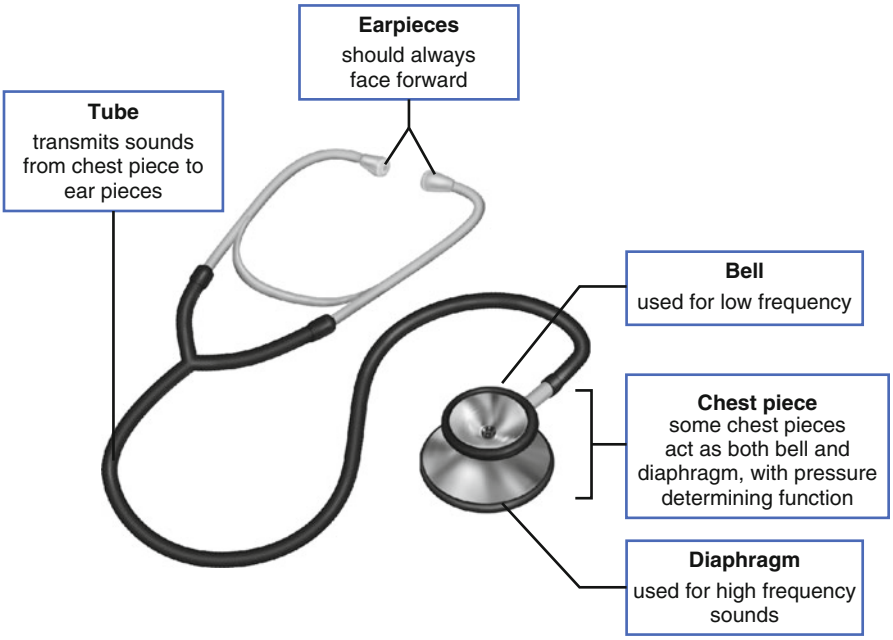



**Fig. 3.1** Acoustic stethoscope

  - The diaphragm is used for high frequency sounds.
  - Some chest pieces act as both the bell and diaphragm, with pressure determining function.

- The tube transmits the sound from the chest piece to the ear pieces.
- Earpieces.

  - A variety exist for the comfort of the wearer.
  - Should always face forward.

## *Sound and Physiologic Frequencies (Fig. 3.2)*

- Sound is the oscillation of pressure through a medium, such as air. The frequency of a sound wave is perceived as pitch, and the amplitudes at intensity or loudness [1].
- The average normal hearing range of a person is 20–20,000 Hz [1].
- The range of clinically important heart and lung sounds is 20–1000 Hz [2]. Systolic murmurs, mitral diastolic murmurs, and S1 – S4 sounds range from 20 to 115 Hz, pericardial rubs, pulmonary regurgitation, and aortic regurgitation range from 140 to 600 Hz [2], while mechanical heart sounds are heard at ranges over 1000 Hz [3].

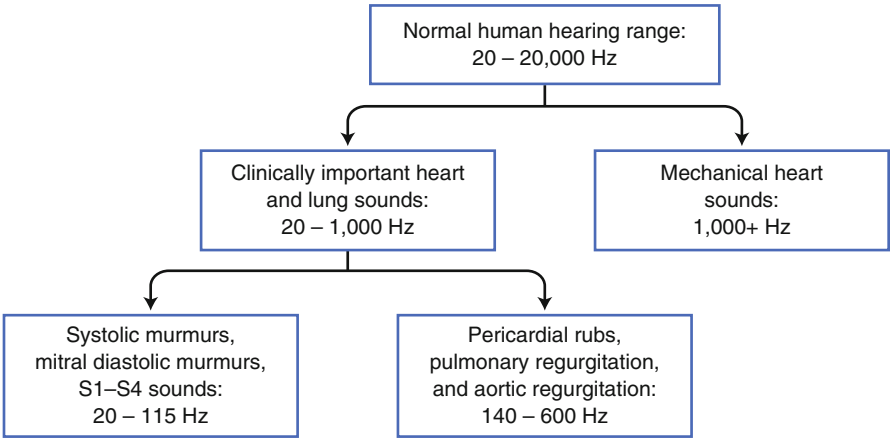



**Fig. 3.2** Ranges of sound frequency (Data from Welsby and Earis [1]; and from Abella [2]; and from Grenier et al. [3].)

- In the clinic and scientific literature, cardiac sounds are commonly characterized using ambiguous terms such as "low" and "high" frequency.

## *Characteristics of the Ideal Acoustic Stethoscope*

- Largest ear tips possible for a good seal in the external auditory canal.
- Adjustable angled metal headpiece.
- Internally smooth double vinyl tubing.
  - Shorter tubing provides less sound loss in transmission.
- Separate bell and diaphragm.
  - Large diameter bell for low frequencies.
  - Smooth, stiff, and thin diaphragm for high frequencies.

## *Physical Factors Affecting Sound Transmission*

From the patient's body surface to the earpiece, factors influencing sound transmission include [2]:

- Thickness of clothing worn by patient [4].
- Pressure and degree of mechanical contact on the body surface by the chest piece.
- Size and volume of bell.

- Surface hardness of the bell cavity.
- Diaphragm thickness, size, and tautness.
- Inside diameter of the tube.
- Rigidity, length, and interior surface smoothness of the tube.
- Acoustical characteristics of the human ear.
- Air leaks between components, such as chest piece and body surface or at the ears.
- Ambient noise limiting auscultation [5].

## *Selection of an Acoustic Stethoscope*

- In 1940, a study found that medical professionals choose stethoscopes not based on the acoustic properties of the instrument, but rather on the basis of exterior finish and features, as well as on the recommendation of mentors and peers [2]. This seems true even today.
- Currently there is no gold standard or guideline in selecting a stethoscope. This is mainly due to limited data. Furthermore, the little evidence available suggests differences may be subtle [2], with unknown clinical relevance.

## *Comparisons Between Acoustic Stethoscopes*

- One study by Iversen et al. compared the clinical performances of a high cost advanced stethoscope to a low cost basic stethoscope [6].
  - They used the 3M™ Littmann® Master Cardiology™ stethoscope (3 M, Cerritos, CA, USA) (higher cost and advanced) and the 3M™ Littmann® Classic II™ SE stethoscope (3 M, Cerritos, CA, USA) (lower cost and basic).
  - The two stethoscopes were randomly distributed to 72 house officers without formal training in auscultation in 10 different hospitals. After using the stethoscopes for 4 weeks, participants examined 20 patients (16 with murmurs). Diagnostic accuracy was measure.
  - 33 % of patients were diagnosed correctly with the simple scope, while 35 % were diagnosed correctly with the advanced stethoscope (no statistically significant difference).
  - The authors concluded that using a more advance and expensive stethoscope does not improve the rate of murmur detection and diagnosis made by house officers.
- A limited number of articles in recent scientific literature have compared the acoustic properties of different brand stethoscopes [2, 7, 8].
  - One study [2] analyzed six stethoscopes including the Littmann® Classic II™ (3M™, St. Paul, MN, USA), the Littmann® Cardiology II™ (3M™,

**Table 3.1** Comparison of six different brand stethoscopes examined by Abella et al. The three diaphragms that amplified the low frequency sounds were all Littmann® (3M, Cerritos, CA, USA) stethoscopes

| | Bell – amplification | Bell – attenuation | Diaphragm – amplification | Diaphragm – attenuation |
|---|---|---|---|---|
| Low frequencies | 6 | – | 3 | 3 |
| High frequencies | – | 6 | – | 6 |

Data from: Abella et al. [2]

St Paul, MN, USA), the Littmann® Master™ (3M™, St. Paul, MN, USA), the Hewlett-Packard® Rappaport-Sprague™ (Hewlett-Packard®, Palo Alto, CA, USA), the Tycos® Harvey™ Triple Head (Welch Allyn®, Skaneateles Fall, NY, USA), and the Allen® Medical Series 5A™ (Allen®, Acton, MA, USA) (Table 3.1).

- The acoustic transfer function (ratio of sound pressure at the earpiece to sound pressure at the chest piece) was used to compare the stethoscopes.
- At low frequencies (37.5–112.5 Hz), all six bell pieces amplified the sound. Only the three Littmann diaphragms, however, amplified the low frequency sounds. Relative lower performance was statistically significant for Tycos® Harvey™ Triple Head ribbed diaphragm, the Hewlett-Packard® small diaphragm, and the Allen® Medical Series 5A™ diaphragm.
- At high frequencies (125–1000 Hz), all six bell pieces and diaphragms attenuated but did not amplify the sound. Of the diaphragms, attenuation by the Tycos® Harvey™ Triple Head ribbed diaphragm was statistically significantly lower.
- The authors concluded the Littmann® Cardiology II™ had the best overall performance. Generally speaking, sound attenuation between stethoscopes was not significantly different.

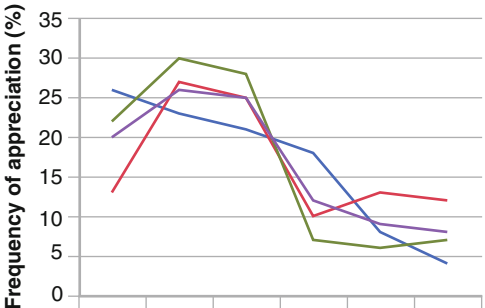
## Characteristics of Electronic Stethoscopes (Fig. 3.3)

- The basic structure of an electronic stethoscope resembles a conventional stethoscope [3].
  - Head and chest piece.
  - Sound transducer.
  - Adjustable gain amplifier.
  - Frequency filters.
  - Mini-speaker.
  - Batteries.

**Fig. 3.3** Example of Electronic Stethoscope: 3M™ Littmann® Electronic Stethoscope Model 3200 (Copyright © 3M Littman Stethoscopes, St. Paul, MN, USA. Used with permission)

- Some models can be attached to an acoustic stethoscope, converting it into an electronic device [9].
- The chest piece can be switched from a bell to a diaphragm without interruption in auscultation [10]. Certain models also have an automated mute mode to lessen impact noise [3].
- Cardiac sounds are transmitted by a wire; therefore, there is no tubular noise or limit on length [3]. Older models may suffer from background electronic noise [3], although newer stethoscopes have the capabilities to filter electronic noise [10].
- Users can choose whether to amplify all sounds or only certain frequencies, with the user controlling the volume [9, 10]. Ambient noise can be filtered (Littmann.com).

- Visual display for heart rate, or phonocardiogram (Littmann.com).
- Cardiac sounds can be recorded and transferred to a computer or Bluetooth device (Littmann.com). Once on a computer, sounds can be played back at various speeds in conjunction with waveform and spectral displays, stored, and compared. This aspect has been used to record cardiac murmurs for transmission via email to a physician for evaluation [11–13].

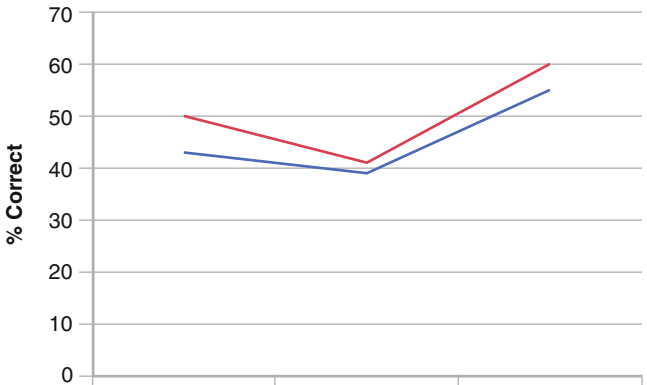



| | Harvey Elite (Welch Allyn) | Cardiology II (Littmann) | Rappaport-Sprague (Hewlett-Packard) | Labtron (Graham Field) | EST40 (Bosch) | ST3 (Starkey) |
|---|---|---|---|---|---|---|
| Nurses | 26 | 23 | 21 | 18 | 8 | 4 |
| General practitioners | 13 | 27 | 25 | 10 | 13 | 12 |
| Cardiologists | 22 | 30 | 28 | 7 | 6 | 7 |
| Mean | 20 | 26 | 25 | 12 | 9 | 8 |

**Fig. 3.4** Comparison of six stethoscopes among different health care professionals. The frequency of appreciation is based on the number of times a stethoscope was preferred over the others for each evaluation performed. The acoustic stethoscopes are Littmann® Cardiology II™ (3M, Cerritos, CA, USA), Tycos® Harvey™ Elite (Welch Allyn®, Skaneateles Fall, NY, USA), and Hewlett-Packard® Rappaport-Sprague™ (Hewlett-Packard®, Palo Alto, CA, USA), and the electronic are Graham Field® Labtron® (Graham Field®, Hauppage, NY, USA), Bosch® EST40™ (Bosch®, Berlin, Germany), and Starkey Laboratories® ST3™ (Starkey Laboratories®, Minneapolis, MN, USA) (Tabular portion used with permission from Grenier et al. [3])

## Comparisons Between Acoustic and Electronic Stethoscopes

- A comparative clinical survey study in the early 1990s found that cardiologists, general practitioners, and nurses preferred acoustic stethoscopes to electronic [3].
  - Three acoustic stethoscopes (Littmann® Cardiology II™ (3M™,St. Paul, MN, USA), Tycos® Harvey Elite (Welch Allyn®, Arden, NC, USA), and Hewlett-Packard Rappaport-Sprague (Hewlett-Packard®, Andover, MA, USA)) were compared to three electronic stethoscopes (Graham Field® Labtron® (Graham Field®, Hauppage, NY, USA), Bosch® EST40™ (Bosch®, Berlin, Germany), and Starkey Laboratories® ST3™ (Starkey Laboratories®, Minneapolis, MN, USA)) (Fig. 3.4).
  - For each patient examined three stethoscopes were randomly assigned. After three successive auscultations, participants evaluated the stethoscope performance on 13 different criteria ranging from sound attenuation to comfort. Overall 378 comparative evaluations and 1134 auscultations were performed.
  - Acoustic stethoscopes were rated superior 71 % of the time, while electronic were preferred only 29 % of the time.
  - Noted limitations of the acoustic stethoscope included lack of amplification and imperfect attenuation of lower frequency sounds. Subsequently, participants had to apply high pressure on the earpiece to hear.
  - Noted limitations of the electronic stethoscope included electronic noise, as well as sensitivity to impact and ambient sounds, no standard bell and diaphragm filtering, and poor design.
- Another study found no significant difference in observer agreement between clinicians using acoustic stethoscopes (Littmann® Classic II SE™ (3M™, Copenhagen, Denmark) acoustic stethoscope) and those using electronic stethoscopes (Littmann® electronic stethoscope, model 4000™ (3M™, Copenhagen, Denmark)) [14].
  - Participants included cardiologists, internal medicine practitioners, specialist registrars, senior house officers, house officers, and medical students. The two stethoscopes were randomly and evenly distributed to participants in each group. After using the assigned stethoscope for 4 weeks, 26 patients (1008 examinations) were evaluated by participants in 14 categories, including cardiac and lung sounds.
  - Agreement was statistically stronger between participants using the electronic stethoscope when diagnosing systolic murmurs at the apex of the heart, and lung rhonic sounds compared to agreement between acoustic stethoscope users. Otherwise, there was no significant difference in agreement between the two groups in the other 12 categories, or when combining all sounds.
- Similarly, data shows that using an acoustic or electronic stethoscope in training does not improve performance on cardiac auscultation [15].




| | Grading of murmurs | Characterization of murmurs | Report of false murmurs |
|---|---|---|---|
| Electronic stethoscope | 43 | 39 | 55 |
| Acoustic stethoscope | 50 | 41 | 60 |

**Fig. 3.5** Comparison of student performance after training with an acoustic stethoscope vs. an electric. No significant difference was found between the two (Tabular portion used with permission from Hoyte et al. [15].)

**Table 3.2** Comparison of electronic and acoustic stethoscopes aboard a Boeing C135 and a Falcon 50 (cardiac auscultation)

| | Electronic stethoscope | Acoustic stethoscope | *P* – value |
|---|---|---|---|
| Boeing C135 | 85 ± 11 | 53 ± 24 | 0.0024 |
| Falcon 50 | 6.4 ± 1.9 | 5.8 ± 1.5 | 0.018 |

Data from: Tourtier et al. [16, 17]
Values are based on a visual rating scale for the C135 (0 – I hear nothing, 100-I hear perfectly) and a numerical rating scale for the Falcon 50 (0 – I hear nothing, 10 – I hear perfectly)

  - Of the 48 third year medical students enrolled in a four-month class, half used an acoustic stethoscope of their choice, and half were assigned an electronic stethoscope (Fig. 3.5).
  - Patients in the study were examined by two cardiologists using acoustic stethoscopes, and afterwards by the medical students. Questionnaires were collected from the students and graded.
  - No significant difference in performance was observed between the group of students using the electronic stethoscope and those using the acoustic.

- Two auscultation studies performed aboard airplanes, however, suggest electronic stethoscopes may improve the subjective perception of cardiac sounds.

- In both cases the acoustic stethoscope used was a Littmann® Cardiology III™ (3M™, St. Paul, MN, USA) stethoscope. The electronic stethoscope was a Littmann® Electronic Stethoscope Model 3000™ (3M™, St. Paul, MN, USA) in the study aboard a Boeing C135 [16], and a Littmann® Electronic Stethoscope Model 3100™ (3M™, St. Paul, MN, USA) in the study aboard a Falcon 50 [17]. See Table 3.2.
- On the C135 (88 dB ambient noise), physicians, experienced in medical air transport, made 36 comparative evaluations. Stethoscopes were randomly selected for each patient. A visual rating scale of 1–100 was used to evaluate perception of cardiac and pulmonary sounds. Improved perception of sound when using the electronic stethoscope compared to the acoustic was statistically significant for both cardiac and pulmonary sounds.
- On the Falcon 50 (77 ± 1 dB ambient noise), 32 comparative evaluations were made by physicians experienced in medical air transport. Participants were blinded with a mask, while an independent physician placed the randomly selected stethoscope on the patient. A rating scale of 0–10 was used to describe perception of sound. On cardiac examination the small perceived improvement using the electronic stethoscope was statistically significant. There was no significant difference in pulmonary sound auscultation using the electronic stethoscope compared to the acoustic.

## Beyond the Stethoscope: Precautions

Ultimately, a stethoscope is only as good as the person using it. In a study, 46 % physicians reporting "good" hearing were shown to have audiometric hearing loss. Increasing age or hearing threshold levels were not a predictor of self-reported stethoscope difficulties; 51 % of participants never took precautions when around loud noises [18]. After finding a stethoscope they are comfortable with, medical personnel should take measures to protect their ear function.

## Stethoscope Apps

This list is meant to help introduce the reader to app based clinical tools for auscultation; it is not exhaustive and not all apps may be available.

- 3M™ Littmann® SoundBuilder (3M™, St. Paul, MN, USA) (Free) – 14 lessons on key heart sounds.
- Thinklabs® iMurmur 2 App (Thinklabs®, Centennial, CO, USA) ($5.99) – 16 cardiac sounds with phonocardiograms and clinical notes.
- iStethoscope Expert 2013 (Anna Chan) ($0.99) – Assess sounds recorded with the iPhone.
- Mobile Stethoscope ($3.99) (Keaten House, Ltd,) – Record heart sounds using iPhone; phonocardiogram display.

- Thinklabs® Stethoscope App (Thinklabs®, Centennial, CO, USA) ($3.99) – Record a cardiac sound with an electronic stethoscope or iphone; real time waveform and spectral display; save, recall, and email.

## Future of Stethoscopes

- Wireless auscultation was first developed in the late 1980s to help anesthesiologists monitor patients during surgery [19]. More recently tele-stethoscope systems allow physicians to monitor patients in rural areas [20].
- An "auscultation jacket" with embedded electronic stethoscopes and processing software was developed for semi-automated diagnosis; this may be especially helpful in underserved regions [21].

## Conclusions

- Ironically, the first stethoscope was invented not to improve auscultation, but for a more "aesthetic" reason; namely to avoid the embarrassment of placing one's ear on a lady's chest. This legacy is still in existence today as stethoscopes are not chosen based on their acoustic properties.
- There are few completely objective or blind studies comparing stethoscope performance. Results should be interpreted with caution, especially surveys or comparative studies based on participant opinion.
- Differences between acoustic stethoscopes are subtle. Using an acoustic or electronic stethoscope does not change clinical outcomes. Because of the limited data, stethoscope selection will probably continue to be based on personal preference.

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# Part II
# Valvular Lesions: Aortic Valve

# Chapter 4
# Aortic Sclerosis

**Armond Esmaili, Robert A. Christian, and Ashley C. Pfaff**

## Key Teaching Points

- Aortic valve sclerosis (AVS) is a common, acquired valvular condition characterized by fibrosis, thickening, and calcification of the aortic cusps without concomitant absence of outflow obstruction.
- AVS shares similar risk factors to atherosclerosis and is associated with increased risk of coronary artery disease (CAD) and myocardial infarction (MI). AVS may be a marker of CAD.
- AVS has been described as a "50–50 murmur," meaning that it is present in approximately 50 % of the population at age 50.
- Auscultation findings include the presence of an early to mid-systolic ejection murmur (often soft), normally split S2, no click at the 2nd right interspace (aortic valve area).
- Carotid pulses are normal in cases of AVS and help distinguish AVS from murmurs associated with ventricular outflow obstruction.
- AVS is not associated with aortic regurgitation. If aortic regurgitation is found on auscultation, AVS as the sole abnormality is likely not present.
- Due to its similar pathologic appearance to atherosclerosis, coronary risk factor modification could potentially slow AVS progression.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_4) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- A 63-year-old male presents to his cardiologist for an annual check-up. He has a 35-pack-year history of smoking and a past medical history characteristic of hypertension and hyperlipidemia. The patient remarks that he has been trying to control his cholesterol for years with diet and exercise modifications.

### *Physical Exam*

- Vital Signs: BP 138/90 mmHg, Pulse 62 beats per minute, BMI 27.8 kg/m$^2$.
- Physical examination was largely unremarkable except for a soft, early to mid-systolic ejection murmur in the 2nd right interspace with a normally split S2 without a click (Fig. 4.1).
- The carotid pulses were normal.

### *Test Results*

- LDL 170 mg/dL, TG 330 mg/dL, HDL 35 mg/dL.
- An echocardiogram was performed showing aortic valve nodular thickening with an upper normal aortic jet velocity of 1.9 m/s (Fig. 4.2).

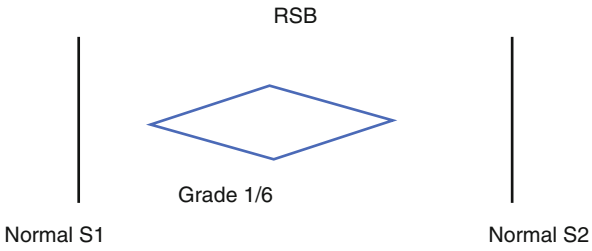


**Fig. 4.1** Aortic valve sclerosis is characteristically a soft, early to mid-systolic ejection murmur in the 2nd right interspace with a normally split S2 without a click

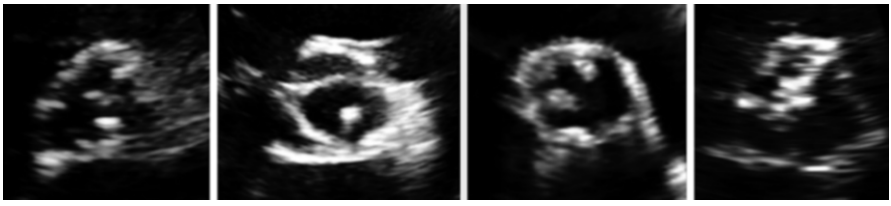

**Fig. 4.2** Images showing echocardiographic appearance of aortic valve sclerosis in the parasternal short axis view. Images show from *left* to *right*: Mild AVS in its typical location in the noncoronary cusp, mild AVS in an atypical location involving the left coronary leaflet, Moderate aortic valve sclerosis, and severe AVS

## Clinical Basics

### *Definition*

- AVS has been variably defined across literature. In general, AVS is characterized using echocardiographic imaging by [1, 2]:
  - Calcification and thickening of a tri-leaflet aortic valve.
  - Absence of ventricular outflow obstruction.
  - Aortic jet velocity <2.0 m/s on echocardiogram.
- Variant criteria describing AVS have also involved: irregular, non-uniform thickening of portions of the aortic valve leaflets and/or commissures; thickened portions of the aortic valve with calcific appearance; non-restricted or minimally restricted opening of the aortic cusps; and aortic jet velocity <2.5 m/s [2, 3].

### *Etiology*

- The etiology of AVS may stem from the fibrosis, thickening, and calcification of aortic cusps. In this way, the precipitating factors of AVS closely resemble those of atherosclerosis [4].
- Inflammatory cell infiltrates, oxidized LDL, and osteopontin calcification characterize sclerotic lesions of the aortic valve. These lesions differ from atherosclerotic plaques, however, because AVS lesions have a greater calcium load, uncoupled nitric oxide synthase, and are absent of smooth muscle cell proliferation [2].
- Current studies suggest that leaflet and aortic changes are due to an active disease process characterized by sub-endothelial lesions on the aortic side of the leaflets [1]. Theories propose that these changes may be due to calcium spurs on aortic valve cusps or atherosclerotic plaques in the ascending aorta that contribute to turbulent flow [3]. This stands in contrast to previous beliefs that leaflet and aortic changes are due to a non-specific, age-related degenerative process.

### *Signs and Symptoms*

- AVS is an asymptomatic condition that is usually only apparent with auscultation. Its sole sign is an ejection flow murmur with a normally split S2 [4].
- Click here to listen to an example of an elderly patient with an early mild ejection murmur, classically referred to as the “innocent murmur of the elderly,” unrelated to stenosis of the aortic valve, as described by Dr. W. Proctor Harvey (Video 4.1).

### *Prevalence*

- The prevalence of AVS is relative to the age of the patient or population [4].
- AVS has been described as a "50–50 Murmur," meaning that it is present in about 50 % of the population at the age of 50 [4, 5]. From a population perspective, AVS remains an important murmur due to its high prevalence in the aging population.
- The prevalence of AVS drops to 30 % of the population at age 50 in more selected patient populations without prevalent cardiovascular disease or left ventricular hypertrophy [3].
- Risk factors associated with AVS are similar to those of atherosclerosis and typically include: increasing age, male gender, smoking, HTN, and elevated LDL cholesterol [1, 2]. However, there is some controversy over the association of AVS with gender. Some evidence suggests that AVS may be twice as likely in females [3].

## Auscultation Differential Diagnosis

- AVS is an ejection murmur.
  - Ejection murmurs are the result of forward bloodflow through a semilunar (aortic or pulmonary) valve during systole. Ejection murmurs begin at the end of the first heart sound (S1), are crescendo-decrescendo in loudness, end before the second heart sound (S2) on the side of the heart from which the murmur originates, and are louder after long diastoles [4].
  - The two most common types of ejection murmurs are systolic flow murmurs (murmurs due to causes other than obstruction to flow) and a semilunar valve stenosis ejection murmur [4].
- AVS can be classified as a systolic flow murmur, meaning there is no obstruction to flow [4]. There are five key causes of systolic flow murmurs, and the differential diagnosis upon auscultation of a systolic flow murmur should include [4]:
  - AVS.
  - Ejection into a dilated artery.
  - Increased stroke volume or rate of ejection (e.g., anemia, hyperthyroidism).
  - Normal 'impulse gradient' (a murmur only perceivable because of a thin chest or quiet room).
  - Still's Murmur.

## Clinical Clues to the Detection of the Lesion

- AVS should be suspected on auscultation by its characteristic hallmarks [4]:
  - Soft, early- to mid-systolic ejection murmur in the second right interspace (aortic valve area).

  - Normally split S2.
  - Normal volume carotid pulses.

- It is important to differentiate AVS from other systolic murmurs, including those due to aortic stenosis, hypertrophic cardiomyopathy, and a bicuspid aortic valve [4].
  - Similar to AVS, bicuspid aortic valves also produce early ejection murmurs that are loudest in the 2nd right interspace. In contrast to AVS, non-stenotic bicuspid aortic valves are commonly associated with a louder A2 than normal and mild aortic regurgitation [4].
  - A murmur due to AVS will typically be low grade in terms of loudness, however, grade 3 or greater murmurs can arise from AVS. Such murmurs can be distinguished from aortic stenosis by palpating the carotids. Palpation of the carotids can typically differentiate between the normal rate of rise of the carotids in AVS and the slow rise of the carotids in aortic stenosis [4].
  - AVS should diminish with maneuvers that diminish ventricular volume and flow (e.g., Valsalva) whereas such murmurs will be accentuated in the setting of hypertrophic cardiomyopathy.
- AVS is rarely associated with aortic regurgitation. Thus, if aortic regurgitation is heard, AVS is likely not present [4].
- Upon suspicion of AVS by auscultation, echocardiography is the gold standard diagnostic tool to confirm AVS. Echocardiography of AVS typically shows mitral annulus calcification, coronary artery calcification, and an aortic jet velocity <2.0 m/s [1, 2].

## Diagnostic Implications of the Auscultation Features

- Currently, there are no objective and established guidelines to classify the severity of AVS according to auscultation features.
- Several studies have attempted to characterize AVS severity according to echocardiography features. AVS severity has been graded on a scale from 1–3 based on the amount of aortic leaflet calcification, echocardiography density, aortic valve calcification thickening, aortic leaflet motion, and aortic valve pressure gradient [6, 7] (Fig. 4.2).
  - Grade 1 or ‘mild’ involves minor calcification of one leaflet and increased echocardiography density.
  - Grade 2 or ‘moderate’ involves minor calcification of two leaflets or major calcification of one leaflet with valve thickening of calcific deposits >3 mm.
  - Grade 3 or ‘severe’ involves calcification of all three leaflets or extensive calcification of two leaflets, calcific deposits >3 mm, mildly restricted motion of aortic leaflets, and an aortic valve pressure gradient <16 mm.
- It is unknown if auscultation can distinguish between mild, moderate, and severe aortic sclerosis as defined by imaging. However, as noted below, an auscultation diagnosis of AVS may increase the need for surveillance for progression to aortic stenosis.

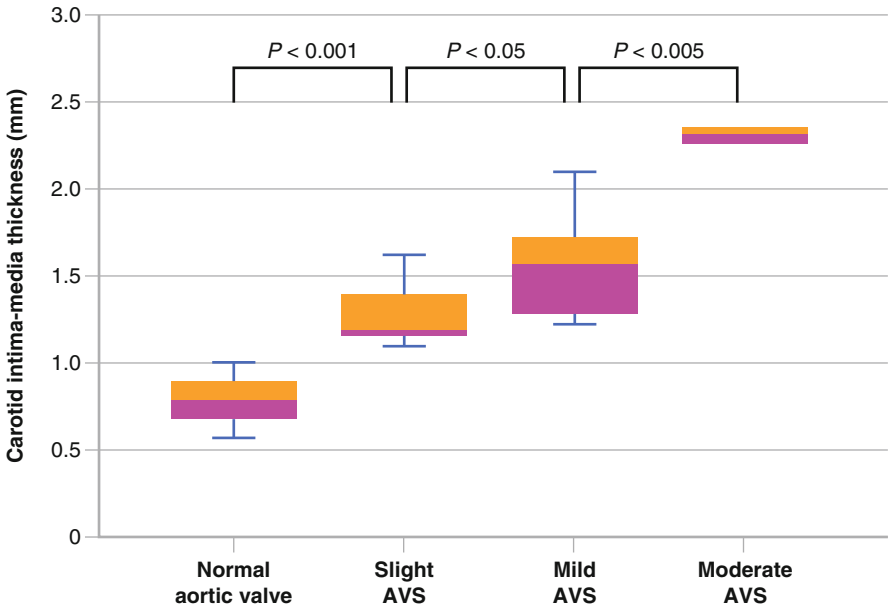


**Fig. 4.3** Among a Japanese study of 252 health volunteers aged between 25 and 65 years old, echocardiography and carotid ultrasonography showed that carotid intima media thickness was significantly greater in those with aortic valve sclerosis, which persisted after adjustment for cardiovascular risk factors (Used with permission from Yamaura et al. [8])

- AVS is associated with both subclinical atherosclerosis and coronary artery disease.
  - Among a Japanese study of young to middle age individuals, carotid intima media thickness was greater in those with AVS, which persisted after adjustment for cardiovascular risk factors (Fig. 4.3) [8].
  - Particularly in younger individuals (<65 years of age), AVS suggests increased odds of coronary artery disease (threefold) (Fig. 4.4).

## Prognostic Implications of the Auscultation Features

- AVS is considered a potential 'precursor lesion' to aortic stenosis. Patients with AVS are at higher risk for developing aortic stenosis with left ventricular outflow obstruction [1–3, 9, 10].
  - Calcification, fibrosis, and leaflet stiffness in AVS can increase progressively. This can lead to a reduced systolic opening and an increase in forward velocity that causes hemodynamic abnormality [1–3, 9, 10].

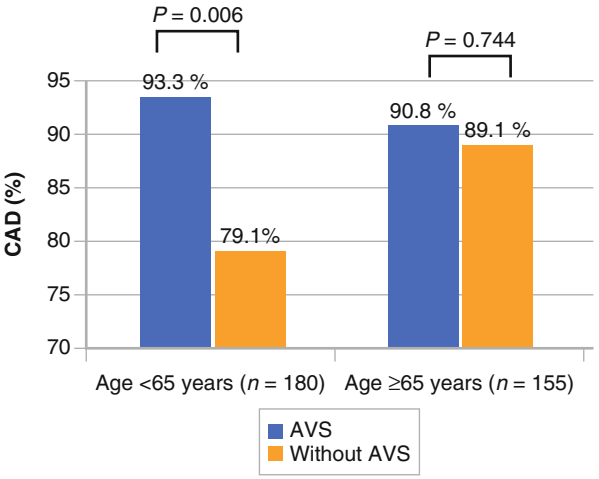


**Fig. 4.4** Study of 367 Chinese men and women showing an odds ratio of 3.18 for presence of significant coronary artery disease with aortic valve sclerosis is present (Used with permission from Hsu et al. [22])

  - In one prospective trial of 2,131 patients with AVS followed over 7 years, 16 % of patients developed aortic stenosis [11].
  - In another study with 400 AVS patients, almost one-third (32.8 %) of patients developed aortic stenosis within 14–74 months. After 5 years, 8 % of patients developed severe aortic stenosis and 44 % developed mild aortic stenosis [12].

- There is a strong association between AVS and cardiovascular mortality and morbidity both in patients with and without known CV disease (Table 4.1).
  - In a retrospective study of 5,621 adults in the community age 65 or older participating in the Cardiovascular Health Study, AVS was associated with a 23 % increased risk of all-cause mortality and a 45 % increase in CV mortality after 5 years. AVS was also associated with 17 % increased odds of MI and 24 % increased odds of angina. Higher risk of MI and CHF were also observed in AVS patients without CAD compared to patients with CAD [13].
  - In a prospective study of 1,980 older adults (mean age 81), AVS was associated with a 76 % increase in the risk of MI or sudden cardiac death [14].
  - In a retrospective subgroup analysis of 945 patients with hypertension in the LIFE trial, AVS was associated with a 1.5-fold increased risk of the composite outcome of CV death, stroke, or MI [15].
  - In a retrospective study of 814 patients with CAD, AVS was associated with a 2.4-fold increased risk of MI [16].

- Importantly, the association between AVS and increased risk for serious cardiovascular events and mortality appears to persist even when age, sex, CV disease risk factors, treatment status, and known CV disease are controlled [15, 17]. Thus, AVS may serve as an objective marker of other forms of cardiovascular

**Table 4.1** Base-line characteristics of the subjects with normal aortic valves, those with sclerotic valves, and those with stenotic valves, and event rates in a mean 5 year follow-up

| Characteristic | Normal aortic valves (N = 3,919) | Aortic sclerosis (N = 1,610) | Aortic stenosis (N = 92) | P value for trend |
|---|---|---|---|---|
| Mean ± SD age—year | 72.1 ± 5.2 | 74.7 ± 6.0 | 75.8 ± 6.1 | < 0.001 |
| | | *Number* (*percent*) | | |
| Sex—no. (%) | | | | |
| Female | 2,372 (60.5) | 818 (50.8) | 45 (48.9) | <0.001 |
| Male | 1,547 (39.5) | 792 (49.2) | 47 (51.1) | |
| Current smoking—no. (%) | 452 (11.6) | 191 (11.9) | 13 (14.1) | 0.43 |
| History of hypertension—no. (%) | 1,724 (44.0) | 833 (51.7) | 47 (51.1) | <0.001 |
| History of diabetes—no. (%) | 446 (11.4) | 211 (13.1) | 6 (6.5) | 0.90 |
| Coronary heart disease—no. (%) | 673 (17.2) | 383 (23.8) | 22 (23.9) | <0.001 |
| Renal Insufficiency—no. (%)[a] | 182 (4.8) | 123 (8.1) | 16 (17.8) | <0.001 |
| Impaired ability to perform activities of daily living—no. (%)[b] | 1,039 (26.6) | 526 (32.8) | 28 (30.8) | <0.001 |

| Event | Normal aortic valves (N = 3,919) | Aortic sclerosis (N = 1,610) | Aortic stenosis (N = 92) | P value for trend |
|---|---|---|---|---|
| Death from any cause | 583 (14.9) | 353 (21.9)[a] | 38 (41.3)[a] | <0.001 |
| Death from cardiovascular causes | 238 (6.1) | 162 (10.1)[a] | 18 (19.6)[a] | <0.001 |
| Myocardial infarction[b] | 217 (6.0) | 123 (8.6)[+] | 9 (11.3)[+] | <0.001 |
| Angina[b] | 358 (11.0) | 160 (13.0) | 17 (24.3)[a] | 0.001 |
| Congestive heart failure[b] | 337 (8.9) | 192 (12.6)[a] | 21 (24.7)[a] | <0.001 |
| Stroke[b] | 238 (6.3) | 122 (8.0)[++] | 10 (11.6)[++] | 0.003 |

Modified with permission from Otto et al. [13]

[+]p < 0.01 for the comparison with the group of normal aortic valves

[++]p + 0.002 for the comparison with the group of normal aortic valves

[a]Data were missing for 131 patients with normal aortic valves, 88 patients with aortic sclerosis, and 2 patients with aortic stenosis

[b]Data were missing for seven patients with normal aortic valves, four patients with aortic sclerosis, and one patients with aortic stenosis

disease [18]. In particular, AVS may serve as an important clinical marker of left ventricular hypertrophy (LVH) and CAD [1, 19].

- AVS is independently associated with higher left ventricular mass and wall thickness. Although there is no evidence showing that either normalization or progression of AVS impacts LVH, AVS may still be seen as a clinically useful marker of LVH and its related CV risks [19].
- Because AVS and CAD share many risk factors, it seems possible that AVS may serve as an objective marker of CAD [1].

- There is emerging evidence that risk-factor modification proven to have a beneficial influence on the progression and outcomes of CAD (such as the reduction of LDL cholesterol) may also be able to slow the progression of AVS.
  - Treatment with a statin has been shown to slow progression of AVS to aortic stenosis compared to untreated patients and has been shown to significantly reduce mortality in patients with AVS [20, 21].

## Statement on Management

- Currently, there are no specific management guidelines for AVS.
- The ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease recognize AVS as a potential precursor lesion to aortic stenosis and cite evidence of the association of AVS with an increased risk for MI and CV death [18].
- The presence of a soft ejection systolic murmur in the aortic area with a normally split S2 and normal volume carotid pulse is clinically suspicious of AVS. Therefore, given the likelihood of progression to aortic stenosis and the clinical significance of this lesion in poor CV outcomes, this auscultation finding should be confirmed with echocardiography.
  - It is difficult to assess disease severity and progression on auscultation, therefore an echocardiogram should be performed. Echocardiography may be useful in grading the severity of AVS and the risk of progression to aortic stenosis [18, 21].
  - Confirmatory diagnosis of aortic sclerosis by echocardiography can be considered a marker for CAD, and warrants further screening for CAD [1].
- Given similar pathogenesis between AVS and ATH and the strong association between AVS and cardiovascular events, managing patient risk factors for AVS – especially lowering serum LDL cholesterol levels and managing hypertension – may help slow progression of AVS and decrease the incidence of CV events [1–3, 9].

## Clinical Summary of the Case

This 63 year old patient has a common valvular degenerative condition, aortic sclerosis, characterized by a mild early to mid systolic murmur without a click. The condition is reflective of his cardiovascular risk factors, including hyperlipidemia. The interesting association between a murmur of aortic sclerosis, and its potential implication for risk of cardiovascular events, recognizes the common pathologic appearance of aortic sclerosis to atherosclerosis, and prompts further evaluation and treatment for heart disease prevention.

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# Chapter 5
# Aortic Stenosis

**Julia M. Kammel, Christina M. Bence, Adam J. Money, and Steven T. Swinford**

## Key Teaching Points

- A crescendo-decrescendo systolic ejection murmur which may affect the quality of the carotid pulses is characteristic of aortic stenosis.
- Auscultation findings that aid in the diagnosis of aortic stenosis include an increase in the murmur after a pause, such as an extrasystole, and diminished aortic component of the second heart sound (S2).
- Increased intensity of the murmur, and higher murmur pitch, in addition to reduced and delayed carotid artery upstrokes, suggest a more severe stenosis.
- There are no medical therapies for aortic stenosis. Surgery for aortic valve replacement is typically reserved for individuals with symptoms related to AS.

## Case Description

### *History*

A 59 year old man presents with a history of a heart murmur since childhood and was diagnosed with aortic valve disease in the late 1980s. The patient runs every other day but has noticed a recent reduction in stamina, occasional chest pain, and intermittent dizziness. He has no significant past medical history or family history of heart disease.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_5) contains supplementary material, which is available to authorized users.

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## *Physical Exam*

- BP: 131/76 mmHg.
- Pulse: 65 bpm, regular.
- Cardiac: No abnormal impulses.
- Carotids: Somewhat difficult to palpate, therefore moderately diminished; delayed upstrokes noted.
- Auscultation (Fig. 5.1).

## *Text Results*

- Echo: Aortic Valve Area (AVA) 0.8 $cm^{2,}$ AV gradient 2.84 m/s (Fig. 5.2).
- ECG: LV hypertrophy, left atrial hypertrophy, T wave inversion and ST segment depression (in leads I, AVL, V5, V6) (Fig. 5.3).

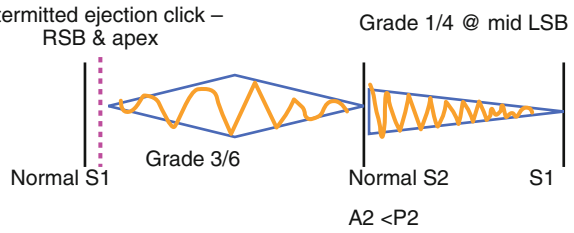



**Fig. 5.1** Representation of the patient's auscultation exam. A systolic crescendo-decrescendo murmur grade 3 and diastolic decrescendo murmur grade 1 is present. S1 normal, however the aortic component of the S2 is diminished, with an intensity beneath that of P2

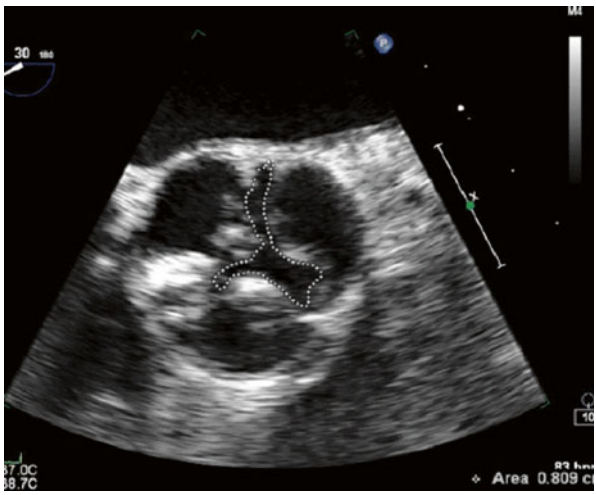



**Fig. 5.2** Echocardiogram showing a parasternal short axis view of the aortic valve with an aortic valve area by planimetry of 0.8 $cm^2$

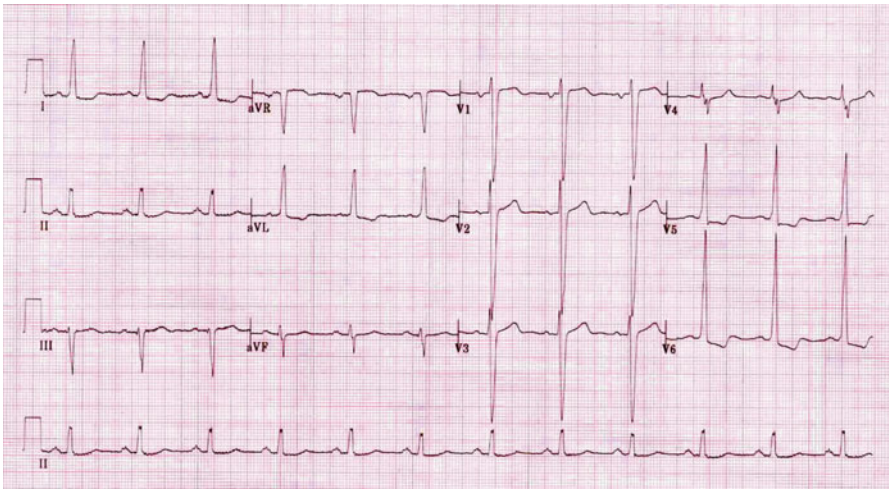



**Fig. 5.3** ECG shows LV hypertrophy, ST depression

## Clinical Basics

### *Normal Anatomy*

- The normal aortic valve has three leaflets, the right, left and noncoronary leaflet. The right coronary artery arises from the right cusp, and the left coronary artery arises from the left cusp.
- The normal aortic valve has an area of 3–4 $cm^2$.

### *Definition*

- Aortic stenosis is a pathologic narrowing of the aortic valve.

### *Causes*

- Causes of AS include congenital aortic stenosis, bicuspid calcific aortic stenosis, tricuspid aortic valve sclerosis and calcific stenosis.

### *Prevalence*

The prevalence of AS increases with age:

- 0.02 % at age 18–44 years.
- 0.1 % at age 45–54 years.

- 0.2 % at age 55–64 years.
- 1.3 % at age 65–74 years.
- 2.8 % at age 75 years and older.

### *Pathophysiology*

- Stenosis of valve usually occurs gradually over time due to calcification.
- The narrowing of the valve causes an increased pressure gradient across the valve leading to high velocity, turbulent ejection of blood.
- The increased pressure gradient leads to decreased ejection fraction which subsequently causes hypertrophic changes of the heart, specifically, left ventricular hypertrophy which maintain ejection fraction.
- The increased muscle mass of the heart puts it at an increased risk for left ventricular failure, reduced coronary blood flow per gram of muscle, and limited coronary vasodilator reserve.

### *Symptoms*

Hallmark symptoms of aortic stenosis include:

- Angina.
- Syncope.
- Heart failure.

## Key Auscultation Features

- Crescendo-decrescendo systolic ejection murmur with ejection click that is heard best at the base of the heart and may radiate to the carotids. The underlying physiologic cause is turbulent flow through a narrowed aortic valve.
- Murmur intensity increases following a post-extrasystolic pause (post-extrasystolicaccentuation) and during the release phase of the Valsalva maneuver.
- Loss of splitting of S2 (loss of A2) due to inflexible aortic leaflets closing inaudibly.
- Presence of S4 due to vigorous atrial contraction in the face of a partially closed mitral valve during presystole.
- Auscultation examples of aortic stenosis.
  - Click here to listen to an example of moderate aortic stenosis and see an image of the phonocardiogram (Video 5.1). The peak to peak gradient was 60 mmHg.
  - Click here to listen to an example of severe aortic stenosis as described by Dr. W. Proctor Harvey (Video 5.2).

## Differential Diagnosis of Key Auscultation Features

- A systolic murmur with ejection may arise from:
  - pulmonary valve stenosis.
  - atrial septal defect.
  - mitral regurgitation.
  - tricuspid regurgitation.
  - high cardiac output state.
  - hypertrophic obstructive cardiomyopathy.
- High-pitched decrescendo diastolic murmur due to regurgitation through a compromised aortic valve.
  - Differential diagnosis for a diastolic murmur.
    - aortic regurgitation.
    - pulmonary regurgitation.
    - mitral valve stenosis.
    - tricuspid valve stenosis.
    - atrial septal defect.

## Clinical Clues to the Detection of the Lesion

Other clinical findings to aid in the diagnosis of aortic stenosis are below:

- Carotid pulsus parvus et tardus on palpation caused by reduced stroke volume and a prolonged ejection phase.
- Echocardiography.
  - Reduced aortic valve area (AVA) indicative of a calcified aortic valve unable to open fully.
  - Increased velocity through the aortic valve due to elevated blood flow through a narrowed aortic valve.
  - Increased systolic pressure gradient between the left ventricle and the aorta (AV gradient) caused by left ventricular outflow obstruction in the face of a narrowed aortic valve.
- ECG.
  - Left ventricular hypertrophy caused by the prolonged elevation of left ventricular contractile force required to eject blood through a stenotic aortic valve.
  - T wave inversion and ST segment depression (leads I, AVL, V5, V6) indicative of myocardial ischemia due to left ventricular dysfunction and decreased myocardial $O_2$ supply.
  - Left atrial hypertrophy secondary to the elevated contractile force necessary to eject blood into an over-filled and hypertrophic left ventricle.

## Classification of the Severity of Aortic Stenosis

See Fig. 5.4.

## Diagnostic Implications of the Auscultation Features

- Auscultation findings aid in the diagnosis of the severity of AS.
  - Increased intensity of murmur indicative of a higher pressure gradient.
  - Increased pitch of murmur correlates with a higher pressure gradient (Fig. 5.5) [1].
  - A murmur with easily heard high frequency sounds correlates to a transvalvular pressure gradient of at least 40 mmHg.
  - Later peak of murmur indicates later peak flow.
  - Single S2 due to the reduction or loss of an A2 sound.
- Carotid upstroke delay and reduction due to the valve impeding ejection. The accuracy of these findings is shown in the Table 5.1.
  - A murmur grade 3 or greater, and peak in mid or late systole has the highest negative predictive value for predicting a peak velocity >3.5 m/s.
  - Abnormal carotid amplitude or delay has the highest positive predictive value for predicting high valve gradients (Fig. 5.6).

## Prognostic Implications of the Auscultation Features

### *Severity [2]*

- AS that is severe on exam may indicate increase risk for mortality. Severe AS is associated with a fourfold increased risk of intermediate term (4-year) all-cause and CVD mortality.
- Symptoms are a key determinant of prognosis. “Once moderate to severe AS is present, prognosis remains excellent as long as the patient remains asymptomatic.”

### *Asymptomatic Patients*

- Aortic valve jet velocity on echocardiography. Graph demonstrates that reduced Vmax indicates a more severe form of stenosis and is associated with a reduced duration of event-free survival (Fig. 5.7) [3].

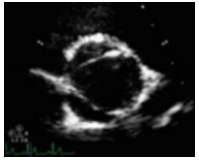
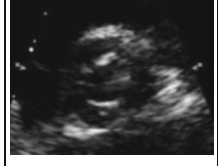
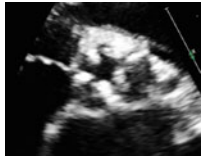
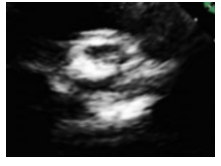
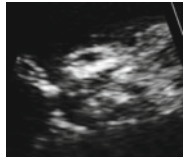
| Echo finding | Normal | Mild AS | Moderate AS | Severe AS | Critical AS |
|---|---|---|---|---|---|
| AVA ($cm^2$) | 3.0–4.0 | >1.5 | 1.0–1.5 | <1.0 | <0.7 |
| AV velocity (m/s) | <2.5 | <3.0 | 3.0–4.0 | >4.0 | |
| AV gradient (mmHg) | ~0 | <25 | 25–40 | >40 | >50 |
| Echo image |  |  |  |  |  |

**Fig. 5.4** Echocardiographic characteristics of grades of aortic stenosis

  - >4 m/s implies 21 % 2-year free of symptoms.
  - <3 m/s implies 84 % 2-year free of symptoms.

- Carotid Amplitude: A moderate to severe decrease indicates reduced event-free survival rates (Fig. 5.8) [4]. This figure indicates the correlation between carotid amplitude and duration of survival without an event. A moderate to severe decrease in carotid amplitude indicates a reduced duration of event-free survival.

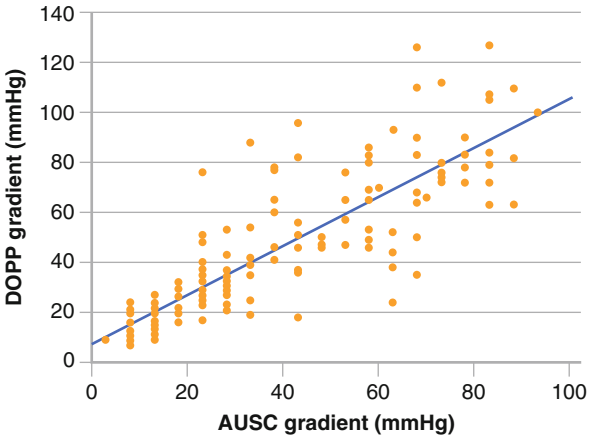



**Fig. 5.5** Relationship between estimated auscultated murmur pressure gradient (*AUSC*) and the pressure gradient across the aortic valve as measured by Doppler ultrasound (*DOPP*). AUSC was determined by pitch of the murmur; higher frequency murmurs were assigned higher pressure gradient estimates. A clear positive correlation can be seen between Doppler-measured pressure gradients and the frequency murmurs on clinical exam ($r = 0.84$, $p < 0.0001$) (Used with permission from Phoon [1])

**Table 5.1** Accuracy of physical examination characteristics for prediction of a maximum Doppler echocardiographic velocity of >3.5 m/s

| | Vmax >3.5 m/s | | | |
|---|---|---|---|---|
| | Sens (%) | Spec (%) | PPV (%) | NPV (%) |
| Physical examination | | | | |
| Murmur grade ≥3 | 22 | 100 | 100 | 48 |
| Murmur grade ≥2 | 88 | 27 | 63 | 62 |
| Systolic murmur peak in late systole | 22 | 97 | 94 | 39 |
| Systolic murmur peak in mid or late systole | 94 | 20 | 62 | 71 |
| Carotid delay, 3–4+ | 12 | 100 | 100 | 46 |
| Decreased carotid amplitude, 3–4+ | 11 | 100 | 100 | 46 |
| Single S2 | 80 | 46 | 66 | 64 |
| Combinations of physical examination findings late systole | 93 | 23 | 62 | 71 |
| Peak in mid- or late systole or single S2 | 92 | 17 | 60 | 60 |

Used with permission from Munt et al. [4]

### *Symptomatic Patients [5]*

- 2-year survival is 50 % without aortic valve replacement.
- 5-year survival is 20 % without aortic valve replacement.

## Statement on Management

### *Medical Therapies*

- In patients with rheumatic aortic stenosis antibiotic prophylaxis is indicated, to prevent against recurrent rheumatic fever.

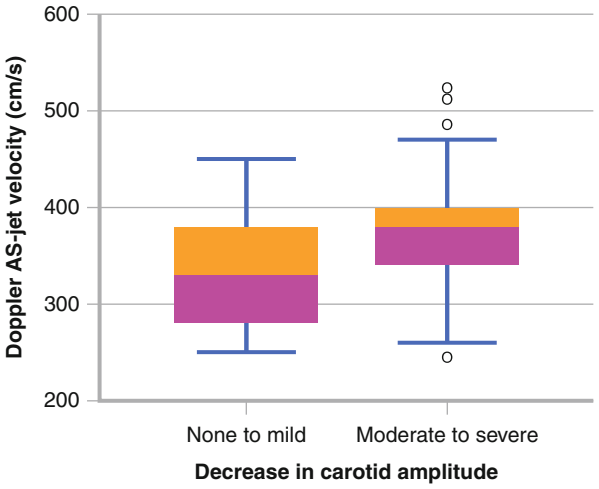



**Fig. 5.6** Relationship between peak aortic valve flow velocities measured by Doppler ultrasound and the degree of carotid upstroke amplitude reduction as assessed on physical exam. Moderate and severe reductions in amplitude on clinical exam correlate with elevated peak velocities (Used with permission from Munt et al. [4])

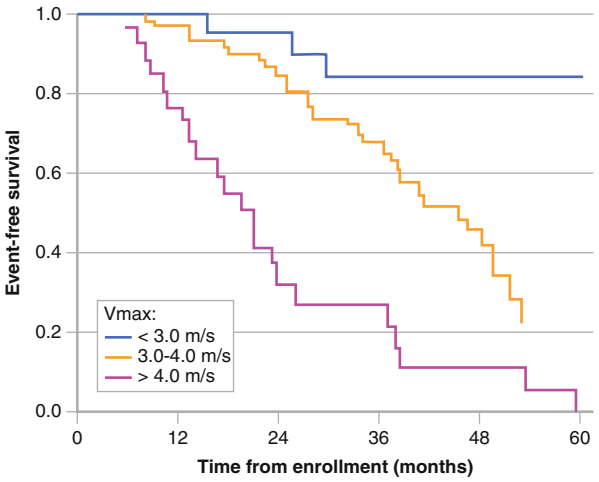



**Fig. 5.7** Natural history of asymptomatic patients with aortic stenosis. Initial aortic jet velocity (Vmax) stratifies patients according to the likelihood that symptoms requiring valve replacement will develop over time. Most events in this series were the onset of symptoms warranting aortic valve replacement (Used with permission from Otto et al. [3])

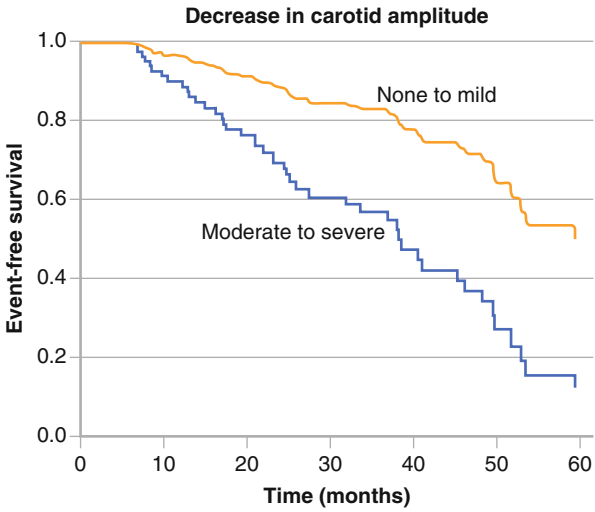



**Fig. 5.8** Event-free survival of patients with aortic stenosis stratified by severity of carotid upstroke amplitude reduction. Patients with moderate to severe carotid upstroke amplitude reduction on physical exam demonstrated a higher rate of mortality or valve replacement surgery than those patients with normal to mildly reduced carotid upstroke amplitude (Used with permission from Munt et al. [4])

- Currently there is no medical therapy that has been proven to prolong life or delay the disease progression.
- Since there is no medical therapy currently indicated, if a patient becomes symptomatic surgery is indicated.

## *Physical Activity*

- In patients who are asymptomatic and have mild AS there are no restrictions on the level of physical activity.
- Limitations are recommended for patients with moderate to severe AS. These patients should not partake in competitive sports that are highly physically demanding.
- Exercise tests can be carefully performed to determine which levels of activity are safe for the patient.

## *Aortic Valve Replacement [6]*

### Recommendations for Symptomatic Patients

- In these patients aortic valve replacement (AVR) has been shown to decrease symptoms and increase survival.
- AVR is the only effective treatment in adult patients with severe symptomatic AS.

  - Since sudden death can occur soon after symptoms present rapid progression to AVR is recommended.
  - There are generally no age limits for this surgery, though risks of the operation should be taking into account when recommending the surgery.
  - Surgical AVR is now being complemented by transcutaenous AVR in patients that are poor surgical candidates.
- It is recommended that patients with severe AS who are undergoing heart surgery such as a coronary artery bypass graft procedure or a procedure on another valve should have AVR done. This is also recommended for asymptomatic patients.

**Recommendations for Asymptomatic Patients**

- Though there is some debate it appears that most physicians believe that the risks associated with AVR outweigh the benefits when the patient is still asymptomatic.
  - Based on the STS database the mortality associated with AVR in the average hospital ranges from 3 to 4 % (and increases to 5.5–6.8 % with concurrent coronary artery bypass graft).
  - An analysis of Medicare data found that in patients over 65 the mortality rate for AVR is 8.8 %.
  - In younger patients when considering AVR with bioprothesis the breakdown of the valve over time needs to take into consideration.
  - Ultimately the risk for sudden death that can occur without the AVR needs to be weighed against the risk of the procedure. The rate of sudden death is <1 % per year.

**Recommendations for Aortic Balloon Valvotomy**

- This treatment has some application in younger patients with AS.
- It is not recommended for older patients.
- There is a high risk of acute complications (10 %) and the majority of patients experience restenosis of the valve within a year of the procedure.

## Clinical Summary of the Case

The patient presents with typical symptoms of aortic stenosis (reduced exertional capacity, chest pain and dizziness), in the setting of severe aortic stenosis suggested by a grade 3 murmur with abnormal carotid upstrokes. These findings predict a worse clinical outcome, and, in the setting of symptoms, warrant surgical aortic valve replacement.

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# Chapter 6
# Bicuspid Aortic Valve

**Peter C. Johnson and Michael DeLuca**

## Key Teaching Points

- The prevalence of a congenital bicuspid aortic valve (BAV), 1–2 %, is high enough to warrant attention for diagnosis during auscultation of the heart.
- A BAV can produce a variety of sounds and murmurs and should therefore always be considered as a cause or as a contributor to unexplained heart sounds.
  - An ejection click associated with S1 is frequently associated with BAVs.
  - Aortic regurgitation (AR) can result and is associated with younger age (less than 40 years of age).
  - Aortic stenosis (AS) can result and is more likely as a patient ages, especially after 50 years of age.
- To definitively diagnose a BAV, the patient requires an echocardiogram.

## Case Description

### *History*

- A 52 year old man presents with a known BAV and moderate AR (as diagnosed by echo). He is currently asymptomatic and denies dyspnea and edema.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_6) contains supplementary material, which is available to authorized users.

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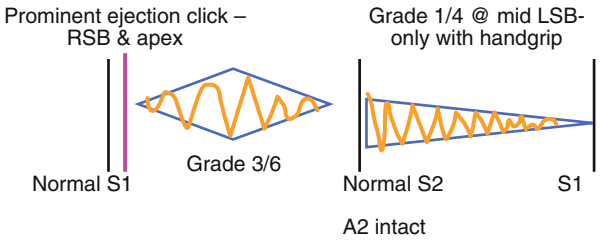



**Fig. 6.1** Diagram of the patient's auscultation findings including a prominent ejection click, a diastolic crescendo decrescendo murmur and systolic decrescendo murmur

- Other significant history is hyperlipidemia, for which he takes atorvastatin, and for hypothyroidism, treated with thyroid hormone replacement therapy.
- His family history is significant for a brother that had surgery at 2 years old to correct a narrow aortic valve.

## *Physical Exam*

- Vital signs: BP 117/73 mmHg, Pulse 72 beats per minute.
- His jugular venous pressure is normal, his chest is clear to auscultation, he has no abnormal cardiac impulses, and his carotids are notable for normal upstroke.
- Cardiac auscultation.
  - Prominent ejection click at the right sternal border (RSB) and apex that is a grade 3 out of 6 with a normal S1.
  - The patient's AR is unnoticeable at rest; however, a handgrip accentuates a grade 1 out of 4 holodiastolic murmur at the mid-left sternal border (LSB). The S2 is normal and A2 is intact (Fig. 6.1).

## *Test Results*

- Electrocardiogram is normal (Fig. 6.2).
- Echocardiogram:
  - A BAV can be seen (Fig. 6.3).
  - Normal left ventricular size and function.
  - The aortic root diameter is upper normal (3.6 cm).
  - Echo Doppler shows mild AR and mild AS (2.1 m/s).

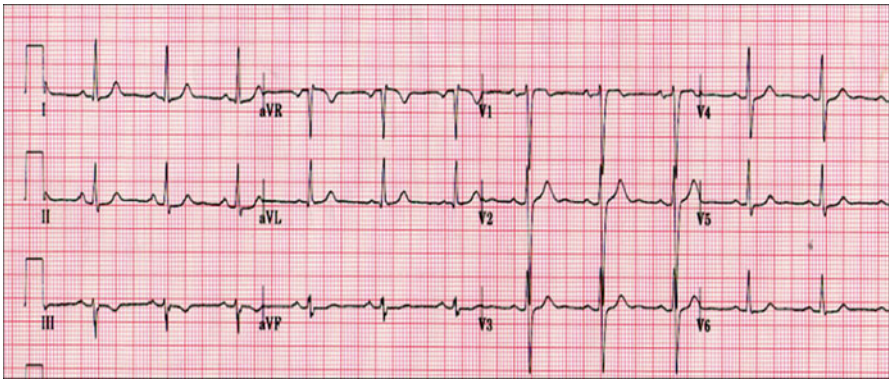



**Fig. 6.2** Normal electrocardiogram in the setting of BAV

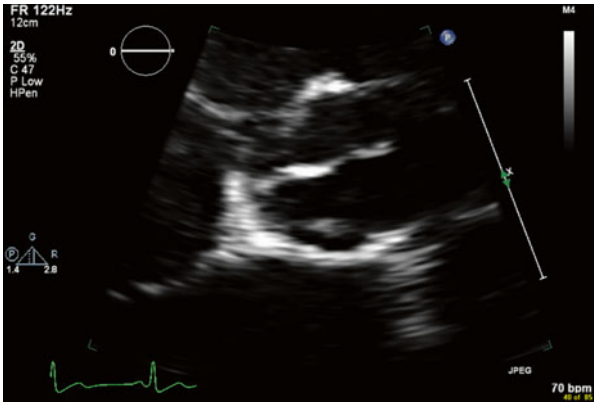



**Fig. 6.3** Echocardiogram showing BAV

## Clinical Basics

### *Definition*

- Most commonly, a BAV is associated with the congenital fusion of right and left coronary cusps, which is seen in 70–80 % of cases (Fig. 6.4). The other, less common fusion is of the right cusp and the posterior (noncoronary) cusp, which is seen in the other 20–30 % of cases [1].
- Median raphe is typically (60 %) in the conjoint cusp. Differential point for acquired bicuspid AV: Raphe does not reach cusp margin.

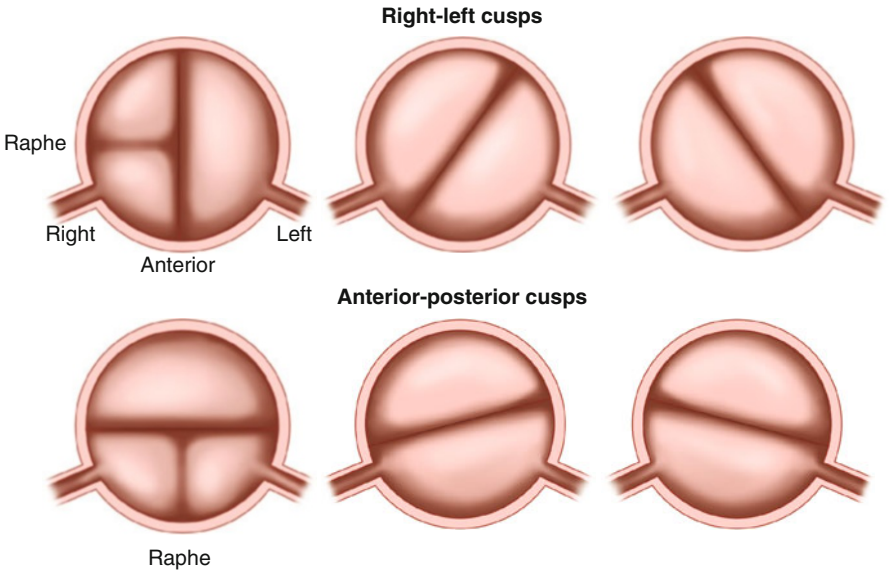



**Fig. 6.4** There are several types of malformations characteristic of a bicuspid aortic valve

## *Prevalence*

- BAV is a congenital disorder that affects 1–2 % of the population [2]. Males make up 70–80 % of cases. It is the most prevalent congenital heart abnormality.

## *Etiology*

- BAV accounts for approximately half of all cases of AS, with a presentation typically in the 5th–6th decade. It also accounts for about one-fourth of all cases of AR, commonly presenting earlier in life.
- A 2012 study of patients at necropsy found that 61 % of those with BAV had aortic stenosis [3, 4]. There is a significant association with aortic dilatation, with studies varying from 33 to 79 % prevalence depending on the study criteria. Increased risk for endocarditis has also been associated with BAV [4].
- There does appear to be a significant genetic component to BAV. One epidemiological study showed a prevalence of 14.6 % of BAV in affected families, which is a much higher rate than the general population [5]. The risk of BAV among 1st degree relatives of an affected individual is 10 % [2]. A family history of BAV should raise suspicions during evaluation.
- There is also a high association of BAV with other congenital anomalies including aortic coarctation, interrupted aortic arch, and other aortopathies [2].

**Table 6.1** Key auscultation characteristics associated with BAV

| Feature | Description |
|---|---|
| Ejection click [6–8] | S1 is split in 85 % of cases<br>Ejection click in BAV associated with aortic valve opening<br>Halting of opening of AV<br>Intensity equal to or greater than M1<br>Intensity constant throughout respiration<br>Heard over entire precordium<br>At apex, true "splitting" of S1 is generally not audible<br>Associated with a loud A2<br>Short and sharp ejection "click"<br>Timing:<br>T1 <50 ms (pa-da)<br>A1 >50 ms (pa-ta)<br>Mitral/tricuspid closure represents non-pathological splitting |
| Systolic murmur | Early to mid systolic<br>Flow related |
| S2 | Increased 1.5–2 fold in uncomplicated BAV<br>A decrease might suggest a degree of AS |
| Diastolic murmur | AR is common<br>Frequently mild |

While the ejection click is most typical of BAV, systolic and diastolic murmurs in addition to alterations in S2 may be heard

### *Signs and Symptoms*

- Commonly asymptomatic and may be found as an incidental finding on an echo for another reason.
- Symptoms of BAV are related to the pathologies closely associated with the anomaly, including AR, AS, and aortopathies.

## Key Auscultation Features

- There are several key auscultation features associated with BAV [6]. Table 6.1 describes the auscultation characteristics of the anomaly.
- It is important to differentiate between non-pathological splitting of S1 and a true ejection click. A true BAV ejection click is related to the halting of the opening of the aortic valve, and the sound occurs later than a typical split S1 (Fig. 6.5).
- One should also note that the auscultatory hallmarks of BAV may vary depending on whether aortic stenosis or regurgitation is present.
- Auscultation examples of bicuspid aortic valve.
  - Click here to listen to an example of bicuspid aortic valve showing an ejection click, with a mild (15 mmHg) gradient, and see an image of the phonocardiogram (Video 6.1).

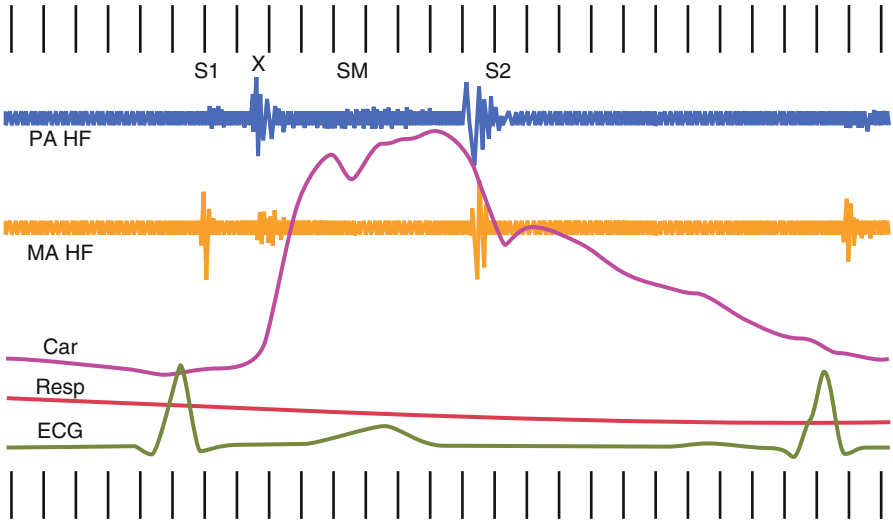



**Fig. 6.5** Phonogram of aortic ejection click heard in bicuspid aortic valve. Note the timing of the click relative to M1 and T1, distinguishing it from non-pathological splitting of S1. Note also the loud S2 (Used with permission from Leech et al. [6])

- Click here to listen to an example of an ejection sound, as described by Dr. W. Proctor Harvey (Video 6.2).

## Auscultation Differential Diagnosis

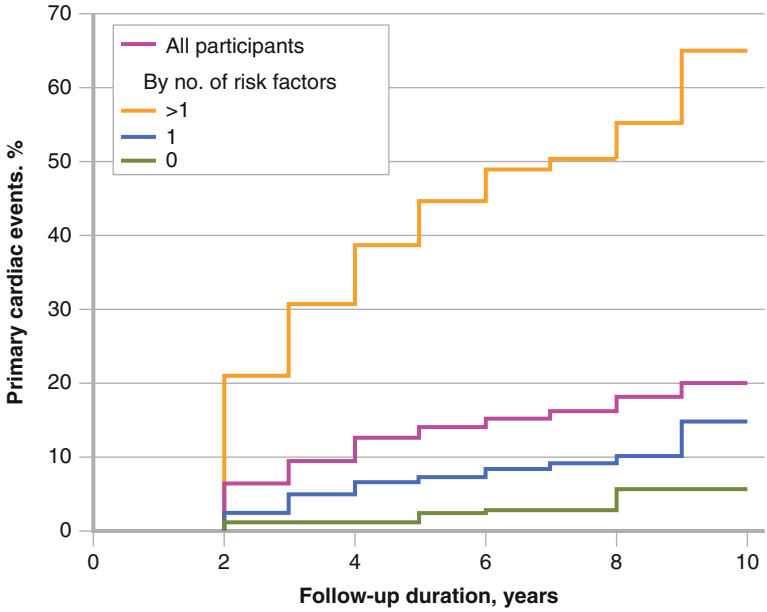
- It is important to distinguish BAV from other disorders involving an ejection click. There are several pathological processes that may present with an ejection click in addition to BAV. Key elements of the differential diagnosis of an ejection click are listed here:
  - Stiff AV associated with hypertension.
  - Pulmonary hypertension leading to delayed ejection.
  - S4 gallop timing affected by volume and respirations or apical location.
  - Tricuspid valve closure in the setting of right sided volume or pressure overload conditions.
  - Mitral valve prolapse.
- In general, clicks that are late, loud, non-varying, and apical are likely to be from bicuspid AV. However, there is a relatively low positive predictive value of ejection sounds for BAV given the differential listed above. It is important to evaluate family history and determine the presence of the other key auscultatory features.

## *Diagnostic Implications of the Auscultation Features*

- The most specific feature for BAV may be the presence of an aortic ejection sound (an ejection "click"). BAV is found in 22 % of ejection clicks [7]. The presence of an ejection click in the absence of any other murmur, such as AS, is mostly likely a non-stenotic BAV [6].
  - Factors that increase the likelihood of BAV [6]:
    - The ejection sound is loud, and the intensity remains constant during expiration.
    - The ejection sound is heard over the entire precordium, and true "splitting" of the S1 is not heard at the apex.
    - The A2 is generally loud.
- The aortic ejection sound can be heard from the second right interspace to the apex in a slash pattern [7].
  - In patients with mild AR, an ejection click followed by an early ejection murmur heard loudest in the second right interspace suggests BAV [8].
  - In patients with AS, the click may be difficult to hear at the second left interspace and left sternal border due to a loud AS murmur. The click would be most obvious at the apex [8].
- Due to the high prevalence of AS and AR in patients with BAV, patients with these conditions should be evaluated for BAV by echo.
  - In a study of 152 autopsies of patients with BAV:
    - 28 % of all deceased patients with BAV had AS. The likelihood of AS increased as the patients aged with one-third of patients aged 40–60 having evidence of the condition and over two-thirds of patients over age 70 [9].
    - 40 % of all deceased patients with BAV had AR. The likelihood was higher amongst younger patients with 64 % of deceased patients 20–29 years old showing evidence of AR. The prevalence of AR in older populations (5th and 6th decades of life) was only one-fourth [9].

## *Prognostic Implications of the Auscultation features*

- Several studies have prospectively followed patients with BAV and reported clinical outcomes (Figs. 6.5 and 6.6).
- 642 ambulatory patients at a Canadian Cardiac Center 1994–2001 followed for a mean period of 9 years [10]:
  - 280 patients (45 %) had a dilated aortic sinus and/or ascending aorta [10].




No. at risk

| | | | | | | |
|---|---|---|---|---|---|---|
| All participants | 642 | 639 | 533 | 413 | 309 | 198 |
| By no. of risk factors | | | | | | |
| >1 | 142 | 141 | 95 | 66 | 51 | 36 |
| 1 | 306 | 305 | 261 | 204 | 153 | 93 |
| 0 | 194 | 193 | 177 | 143 | 105 | 69 |

**Fig. 6.6** Development of cardiac events in patients with BAV. This illustrates the risk of developing a cardiac event over 10 years after confirmed BAV. The risk factors include 30 years or older, moderate/severe aortic regurgitation, and/or moderate/severe aortic stenosis (Used with permission from Tzemos et al. [10])

  - 161 patients (25 %) suffered from one or more cardiac events [10].
  - 142 patients (22 %) required intervention on the ascending aorta or aortic valve [10].
  - 11 patients (2 %) suffered from an aortic dissection or aneurysm [10].
  - Predictors of cardiac events included: older than 30 years old, moderate or severe AS, and moderate or severe AR [10].
- 416 consecutive patients with BAV in Olmstead County, Minnesota, from 1980 to 1999 with the last follow-up in 2008–2009:
  - 2 patients suffered an aortic dissection, which translates to an age-related relative risk of 8.4 compared to the general population of the county. The incidence is still low, but it is much higher than the general population [11].

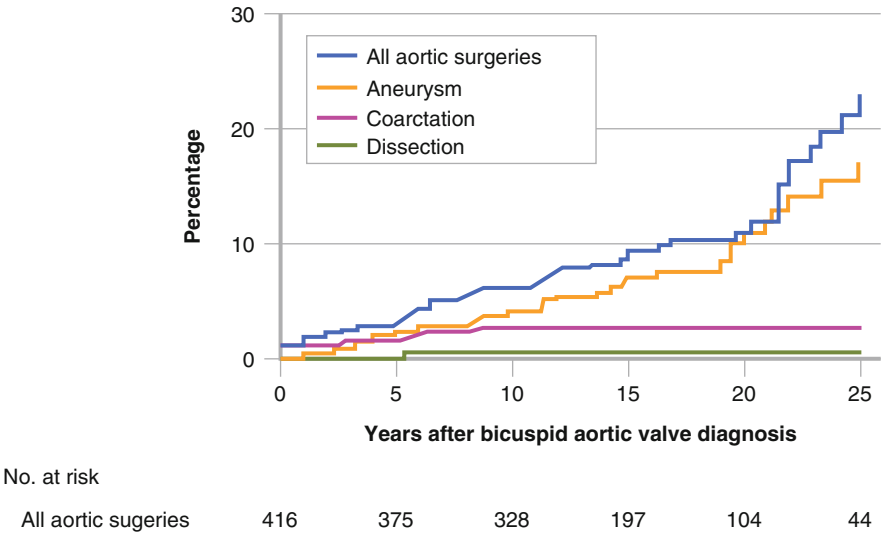



**Fig. 6.7** Risk of aortic surgery in BAV. This illustrates the Kaplan-Meier risk of aortic surgery over 25 years after a confirmed BAV (Used with permission from Michelena et al. [11])

  - 49 patients developed an aneurysm (out of a total of 384 who did not have an aneurysm at baseline), which translates to an age-related risk of 86.2 compared to the general population of the county [11].
  - Over 25 years, the rate of aortic surgery was 25 %, aneurysm formation was 26 %, and valve replacement was 53 % [11].
  - As in the previous study, while morbidity was high, the mortality rate over 25 years was not significantly elevated [11].
- Coarctation of the aorta, as may be detected clinically as differential blood pressures between the upper and lower extremities, represents another congenital abnormality that is associated with BAV in a minority (fewer than 10 %) of individuals, and therefore should be clinically considered.

## Management

There is no treatment to prevent the progression of this congenital abnormality. Guidelines from ACC/AHA do suggest the following:

- First degree relatives of an affected individual should be screened for BAV and other thoracic aorta abnormalities [12].
- Individuals with BAV should be assessed for aortic dilatation with an initial transthoracic echocardiogram [12, 13].

- Yearly evaluation of aortic dilatation should be undertaken in patients with known BAV (with diameter >4 cm) [13].
- Surgical repair of the dilatation may be necessary with severe dilatation (>5 cm or 4.5 cm if AR present) [13].
- Aortic regurgitation (decreased likelihood with aging) and aortic stenosis (increased likelihood with aging) should be evaluated and managed. Additionally, it has been suggested that blood pressure management be emphasized to reduce aortopathy risk with the use of beta blockers [2].
- Angiotensin II blockade may be a potential future intervention as it has been shown to reduce the rate of aortic root dilation in Marfan's syndrome [14].

## Clinical Summary of the Case

The patient, with an apparent family history of aortic valve disease, has typical findings of "mid-stage" bicuspid valve, with a prominent click, yet the early onset of aortic stenosis, and characteristically mild AR. The click is characteristically heard across the precordium. The normal blood pressure suggests against the presence of coarctation. With this established diagnosis, monitoring the patient for progression of AR or AS, and evaluating for associated conditions, such as aortic root enlargement and its consequences is required.

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# Chapter 7
# Aortic Regurgitation

**Kamil Stefanowski, Mary Catherine Daly, and Matthew J. Moynihan**

## Key Teaching Points

- Aortic regurgitation (AR) is most commonly caused by aortic root enlargement and congenital heart valve abnormalities.
- Characterized by a diastolic decrescendo murmur at the left upper sternal border which can be accentuated by maneuvers that increase afterload.
- Auscultation of aortic regurgitation can provide clues to the severity and mechanism of the disease. Auscultation of the murmur at right upper sternal border suggests an etiology of aortic root enlargement or displacement. A murmur at the left lower sternal border is indicative of valvular abnormality.
- In cases of severe, symptomatic aortic regurgitation, echocardiographic screening is necessary to evaluate left ventricular dysfunction.
- Postoperative prognosis for aortic regurgitation is better without left ventricular dysfunction.
- Recent onset left ventricular dysfunction tends to resolve postoperatively.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_7) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- 44 year old male with known aortic regurgitation diagnosed 10 years ago as an asymptomatic clinical finding. He denied chest pain or dyspnea.
- Past medical history is notable for glaucoma. He takes nifedipine 30 mg daily.

### *Physical Exam*

- Blood pressure 157/70 mmHg; Pulse 60 bpm, regular.
- Chest: Clear to auscultation.
- Cardiac: Normal precordial palpation, JVP within normal limits.
- Increased radial and carotid pulse volume.
- Other findings: Qwinke's pulses, Pistol shot pulses.
- Auscultation (Fig. 7.1):
  - An early ejection sound is present along with an early diastolic murmur.
  - Normal S2.
  - Grade 2/4, low pitch murmur at the mid right sternal border.
  - S4 gallop.

### *Test Results*

- Normal ejection fraction with left ventricular enlargement:
  - End diastolic dimension: 56 mm.
  - End systolic dimension 35 mm.
- AV: trileaflet (appeared functional bicuspid) with calcified anterior leaflet, and limited mobility.
- Severe AR by color flow imaging (Fig. 7.2).

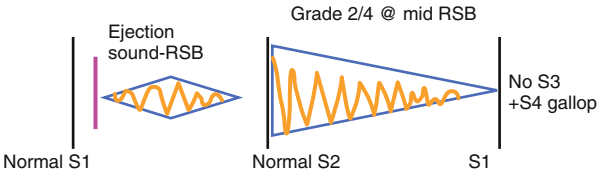



**Fig. 7.1** A diagrammatic representation of the AR murmur

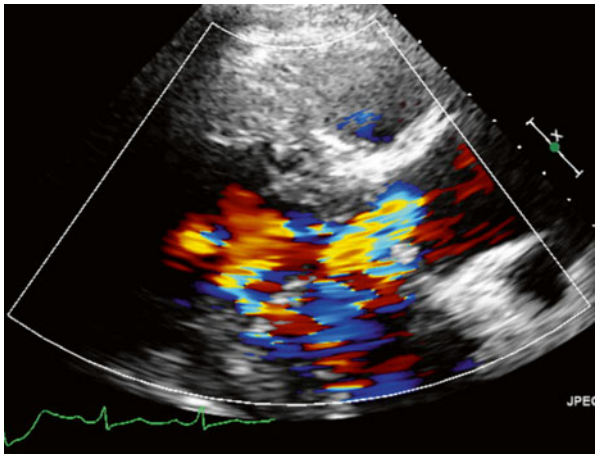


**Fig. 7.2** Echocardiogram of the described patient case demonstrating retrograde blood flow across the valve in AR

- Eccentric jet onto anterior mitral valve leaflet.
- Compressed mitral valve- limited diastolic excursion with anterior mitral valve leaflet fluttering.
- Pressure half time ~300 ms (moderate to severe).
- Holodiastolic aortic flow reversal.

## Clinical Basics

### *Normal Anatomy*

- The normal aortic valve is composed of three leaflets with approximately 2 % of the population having two leaflets ("bicuspid valve").
- The AV controls flow from the LV to the aorta and is open during systole. It contributes to the S2 heart sound.

### *Definition*

- Aortic regurgitation refers to abnormal retrograde blood flow through the aortic valve during diastole. The abnormal blood flow through the valve causes an increase in LV end-diastolic volume. See Fig. 7.3.

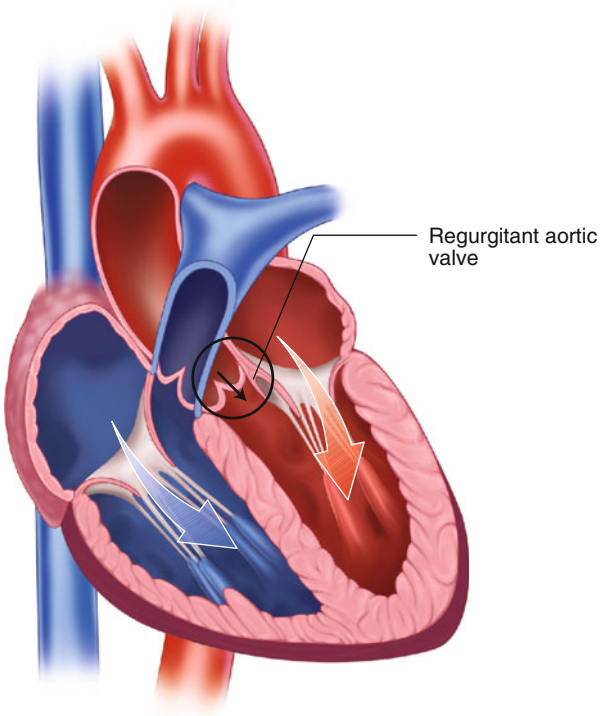



**Fig. 7.3** Area in heart producing early diastolic aortic regurgitation murmurs

## *Etiology*

- Aortic regurgitation is considered to be a result of aortic root dilation (35 %), congenital defects (20 %), or valvular pathology. Bicuspid aortic valve is the most common congenital cause.

## *Signs and Symptoms*

- Most patients are asymptomatic early in the disease and aortic regurgitation is most commonly discovered incidentally. Late stage or progressive symptoms can include angina, dyspnea, and fatigue that signify left ventricular dysfunction and pulmonary venous congestion.

## *Prevalence*

- Aortic regurgitation has been found in approximately 0.75 % of patients in the United States [1].

## Key Auscultation Features (Fig. 7.4)

- *Diastolic decrescendo murmur at the left upper sternal border* which can be accentuated by maneuvers that increase afterload. Auscultation of this murmur at the right upper sternal border is suggestive of aortic root enlargement or displacement. A left lower sternal border location is suggestive of a valvular abnormality.
  - *S1 is soft* due to increased left ventricular filling pressure decreasing the force of MV closure.
  - The presence of an ejection click suggests an etiology of bicuspid valve.
- Brief early systolic murmurs can be auscultated due to flow disturbances.
- An S3 signifies LV dysfunction, but does not indicate the severity of aortic regurgitation.
- Auscultation examples of aortic regurgitation.

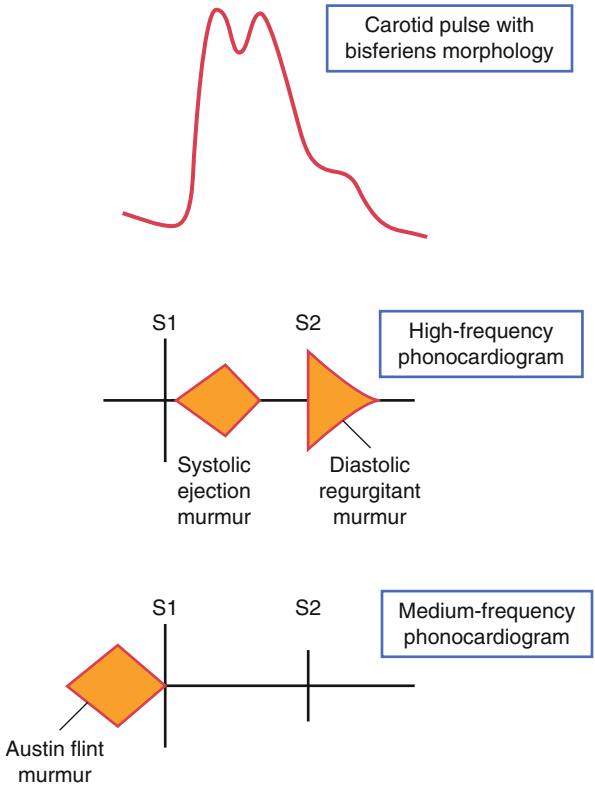



**Fig. 7.4** Key features of AR auscultation

  - Click here to listen to an example of an AR murmur and see an image of the phonocardiogram (Video 7.1).
  - Click here to listen to an example of mixed AS with AR and see and image of the phonocardiogram (Video 7.2).
  - Click here to listen to examples of several patients with AR, as described by Dr. W. Proctor Harvey (Video 7.3).

## Auscultation Differential Diagnosis

- Mitral regurgitation: distinguished by a right ventricular heave and a pansystolic murmur at apex radiating to axilla.
- Mitral stenosis: distinguished by a loud S1 with an opening snap and rumbling mid-diastolic murmur.
- Aortic stenosis: distinguished by patient presentation of dyspnea, dizziness, syncope, and congestive cardiac failure. Auscultation reveals an ejection systolic murmur that radiates towards carotids with an ejection click.
- Pulmonary regurgitation: distinguished by a crescendo-decrescendo diastolic murmur heard at the left upper sternal border which is increased with inspiration.
- Arterial-venous fistula- can widen pulse pressure, and can create murmurs in the setting of high venous flow.

## Clinical Clues to the Detection of the Lesion

- *Widened pulse pressure* is frequently seen in aortic regurgitation due to the increased LV ejection volume (thereby increasing systolic pressure) and reduced diastolic pressure from the regurgitant volume and the low peripheral resistance.
  - Potential false positive: Older patients may have increased pulse pressure as a function of reduced arterial compliance.
  - Potential false negative: Young patients with highly compliant vessels may not show early changes of widened pulse pressure.
- Key physical signs that may contribute to accuracy (Table 7.1) include [2]:
  - Qwinke's sign – nail beds blanch with pulse.
  - Traube's sign – systolic sound over the expanding femoral artery.
  - Duroziez's sign – to-and-fro murmur in the femoral artery.
  - Hill's sign – large difference (>60 mmHg) between upper and lower extremity systolic pressure.
  - Corrigan pulse – rapidly swelling and falling arterial pulse by palpation.

**Table 7.1** Physical diagnosis signs associated with more accurate detection of AR

| Sign | Specificity % | Sensitivity % |
|---|---|---|
| Austin Flint murmur | Not applicable | 25–100 |
| Corrigan pulse | 16 | 38–95 |
| Duroziez sign | 35–100 | 33–81 |
| Hill sign | 71–100 | 0–100 |

Used with permission from Babu et al. [2]

## Diagnostic Implications of the Auscultation Features

### *Acute, Severe AR*

#### Quality

- Acute AR involves large diastolic flow volumes and therefore results in a low or medium-pitched murmur. Severe AR can often be described as harsh sounding.
- S1 may be diminished or absent due to early closure of the mitral valve. The premature closing results when left ventricular pressure is elevated above that of the left atrium during mid-diastole [3].

#### Timing

- Acute AR may also result in a shorter diastolic murmur. This occurs when the left ventricular pressure rapidly increases limiting the pressure difference between the left ventricle and aorta and decreasing regurgitant flow.
- One must be sure not to confuse the murmur with a systolic ejection murmur when the patient is in sinus tachycardia [3].

#### Gallop Rhythm

- S3 may be present in acute AR also correlating with effects of increased left ventricular end diastolic volume [3].

### *Chronic AR*

#### Quality

- In *mild* AR, the murmur is diastolic and high-pitched due to the regurgitant flow being characterized by small volume and high velocity. It is often described as a blowing sound. Listening for the murmur with the breath held at the end of expiration may prevent confusion with breath sounds and increase the examiner's ability to identify the murmur.

  - The murmur can be distinguished from pulmonic regurgitation as it occurs just after A2, not P2 [4].

- In *moderate* AR, the murmur may have mixed frequencies as diastolic flow volume increases but overall remains largely high-pitched.
- *Severe* AR results in a low or medium-pitched harsh sounding murmur.
- A musical AR murmur frequently indicates everted (syphilis) or perforated (infective endocarditis) leaflets or rupture of an aortic sinus of Valvalsa [5].

### Intensity

- AR severity cannot be inferred from murmur intensity as the case may be with other types of murmurs. The murmur of severe AR has the potential to sound soft [3].

### Duration

- Severity of AR is known to correlate with the duration of the murmur.
- A pandiastolic murmur indicates that AR is moderate or perhaps severe compared to a less severe murmur that is contained within early diastole [5].

### Location

- Auscultation of the murmur on the right between the second and fourth intercostals spaces is likely to indicate aortic root enlargement as the etiology of AR.
- Auscultation at the left sternal border suggests a valvular etiology [3].

### Systolic Murmur

- In moderate or severe AR, diastolic ventricular volume will be markedly increased. Ejection of the increased stroke volume may cause a systolic ejection murmur [3].
- Differentiation from aortic stenosis may be based on a higher-pitched murmur and radiation to the carotid vessels in AR [4].

### Austin Flint Murmur

- Severe AR may result in functional mitral stenosis from high ventricular diastolic pressures leading to early closure of the mitral valve. A low frequency, mid-diastolic rumble at the apex of the heart indicates severe AR [3].

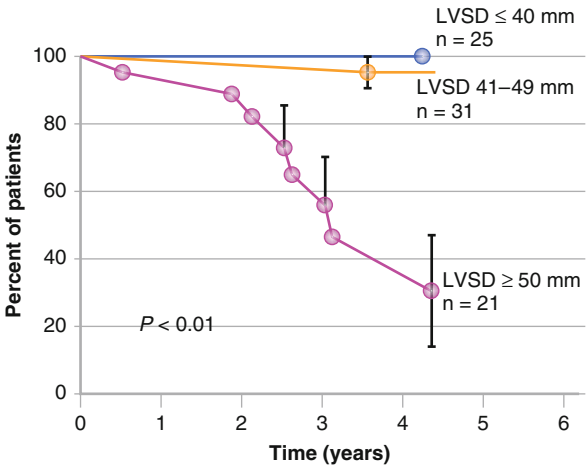



**Fig. 7.5** The graph of the data from Bonow et al., indicating increased left ventricular systolic volumes correlated with worse survival rates at 5 years (Used with permission from Bonow et al. [6])

## Prognostic Implications of the Auscultation Features

- An enlarged left ventricular end-systolic dimension puts the patient at significant risk of developing left ventricular dysfunction or symptoms.
  - Apical displacement identified on physical exam may indicate left ventricular enlargement.
- In a study of 77 patients, only 31 % of those with an initial left ventricular end-systolic volume >50 mm were asymptomatic (Fig. 7.5) [6].
- Exam assessment of murmur pitch suggesting mild, moderate or severe AR has potential prognostic significance. In a study of 251 asymptomatic patients with AR, cardiac event rates (cardiac death, congestive heart failure, and new atrial fibrillation) were more frequent in individuals with a higher grade condition. Using the QASE (Quantitative American Society of Echocardiography) scale, mild AR, moderate AR, and severe AR had cardiac event rates of 5 %, 27 %, and 47 % at 5 years respectively (Fig. 7.6) [7].
- Symptoms are a major predictor of prognosis with mortality rates significantly higher in symptomatic patients compared to those who are asymptomatic. In a study in which patients were stratified by no dyspnea (New York Heart Association class 1 (NYHA), mild dyspnea (NYHA II), and severe dyspnea (NYHA II–IV), 5-year survival rates were calculated to be 87 ± 3 %, 73 ± 8 %, and 28 ± 12 % respectively (Fig. 7.7). This study again suggests the need for immediate intervention when symptoms are present [8].

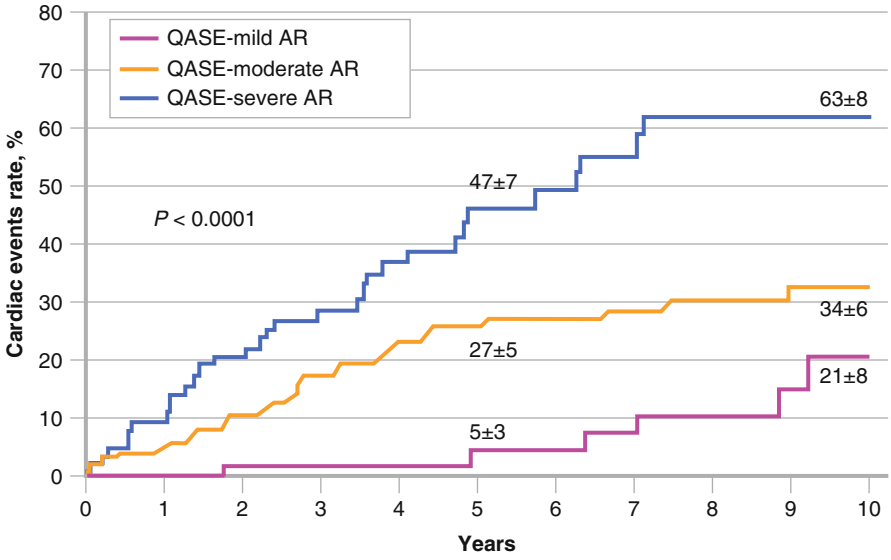
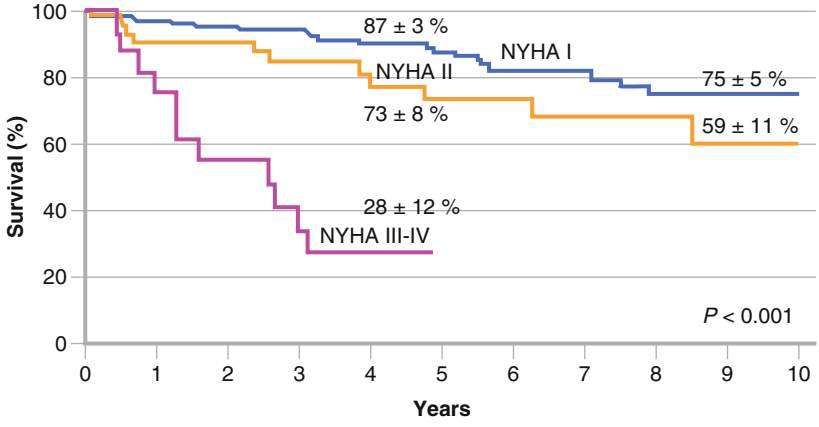



**Fig. 7.6** The graph of cardiac event rates progression in patients with AR (Used with permission from Detaint et al. [7])




| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| NYHA I | 122 | 100 | 91 | 88 | 81 | 71 | 55 | 48 | 37 | 31 | 16 |
| NYHA II | 64 | 37 | 31 | 26 | 21 | 19 | 16 | 9 | 9 | 6 | 4 |
| NYHA III–IV | 60 | 11 | 8 | 5 | 4 | 2 | | | | | |

**Fig. 7.7** The graph of this data shows a correlation of more severe AR symptoms, specifically dyspnea, with a markedly decreased survival rate at 5 years (Used with permission from Dujardin et al. [8])

## Statement on Management [9]

### *Diagnosis and Evaluation*

- Echocardiography is recommended for the diagnosis of AR, assessment of severity, and periodic reevaluation in patients with severe AR or new or changing symptoms.
- Exercise stress testing, and cardiac catheterization may also serve as more advanced diagnostic tools.

### *Aortic Valve Repair*

- Surgical intervention is recommended for symptomatic patients with severe AR regardless of the degree of left ventricular dysfunction.
- Surgical intervention is also recommended for asymptomatic patients with left ventricular dysfunction (LV ejection fraction ≤0.50) or increased left ventricular end systolic diameter (>55 mm).

### *Vasodilator Therapy*

- Definitive recommendations on vasodilator use have proven difficult due to conflicting studies both showing delayed appearance of symptoms with treatment and studies showing no benefit of treatment.
- Chronic therapy is not recommended in symptomatic patients with severe AR due to its propensity to cause additional cardiac and non-cardiac effects.
- The only situations in which the AHA may indicate vasodilator use are for short-term therapy to improve hemodynamic factors preceding atrial valve repair in patients with severe heart failure symptoms (IIa-C) and long term therapy in asymptomatic patients with severe AR, LV dilation, and normal systolic function (IIb-B).

## Clinical Summary of the Case

The patient presents with moderate to severe aortic regurgitation with a high pitched, right sided murmur and ejection sound, and findings of a large regurgitant volume including a wide pulse pressure. The near term prognosis is excellent; nevertheless, he requires continued monitoring for progression to surgical indications with periodic clinical and echocardiographic evaluations.

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# Chapter 8
# Hypertrophic Obstructive Cardiomyopathy

**Joanna Leigh Shechtel**

## Key Teaching Points

- HCM is due to a myocardial abnormality that causes a hypertrophied interventricular septum and may involve the left ventricle (LV) free wall leading to dynamic obstruction of ventricular outflow.
- Systolic anterior motion of the anterior leaflet of the mitral valve results in mitral-septal contact, contributing to LV outflow obstruction.
- HCM is one of the most common causes of death in young athletes under 30 years old.
- The characteristic systolic murmur of HCM is a mid-late peaking systolic ejection murmur that is intensified by the squat-to-stand maneuver.
- Murmur intensity is dependent on the volume of blood in the LV. As venous return decreases (i.e., in exercise with a high heart rate), the outflow tract obstruction, and thus murmur intensity, increases.
- Subaortic membrane is another, rare cause of LV outflow tract (LVOT) obstruction with a fibrous membrane below the aortic valve that may involve the ventricular septum, anterior leaflet of the mitral valve, and the aortic valve itself.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_8) contains supplementary material, which is available to authorized users.

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A.J. Taylor (ed.), *Learning Cardiac Auscultation: From Essentials to Expert Clinical Interpretation*, DOI 10.1007/978-1-4471-6738-9_8

## Case Description

### *History*

- 50 year old fireman.
- Murmur first detected at age 7. Had a cardiac catheterization but no diagnosis was carried forward.
- Noted to have a lifelong murmur.
- In his 40s, began having symptoms including:
  - Dyspnea- The patient smokes tobacco.
  - Angina- only with running.
  - Intermittent lightheadedness.
  - No syncope.
- A murmur was detected on routine exam, and he was referred for further testing with a provisional diagnosis of HCM.

### *Physical Exam*

- VS: BP 140/90 mmHg; Pulse 65 bpm, regular.
- JVP normal, Carotids: diminished, no thrill.
- Chest: CTA.
- Cardiac: Nondisplaced apical impulse; normal palpation.
- Crescendo-decrescendo systolic murmur that increases with the Valsalva maneuver and changes with the squat-to-stand maneuver (Fig. 8.1).

### *Test Results*

- Echo.
  - Echocardiogram (Fig. 8.2) shows an enlarged interventricular septum and LVOT obstruction during systole (arrow) in a patient with HCM. Asymmetrical LV hypertrophy is noted with septal thickening.

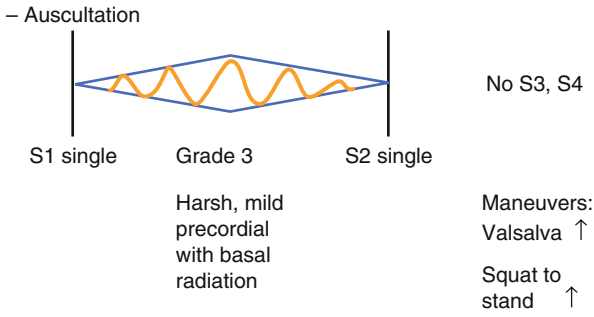


**Fig. 8.1** Depiction of auscultation findings for HCM

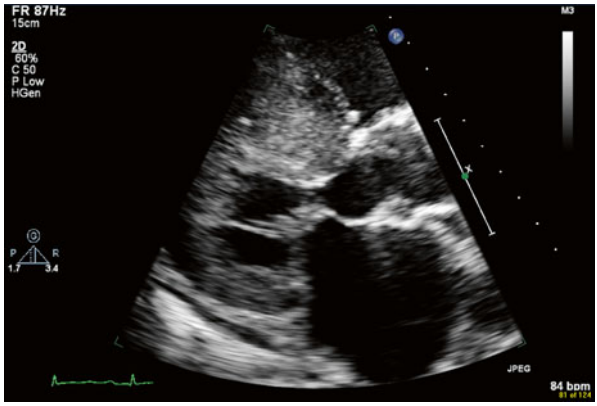


**Fig. 8.2** Echocardiogram showing the increased septal thickness and systolic anterior motion of the mitral leaflet into the left ventricular outflow tract

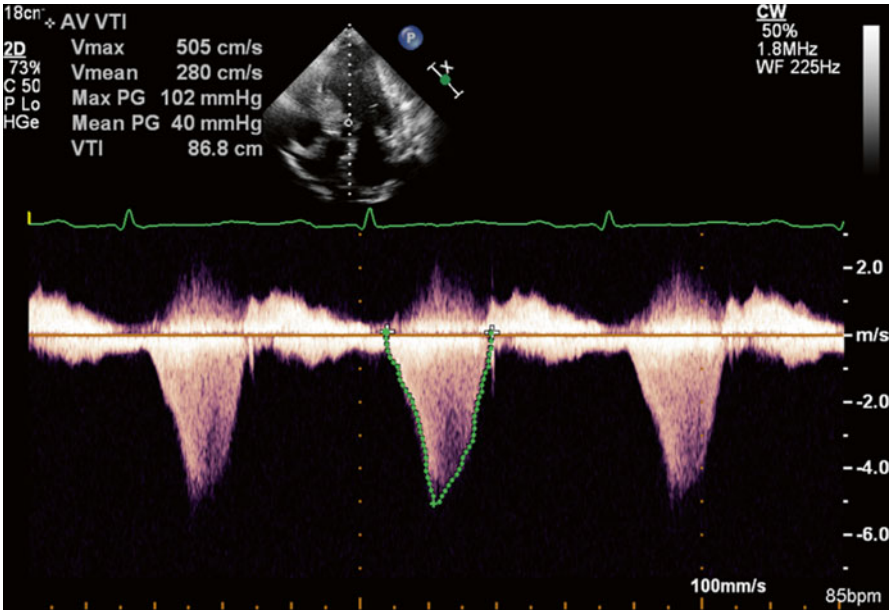


**Fig. 8.3** Doppler ultrasound showing severely increased left ventricular outflow velocity due to dynamic obstruction of the outflow tract

- Doppler.
  - Doppler ultrasound (Fig. 8.3) shows increased blood ejection velocity from the LV. There is a presence of late-peaking systolic velocity due to the LVOT obstruction.
  - Subaortic velocity acceleration is noted by turbulence of blood flow.
  - LVOT peak velocity of 4–6 m/s.
  - Systolic anterior motion of the anterior mitral valve leaflet.
  - Grade 2 aortic regurgitation.

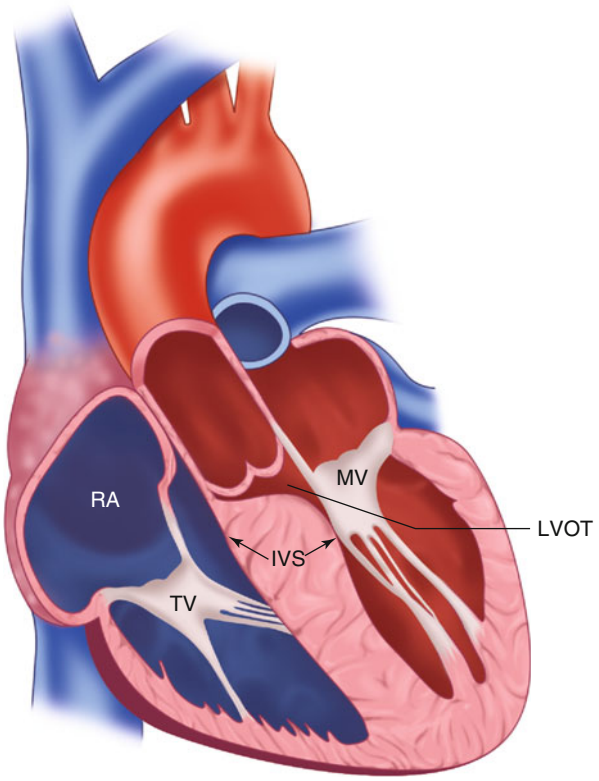


**Fig. 8.4** Illustration of the myocardial abnormalities in hypertrophic cardiomyopathy, including cardiomegaly with an asymmetrically thickened interventricular septum

## Clinical Basics

### *Normal Anatomy*

- HCM pathophysiology arises from obstruction of aortic valve/outflow tract due to excessive cardiac muscle build up.
  - 50–75 % have subaortic stenosis from ventricular septum obstruction.
  - left ventricular outflow tract plaque (scarring from anterior mitral valve leaflet rubbing against the outflow tract).
- There is reduced left ventricular compliance in conjunction with left atrial dilation.
- Myocardial abnormalities include cardiomegaly, enlarged asymmetric ventricular septum, and asymmetric LV thickness, with the interventricular septum being hypertrophied more so than the left ventricle free wall (Fig. 8.4).
- On histology, there is cardiac myofiber disarray and thickened intramural coronary arteries.

## *Etiology*

- 50 % hereditary.
  - Family member with exertional syncope or sudden death.
  - Most common familial heart disease.
- Sarcomere protein abnormality (usually beta-myosin heavy chain).
- Male predominance.
- 1 % of all congenital heart disease.
  - Often associated with other congenital heart diseases.
  - Potential hemodynamic cause.
    (a) Steeper aorto-ventricular angle with increased aortic override.
- Four morphological variants.
  - Thin discrete membrane.
  - Fibromuscular ridge at base of intraventricular septum.
  - Ring of tissue attached to LV outflow tract and base of mitral valve.
  - Fibromuscular tunnel in LV outflow tract.
  - Types 1 and 2 account for 75 % of cases.

## *Signs and Symptoms*

- Often related to exertion.
- Shortness of breath or dyspnea (most common symptom) especially in the setting of atrial fibrillation.
- Dizziness or syncope.
- Angina.
- Arrhythmias common.
- Sudden death (often exercise related) usually with very high LVOT gradients.
- Rapid or quick-rise (“flip”) pulse.

## *Prevalence*

- The prevalence of HCM is 20/100,000.
- Typical age of onset is 20–50 years old.
- The disease occurs with a male predominance (1.5:1).

## Key Auscultation Features

- Systolic murmur.
  - Occurs in early to mid systole with a peak around mid systole.
  - Best heard at the apex and left sternal border (aortic area).
  - May not radiate.
  - Has a crescendo-decrescendo pattern (Fig. 8.1).
  - Low pitched, murmur intensity grade 2–4/6.
- The murmur of HCM is highly dependent on the volume of blood in the LV.
  - With less blood, the LV outflow tract can be increasingly obstructed because the septum and the mitral valve become closer together, thus the murmur gets louder.
  - Conversely, increased venous return will increase volume in the LV and decrease the murmur intensity.
- Normal S1.
- S2- often single due to prolonged LV systole.
- No ejection click.
- Changes with maneuvers [1]:
  - In a majority of cases (90 % of the time), the murmur intensity will decrease on inspiration and increase on expiration.
  - Increase in intensity with Valsalva maneuver (65 % sensitivity, 96 % specificity).
  - Increase in intensity from squatting to standing (95 % sensitivity, 84 % specificity).
  - Decrease in intensity with passive leg elevation (85 % sensitivity, 91 % specificity).
  - Decrease in intensity with handgrip maneuver after 1 min of maximal contraction (85 % sensitivity, 75 % specificity).
- Valsalva maneuver and standing increase murmur intensity; handgrip maneuver, passive elevation of the lower extremity, and squatting each decrease the murmur intensity (Fig. 8.5).
- Other heart sounds may be affected in HC including paradoxical splitting of S2, and an S4 gallop.
  - Auscultation examples of hypertrophic cardiomyoapthy.
- Click here to listen to an example of a murmur of a patient with HC, including the effect of squatting, as described by Dr. W. Proctor Harvey (Video 8.1).

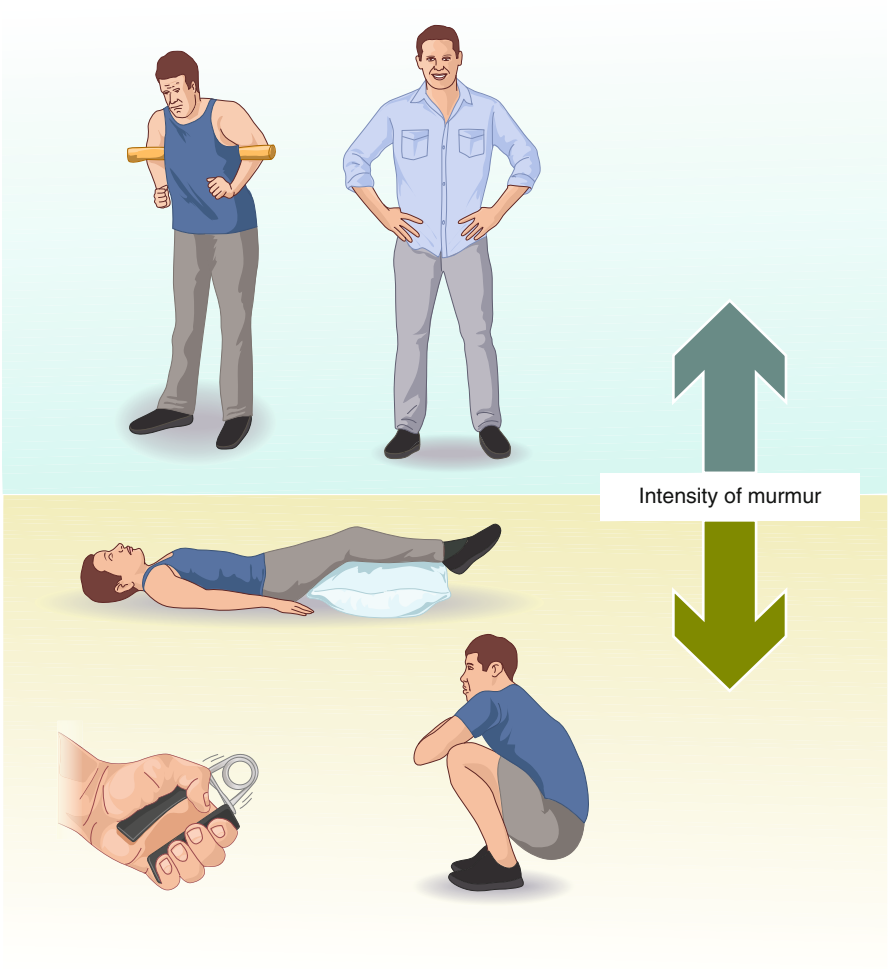


**Fig. 8.5** Maneuvers to accentuate or diminish the intensity of the systolic murmur heard in patients with HCM

## Auscultation Differential Diagnosis

- Many different cardiac murmurs can present similarly on auscultation. Thus, an algorithm can be used to help the examiner discern which cardiac pathology the murmur represents (Fig. 8.6).
- Aortic stenosis (AS) (valvular or supravalvular)- can cause similar symptoms due to LV outflow tract obstruction and will also have an associated systolic murmur.

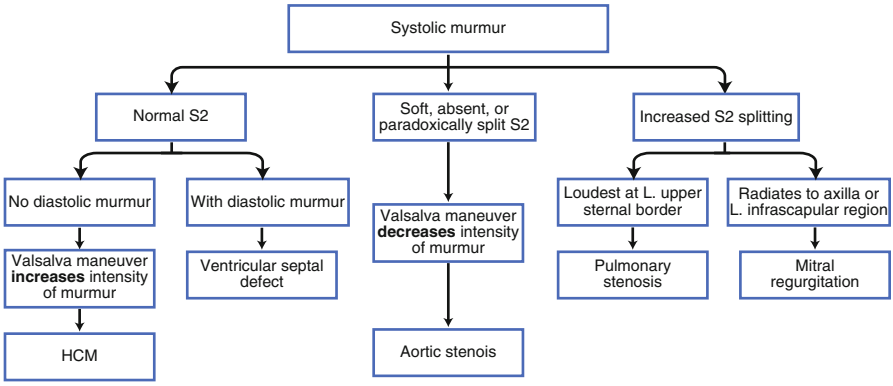


**Fig. 8.6** Flow chart of diagnostic algorithm for murmurs to be considered in the differential diagnosis of a systolic murmur

- *Valsalva maneuver* is a key differentiating feature for HCM versus AS. Valsalva *decreases intensity of AS systolic murmurs but increases the intensity of HCM systolic murmur.*
- Both may have an accentuated LV impulse or heave palpated over the fifth left intercostal space within the midclavicular line.
- To differentiate between AS and HCM, feel the arterial pulse, palpate the precordial pulsations, and take the patient's blood pressure.
  - HCM will have a quickly rising pulse that peaks in early systole.
    (a) See Fig. 8.7. The carotid pulse (bottom) peaks shortly after the S1 sound is heard and systole begins (top).
    (b) Carotid pulse volume decreases with thrill.
  - HCM may have a presystolic and double-systolic impulse ("triple ripple").
    (a) Three component apical impulse which can be palpated on the chest wall.
    (b) See Fig. 8.8, where the three components of the impulse are indicated with the letters "A," "E," and "L."
- AS will have a pulse with a small amplitude that is late peaking or delayed (pulsus parvus et tardus) and may have a palpable shudder. Narrow pulse pressure is usually a late finding in patients with severe AS.

## Clinical Clues to the Detection of the Lesion

Harvey's Formula for diagnosis of HCM (Fig. 8.9). A patient with HCM will have a quick pulse, no diastolic murmur, and the characteristic systolic murmur which changes with the squat-to-stand maneuver.

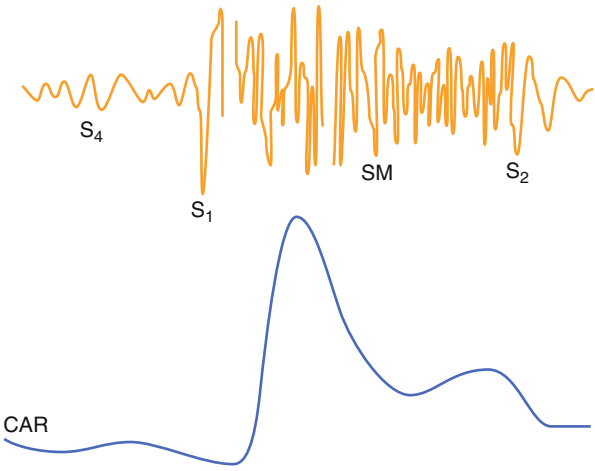


**Fig. 8.7** Biphasic "spike and dome" arterial pulse due to mid-systolic aortic valve closure during LVOT obstruction. Pulse waveform of carotid artery shown (Modified with permission. Original published in Harvey [5]. Copyrighted by Laennec Publishing, Inc. All rights reserved). *SM* systolic murmurs

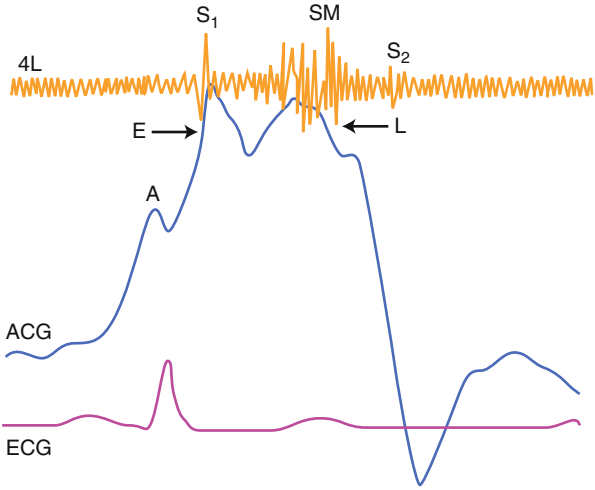


**Fig. 8.8** "Triple Ripple" apical impulse typical of HCM. The three waves are due to presystolic distention of the LV (A), early systole (E), and late systole (L) which occurs after the LVOT obstruction (Used with permission from Vanden Belt et al. [6]). *SM* systolic murmurs, *ACG* apex cardiogram

## Diagnostic Implications of the Auscultation Features

- Differential diagnosis may include other etiologies for ventricular hypertrophy, including hypertension and "athlete's heart" [2].
  - HCM can be a more severe etiology than these, and is managed differently. Confirming the etiology as HCM can be accomplished by assessing sarcomere mutations or LVOT obstruction on echo. There will also be an absence of cardiac chamber enlargement, which is often found in athlete's heart.
- The outflow tract obstruction is dynamic (not fixed like in aortic stenosis). Drugs that reduce LV volume or chamber size (e.g., nitrates, diuretics) or enhance LV

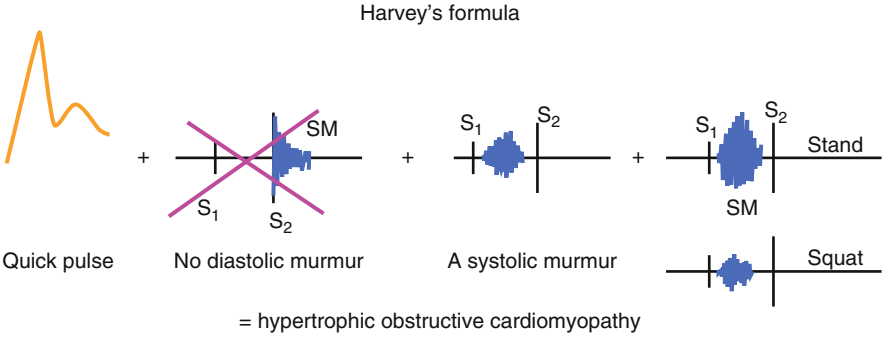


**Fig. 8.9** Four diagnostic features of HCM. The "1, 2, 3, 4" diagnosis of hypertrophic cardiomyopathy as classically taught by Dr. W. Proctor Harvey. 1. A quick rise in the arterial pulse (radial or carotid most frequently used) is noted. 2. AR is suspected as a possibility; however, no aortic diastolic murmur (DM) is present. 3. Instead, a systolic murmur is heard. 4. On squatting, the systolic murmur (SM) becomes softer or disappears. On standing, the systolic murmur becomes significantly louder. Following these clues, the diagnosis of hypertrophic cardiomyopathy can be made or strongly suspected (Modified with permission and courtesy of W. Proctor Harvey, MD, MACC, Jules Bedynek, MD and David Canfield. Original published by Laennec Publishing Inc., Fairfield, NJ, and copyrighted by Laennec Publishing, Inc. All rights reserved.)

contractility (e.g., digitalis or other inotropic agents) will exacerbate any chest pain or other HCM symptoms.

- Complications exist for HCM that are not evident with other systolic murmurs.
  - LVOT obstruction, diastolic dysfunction, myocardial ischemia and infarction of hypertrophied tissue, abnormal systolic blood pressure response to exercise.
    - Abnormal systolic blood pressure response results in an inadequate blood pressure increase due to the LVOT obstruction, and may be associated with inappropriate bradycardia.
  - Secondary mitral regurgitation.
    - The systolic anterior motion of the LVOT can distort the mitral valve. The more severe the LVOT, the more severe the mitral regurgitation is likely to be.

## Prognostic Implications of the Auscultation Features

- Family history is the key predictor of sudden death.
- Progressive disease [3].
- Over a lifetime, patients may be mostly asymptomatic with a benign course, develop heart disease or atrial fibrillation as complications, or may experience sudden death (Fig. 8.10) [2].

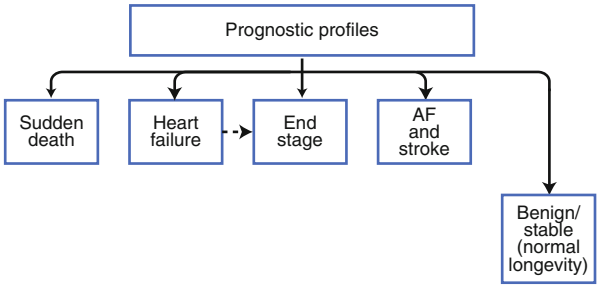


**Fig. 8.10** Different prognostic outcomes possible for patients with HCM (Used with permission from Maron et al. [7] and from Gersh et al. [1])

  - LVOT gradients increase over time.
  - Aortic regurgitation may appear but is usually mild.

- 10 year survival rate is 70 %.
- can lead to LVOT obstruction, especially on exertion, and a non-compliant hypertrophied LV which may evolve into heart failure.
  - For confirmation, electrocardiography should show LVH and deep Q waves ("pseudo-infarction" pattern) due to septal hypertrophy in the inferior or lateral precordial leads).
- Echocardiography: Doppler echocardiography can be used to estimate the pressure gradient, eliminating the need for routine cardiac catheterization.
  - The probability of death due to HCM is significantly greater in those with outflow obstruction compared to those without obstruction (RR = 2) [4].
  - Progression to severe NYHA functional class II or IV symptoms or death from heart failure or stroke has a RR = 4.4 compared to those without obstruction [4].
- Disease complications are most common in patients older than 40 years old.

## Statement on Management

### *Symptomatic Patients*

- Pharmaceutical therapy- focus on negative inotropic drugs.
  - beta blocker.
  - calcium channel blocker (verapamil).
  - anti-arrhythmic (disopyramide), if indicated.
- Invasive therapy.
  - Used if patient has persistent symptoms on medications.
  - Surgical septal reduction (myectomy).
    - Class IIa recommendation [2].

  - Alcohol ablation.
    - Class IIb recommendation [2].
    - Perform if not an acceptable surgical candidate.
- Implantable Cardiac Defibrillator.
  - Class Ia recommendation if patient had prior cardiac arrest or sustained ventricular tachycardia [2].
  - Class IIa indication for use if patient has family history of sudden cardiac death, LV wall thickness >30 mm, recent unexplained syncope, or other sudden cardiac death risk factors [2].

### *Asymptomatic Patients*

- should be treated for their comorbidities which may contribute to cardiovascular disease and should perform low-intensity aerobic exercise [2].
- Beta blocker and calcium channel blocker may be prescribed, but usefulness is not well defined.
  - See Fig. 8.11 for a treatment algorithm to be used for patients with HCM [2].

## Clinical Case Summary

The patient presents with symptomatic hypertrophic cardiomyopathy, with a high LVOT gradient inducible by typical exam maneuvers. Symptoms may be improved by the introduction of negative inotropic drugs. If symptoms are persistent, a procedural approach to septal reduction may be warranted. Prognostic considerations rely on surveillance for syncope, arrhythmias or severe increases in wall thickness.

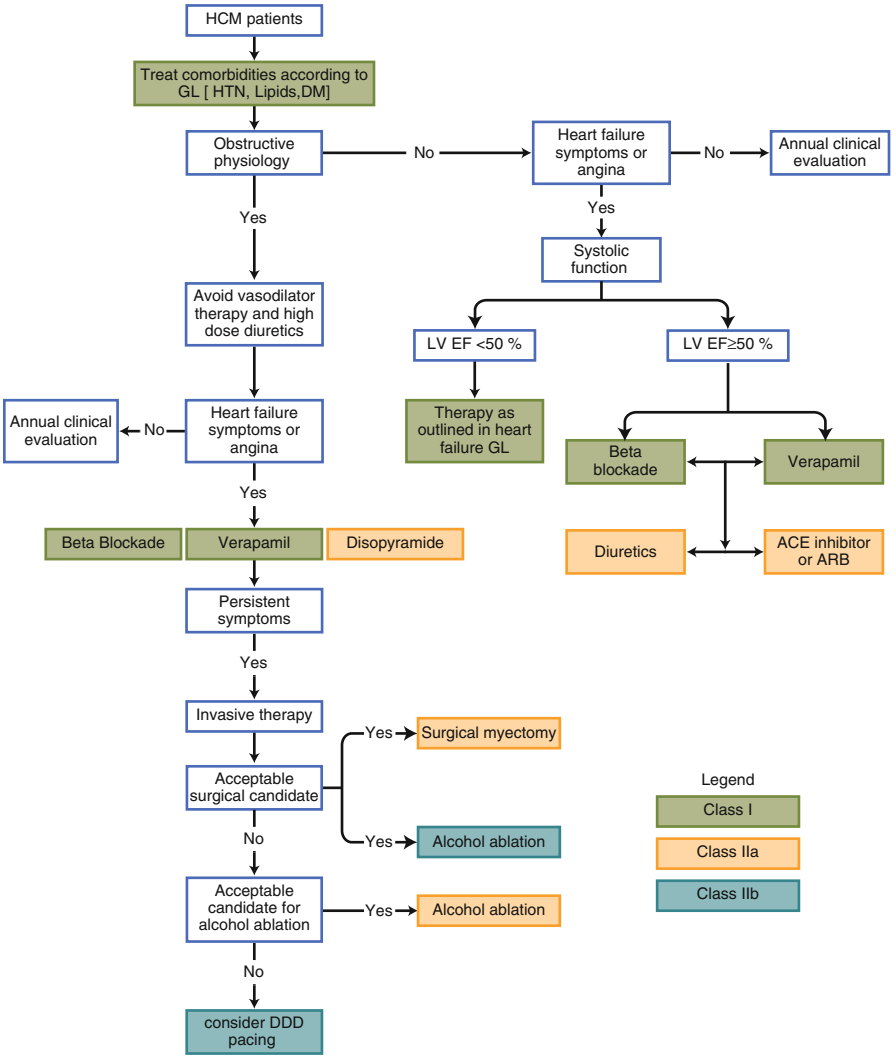


**Fig. 8.11** ACC 2011 Guidelines depicting the HCM treatment algorithm (*ACE* angiotensin-converting enzyme, *ARB* angiotensin receptor blocker, *DM* diabetes mellitus, *EF* ejection fraction, *GL* guidelines, *HCM* hypertrophic cardiomyopathy, *HTN* hypertension, *LV* left ventricular) (Used with permission from Gersh et al. [1])

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# Part III
# Valvular Lesions: Mitral Valve

# Chapter 9
# Mitral Regurgitation

**Bridget Kaufman, Christopher Sonne, and Anly K. Tsang**

## Key Teaching Points

- Mitral Regurgitation results from the systolic backflow of blood into the left atrium.
- The clinical presentation depends on severity (mild, moderate or severe) and chronicity (acute versus chronic).
- Severity can be estimated based on the intensity of the murmur, changes to S2, and presence or absence of S3.
- The general auscultation characteristic finding is an apical holosystolic murmur with radiation to axilla in chronic MR, and crescendo-decrescendo systolic murmur in acute MR.

## Case Description

### *History*

- An 85-year-old male presented to the emergency department with infrequent chest tightness and a systolic murmur.
- He reported a history of atrial fibrillation, congestive heart failure, left bundle branch block, hypertension and renal calculi.
- His current medications include: furosemide, aspirin, pentoxyfilline, lisinopril, spironolactone, levothyroxine and prazosin.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_9) contains supplementary material, which is available to authorized users.

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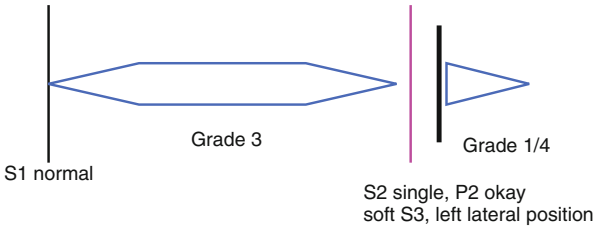


**Fig. 9.1** Auscultation Findings of Patient Case. This figure illustrates auscultation findings of a 85-year-old male who presented with chest tightness and new systolic murmur. It demonstrates the classic findings of a mitral regurgitation murmur: holosystolic murmur with radiation towards the axilla along with a S3 heart sound. Other findings of mitral regurgitation include left atrial enlargement, left ventricular hypertrophy pulmonary hypertension

## *Physical Examination*

- Vital signs: BP of 179/94 mmHg and pulse of 71 with an irregularly irregular rhythm.
- He had a normal JVP and no edema.
- Chest was clear to auscultation.
- On cardiac palpation, he had a brisk, hyper-dynamic and laterally displaced apical impulse as well as a parasternal impulse.
- Auscultation (Fig. 9.1) demonstrated a grade 3 mid-systolic murmur and grade ¼ early diastolic murmur with a normal S1, single S2 (normal P2) and soft S3 in the lateral decubitus position. The murmur radiated to the axilla.
- His arterial pulses demonstrated a brief rapid upstroke.

## Test Results

- Electrocardiogram demonstrated atrial fibrillation, septal myocardial infarction, right bundle branch block, left anterior fascicular block, left ventricular hypertrophy, and primary T wave changes (Fig. 9.2).
- Echocardiography revealed a decreased left ventricular ejection fraction of 40–45 % and left ventricular hypertrophy with a left ventricular internal diastolic dimension of 62 mm. Other findings included: left atrial enlargement, AV sclerosis, 3+ mitral regurgitation (MR), centrally directed, through a morphologically normal mitral valve (MV), and moderate tricuspid regurgitation at 2.6 m/s.

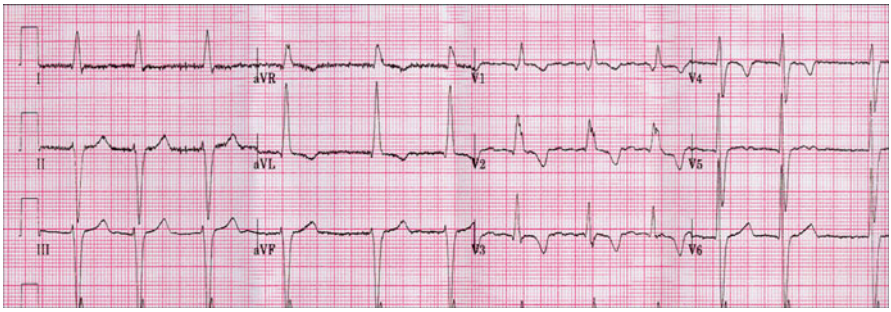


**Fig. 9.2** This presents the patient's previous ECG result obtained in 2004. The ECG shows atrial fibrillation (no true P waves and ventricular rate is irregular), right bundle branch block (wide QRS complexes with terminal R wave in lead V1 and slurred S wave in lead V6), along with septal infarction, left ventricular hypertrophy, and 1° T wave changes

## Clinical Basics

### *Normal Anatomy (Fig. 9.3)*

- The mitral valve is a bicuspid valve that separates the left atrium (LA) and left ventricle (LV). The fibrous mitral annulus sits at the left atrio-ventricular junction and serves as an insertion point for the anterior and posterior leaflets.
- The valve leaflets open into the left ventricle, tethered by papillary muscles on the wall of the LV that extend chordae tendineae attachments to the leaflets. The anterolateral papillary muscle attaches chordae tendineae to the anterior leaflet while the posteromedial papillary muscle attaches chordae tendineae to the posterior leaflet.
- During diastole, the mitral valve is open allowing for LV filling. The mitral valve closes during systole due to increased pressure of the LV, blocking blood flow back into the left atrium. Complete mitral valve closure ensures the unidirectional flow of blood from the LV to the aorta.
- The mitral valve closure is associated with the S1 sound.

### *Definitions*

- *Mitral Valve Regurgitation* (*MR*) occurs when the mitral valve becomes incompetent as a result of compromised or structurally disrupted components of the valve apparatus. This renders gaps in leaflet apposition, allowing for insufficiency, or regurgitation, from the left ventricle back into the left atrium during systole.

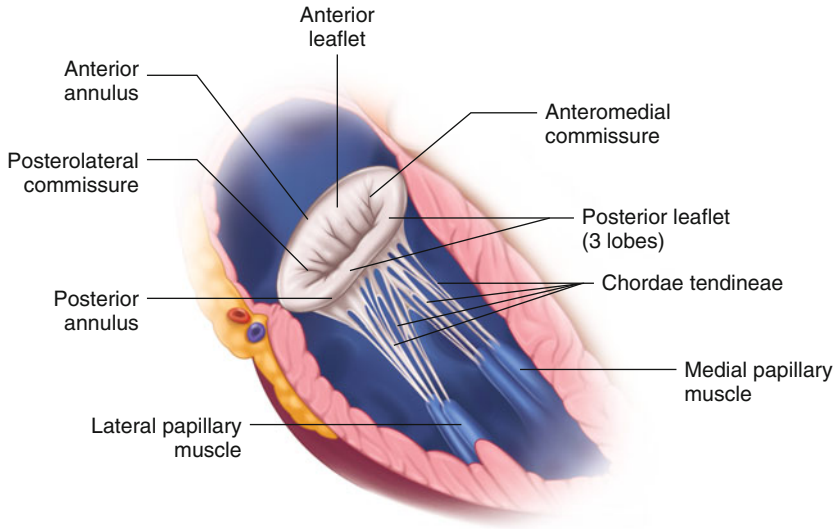


**Fig. 9.3** Internal structures of the left ventricle, showing the anterior view of the left ventricle with normal mitral valve anatomy

- There are two main types MR: Chronic and Acute.
- *Chronic MR* results from progressive deterioration of the mitral valve apparatus with increasing insufficiency over the course of many years. The defect may be within the valve itself, referred to as *organic*, or may appear secondary to pathology within the ventricles without coexisting structural change of the valve, called *Functional MR* [1, 2].
- As a result of any defect, increased volumes within the left side of the heart lead to compensatory dilatation of the left atrium and left ventricle. The resulting increase in LV end-diastolic volume allows for an increased ejection fraction (0.5–0.6), while the enlarged atrial cavity better accommodates the regurgitant volume of blood. These compensations abate the symptoms of MR: pulmonary congestion and forward failure.
- Over the course of 6–10 years, however, the prolonged burden to volume overload causes LV dysfunction and the emergence of MR symptoms [3].
- *Acute MR* is the result of an acute impairment of the mitral valve apparatus without time to establish sufficient compensatory mechanisms. The left atrium and left ventricle experience a sudden volume overload as a result of dramatic backflow of blood coupled with decreased stroke volume and cardiac output. The regurgitant volume increases intra-atrial pressure, preventing flow of blood from the pulmonary circulation into the left atrium and resulting in pulmonary congestion. In acute MR, therefore, the patient experiences reduced forward output, or even shock, along with congestion of the pulmonary vasculature [3].

## *Etiology*

- MR occurs due to a defect to any part of the mitral valve apparatus – the leaflets, chordae tendineae, papillary muscles, or mitral annulus. The location and extent of damage to the apparatus determines whether the pathology presents as Acute or Chronic MR.
- *Acute MR* may be the result of any sudden event that renders one or several component(s) of the valvular apparatus incompetent. Chordae tendineae rupture, as a result of any etiology, is the most common cause of acute MR. Possible etiologies of acute MR include:
  - *Ischemic Rupture of Chordae Tendineae or papillary muscles*: This often results from acute myocardial infarction. If ischemic damage is sudden and severe enough, rupture of the papillary muscles or chordae tendineae will likely result in Acute MR.
  - *Infectious endocarditis* is most frequently affects mitral valve structures [4]. It may lead to rupture of the chordae tendineae and/or enlargement of the posterior portion of the mitral annulus [1].
  - *Acute or Rapidly developing Cardiomyopathy.*
  - *Other acute causes*: Trauma, Surgery and spontaneous rupture.
- *Chronic MR* results from slow, progressive deterioration of the mitral valve apparatus leading to increasingly severe regurgitation across the mitral valve. Common etiologies of Chronic MR include:
  - *Myocardial infarction/Coronary Artery Disease*– Prolonged ischemia and/or infarction to the region of the tensor apparatus weakens the papillary muscles and results in an inability to sufficiently tether the corresponding leaflet to the left ventricle. An alternate hypothesis suggests that an infarct near the base of the papillary muscle may cause disorganized muscle contraction, shifting the position of the leaflet during ventricular contraction and precluding appropriate closure [5]. Others argue that MR results from displacement of papillary muscles as a result of left ventricular remodeling rather than an intrinsic defect with the muscle itself [1]. Regardless of the exact mechanism, MR in the setting of ischemic disease is rarely organic or acute, but is rather Functional MR as a result of left ventricular or papillary muscle pathology [1]. Note: Occlusion in the right coronary artery will affect the posteromedial structures, whereas left anterior descending or circumflex artery occlusion will compromise the anteromedial structures. Due to its single blood supply, posteromedial rupture is more common.
  - *Myxomatous degeneration of mitral leaflet*(*s*): Pathological weakening of the valve connective tissues renders the mitral leaflets floppy and redundant, resulting in mitral valve insufficiency. Degenerative MR is usually associated with mitral valve prolapse. Myxomatous degeneration is the most frequent cause of surgical MR [4].
  - *Rheumatic Fever*: Acquired during childhood, Rheumatic Fever (RF) induces a slow progression of scarring and retraction of the valvular leaflets that mani-

fests as MR and mitral stenosis with fusion of the commissures in middle age. These cardiac sequelae are no longer common in the United States, but are still a frequent cause of MR in countries where RF remains endemic [1].
- *Dilated Cardiomyopathy*: Dilatation of the LV expands the mitral annulus causing incompetence of the valvular apparatus.
- *Mitral annular calcification*: More common in elderly, mitral annular calcification is usually of little clinical significance; however, it may result in MR due to impairment of contraction of the valve annulus and deformation of valve leaflets. Often associated with conditions such as hypertension, aortic stenosis, diabetes and end stage renal disease [4].
- Other less common causes include *congenital connective tissue disorders* (such as Marfan Syndrome, Ehlers-Danlos Syndrome and Osteogenesis Imperfecta), Hypertrophic Cardiomyopathy, Anorectic Drugs (Fenfluramine and Desfenfluramine), Anthracycline Chemotherapy, Radiation Injury, Carcinoid heart disease, and Congenital parachute valve.

## *Signs and Symptoms*

- Depending on the cause, time course of valvular degeneration/destruction, and severity of valvular pathology, MR may remain asymptomatic or lead to severely debilitating symptoms.
- *Chronic MR* (more common) – While compensatory mechanisms are initially successful at maintaining LVEF, continuing pathology leads to symptoms of heart failure and pulmonary hypertension. Of note, patients with an asymptomatic chronic mitral regurgitation may become symptomatic after the imposition of a primary hemodynamic stressor such as pregnancy or infection.
- Symptoms of chronic MR include:
  - Progressive dyspnea upon exertion.
  - Increasing orthopnea from elevated pulmonary pressures.
  - Fatigue.
  - Palpitations from LA dilation leading to arrhythmias (e.g., atrial fibrillation).
- *Acute MR* – Symptoms of acute MR are markedly more severe than those of chronic MR, as the LA and LV have not been able to adapt to the regurgitant blood flow. An immediate and unabated increase in pressure within the LA and LV coupled with a dramatic reduction in cardiac output results in rapid onset of the following symptoms:
  - Severe dyspnea/orthopnea.
  - Pulmonary edema or congestion/ pulmonary hypertension.
  - Weakness.
  - Anxiety / confusion.
  - Fever, if stemming from endocarditis.

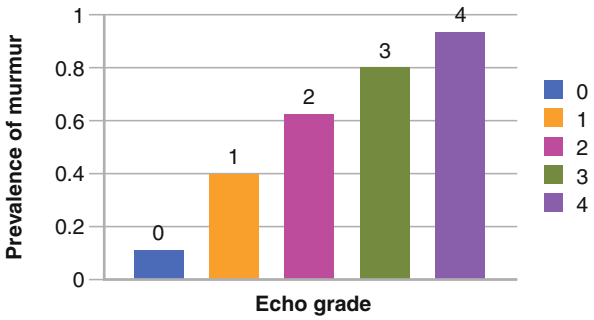


**Fig. 9.4** Prevalence of systolic murmurs based upon echocardiographic grade of mitral regurgitation. Note that although mild MR may go undetected by physical exam, most patients with moderately-severe and severe MR have a murmur present (Used with permission from Rahko [8])

### *Prevalence*

- MR is among the most common valve disease in developed countries, representing nearly one-third of acquired left-sided valve pathology [2].
- Moderate to severe mitral regurgitation affects 1.7 % of the general population with equal gender distribution and increases in prevalence with age, from .1 % among 45–50 year-olds to 9.3 % in those ≥75 years [6].
- The Framingham Heart Study demonstrates that, including mild MR, this condition is found in 19.0 % and 19.1 % in men and women, respectively [7].

## Key Auscultation Features

### *Chronic Mitral Regurgitation*

- The classical holosystolic murmur, commencing immediately after S1 and continuing up to S2. It is most often "blowing" and high pitched in quality.
- Murmur is heard best over the apex.
- The likelihood of auscultating a murmur is proportionately related to the grade of severity of MR on echocardogram. Murmur prevalence increases from 40 % to nearly 90 % with increasing severity of MR to grade 1 through grade 4, respectively [8]. See Figs. 9.4 and 9.5.
- A *widening of S2* may be due to (1) an early A2 with normal P2 indicating a shortened LV ejection time due to an early closure of the aortic valve, or (2) an early A2 combined with delayed P2 indicating the presence of pulmonary hypertension causes the delayed closure of the pulmonic valve.
- Presence of S3 gallop.
- No S4 gallop heard in chronic MR, due to an enlarged, poorly contractile left atrium.
- Auscultation Examples of Mitral Regurgitation.

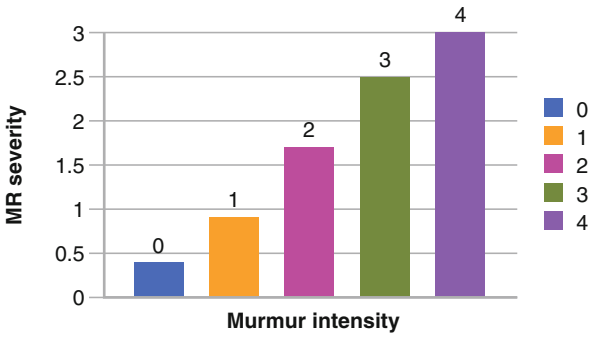


**Fig. 9.5** Relationship between murmur intensity and severity of mitral regurgitation. Note that a general relationship exists with more intense murmurs being more likely in the presence of severe mitral regurgitation (Used with permission from Rahko [8])

- Click here to listen to an example of an MR murmur in the setting of presumptive rheumatic fever and see an image of the phonocardiogram (Video 9.1).
- Click here to listen to an example of moderate to severe MR, as described by Dr. W. Proctor Harvey (Video 9.2).
- Click here to listen to an example of a female patient with chronic significant MR, as described by Dr. W. Proctor Harvey (Video 9.3).

### *Acute Mitral Regurgitation (Fig. 9.6)*

- An apical systolic murmur with early- and mid- systolic crescendo-decrescendo. The diminishment of the late systolic sound is thought to be due to building atrial pressures that soon equalize that of the LV [9, 10].
- Murmur best heard along the left sternal border.
- Prominent S4 gallop: Caused by normal-sized, vigorously contracting left atrium following exaggerated expansion during systole. It is suggestive of acute onset of regurgitation due to the rupture of the chordae tendineae that anchor the valvular leaflets [11].
- Crackles and wheezes from the abrupt onset of pulmonary edema.
- Increased P2: resulting from the pulmonary hypertension that common occurs in acute MR. While the murmur may be soft, generally cases of acute severe MR are loud and rough of a higher grade (grade 4/6) [9].

## Radiation

*Where the murmur will radiate to will depend on the type of MR (acute or chronic), the location of the valvular abnormality, and the severity of chronic MR.*

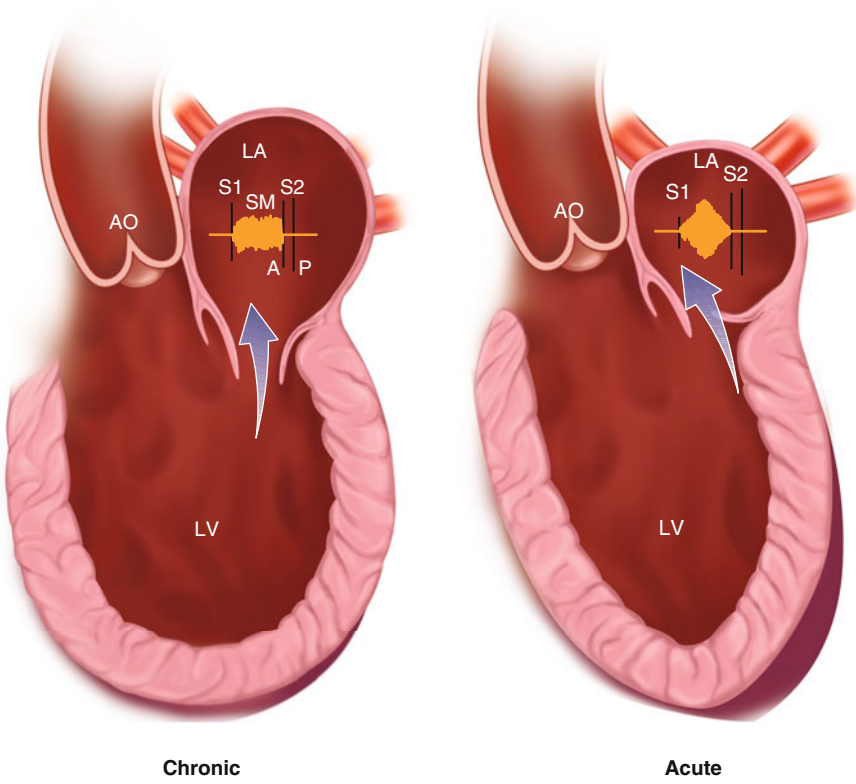


**Fig. 9.6** Acute and chronic mitral regurgitation diagrammatic representation (Modified with permission and courtesy of W. Proctor Harvey, MD, MACC, Jules Bedynek, MD and David Canfield. Originals published by Laennec Publishing Inc., Fairfield, NJ, and copyrighted by Laennec Publishing, Inc. All rights reserved.)

## *Onset*

- Chronic MR: Radiation of the murmur to the axilla or left infrascapular region.
- Acute MR: Radiation towards the base of the heart is more typical.

## *Location of Abnormality in Chronic or Acute MR*

- Posterior Leaflet: Pathology of the posterior leaflet or the leaflet's associated tensor apparatus causes the murmur to radiate toward the sternum and is heard well at the base.
- Anterior Leaflet: Anterior leaflet involvement causes radiation to back, along vertebral column, and to top of head.

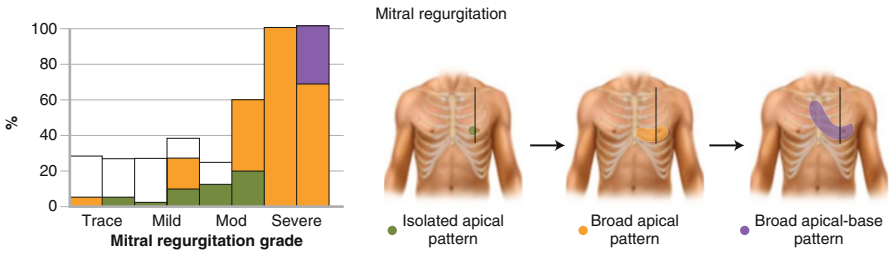


**Fig. 9.7** Radiation of mitral regurgitation based on murmur severity. As the severity of MR increases from mild to severe, the frequency of the murmur increases from 29 to 100 %. Further, the pattern of the murmur changes depending on the severity. The "isolated apical" pattern is only seen in mild to moderate cases, whereas the "broad apical" and less frequently "broad apical-base" patterns are only seen in severe MR. Data is based on 174 patients with isolated mitral regurgitation (AV peak velocity <1.8 m/s and without significant tricuspid regurgitation) (Used with permission from McGee [12])

### *Severity of Chronic MR*

- Radiation of murmur often correlates with the severity of chronic MR (Fig. 9.7).
  - Mild- moderate: Usually present with isolated apical pattern.
  - Severe: Broad apical or apical-base pattern [12].

### *Accentuation of Murmur*

- MR murmurs can be accentuated by the handgrip maneuver with 67 % sensitivity or arterial occlusion with 77 % sensitivity [13].
- During the squatting maneuver, the MR murmur will increase in intensity. Murmur intensity will decrease during return to standing position [13].

## Auscultation Differential Diagnosis

- Mitral valve prolapse: Unlike mitral valve prolapse, MR displays absence of a mid-systolic click and is a blowing holosystolic rather than harsh mid- to late systolic murmur [4].
- Tricuspid regurgitation: The intensity of the murmur of MR does not increase with inspiration, radiates towards axilla rather than the right of sternum, and involves a displaced apical beat.

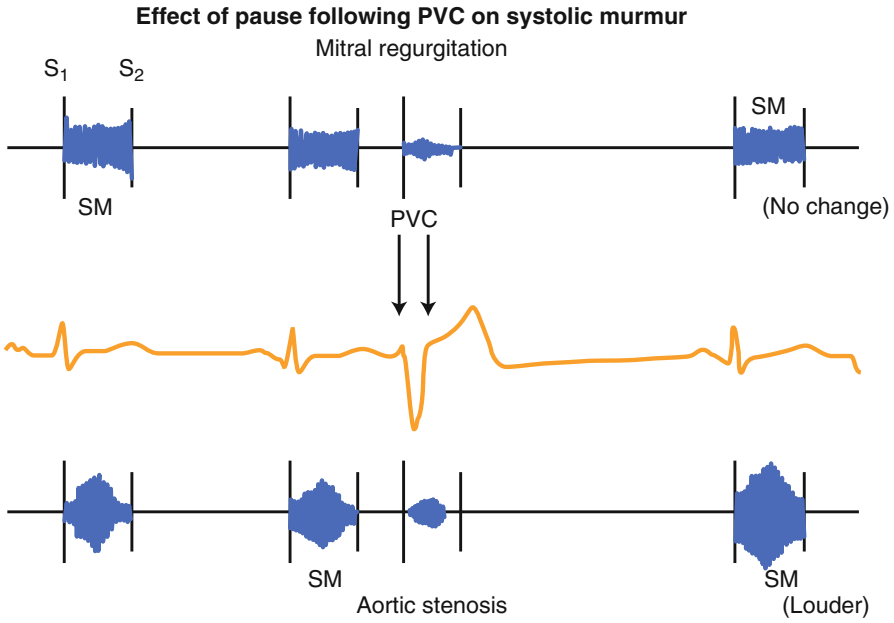


**Fig. 9.8** Effect of pause following PVC on systolic murmur. Systolic murmur (SM) of mitral regurgitation remains unchanged in intensity after pause. In contrast, SM of aortic stenosis louder after pause following premature beat (Modified with permission and courtesy of W. Proctor Harvey, MD, MACC, Jules Bedynek, MD and David Canfield. Originals published by Laennec Publishing Inc., Fairfield, NJ, and copyrighted by Laennec Publishing, Inc. All rights reserved.)

- Ventricular septal defect: MR is a high pitched murmur heard loudest at apex with a diminished S1 rather than a harsh, low-pitched murmur at the lower left sternal border with a normal S1.
- Aortic stenosis: MR, especially acute MR, can be difficult to differentiate from the murmur of aortic stenosis as both are systolic murmurs that radiate to the base of the heart. The murmur of MR, however, can also radiate towards the sternum (when posterior leaflet is involved), and may not radiate to the carotid arteries [9, 14].
  - Further differentiation of MR from aortic stenosis can be achieved upon auscultation after a premature ventricular beat (PVC) (Fig. 9.8). Diastolic left-ventricular filling time increases after a PVC, and peripheral resistance is diminished. The intensity of an MR murmur, therefore, remains unchanged after a PVC while the murmur of aortic stenosis becomes louder and longer [15].
  - *Auscultation after a premature ventricular beat can help differentiate MR from aortic stenosis.*

**Table 9.1** Auscultation characteristics distinguishing chronic mitral regurgitation from other murmurs

| Chronic MR | MVP | TR | VSD |
|---|---|---|---|
| **Loudest at apex** in left lateral decubitus position | Loudest at apex | Best heard at left upper sternal border | **Loudest at LLSB** |
| **High pitched** | | | Harsh, low pitched |
| **Soft S1** | | | Normal S1 |
| **Blowing holosystolic murmur** | Harsh mid- to late-systolic murmur with ejection click | Holosystolic murmur | Blowing holosystolic murmur (smaller) |
| **Radiates to axilla** (posterolateral jet) | | Radiates to right of sternum | Radiates to right lower sternal border |
| **Murmur accentuated with hand grip, arterial occlusion, or standing to squatting maneuver No change with inspiration** | Murmur accentuated by standing and Valsalva maneuver. | Murmur accentuated with inspiration (Caravallo's sign) | Murmur accentuated with handgrip, arterial occlusion, and squatting. |

Sources: http://cmbi.bjmu.edu.cn/uptodate/cardiac%20evaluation/Auscultation%20of%20cardiac%20murmurs.htm; and http://depts.washington.edu/physdx/heart/teaching.html

  - The MR murmur will remain unchanged (lack of accentuation) while the murmur from aortic stenosis will become louder and more intense. See Table 9.1.

- *Differentiating between three holosystolic murmurs* (Fig. 9.9). Chronic MR is a "blowing" holosystolic murmur that is *loudest at apex* in left lateral decubitus position and that radiates to the axilla. Tricuspid Regurgitation is a holosystolic murmur that increases in intensity upon inspiration. The murmur of ruptured ventricular septum will alternate in intensity and can radiate to the right sternal boarder.

## Diagnostic Implications of the Auscultation Features

### *Grading of MR Severity Clinically (Table 9.2)*

- Mild: No pulmonary hypertension.
  - *Normal S2.*
  - *Normal or hyperdynamic apical impulse.*
  - *Murmur ≤ grade 2 suggests mild MR* and accurately rules out severe MR between 88 % (fraction) and 100 % (volume) of the time, depending on whether the auscultation findings were compared to regurgitant fraction or regurgitant volume [16].

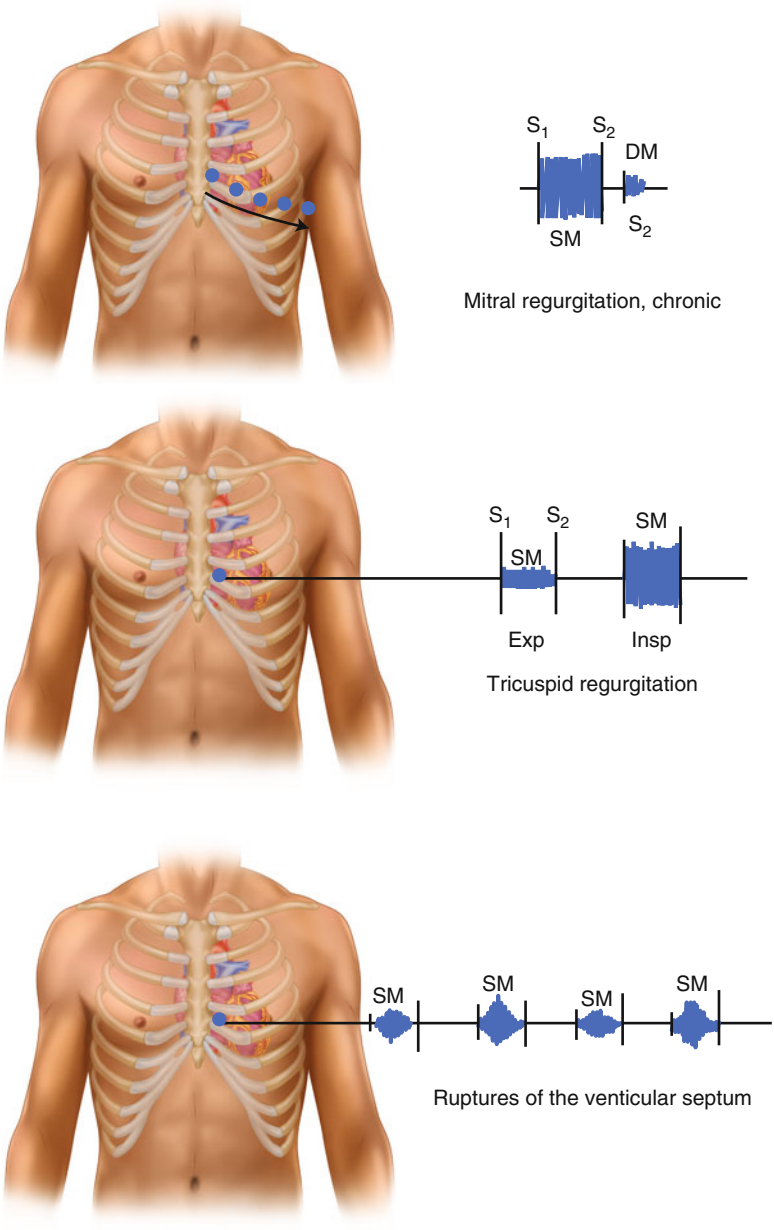


**Fig. 9.9** Differentiating holosytolic murmurs of mitral regurgitation, tricuspid regurgitation, and ventricular septal defect based on auscultation. *Top*: the holosytolic murmur of chronic MR radiates in a "band-like" manner from the apex to the left axilla and posterior lung base. An S3 gallop and short diastolic murmur may also be heard. *Middle*: the murmur of tricuspid regurgitation is best heard over the lower left sternal border. The intensity increases during inspiration. *Bottom*: The murmur of an acute VSD (due to rupture of the intraventricular septum) leads to a systolic murmur with alternating intensity as a result of cardiac decompensation (*SM* systolic murmur, *DM* diastolic murmur) (Used with permission from Chizner [10])

**Table 9.2** Qualitative and quantitative features of cardiac catheterization and echocardiography in mild, moderate and severe mitral regurgitation

| Mitral regurgitation | | | |
|---|---|---|---|
| | Mild | Moderate | Severe |
| **Qualitative** | | | |
| Angiographic grade | 1+ | 2+ | 3–4+ |
| Color Doppler jet area | Small, central jet (less than 4 $cm^2$ or less than 20 % LA area) | Signs of MR greater than mild present but no criteria for severe MR | Vena contracts width greater than 0.7 cm with large central MR jet (area greater than 40 % of LA area) or with a wall-impinging jet of any size, swirling in LA |
| Doppler vena contracts width, cm | Less than 0.3 | 0.3–0.69 | Greater than or equal to 0.70 |
| **Quantitative (cath or echo)** | | | |
| Regurgitant volume (ml per beat) | Less than 30 | 30–59 | Greater than or equal to 60 |
| Regurgitant fraction (%) | Less than 30 | 30–49 | Greater than or equal to 50 |
| Regurgitant orifice area ($cm^2$) | Less than 0.20 | 0.2–0.39 | Greater than or equal to 0.40 |
| **Additional essential criteria** | | | |
| Left atrial size | | | Enlarged |
| Left ventricular size | | | Enlarged |

Based on table from the following source: Bonow et al. [3]

- Moderate: Pulmonary hypertension.
  - *Wider split of S2 in* pulmonary hypertension: results from delayed P2; indicate advanced disease and worse prognosis. Jugular venous distension, right ventricular impulse, or a loud P2 sound can be heard either in combination or individually [9].
- Severe:
  - *Presence of S3*: LV volume overload, S3 is prolonged in severe chronic mitral regurgitation and possible heart failure. A pulsus alterans felt upon palpation of the radial pulse should cause suspicion of the presence of an S3 and the systolic murmur of MR that often accompany acute heart failure [14].
  - *Apex thrusting and displaced*: Severe MR may produce a more forceful, brisk left parasternal thrust or lift, predominantly in late systole, as a result of a recoil phenomenon related to the regurgitant jet of blood into the left atrium pushing the heart forward against the chest wall ("left atrial rock") [11].
  - *Grade 4 murmur or greater*: Auscultation of MR murmur ≥ grade 4 predicts severe MR in 91 % of patients (based on regurgitant volume and regurgitant fraction) [16].

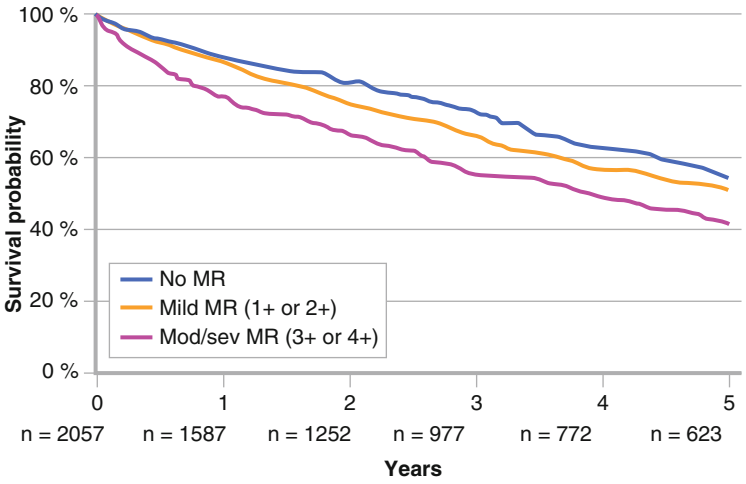


**Fig. 9.10** Adjusted survival estimates are shown. Patients with moderate to severe (Mod/sev) MR are represented by the light line, those with mild MR by the dashed line, and those with no MR by the dark line (Used with permission from Trichon [17])

## Prognostic Implications of the Auscultation Features

- Enriquez-Sarano's review (1) on mitral regurgitation found that patients with left ventricular enlargement (and resulting volume overload) experienced the highest mortality risk of patients with MR. Patients with NYHA class III–IV symptoms incurred the highest risk of mortality, at 12 % per year, whereas asymptomatic patients with normal ejection fraction and sinus rhythm had a much lower prevalence of 0.8 % per year.
  - Of patients diagnosed with severe MR, patients under 50 years old and those who had progressed from moderate MR exhibited lower rates of mortality.
  - Regardless of symptom severity, patients over age 50 with severe organic mitral regurgitation have a 6 % risk of mortality whereas those with moderate regurgitation have a 3 % risk.
  - Patients with severe mitral regurgitation have cardiac event rates of 10–12 %, most commonly congestive heart failure and atrial fibrillation.
  - Within 10 years of diagnosis of severe mitral regurgitation, 90 % of patients will die or undergo surgery for MR.
  - Predictors of poor survival in those under medical management include: class III or IV CHF symptoms, reduced ejection fraction, and effective regurgitant orifice of 40 $mm^2$ or above (or corresponding murmur ≥ grade 4 (16)) [1].
- A 2003 study by Trichon et al. also found that the presence and severity of MR independently predicted decreased survival in patients with LV systolic dysfunction (Fig. 9.10). Of the 2057 studied patients with LV systolic dysfunction 56.2 % also had MR. Those with severe MR (grades 3+ or 4+, which correlate to murmur grades

≥4/6 (16)) had significantly decreased 3- and 5-year survival (51.3 and 39.9 %, respectively) compared to those with no MR (71.8 and 54.2 %, respectively) [17].

- Symptoms associated with MR predict prognosis. In a retrospective study by Delahaye et al. [18], the course of MR was divided into three periods: an asymptomatic period, the symptomatic pre-hospital period, and the post-hospital period divided into a surgical and non-surgical group.
  - The average time between initial MR murmur and the onset of MR-related symptoms (the asymptomatic period) is approximately 16 years. During this phase, the prognosis of the asymptomatic patients was good. The onset and progression of MR symptoms closely correspond to onset and progression of myocardial dysfunction.
  - The time between when patients begin to have MR-related symptoms and reparative or replacement surgery is 3–6 years. During that time the average LVEF decreases by 5 % each year.
  - For patients who are not operated on, prognosis is poor. Matching LVEF in patients in the surgical and non-surgical groups, 5-year survival rate was 81 % vs. 51.5 %, respectively.

## Statement on Management

### *Chronic MR (Fig. 9.11)*

- Asymptomatic with Normal LV Function.
  - There are no guidelines for the management of asymptomatic MR if the patient remains in sinus rhythm with normal LV and LA dimensions. Such patients can exercise without restriction. No pharmacological treatments have been consistently indicated for the sole treatment of MR.
  - Ideally, vasodilators decrease systemic vascular resistance, increase LVEF and alleviate tendency for regurgitant flow. However, while vasodilators reduce symptoms associated with systolic dysfunction associated with MR, there is no data to support use of vasodilators on asymptomatic patients with MR. In general, medical therapy is only suitable to treat the symptoms of chronic MR, or otherwise to treat secondary conditions arising from chronic MR – cardioversion and anticoagulants for atrial fibrillation, ischemic disease prevention, etc.
  - However, for these patients clinical and echocardiogram evaluations are suggested every 6 months.
- Symptomatic or Abnormal LV Function.
  - Patients with LV or LA enlargement, any degree of pulmonary hypertension should be advised against exercise in competitive sports.
  - Pharmaceutical management should be focused on decreasing preload and afterload on the LV.

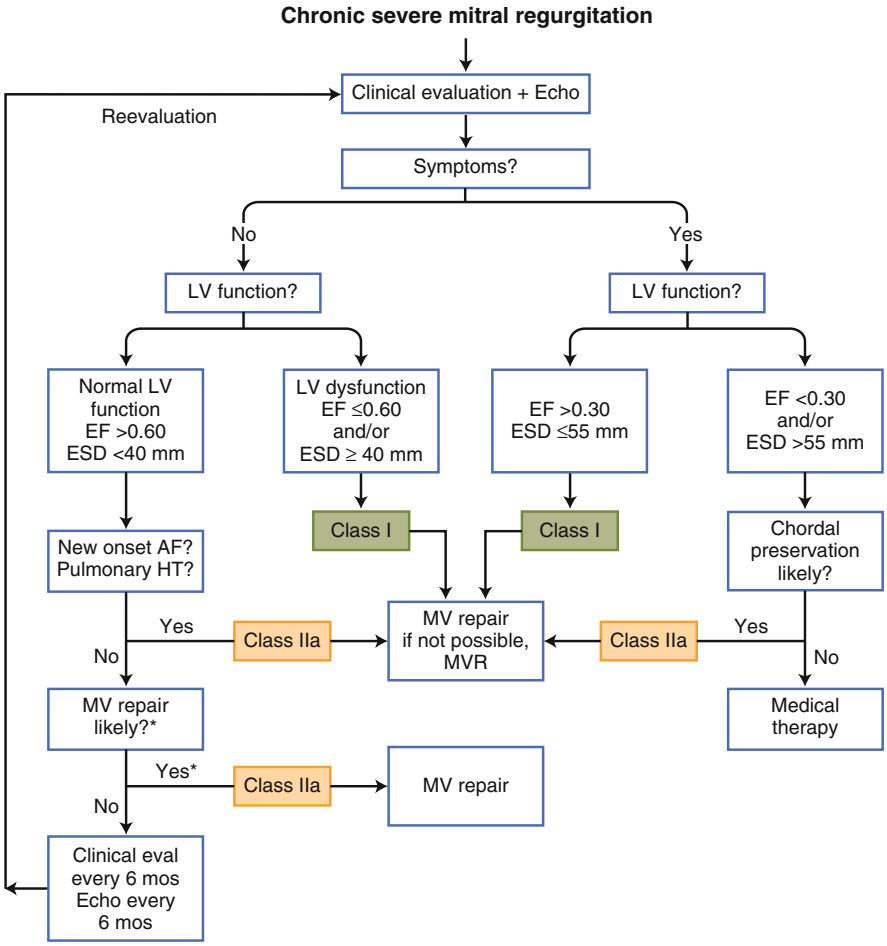


**Fig. 9.11** Management strategy for patients with chronic severe mitral regurgitation. *Mitral valve (MV) repair may be performed in asymptomatic patients with normal left ventricular (LV) function if performed by an experienced surgical team and if the likelihood of successful MV repair is greater than 90 %. *AF* indicates atrial fibrillation, *Echo* echocardiography, *EF* ejection fraction, *ESD* end-systolic dimensions, *eval* evaluation, *HT* hypertension, and *MVR* mitral valve replacement (Used with permission from Practice Guideline: Bonow et al. [19])

- Surgery.
  - Options.
    - Mitral valve repair – Generally better outcomes, but is more time-intensive and is dependent on the clinical expertise available.
    - Mitral valve replacement.
  - Indications.
- Surgical repair or replacement of the dysfunctional valve is indicated in symptomatic patients with severe chronic MR. Surgery is also recommended

in asymptomatic patients with severe MR once any indication of early systolic dysfunction become identifiable. Such indicators include an end-systolic ventricular dimension of 45 mm or more or an LVEF of ≤60 %.

### *Acute MR*

- Management should be centered on keeping the patient hemodynamically stable while awaiting surgery for mitral valve repair or replacement.
- If the patient is normotensive, reducing pulmonary hypertension and increasing forward output can be accomplished by administration of nitroprusside.
- If the patient is hypotensive, inotropic agents such as dobutamine need to be added.
- If the cause of the MR is determined to be infectious, appropriate antibiotics should be administered.

## Clinical Case Summary

The patient presents with moderate to severe MR by exam, as evidenced by a grade 3 murmur, with a diastolic flow murmur, and S3 gallop. LV enlargement is present, along with reduced ejection fraction. The findings of LV enlargement and the severe MR predict a poor prognosis. Decision making on surgical management is difficult due to the patients advanced age, and left ventricular systolic dysfunction.

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# Chapter 10
# Flail Mitral Leaflet

**Haley Bunting, Megan E. Murphy, and Heather Pemberton**

## Key Teaching Points

- The cause of flail mitral leaflet (FML) is most commonly myxomatous valve changes accompanied by rupture of chordate tendinae of the mitral valve.
- The hallmark finding on auscultation is a holosystolic murmur with features of severe mitral regurgitation (MR), typically a grade 3 or 4 murmur.
- Specific features include a decrescendo murmur with eccentric radiation, soft S1 and loss of the click often associated with mitral valve prolapse.
- The MR can be accentuated by hand-grip and vascular occlusion, but echocardiogram is key for diagnosis.
- FML should generally be treated with surgical valve repair or replacement.

## Case Presentation

### *History*

- A 64 year old woman presents with a history of Mitral Valve Prolapse (MVP) for 20 years.
- History reveals slowly progressive dyspnea on exertion, fatigue for months, worsening over the week prior to admission.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_10) contains supplementary material, which is available to authorized users.

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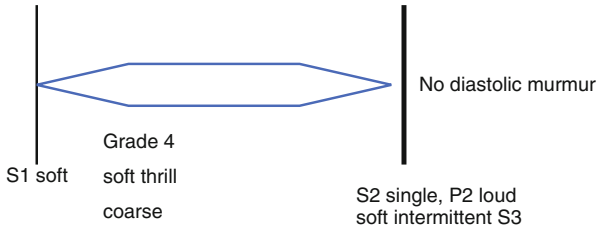


**Fig. 10.1** This figure illustrates auscultation findings of a flail mitral leaflet with its hallmarks of an intense murmur, a palpable thrill, a soft S1 reflecting high intracardiac pressure, and indicators of pulmonary hypertension

- She denies orthopnea, paroxysmal nocturnal dyspnea (PND) and chest pain. She has had mild lower extremity (LE) edema for 2 days.
- Past medical history reveals toxic multinodular goiter/Hashimoto's thyroiditis. She is not currently taking any medications.

## *Physical Exam*

- Vital Signs: Blood Pressure 109/77 mmHg; Pulse 86, regular.
- Jugular Venous Pressure (JVP): Increased, normal contour.
- Chest: Clear to auscultation.
- 1+ LE edema.
- Auscultation (Fig. 10.1):

  – The apical impulse is enlarged. A parasternal impulse is noted synchronous with the radial pulse. The pulmonic closure sound (P2) is palpable in the left second interspace.
  – Soft S1.
  – Grade 4 coarse systolic crescendo decrescendo murmur with soft thrill.
  – Single S2 with loud P2.
  – Soft intermittent S3.
  – No diastolic murmur.

## *Test Results*

- Electrocardiogram shows normal sinus rhythm (NSR), rightward axis, RV strain pattern, increased voltage and left atrial enlargement (LAE) criteria for left ventricular hypertrophy (LVH).
- Echocardiography shows the following (Fig. 10.2a, b):

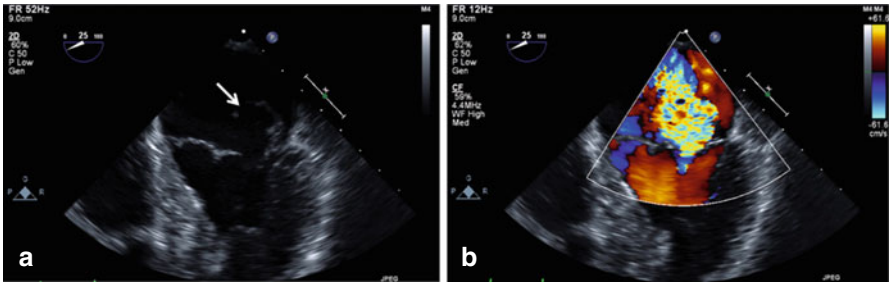


**Fig. 10.2** (**a**, **b**) Echocardiogram of a flail leaflet of the mitral valve resulting in severe mitral regurgitation. (**a**) Posterior leaflet displaced into the *left* atrium during systole. (**b**) Color Doppler showing severe mitral regurgitation (MR)

- Ejection fraction (EF): 65 %.
- D-shaped septum in systole.
- Left ventricular end diastolic dimension: 48 mm.
- Left atrium minimally enlarged.
- Mitral valve: Shows myxomatous features and partial flail.
- Severe MR: eccentric.
- Tricuspid Regurgitation: Moderate (3.6–4 m/s).
- Pulmonary hypertension pattern on pulmonary valve m-mode.
- Increased velocity of mitral valve inflow (>2 m/s).
- Dilated hepatic veins and inferior vena cava: Inspiratory flow reversal.
- Vena contracta width: 0.77 cm.

## Key Auscultation Features of the Lesion

- Basic auscultation features of FML include severe MR with decrescendo, mixed frequency murmur and eccentric radiation.
- The murmur is classically holosystolic, extending from S1 through to S2. It can also be early systolic, mid systolic or late systolic.
- Soft S1 heart sounds may be heard and the click associated with MVP may disappear.
- S2 splitting due to early A2 is frequently heard.
- Occasionally, an early to mid diastolic murmur is present due to increased mitral flow or MV pre-closure.
- FML classically radiates to the axilla or left intrascapular region, but the jet direction can influence murmur radiation [1].
- In an observational study conducted by the Mayo clinic of 229 patients with isolated MR due to FML, 87 % had grade 3 or 4 murmur, classified as severe MR. Therefore, auscultation findings consistent with severe MR are often used to help diagnosis FML [2].

- Auscultation examples of severe MR.
  - Click here to listen to an example of severe MR in the setting of progressive valve destruction in infective endocarditis in a patient with a history of mitral valve prolapsed, as described by Dr. W. Proctor Harvey (Video 10.1).

## Auscultation Differential Diagnosis

Upon hearing a holosystolic murmur, one should be suspicious of MR. Recall, 87 % of individuals with isolated FML presented with a grade 3 or 4 severe MR murmur [2]. However, several other clinical features may mimic this and should be considered in the differential diagnosis:

- **Aortic Stenosis (AS)**: In a posterior chordae rupture leading to a flail posterior cusp, the stream of regurgitation may strike the atrial septum in such a way that mimics the shape and radiation into the carotids typical of AS. Radiation of a posterior chordae rupture may be better heard into the lower back opposed to the neck. Rarely, anterior chordae ruptures may also mimic AS. The reason is unknown, but anterior chordal rupture may radiate along the spine and to the top of the head [3].
- **Tricuspid Regurgitation (TR)**: TR, another holosystolic murmur, is heard best along the left sternal border and is augmented by inspiration. It presents with a prominent v wave and y descent in the JVP [3].
- **Gallavardin Phenomenon**: Gallavardin phenomenon is an aortic ejection murmur seen in elderly patients with calcific aortic stenosis. The aortic valve will lack commissural fusion, allowing the cusps to vibrate and produce pure frequencies. The musical sounding murmur is prominent in the apex with high frequency components, suggestive for MR. However, Gallavardin phenomenon does not radiate to the left axilla like FML and is accentuated by a slowing of the heart rate while MR does not change with a slowed heart rate [3].
- **Ventricular Septal Defects (VSD)**: MR usually radiates best to the axilla and to the left posterior intrascapular area of the chest. If loud enough, MR radiates to the right, but to a lesser degree. Conversely, VSD murmur from ventricular septal rupture will be loudest near the apex [3, 4].
- **Corrected Transposition of Great Vessels**: Corrected transposition of the great vessels may mimic severe MR if the tricuspid valve becomes regurgitant, for example in Ebstein's anomaly (downward displacement of a deformed tricuspid valve). This is not uncommon in corrected transpositions. Additionally, anomalous insertion of chordae into the left tricuspid valve has also been found to be a cause and likewise mimics MR [3].

## Clinical Clues to the Detection of the Lesion

- In addition to the auscultation features listed above, clues of severe MR may help identify FML:
  - A decreased arterial pulse with a brief, rapid upstroke and a normal JVP.
  - On palpation, the apex beat is brisk, hyperdynamic and laterally displaced and a parasternal impulse may be present.
  - A diastolic flow murmur may or may not be present.
  - A wider S2, S3 gallop, and louder and longer apical systolic murmur are also associated with severe MR.

## Diagnostic Implications of the Auscultation Findings

Auscultation maneuvers to accentuate the murmur intensity:

- Because the majority of patients with FML present with signs of severe MR, bedside maneuvers that augment or decrease the intensity of MR murmurs will aid in differentiating mitral flail from other conditions that present with systolic murmurs. Specifically, the maneuvers listed below were found to be particularly helpful in the diagnosis of MR.
- Isometric Handgrip Exercise: augmented the murmurs of MR with 68 % sensitivity and 92 % specificity. This maneuver is helpful in distinguishing MR from the murmurs of aortic stenosis, hypertrophic cardiomyopathy and to a lesser degree, right-sided murmurs where the majority of cases showed no change or a decrease in murmur intensity. However, a parallel increase in murmur intensity was seen with VSD and therefore the MR murmurs could not be distinguished from VSD solely on the basis of the response to handgrip [1].
- Transient Arterial Occlusion: augmented the murmurs of mitral regurgitation with 78 % sensitivity and 100 % specificity. This augmentation was also seen with the murmurs of VSD. The majority of all other systolic murmurs did not change or decreased in intensity with transient arterial occlusion [1].
- Amyl Nitrite Inhalation: a decrease in murmur intensity in those with MR was seen with 80 % sensitivity and 90 % specificity. A similar decrease in murmur intensity was observed in patients with VSD. Conversely, inhalation of amyl nitrite augmented the murmurs of right-sided valvular disease, aortic stenosis and hypertrophic cardiomyopathy [1].
- Radiation of MR versus VSD: Because the murmurs of MR and VSD have parallel responses to all of the maneuvers listed above, the two entities can often be distinguished based on where they radiate. Specifically, MR radiates to the axilla

and the left infrascapular regions whereas the murmurs of VSD will be loudest at the apex of the heart [1, 3].

Although these bedside maneuvers aid in the diagnosis of mitral flail, echocardiography is necessary for confirmation.

## Prognostic Implications of the Auscultation Features

Because of its unique pathophysiologic process, MR due to FML has posed a challenge to the clinician for years.

- Symptoms may be absent despite severe regurgitation. Ten years after the diagnosis of FML, however, death or surgical repair of the valve is almost unavoidable [5].
- In effort to better understand the prognostic implications, one landmark study evaluated 229 patients with isolated mitral regurgitation due to flail leaflet [2]. This study found that there were certain factors related to a poorer prognostic outcome (Table 10.1), each of which is discussed in further detail below:

  – Medical treatment (vs. surgery).
  – Older age of the patients.
  – Advanced symptoms.
  – Reduced ejection fraction at diagnosis.

Additionally, this study uncovered factors that did not correlate with a poor prognosis. Most remarkably, atrial fibrillation during follow-up was not associated with excess mortality (Fig. 10.3; P = 0.19) [2].

## Effect of Treatment on Prognosis

A study found that among the patients treated medically there was an excess mortality directly related to cardiac disease, whereas in those that received surgery there was not. The 86 patients who were treated medically had a mortality rate significantly higher than expected (6.3% yearly, P = 0.016 for the comparison with the expected rate in the US population). This is depicted in the Kaplan-Meier survival curve in Fig. 10.4. Conversely, among the 143 patients that underwent surgery, survival at 5 and 10 years was 79 ± 3 and 66 ± 4% respectively (97 and 100 % of the expected survival, respectively; P = 0.68) [2]. Thus, when the effect of surgery on survival was considered, no excess mortality was observed.

**Table 10.1** Multivariate predictors of the outcome of mitral regurgitation due to flail leaflet

| Outcome | No. pts in model | No. of events | Adjusted HR | P-value |
|---|---|---|---|---|
| Survival with medical treatment | 228 | 44 | | |
| Age | | | 1.08 (1.05–1.12) | 0.001 |
| NYHA class | | | 1.93 (1.45–2.59) | 0.001 |
| Ejection fraction | | | 0.96 (0.93–0.98) | 0.001 |
| Congestive heart failure | 196 | 48 | | |
| Age | | | 1.06 (1.02–1.09) | <0.001 |
| NYHA class | | | 1.39 (0.96–2.01) | 0.084 |
| Ejection fraction | | | 0.95 (0.91–0.98) | 0.035 |
| Left atrial dimension | | | 1.05 (1.01–1.09) | <0.001 |
| Survival with medical and surgical treatment | 228 | 63 | | |
| Age | | | 1.09 (1.06–1.12) | <0.001 |
| NYHA class | | | 1.60 (1.25–2.05) | <0.001 |
| Ejection fraction | | | 0.96 (0.94–0.98) | 0.001 |
| Mitral-valve surgery | | | 0.29 (0.15–0.56) | <0.001 |
| Survival with medical treatment | 228 | 63 | | |
| Age | | | 1.09 (1.06–1.12) | <0.001 |
| NYHA class | | | 1.62 (1.26–2.09) | <0.001 |
| Ejection fraction | | | 0.96 (0.94–0.98) | <0.002 |
| Mitral-valve surgery | | | 0.28 (0.15–0.55) | <0.001 |
| Co-morbidity index | | | 1.07 (0.83–1.37) | 0.61 |

Used with permission from Ling et al. [2]

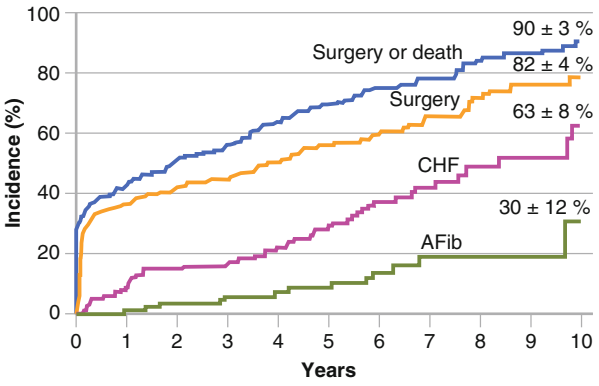


**Fig. 10.3** Incidences of atrial fibrillation (AFib), congestive heart failure (CHF), mitral valve surgery and surgery or death. Values for each endpoint are means ± SEM incidences after 10 years (Used with permission from Ling and Enriquez-Sarano [5])

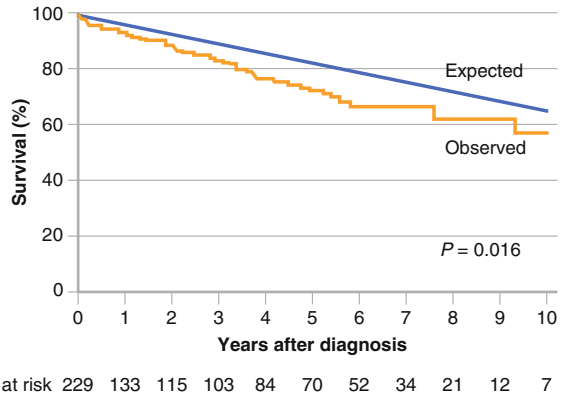


**Fig. 10.4** Long-term survival with medical treatment, as compared with expected survival, in 229 patients with Mitral Regurgitation due to Flail Leaflet (Used with permission from Ling et al. [2])

## Effect of Age on Prognosis

One of the earliest studies looking at outcomes of mitral regurgitation found that in the surgical cohort, age was predictive of survival. When compared to the younger patients, older patients (>61 years) had significantly poorer survival probability (P = 0.0003). This is depicted below in Fig. 10.5 [6].

One of the multivariate predictors of the development of congestive heart failure was age (Table 10.1; P < 0.001). Therefore, the conclusion drawn was that older age can be used as a base-line predictor of death [2].

## Effect of Symptoms on Prognosis

The presence of symptoms is a major predictor of survival. In this study, the outcome for patients in New York Heart Association (NYHA) class III or IV at baseline was worse than the outcome for patients in class I or II (hazard ratio, 8.23; 95 % CI 4.22–16.05; P < 0.001). This is illustrated in the Kaplan-Meier survival curve shown in Fig. 10.6. It was concluded that the presence of class III or IV symptoms, even if transient, should trigger the consideration of immediate surgery [2]. These symptoms include:

- Class III: marked limitation of physical activity, with the patient easily fatigued or dyspenic.
- Class IV: unable to carry out physical activity without discomfort and have symptoms of cardiac insufficiency at rest.

## Effects of Ejection Fraction on Prognosis

Outcome was also influenced by left ventricular function, as measured by ejection fraction. A low EF (<60 %) correlated with poorer survival (Table 10.1, Fig. 10.7).

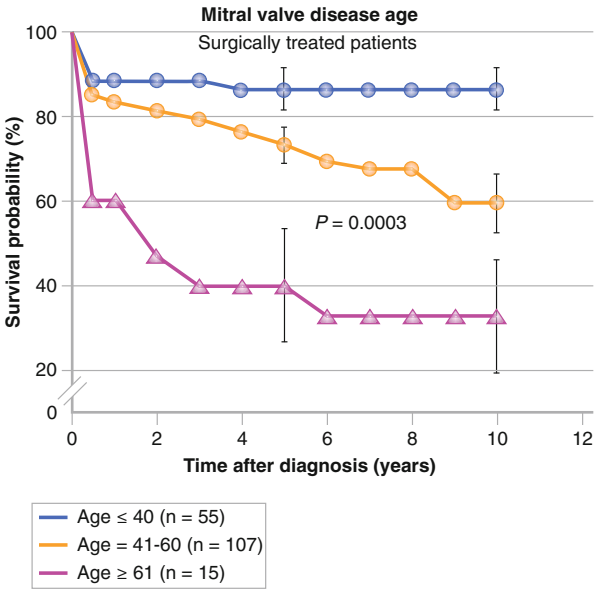


**Fig. 10.5** Survival curve of surgically treated mitral valve disease in patients demonstrating significantly different (P = 0.0003) survival when they are grouped according to age (Used with permission from Hammermeister et al. [6])

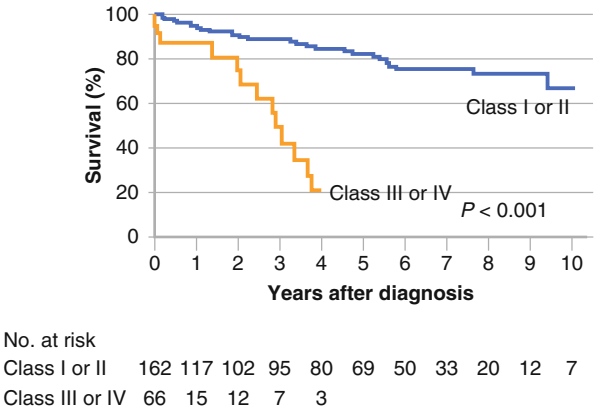


**Fig. 10.6** Long-term survival with medical treatment, according to the New York Heart Association (NYHA) Class (Used with permission from Ling et al. [2])

Even a mildly decreased EF (<60 %) carries an increased risk of late mortality and heart failure and should lead to the consideration of immediate surgery [2].

FML is the most common cause of surgical treatment of mitral regurgitation in the United States [5]. Older age, decreased ejection fraction and symptoms of moderate and severe heart failure have been correlated with decreased survival rates. If a patient presents with these factors, the prognosis is poor and immediate surgery should be considered. Overall, surgical correction has been shown to improve survival. Therefore, surgery should be considered early in the disease in patients who are surgical candidates with repairable valves.

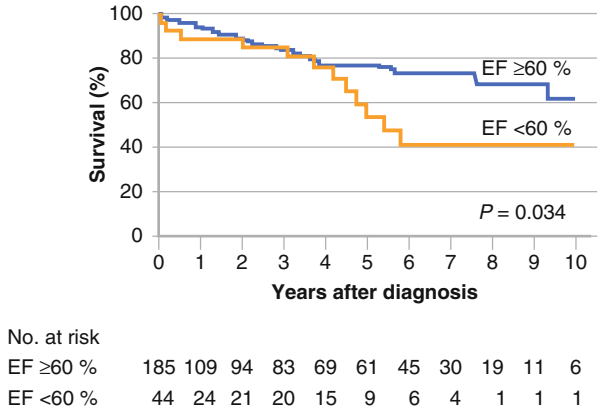


**Fig. 10.7** Long-term survival with medical treatment, according to ejection fraction (Used with permission from Ling et al. [2])

## Statement on Management

According to ACC/AHA 2006 guidelines for the management of patients with valvular heart disease:

- Management of FML requires surgical intervention.
- If possible, repair of the FML is preferred and is superior to valve replacement.
- Severe symptoms of mitral regurgitation is predictive of a poor outcome after MV repair or replacement and therefore surgical intervention should be considered early in the disease in patients with a low surgical risk [7].

## Clinical Summary of the Case

The patient presents with worsening dyspnea with a history of mitral valve prolapse. Current auscultation features with a soft S1, and grade 4 MR murmur, including findings of potential pulmonary hypertension, indicate the potential for flail mitral leaflet. Imaging findings confirmed the diagnosis, for which surgery is indicated due to improved outcomes with surgical intervention.

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# Chapter 11
# Mitral Stenosis

**Kirti Johal, Lawrence Lau, and M. Elizabeth Card**

## Key Teaching Points

- The predominant cause of mitral stenosis is rheumatic fever.
- Characteristic changes to the mitral valve in mitral stenosis include thickening at the leaflet edges, fusion of the commissures, chordal shortening and fusion, and a "fishmouth" appearance.
- The auscultatory hallmarks of mitral valve stenosis include a loud S1 at the apex, an opening snap following S2 at the apex and a diastolic, decrescendo-type murmur accentuated by expiration.
- Markers of severe mitral valve stenosis include biphasic P waves on EKG, a high left atrioventricular pressure gradient on Doppler echocardiography, an early opening snap following S2, a loud P2, and pulmonary hypertension.
- Defining elements of pulmonary hypertension (i.e., pulmonary fibrosis, delayed P2) and/or atrial fibrillation are important in determining the appropriate time for surgical intervention in patients with mitral stenosis.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_11) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- A 51 year old male with a 10 year history of mitral stenosis presents with the chief complain of syncope.
- Syncope is always exertional and preceded by shortness of breath and chest pain.
- He otherwise has no past medical history and is on no medications.

### *Physical Examination*

- VS: BP 120/80 mmHg; pulse 60 bpm, regular.
  - JVP normal.
  - Slight right ventricular heave.
  - Cardiac (Fig. 11.1):
    - Loud S1 at the left sternal border.
    - Opening snap following S2 at the left lower sternal border and apex.
    - Decrescendo-type diastolic rumble, best heard when the patient expires.
    - Auscultation.

## Test Results

- Echocardiography (Fig. 11.2a, b) shows mild right ventricular enlargement, no aortic stenosis. There is moderate MR with a right ventricular systolic pressure of 34 mmHg. The mitral valve gradient was 4 mmHg, and the mitral valve area was 1.5 $cm^2$.
- The Doppler echocardiography demonstrates an increased left atrioventricular pressure gradient (Fig. 11.3).

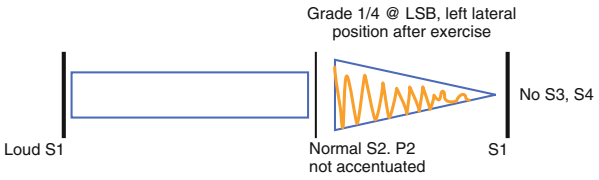


**Fig. 11.1** Typical auscultatory findings associated with mitral valve stenosis include loud S1 and decrescendo-type diastolic rumble. Note that MS is best heard with the patient in the *left* lateral decubitus position (LLDP) after exercise. The LLDP bring the apex of the heart closer to the chest wall and exercising increases cardiac output and thus the volume of blood being forcibly pumped through the stenotic mitral valve

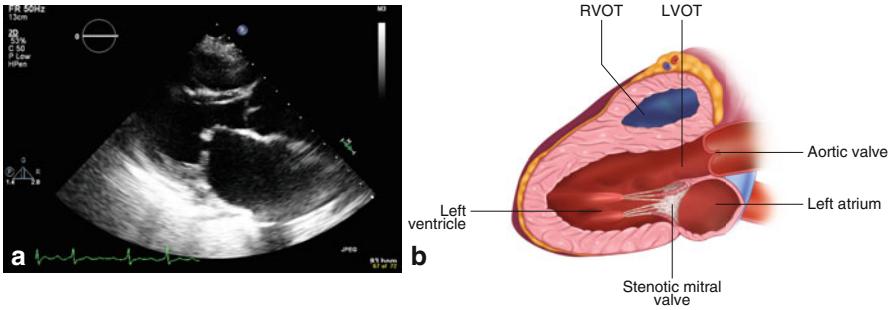


**Fig. 11.2** (**a**) Echocardiogram (parasternal long axis view) showing the mitral valve with hallmarks of mitral stenosis including thickening of the valve and tethering of the anterior mitral valve leaflet. (**b**) Artist rendering of a parasternal long axis view of the myocardium on echocardiogram. Note the thickened calcified valves characteristic of mitral valve stenosis. Symptoms typically occur once the MV area measures between 1.2 and 1.6 $cm^2$

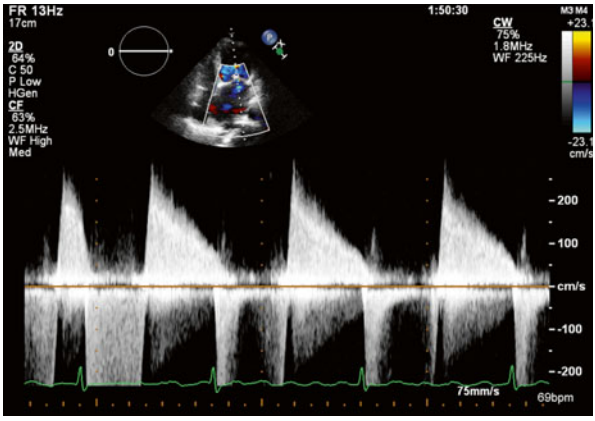


**Fig. 11.3** The thickened valves MS causes seen on 2D echocardiography lead to persistently increased left atrioventricular pressure which is seen in the continuous wave Doppler profile showing high diastolic velocity with a reduced rate of decay (i.e., the velocity remains high throughout diastole). The left atrial pressure, for which the A2-opening snap interval is a surrogate, is an important prognostic indicator of the severity of the disease

## Clinical Basics

### *Normal Anatomy Valve*

- Bileaflet valve with the aortic leaflet in fibrous continuity with the noncoronary cusp of the aortic valve.
- Supported by two papillary muscle groups: anterolateral and posteromedial.
- There is considerable variation in the morphology of the papillary muscles.

## *Definition*

- Occurs from left ventricular inflow obstruction due to thickening and immobilization of the mitral valve leaflets.
- Results in increased left atrial pressure, pulmonary HTN, right ventricle enlargement.
- Left ventricle is unaffected in isolated MS.

## *Etiology (Fig. 11.4a, b)*

- The predominant cause of MS is rheumatic fever.
- Rare complication of.
  - Malignant carcinoid disease, SLE, RA, Fabry disease, and Whipple disease.
  - 25 % of all patients with rheumatic heart disease have isolated MS.
  - 40 % have combined MS and MR.
- Multivalve involvement occurs in 38 % of MS patients.
  - Aortic valve affected in about 35 %.
  - Tricuspid valve in about 6 %.
  - Pulmonic valve is rarely affected.
- Rheumatic fever results in characteristic changes of the mitral valve.
  - Thickening at the leaflet edges.
  - Fusion of the commissures.

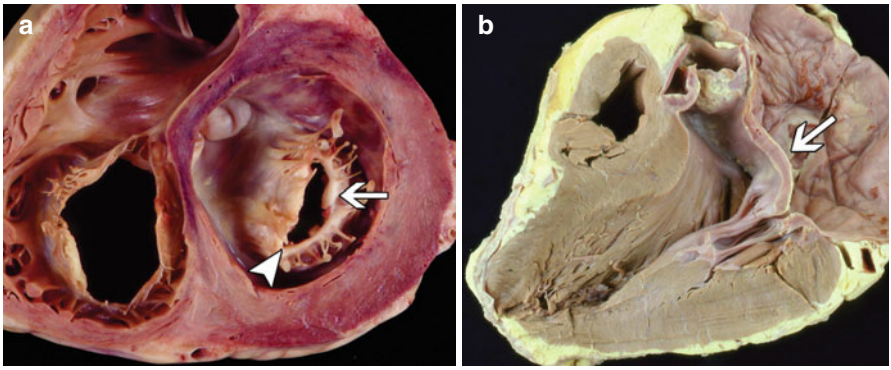


**Fig. 11.4** (**a**) The heart of a 44 year old woman with rheumatic mitral stenosis. Fibrous thickening of the mitral leaflets and fusion of the commissures create a fish mouth appearance (*arrowhead*). (**b**) A three chamber view of a 55 year old woman's heart with rheumatic mitral stenosis. The mitral valve leaflets and chordae show significant thickening. The *arrow* depicts the bowing of the anterior leaflet (With permission of Dr. William D. Edwards, Department of Pathology, Mayo Clinic, Rochester, MN.)

  - Chordal shortening and fusion.
  - "Fishmouth" appearance.
- Congenital MS is uncommon and typically is diagnosed in infancy or early childhood.
- Estimated risk of endocarditis in patients with MS is 0.17/1000 patient-years.

### *Signs and Symptoms*

- Common symptoms of mitral stenosis include:
  - Exertional dyspnea.
  - Fatigue.
  - Orthopnea.
  - Paroxysmal nocturnal dyspnea.
  - Pulmonary edema or right-sided heart failure.
- Complications occurring with increased age include:
  - Atrial fibrillation (increasing probability).
  - Heavy calcification, fibrosis of valve leaflets.
  - Subvalvular fusion.

### *Prevalence*

- United States and Western Europe have low incidence due to low prevalence of rheumatic fever.
- Lack of primary and secondary prevention methods in developing countries elevates statistics of MS development and its severity.
- 2/3 of all patients with rheumatic MS are female.

## **Key Auscultation Findings** (Fig. 11.5)

- Low pitched decrescendo-crescendo diastolic murmur.
- Heard best at the apex with patient in left lateral decubitus position.
- Loud, accentuated S1.
- Opening snap heard after S2.
- Short A2-OS interval indicates worse prognosis.
- Loudness of murmur does not correlate with severity of MS.
- Length of murmur correlates with severity of MS.

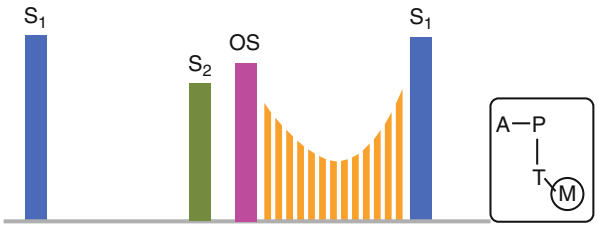


**Fig. 11.5** Graphic depiction of the auscultation features of mitral stenosis. Notice the decrescendo-crescendo diastolic murmur with a preceding opening snap (Source: Based on a figure in http://morningreporttgh.blogspot.com/2010/03/mitral-stenosis.html)

- Diastolic rumbling murmur at apex due to low pitch.
  - Best heard with patient in left lateral decubitus position after limited exercise.
    - Listen with the bell at apex.
    - May radiate to axilla or LLSB.
  - Low frequency caused by large volume of blood going through MV under low levels of pressure, leading to turbulence after OS.
  - Will feature a presystolic crescendo to the loud M1, usually at a higher frequency than the diastolic rumble.
  - Mild exercise will increase cardiac output, and may help to enhance detection of the murmur.
    - Increased volume flow through a stenosed valve will cause more turbulence.
- There is no murmur in the systolic phase.
- Loud S1 from stenotic leaflet closing.
  - Loud S1 is not specific for MS; may be palpated.
  - Calcification or thickening reduces the intensity of S1.
    - Prolonged Q-S1 is indicative and represents increased LA pressure.
- S2/P2 loud with pulmonary HTN.
  - Heard in both mitral and aortic areas.
  - Heard best at cardiac base.
  - Evolves to single S2 in cases of pulmonary HTN.
- Opening snap following S2.
  - OS high-pitched and literally snapping; do not confuse with P2.
    - Between LLSB and apex.
  - Most audible in expiration, at or just medial to apex, with diaphragm of stethoscope.

- Due to sudden deceleration/tensing of opening mitral leaflets; mobility necessary.
- OS will disappear when stenosis immobilizes leaflets.
  - S2-OS will shorten as the severity of MS progresses.
- Auscultation examples of mitral stenosis.
  - Click here to listen to an example of mitral stenosis, as described by Dr. W. Proctor Harvey (Video 11.1).

## Auscultation Differential Diagnosis

In most developed countries MS is rare. Generally, group A Streptococcus infections are appropriately treated in a timely manner, thus most diastolic murmurs are due to other etiologies. It is particularly unlikely that a presenting patient has MS if an S3 occurs before a short murmur, no clear presystolic crescendo is heard, or if a loud S1 or an opening snap is absent. The following list of differential diagnoses must be considered in addition to MS when a diastolic murmur is heard during auscultation.

### *Left Atrial Myxoma*

- The left atrial tumor may prolapse and obstruct blood flow across the mitral valve in early diastole. A characteristic loud S3-like "tumor plop" sound will likely precede a low pitched diastolic rumble, as blood attempts to circumvent the blockage.
- Hemodynamic changes, dyspnea and a diastolic murmur will be similar to those found in mitral stenosis. The diastolic murmur will be due to increased turbulence, related to excessive flow across the mitral valve.
- Auscultatory findings of a left atrial myxoma will vary with body positioning, differentiating a diastolic murmur produced by a tumor from that of mitral stenosis.

### *Ventricular Septal Defect*

- Excessive flow across the MV may cause a diastolic flow murmur due to increased turbulence with a ventral septal defect, as blood is shunted from the right side of the heart to the left side of the heart. This is commonly a result of Eisenmeiger's syndrome.

### *Severe Aortic Regurgitation*

- A diastolic flow murmur, the Austin-Flint murmur, may be heard in severe Aortic Regurgitation due to severe backflow impeding the anterior leaflet of the Mitral Valve from opening fully. (See Chap. 12 on Austin Flint Murmur).
- Like the diastolic murmur of Mitral stenosis, this murmur is best heard at the apex; however, the Austin-Flint murmur is not intensified in presystole and sounds more like an apical mid-diastolic murmur with a late diastolic rumble.
- In general, the diastolic murmur is more likely to be an Austin-Flint murmur as opposed to a murmur caused by MS if an S3 heart sound is heard, or if there is no opening snap. Amyl nitrite, an arterial dilator, will accentuate a murmur caused by MS, and soften an Austin-Flint murmur.

### *Hypertrophic Cardiomyopathy*

- A diastolic rumble may be heard in some patients with hypertrophic cardiomyopathy due to early diastolic flow into a hypertrophied, nondistensible left ventricle.
- A medium-pitch systolic ejection murmur at the LLSB and apex is due to outflow obstruction. This murmur varies in intensity with the magnitude of the subaortic gradient, increasing with the Valsalva maneuver, during/after exercise, or with standing.
- Loud murmurs $\leq$ grade 3/6 indicate likely left ventricular outflow gradients >30 mmHg.

### *Mitral Annular Calcification*

- Mitral annular calcification features an apical diastolic murmur, and may actually lead to mitral stenosis due to narrowing of mitral orifice.
- Contrary to MS, no S1 or opening snap are heard in mitral annular calcification.

### *Mitral Regurgitation*

- Mitral regurgitation causes increased antegrade flow across the mitral valve, leading to the development of a significant diastolic murmur at the apex of the heart.

- The diastolic murmur of isolated mitral regurgitation may be distinguished from that of mitral stenosis by auscultation as the latter begins earlier than the former.
  - This murmur is particularly notable in severe mitral regurgitation, as a short diastolic murmur follows an abnormal S3.
- In mitral regurgitation the opening snap and elevated P2 are absent, allowing for greater differentiation from mitral stenosis. S1 is also soft or absent.
- An apical pansystolic murmur of grade 3 or higher in addition to S3 suggests significant mitral regurgitation.

## Diagnostic Implications of the Auscultation Features

Numerous features of the diastolic murmur, presystolic murmur and opening snap are of diagnostic significance in patients with mitral stenosis. Frequently diagnoses are made with the use of echocardiography and chest radiography to better assess flow pressures in addition to degrees of stenosis and anatomical changes, however, cardiac auscultation still remains important.

- Loudness of the diastolic murmur.
  - The loudness of the diastolic murmur correlates with cardiac output, but does not correlate with MS severity.
  - Patients with severe pulmonary hypertension secondary to mitral stenosis may demonstrate soft to inaudible diastolic murmurs. Severe mitral stenosis can cause a decreased cardiac output, which may lead to a quiet or inaudible murmur.
  - Overdiuresed patients who have a decreased blood volume may have a soft murmur despite significant stenosis.
- Length of diastolic murmur.
  - The length of the murmur correlates with the duration of the pressure gradient in diastole.
  - In severe mitral stenosis, the diastolic murmur may be heard throughout the full length of diastole.
- Presystolic murmur.
  - If only a presystolic murmur is heard, without a diastolic murmur, the diagnosis is likely mild mitral stenosis.
  - A presystolic murmur may not be heard if valve is heavily calcified in severe mitral stenosis.
- Opening Snap.
  - The characteristic opening snap of mitral stenosis may become inaudible when leaflets are immobile and scarred with time in severe mitral stenosis.

**Table 11.1** Severity of mitral stenosis

| Severity | A2-OS interval (seconds) |
|---|---|
| Mild | >1.2 s |
| Moderate | 1.0–1.2 s |
| Moderate-severe | 0.8–1.0 s |
| Severe | <0.8 s |

Data from Carabello [2]

  - S2-OS interval decreases with increased obstruction.
    - A short A2-OS (0.05–0.12 s) interval generally indicates severe mitral stenosis.
- Loud or absent S1.
- An increased left atrioventricular gradient increases the degree by which the mitral valve opens, thus allowing for its fast and loud closure on systole.
- In severe MS, the mitral valve leaflets may become so calcified that they become immobile, thereby softening or even eliminating an audible S1.
- Opening snap/A2-opening snap interval (A2-OS) (Table 11.1).
  - The A2-OS interval estimates the severity of the left atrioventricular gradient: The higher the gradient, the more quickly enough pressure builds up in the left atrium to open the mitral valve, thus decreasing the A2-OS interval.
- Diagnostic Comparisons.
  - Auscultation is considered most useful to diagnose moderate-to-severe disease, as more subtle heart sound abnormalities may not be easily heard.
    - Mild exercise will enhance the characteristic heart sounds of mitral stenosis, as the demand for cardiac output rises, diastolic filling time decreases with tachycardia and pressure rises in the right atrium due to impeded flow from the stenotic valve. This is particularly of use in borderline patients.

## Prognostic Implications of the Auscultation Features

### *Atrial Fibrillation (Fig. 11.6)*

- Approximately 40 % of patients with MS develop atrial fibrillation [1, 2].
- As a result of persistently increased left atrioventricular pressures, MS patients' left atrium undergoes cardiac remodeling; thus, even after controlling ventricular rate, cardiac output often does not return to baseline due to the loss of the atrial "kick" [1, 3].
- 9–14 % of patients ultimately suffer a thrombotic embolism; of these patients, 60–75 % of patients experience a cerebral embolism [1, 3].

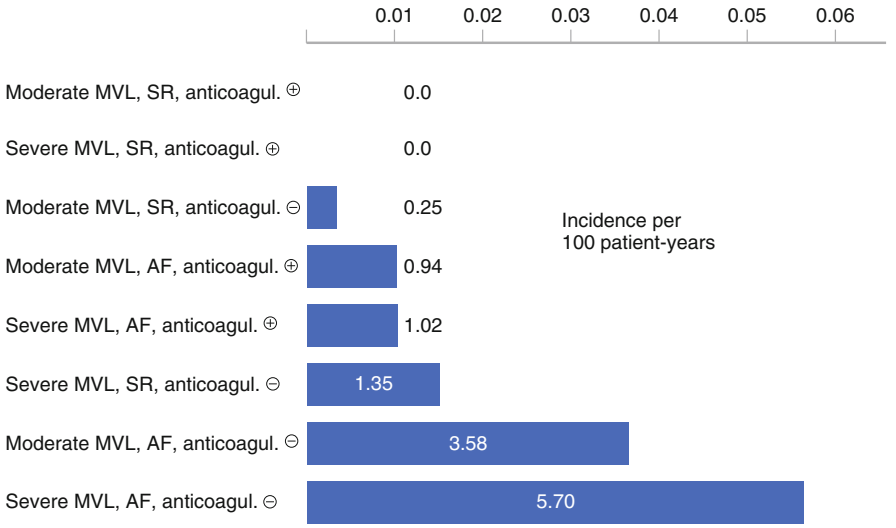


**Fig. 11.6** New risks of thromboembolic events in 300 consecutive patients with mitral stenosis or combined mitral lesions (predominant stenosis) diagnosed between 1967 and 1970. The incidence of thromboembolic complications has been calculated for the different periods of the natural course of mitral valve disease. Atrial fibrillation is an important prognostic indicator for patients with MS. Increased severity of mitral valve stenosis and atrial fibrillation are associated with higher incidences of thromboembolic events (Used with permission from Horstkotte et al. [7])

### *Pulmonary Hypertension (Fig. 11.7)*

- Physical findings suggestive of pulmonary hypertension signify the presence of moderate to severe MS (loud P2, right ventricular heave, JVD).
- Left untreated, MS and associated secondary pulmonary hypertension will progress. In a case review of 21 patients with mitral disease (six of whom had isolated mitral valve stenosis) and extreme pulmonary hypertension (resting pulmonary artery pressure ≥80 mmHg) who refused to undergo corrective valve surgery, the mean survival time was approximately 2.5 years [4].

## Natural History Progression (Fig. 11.8)

In a prospective study examining 159 patients 16 years following onset of rheumatic fever, which accounts for the vast majority of MS cases, 50 % of patients were asymptomatic, 35 % of patients had progressed to NYHA II heart failure and 8 % of patients has progressed to NYHA III heart failure [1, 3, 5].

In patients who refuse valve surgery, common causes of death in descending order of prevalence include right heart failure, refractory lung edema, thromboembolic and/or hemorrhagic complications, myocardial infarction, infective endocarditis and sudden death [1, 3, 5].

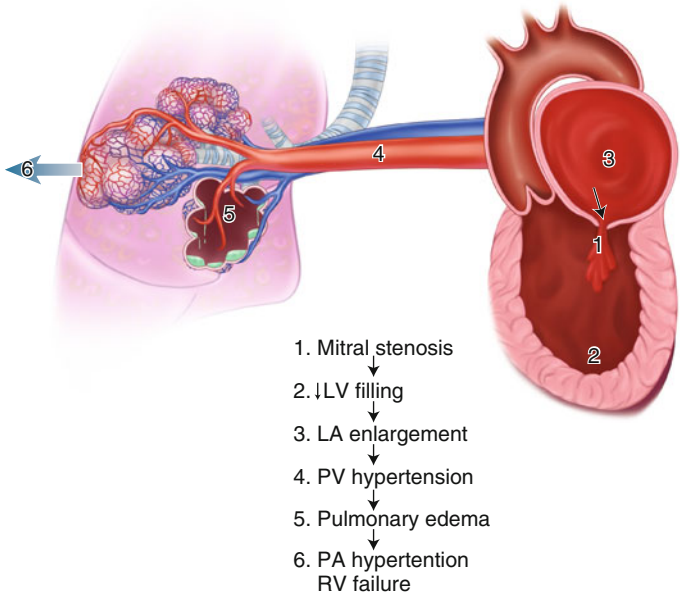


**Fig. 11.7** Severe mitral valve stenosis can cause pulmonary hypertension, a condition that increases morbidity and mortality and adverse perioperative outcomes in MS patients. Over time, as the mitral valve area decreases in size, blood backs up into the pulmonary venous system and can cause pulmonary edema, pulmonary hypertension and, ultimately, right ventricular failure

## General Statement on Management

- Management is directed towards the following:
  - Preventing recurrences of rheumatic fever.
  - Preventing and treating the complications of MS.
  - Monitoring disease progression.
- Treatment of Rheumatic heart disease involves.
  - Penicillin prophylaxis for beta hemolytic streptococcal infections.
- Complication of MS: Systemic Embolism.
  - Treatment should involve anticoagulant therapy.
  - It is indicated for patients with AF, Severe MS, and sinus rhythm with LA enlargement.
- Complications of MS: Hemoptysis.
  - Treatment should involve sedation, placing the patient in an upright position, and diuresis.

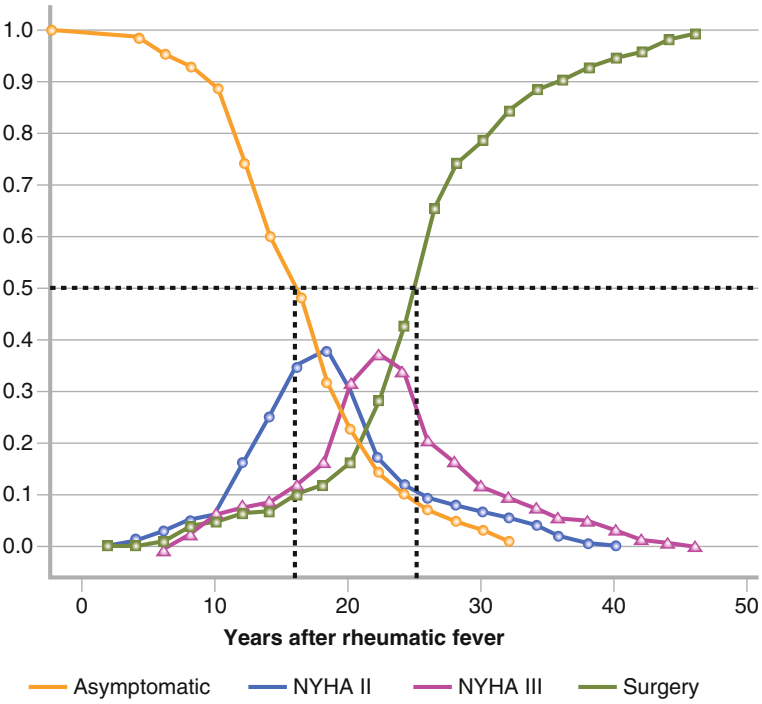


**Fig. 11.8** Progression of symptoms of mitral stenosis of rheumatic origin. O-O asymptomatic, ●-● NYHA II, Δ-Δ NYHA III, ▮-▮ surgery. Rheumatic fever is the predominant precipitating factor for the development of MS. Over time, patients with rheumatic fever-origin MS will develop worsening heart failure (Used with permission from Horstkotte et al. [7])

- Complications of MS: Atrial Fibrillation.
- Atrial fibrillation may be poorly tolerated in AF due to high heart rates, and reduced diastolic filling time, in addition to loss of atrial contraction. Correction of rates, and restoration of normal sinus rhythm may be required [2].
- Conditions of severe MS.
  - Treatment involves the use of oral diuretics and sodium restriction for volume control.
  - Digitalis glycosides may be used to slow the ventricular heart rate in AF.
- Surgical Management [6].
  - Considered with AF and/or pulmonary HTN, or when symptoms are present.
    - Class IA: Indicated in adolescent or young adult with congenital MS with NYHA class III or IV and have mean MV gradient greater than 10 mmHg on Doppler echocardiography (level of Evidence: C).
    - Class IA: Reasonable in asymptomatic adolescent or young adult with congenital MS with pulmonary artery systolic pressure 50 mmHg or

greater and mean MV gradient greater than or equal to 10 mmHg (Level of Evidence: C).
    - Class IIB: Effectiveness is not well established in asymptomatic adolescent or young adult with congenital MS and new-onset atrial fibrillation or multiple systemic emboli while receiving adequate anticoagulation (Level of Evidence C).

– Mitral Valve Replacement.
    - Definitive repair involves mitral valve replacement with mechanical or bioprosthetic mitral valves.
    - MV replacement is especially problematic in patients with a hypoplastic mitral annulus.
        – An annulus-enlarging operation may be necessary.

– Balloon Dilation.
    - Echocardiography results determine eligibility for balloon dilation treatment.
    - Eligibility criteria include.
        – Valve mobility.
        – Extent of involvement of the subvalvular apparatus.
        – Evidence of mitral regurgitation.
        – Extent of valve thickening.
            - Serves as a valid treatment for congenital MS, but has limited benefit in patients with significant stenosis of subvalvular apparatus.

## Clinical Case Summary

Syncope is an unusual symptom in mitral stenosis, thus other causes of syncope should be sought. Exam is most consistent with moderate mitral stenosis, with evidence for mitral regurgitation and normal pulmonary artery pressure. Evaluation of Doppler findings including pulmonary pressures after exercise would be useful given that the patient's symptoms are exertional in nature, and the gradient and pulmonary artery pressure may rise considerably.

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# Chapter 12
# The Austin Flint Murmur

**Mark Real and Mary Jane Reen**

## Key Teaching Points

- The Austin Flint murmur (AF) is a mid-diastolic murmur secondary to severe Aortic Regurgitation (AR).
- AF is heard best using a bell at the apex of the heart. The patient should be in the left lateral decubitus position.
- The etiology is complex. It includes turbulent flow, mitral valve fluttering, and septal bulging secondary to AR.
- While AF sounds like a mitral valve, it is NOT due to functional mitral stenosis (MS).

## Case Description

### *History*

- A 32 yo male recently diagnosed with aortic regurgitation presents for a pre-sports physical exam.
- The patient is asymptomatic with an unremarkable medical history. He is currently taking ramipril.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_12) contains supplementary material, which is available to authorized users.

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A.J. Taylor (ed.), *Learning Cardiac Auscultation: From Essentials to Expert Clinical Interpretation*, DOI 10.1007/978-1-4471-6738-9_12

### *Physical Examination*

- The patient has a BP of 158/40 mmHg (thigh) and 118/42 (arm). Pulse is 65 bpm and JVP are normal.
- Auscultation reveals a grade 2/4 mid-diastolic murmur heard in apical area. The patient has severe AR (Fig. 12.1).

### *Test Results*

- Color M-mode and 2-D echo (Fig. 12.2a–d).
  - Backflow evident in thoracic aorta, demonstrating severe regurgitation.
  - Anterior mitral valve leaflet (AMVL) flutters due to turbulent flow impinging on mitral valve in proto-diastole, mid-diastole and during atrial contraction [1].

## Clinical Basics

### *Normal Anatomy*

- Normal anatomy of the aortic valve can be reviewed in chapters on aortic stenosis and aortic regurgitation.

### *Definitions*

- Though the Austin Flint murmur presents like a mitral murmur, it does not indicate the presence of any mitral valve lesions. Rather, AF accompanies severe aortic lesions coupled with considerable AR.

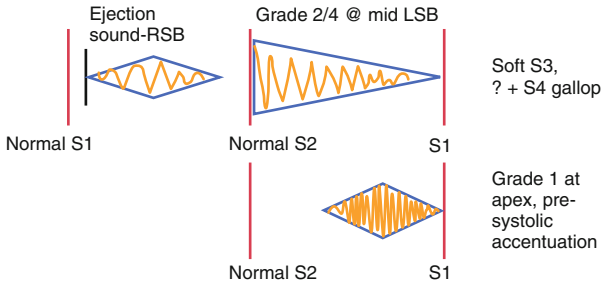


**Fig. 12.1** Graphical representation of auscultation findings in a patient with the Austin Flint murmur

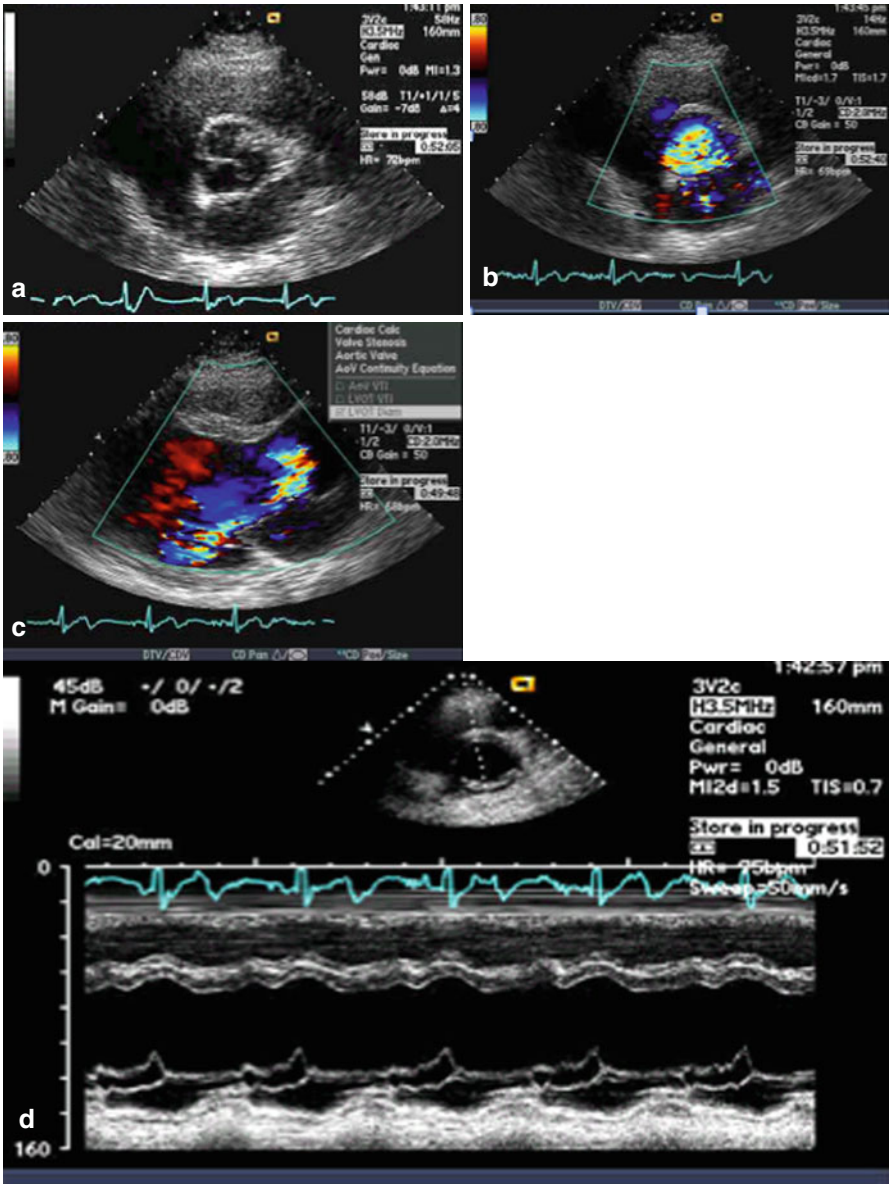


**Fig. 12.2** (**a**–**d**) Echocardiograms. (**a**) An abnormal valve with deformed left coronary leaflet. (**b**) Severe aortic regurgitation on color Doppler. (**c**) The AR jet courses along the anterior mitral leaflet. (**d**) Fluttering and early closure of the mitral valve is shown on M-mode

### *Etiology*

- The etiology behind AF is not completely understood. However, it is agreed that AF is NOT due to functional MS.
- Some commonly accepted mechanisms for AF include:
  - Functional mitral stenosis during ventricular filling. This results from the regurgitant AR jet impinging on the AMVL and restricting atrial-ventricular flow [1].
  - The aortic valve stream contacts the mitral valve stream, with the AMVL vibrating between them. This causes turbulence in the apical area [1].
  - Turbulence caused by the apical irradiation of the regurgitant aortic jet could cause the murmur [1].
  - The regurgitant jet's impact on the left ventricular imaging studies suggests a combined etiology including turbulent flow, mitral valve fluttering, and septal bulging [1].
- The direction of AR flow seems unrelated to the presence of AF.
- While AF is correlated with increased peak mitral inflow velocity there is no temporal relationship between AF and mitral flow (phonocardiography).

### *Presentation*

- Patients with an AF murmur may be asymptomatic or present with progressive exertional dyspnea [2].
- A large-volume collapsing pulse is likely present due to the severity of aortic regurgitation [2].

### *Prevalence*

- One study found that out of 51 patients with AR and a normal MV, 30 exhibited findings suggestive of the AF murmur.

## Key Auscultation Features of the Lesion

- Auscultation findings may include: [2].
  - short-ejection systolic murmur terminating before second heart sound.
  - early diastolic decrescendo murmur.
  - mid-diastolic murmur over apex.

- Best heard with the bell at the heart's apex. Patient should be in left lateral decubitus position for optimal auscultation.
- AF begins in mid-diastole: low-pitched, rough and rumbling murmur.
  - Described as a "blubbering presystolic murmur" that seems characteristic of MS.
- In cases of more severe AR, AF begins and terminates earlier.
- Auscultation examples of the Austin Flint murmur.
  - Click here to listen to examples of the Austin Flint murmur, as described by Dr. W. Proctor Harvey (Video 12.1).

## Auscultation Differential Diagnosis

The differential diagnosis includes mitral stenosis (Table 12.1). In addition to the presence of severe AR, factors favoring an AF murmur over MS include the presence of left ventricular enlargement.

## Diagnostic and Prognostic Implications of the Auscultation Features

- When the AF is present, the clinical exam is indicative of a diagnosis of severe AR. The prognostic implications are therefore those of severe AR (see AR chapter).
- AF and Hill's sign most accurately suggest severe AR (Table 12.2) [3].

**Table 12.1** AF may be confused clinically with MS: Factors favoring MS or AF

| Clinical/laboratory findings | Austin Flint murmur | Mitral stenosis |
|---|---|---|
| Opening snap present | – | + |
| $S_1$ intensity | ↓ | ↑ |
| $S_3$ present | + | – |
| Left ventricular size | ↑ | ↓ |
| Right ventricular size | → | ↑ |
| Murmur increases with afterload maneuvers | – | + |
| Presence of atrial fibrillation | _ | + |

**Table 12.2** Specificity and sensitivity for certain auscultation findings

| | Specificity | Sensitivity |
|---|---|---|
| Sign | % | |
| Austin Flint murmur | Not applicable | 25–100 |
| Corrigan pulse | 16 | 38–95 |
| Duroziez sign | 35–100 | 33–81 |
| Hill sign | 71–100 | 0–100 |

Used with permission from Babu et al. [3]
For AF, sensitivities in moderate to severe AR ranged from 57 to 100 %. In general, sensitivities in all AR ranged from 25 to 100 %. Because AF can only occur in AR by definition, reporting specificities for AF hold no significance

## Statement on Management

- In patients with pure chronic AR, aortic valve replacement (AVR) should be considered only if AR is severe [4].
- Valve replacement surgery in asymptomatic patients remains a controversial topic, but it is generally agreed that valve replacement is indicated in patients with LV systolic dysfunction [4].
- Following valve surgery, careful follow-up is necessary during the early and long-term postoperative course to evaluate prosthetic valve function and assess LV function [4].

## Clinical Summary of the Case

The patient presents with severe AR with a classic AR murmur, including an Austin Flint murmur indicative of more severe AR. There are multiple peripheral findings of severe AR. In the setting of possible symptoms, and dilation of the ventricle at end-systole, aortic valve replacement is indicated.

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# Chapter 13
# Mitral Valve Prolapse

**Steven Kozusko and Joseph J. Raevis**

## Key Teaching Points

- Mitral valve prolapse (MVP) is a syndrome including myxomatous thickening of the mitral valve leaflets, and systolic displacement of the leaflets into the left atrium. It is seen in isolation, and in individuals with Ehler-Danlos Syndrome, Marfan syndrome or polycystic kidney disease.
- Symptoms may include palpitations, dyspnea, fatigue and sometimes chest pain that may be present on physical exertion that is sharp, non-radiating and prolonged [1].
- Auscultation findings classically include an ejection click and late systolic murmur of mitral regurgitation.
- Variations in the auscultation findings can include a click or murmur in isolation.
- The Valsalva maneuver and standing upright will decrease the left ventricular volume resulting in the prolapse occurring sooner and usually more severely. This results in the parachute effect, allowing for a louder murmur [2].
- Management of MVP includes clinical follow up, but serial echocardiography is generally not recommended except for those with high risk characteristics. Endocarditis prophylaxis is not required.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_13) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- A 47 year old female presents to the Emergency Department with sharp pain radiating down her back which started suddenly as she was driving home from work. She states that she did not lose consciousness and admits to be a social drinker.
- Two years ago she had surgery to correct a dislocated lens in her eye that she recalls was due to her having Marfan Syndrome.
- Medications: none.

### *Physical Examination*

- On exam the patient had a mid-systolic click followed by a late systolic crescendo murmur that was heard most prominently at the apex of the heart (Fig. 13.1).
- The Valsalva maneuver altered the systolic click such that it came earlier and the murmur lasted longer, while the opposite occurred with forced expiration, as there was a late systolic click and a shorter murmur.

### *Test Results*

- The ECG was normal.
- A CT scan (Fig. 13.2) as well as a transesophageal echocardiogram (Fig. 13.3) were performed. The CT showed a dissection of the aortic arch with blood

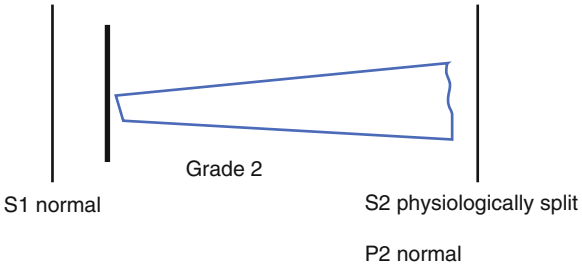


**Fig. 13.1** Graphic depiction of the mid-systolic click followed by a high pitched murmur as seen with mitral valve prolapse. Since the murmur is due to regurgitation, the most effective location to listen for it is at the apex of the heart

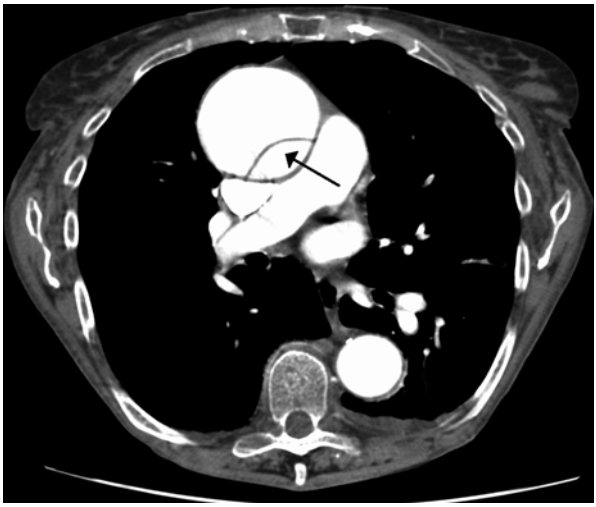

**Fig. 13.2** CT of a Stanford type A aortic dissection of the aortic arch (Image courtesy of James Heilman, MD. Licensed under Creative Commons Attribution-Share Alike 3.0 via Wikimedia Commons – http://commons.wikimedia.org/wiki/File:DissectionCT.png#mediaviewer/File:DissectionCT.png)

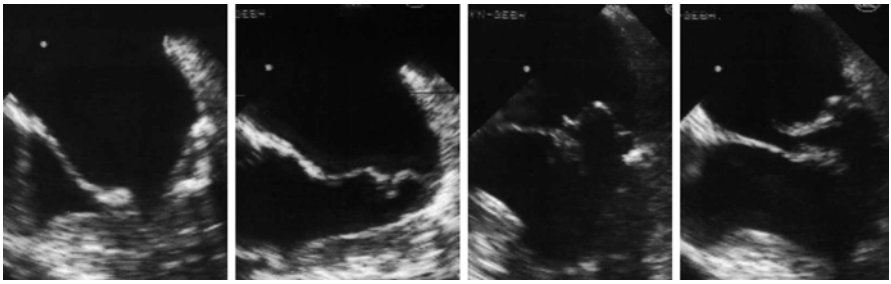

**Fig. 13.3** Transesophageal echocardiogram of the mitral valve with >2 mm displacement of the leaflets beyond the annulus into the left atrium, indicating MVP (Image courtesy of J. Heuser. Licensed under Creative Commons Attribution-Share Alike 3.0 via Wikimedia Commons – http://commons.wikimedia.org/wiki/File:Mitralinsuff_TEE.jpg#mediaviewer/File:Mitralinsuff_TEE.jpg)

entering the media forming a false lumen and the echocardiogram showed prolapse of a mitral valve leaflet into the left atrium.

## Clinical Basics

### *Normal Anatomy*

- The mitral valve is located at the transitional zone between the left atrium and ventricle, consisting of four anatomical structures: annulus, leaflets, chordae tendineae and papillary muscles.

- The *mitral valve annulus* is a junctional ring that not only separates, but gives attachment to the left ventricle and left atrium, while serving as a fulcrum for the anterior and posterior mitral leaflets. The anterior border corresponds to the base of the anterior leaflet. The remainder of the border, composed of muscular tissue, is more dynamic and represents most of the annular circumference, corresponding to the attachment of the posterior leaflet. The annulus moves down toward the LV apex in systole and up toward the LA in diastole due to the contraction of the papillary muscles [3].
- The *anterior leaflet* (Fig. 13.4), which has a rounded edge appearance, occupies approximately a third of the annular circumference, and the *posterior leaflet*, which occupies the remaining circumference, appears long and narrow. The *anterior leaflet* has greater mobility and the *posterior leaflet* plays more of a supportive role [3].
- The *chordae tendinae* (Fig. 13.5) are subdivided into those attached to the free edge of the leaflet which are the majority, and those that are secondary, being

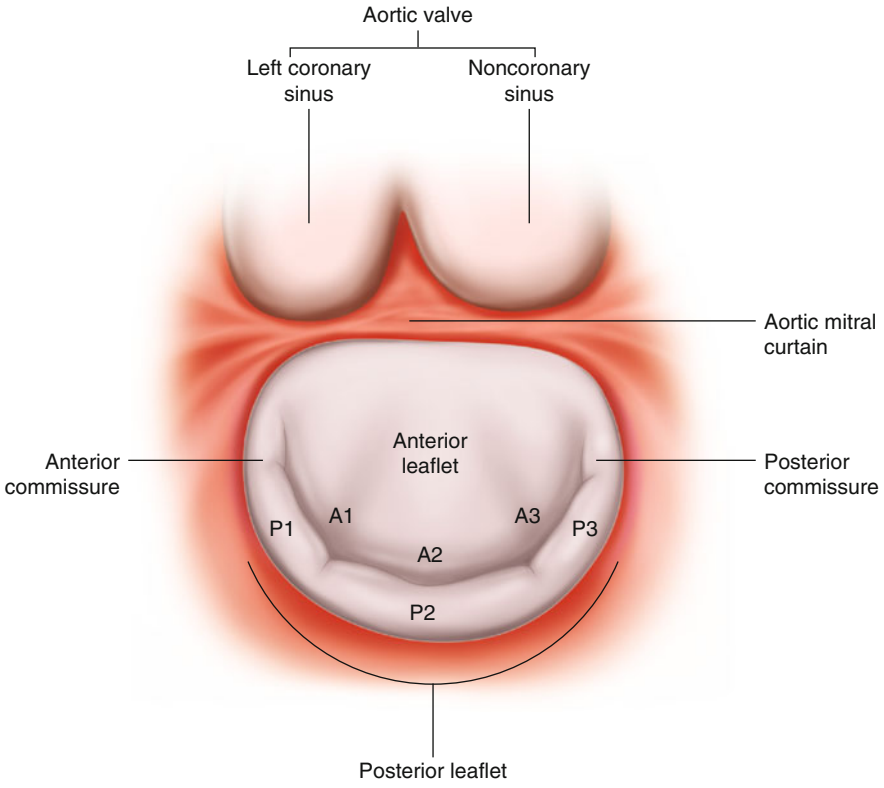


**Fig. 13.4** Mitral valve: segmental anatomy. The Carpentier nomenclature categorizes each leaflet into three segments. The posterior leaflet is termed P and comprises P1, P2, and P3 corresponding to lateral, middle, and medial scallops. The anterior leaflet segments are termed A1, A2, and A3 and correspond to the anterior leaflet scallops

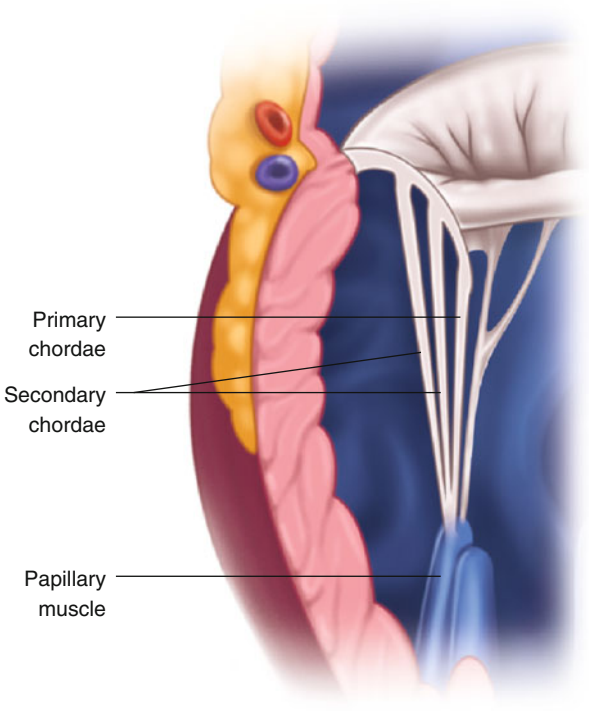


**Fig. 13.5** Mitral valve: subvalvular apparatus. The papillary muscle gives rise to the primary chordae tendineae which attach to the medial region of the anterior and posterior leaflets and the secondary chordae are attached to the more lateral region of the leaflet

attached to the rough zone of the leaflets (and having an anchoring role) [3]. The main role of the chordae is to prevent the free margins of the valve from protruding beyond the annulus into the left atrium during systole [4].

- The two *papillary muscles* emerge as single bodies from the LV wall and then divide into a variable number of heads, serving as anchors for the chordae [3]. The ventricular contraction originates in the papillary muscles allowing for increased tension in the chordae to prevent significant amounts of mitral regurgitation (MR) of blood back into the left atria. The *posterior papillary* muscle is supplied by the right coronary artery in most people or from the third obtuse marginal of the left circumflex artery. The *anterior papillary* muscle is located on the anterolateral LV wall and has an anastomosing blood supply from the obtuse marginal branch of the circumflex coronary artery and the first diagonal branch from the left anterior descending artery [3]. Thus, after a myocardial infarction the posterior papillary is much more likely to be damaged and result in MVP since there is not anastomosis of blood supply.
- Patients with MVP typically have a normal ECG, but sometimes there is ST and T wave depression or T-wave inversion in the inferior leads. This is thought to reflect ischemia created when the prolapsed valve exerts excessive tension on the papillary muscles which stretches the myocardium [1].

### *Etiology*

- MVP is the most common cause of significant MR and if papillary muscle rupture does occur, severe regurgitation will result and can lead to cardiogenic shock.
- Individuals with Ehler-Danlos Syndrome, Marfan syndrome or polycystic kidney diseases are at a higher risk of developing MVP during their lives.

### *Signs and Symptoms*

- The most common complaints of patients with MVP include heart palpitations, dyspnea, fatigue and sometimes chest pain that may be present on physical exertion that is sharp, non-radiating and prolonged [1].

### *Prevalence*

- MVP has a prevalence in the general population of 2.4 %, of which 1.3 % are classical and 1.1 % are non-classical prolapse [5].

## Key Auscultation Features

During systole, one or both of the leaflets of the mitral valve will protrude beyond the annulus into the left atrium. Crisp nonejection clicks are heard and the systolic murmur will endure until the A2 component of the second heart sound. Most commonly, a redundant posterior leaflet will balloon into the left atrium. There are variations in the auscultation findings noted below: [2].

- Midsystolic nonejection click without a late systolic murmur.
- Midsystolic nonejection click with a late systolic murmur.
- Late systolic murmur alone.

The sound that precedes the systolic murmur is called a nonejection click or sound. It should not be called mid-systolic because the click can occur as early as ejection and as late as a widely split S2. It is not uncommon for there to be multiple clicks. If the etiology of the mitral valve prolapse is a myocardial infarction with or without papillary muscle damage, it is unlikely that there will be a click with the murmur [2].

There are a few theories on the origin of the nonejection click that precedes the systolic murmur [2]:

- Chordal Snap Theory: At the point of peak pressure in midsystole, there is a click caused by the sudden stretch of chordae. This theory has been challenged because the papillary muscles contract early putting the chordae under too much pressure to contribute to the click sound.
- Valvular: Due to redundant valve tissue or an abnormality of chordal length there is a valvular sound produced when there is a loss of support of one leaflet by its opposing leaflet. The onset of the mitral valve prolapse murmur is proceeded by the click even though the reverse appears to be the case on auscultation.
- Contraction Ring Theory: There is excessive contraction during midsystole of the left ventricle in a posteroinferior area. This pushes the posterior papillary muscle allowing the chordae to lose tension. With continued systole the chordae then tighten once again, producing the click. This is supported by angiogram evidence showing that 80 % of patients with mitral valve prolapse have LV wall abnormality.

The late systolic isolated MR murmur may be associated with significant adverse LV remodeling, and should be considered evidence of hemodynamically important MR [6].

*Late systolic murmurs* are described as soft or moderately loud, high-pitched murmurs at the left ventricular apex that start well after ejection and end before or at the second heart sound. They can occur with or without mid-systolic clicks, and result from late-systolic regurgitation due to mitral valve leaflet prolapse [6].

The severity of chronic, isolated MR is determined by the extent of LV dilation and augmented stroke volume that is mediated by the Starling mechanism and facilitated by regurgitation into the low-pressure left atrium. This produces the eccentric pattern of LV remodeling in response to an increase in diastolic load as demonstrated in patients [6]:

Auscultation examples of mitral valve prolapse:

- Click here to listen to examples of several patients with mitral valve prolapse, as described by Dr. W. Proctor Harvey (Video 13.1).

## Auscultation Differential Diagnosis

The most common mitral valve abnormality leading to the mitral valve prolapse murmur is myxomatous transformation with elongated chordae. The full differential is listed below [2]:

- Myxomatous transformation (degeneration).
- Marfan's Syndrome.
- Ehlers-Danlos Syndrome.
- Papillary muscle dysfunction due to myocardial infarction or ischemia.

- Dysfunction of muscle adjacent to the posterior leaflet.
- Mitral valve surgery.
- Hypertrophic subaortic stenosis.
- Rheumatic fever.
- Atrial septal defect – primum, secundum, endocardial cushion variants.
- Annular calcification.

## *Annular Calcification*

Calcification of the mitral annulus is commonly found on autopsy, especially in the elderly. Hypertension, aortic stenosis, end stage renal disease, and diabetes are conditions associated with accelerated mitral valve calcification. Other causes include connective tissue disease such as Marfan's and Hurler's. Annular calcification may cause MR via mechanisms including impaired contraction of the valve annulus and deformation of valve leaflets [3].

## *Myxomatous Degeneration*

- Myxomatous degeneration represents the pathological substrate of mitral valve prolapse, which is characterized by floppy, redundant leaflets and associated with progressive MR. The changes seen in the leaflets occur because of defective extracellular matrix, resulting in a thickened spongiosa that impinges on the fibrosa. Interstitial cells in myxomatous valves have features of activated myofibroblasts and express excessive levels of catabolic enzymes and matrix metalloproteinases, which degrade collagen [3].
- Myxomatous degeneration will present with a soft S1 and a nonejection click.

Minimally symptomatic or asymptomatic patients with severe MR secondary to mitral valve prolapse, with normal LV function, progress to surgical indications at an approximate annual rate of 10 % [1].

Chromosomal loci 11, 13, and 16 have been associated with mitral valve prolapse [3].

Human myxomatous mitral valve leaflet specimens were noted to have up to 10 % more *water* content and 30–150 % higher glycosaminoglycan content than normal leaflets. A decreased net loss of collagen was also reported with a shift from type I to type III collagen [3].

Heart failure patients were noted to have 60 % more glycosaminoglycan content in mitral leaflets than normal, suggesting that greater stress on the valvular apparatus may contribute to remodeling of the extracellular matrix of the mitral valve [3].

### *Non-mitral Valve Prolapse Causes of Midsystolic Clicks* [2]

- Patients with coronary disease have a click and a late systolic murmur when squatting.
- Left sided pneumothorax – click due to lingula contacting thoracic wall or cardiac movement displacing air bubbles trapped between the parietal and visceral pleura.
- Pleural-pericardial adhesions – pericardial friction rub.
- Floating balloon catheter contacting the septum in the right ventricle – diastolic sound more common.
- Absence of the pericardium.
- Bicuspid pulmonary valve (with or without right bundle branch block).
- Aneurysm of the atrial septum.
- Aortic regurgitation.
- Tricuspid Valve – prolapse of this valve can produce the same sound as the mitral valve.

## Diagnostic Implications of the Auscultation Features

There are many maneuvers that can be used to manipulate the timing of the nonejection click and the murmur intensity (Table 13.1):

- On auscultation, MVP will present with a crescendo murmur ending at S2 [1]. However, using a phonocardiogram, the murmur is actually crescendo-decrescendo. In most cases the murmur produces a maximum 3/6 grade, unless it is a whoop or a honk.
- Whoops or honks are transient and when they disappear during different stages of respiration they usually produce a regurgitant murmur.

**Table 13.1** Maneuvers and how they affect the timing and intensity of the murmur associated with MVP

| Intervention | Effect | Timing of click | Intensity |
|---|---|---|---|
| Standing upright | Decreased afterload, decreased preload | Earlier | Increased |
| Hand grip | Increased afterload | Earlier | Variable |
| Valsalva | Marked reduction in preload | Earlier | Variable |
| Amyl nitrite | Vasodilation | Variable | Increased |
| Recumbent | Increased preload | Later | Decrease/none |
| Squatting | Increased afterload, increased preload | Later | Decrease/none |

Used with permission from Valentin et al. [1]

- Whoops or honks can be caused by elongated papillary muscles producing a vibration.
- The Valsalva maneuver and standing upright will decrease the left ventricular volume resulting in the prolapse occurring sooner and usually more severely which is in stark contrast to other murmurs. This is due to the doming effect on the redundant mitral valve tissue as it balloons into the left atrium. The diameter of the edges is reduced in a smaller heart. This is because the edges are pulled toward each other as heart size is reduced, which occurs when standing. This results in the parachute effect, allowing for a louder murmur [2]. By having the patient squat or lie in the recumbent position, more blood will fill the left ventricle, allowing for tension to be maintained along the chordae which keeps the valve from prolapsing as quickly, moving the click later. See Fig. 13.6.
- A premature atrial or ventricular contraction will cause a severe and earlier prolapse [2].
- When releasing the Valsalva maneuver, there will be a louder click due to the overshooting of the blood pressure [2].
- Papillary muscle dysfunction murmurs have a loud S1 and a S4 sound present. They become louder with squatting or amyl nitrite [2].
- Prolapsed valve murmurs do not typically have a S4 sound or a loud S1. They are softer with squatting or amyl nitrite [2].

## Prognostic Implications of the Auscultation Features

- The majority of the time, MVP does not cause any symptoms and is associated with a benign prognosis with an age-adjusted survival rate similar to that of individuals without MVP. However, there are times when MVP can progress towards other diseases as is shown in Fig. 13.7.
- The best predictors that MVP will not have a benign course is a left ventricular ejection fraction less then 50% and echocardiographic evidence of thickened MV leaflets greater than 5 mm. Multiple sequelae may be associated with the progression of MVP (ACC/AHA 2006 Guidelines for the Management of Patients with Valvular Heart Disease) [7]:
  - Progressive dilation of the left atrium and ventricle.
  - Left atrial dilation may lead to atrial fibrillation.
  - Severe MR may result in congestive heart failure.
  - Pulmonary hypertension.
  - Fibrin emboli can lead to cerebrovascular accidents and ophthalmic artery occlusions.
- Individuals with connective tissue disease, e.g., Marfan's Syndrome, are at increased risk for mitral valve disruption, leading to sudden worsening of mitral regurgitation.

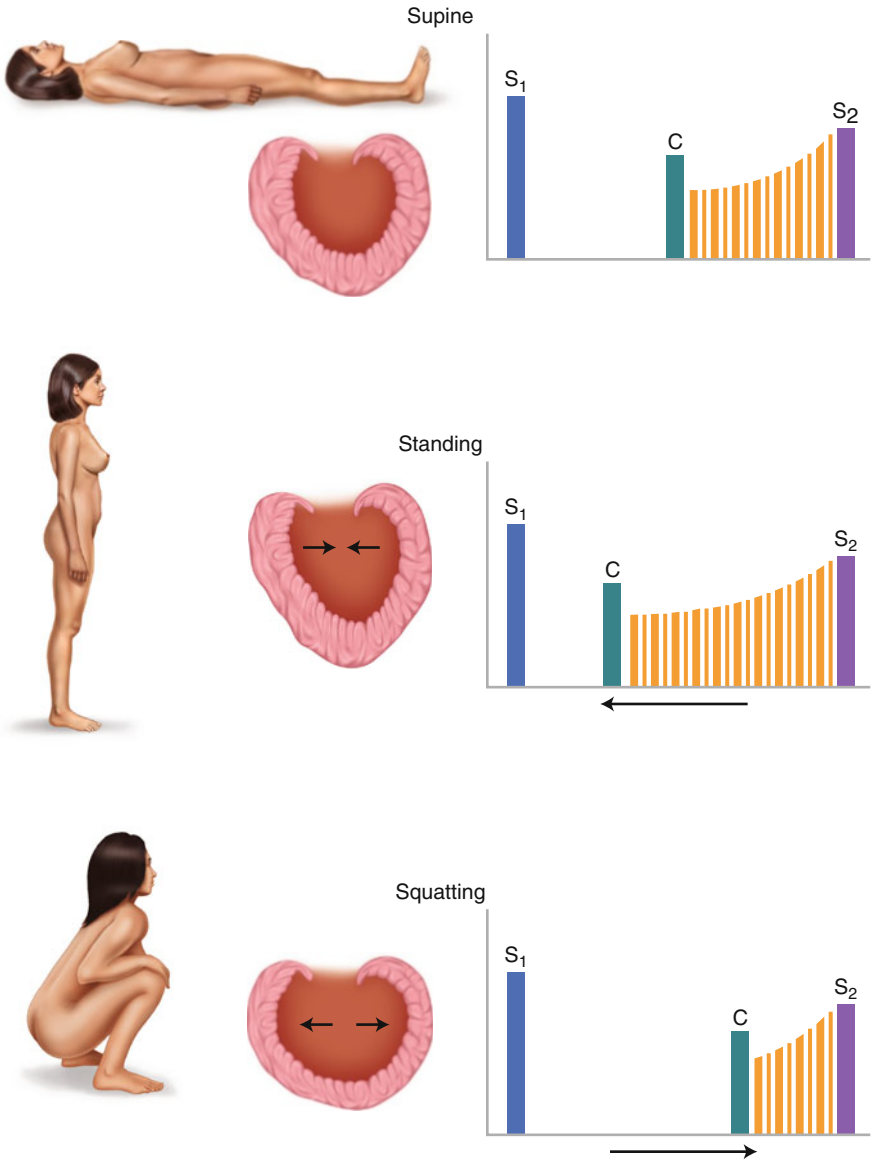


**Fig. 13.6** Diagram of the systolic crescendo nonejection sound associated with MVP. *Top*: a patient is laying supine which allows for a mid-systolic click. *Middle*: standing decreases the left ventricular volume which causes the click to occur earlier in systole. *Bottom*: squatting causes an increase central venous return, which increases end diastolic volume, which leads to a later click and a shorter murmur (Based on figure in the following source: Shaver et al. [10])

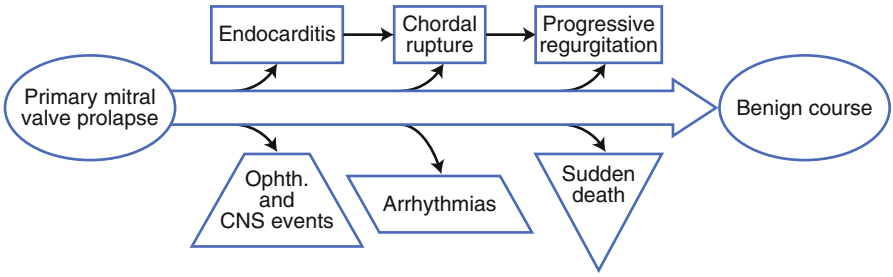


**Fig. 13.7** Most patients with MVP are asymptomatic and have a benign prognosis, but some patients may progress to more severe disorders in some cases. Complications and disease progression most commonly occur in patients with a systolic murmur and thickened redundant valve. Above is the progression of possible outcomes associated with MVP, even though the majority remain benign (Used with permission from Valentin et al. [1])

## Statement on Management

### *Class 1 Recommendations (ACC/AHA)* [7]

- Aspirin therapy (75–325 mg per day) is recommended for symptomatic patients with MVP who experience cerebral transient ischemic attacks.
- Patients with MVP and atrial fibrillation, warfarin therapy is recommended for patients aged greater than 65 or those with hypertension, MR murmur, or a history of heart failure.
- Aspirin therapy is recommended for patients with MVP and atrial fibrillation who are less than 65 years old and have no history of MR, hypertension, or heart failure.
- In patients with MVP and a history of stroke, warfarin therapy is recommended for patients with MR, atrial fibrillation or left atrial thrombus.

### *Class 2a Recommendations (ACC/AHA)* [7]

- In patients with MVP and a history of stroke, who do not have MR, atrial fibrillation or left atrial thrombus, warfarin therapy is reasonable for patients with echocardiographic evidence of thickening (5 mm or greater) and/or redundancy of the valve leaflets.
- In patients with MVP and a history of stroke, aspirin therapy is reasonable for patients who do not have MR, atrial fibrillation, left atrial thrombus, or echocardiographic evidence of thickening (5 mm or greater) or redundancy of the valve leaflets.

- Warfarin therapy is reasonable for patients with MVP with transient ischemic attacks despite aspirin.
- Aspirin therapy (75–325 mg per day) can be beneficial for patients with MVP and a history of stroke who have contraindications to anticoagulants.
- Aspirin therapy (75–325 mg per day) may be considered for patients in sinus rhythm with echocardiographic evidence of high-risk MVP.

## *Dental Procedure Prophylaxis*

- The American Heart Association states that prophylactic antibiotics are no longer required to patients with MVP due to the small absolute risk of infective endocarditis as well as the risk of an allergic reaction to the prophylactic antibiotics [8].
- A multicenter case control study looked at the risks of developing infective endocarditis as a result of MVP, congestive heart disease, rheumatic heart disease, and previous cardiac valve surgery, concluding that dental procedures were not a risk factor for infective endocarditis and that few cases could even be prevented if prophylactic antibiotics were 100 % effective [9].

## *Contact Sports*

- Restriction from contact sports is recommended in those patients with moderate LV enlargement, LV dysfunction, uncontrolled tachyarrhythmias, long QT interval, unexplained syncope, prior sudden death survival, or aortic root enlargement [1].

## *Follow Up*

- Asymptomatic patients with MVP and no significant MR should be evaluated every 3–5 years [7].
- Serial echocardiography is not required, and only recommended for those patients who have high risk characteristics and those who have symptoms consistent with cardiovascular disease or those that have symptoms that suggest a new development of significant MR [7].
- Surgery is indicated with a ruptured chordae tendineae or their marked elongation [1].

## Clinical Summary of the Case

The patient presents with several cardiovascular manifestations of Marfan's Syndrome, including a life-threatening aortic dissection that will require emergency surgery, and, incidentally, mitral valve prolapse. Clues to the detection of MVP include auscultation for the characteristic click, and its dynamic nature with Valsalva. Most patients have a benign course; however, there is heightened risk for progression of mitral regurgitation as the primary adverse outcome particularly in patients with connective tissue disorders.

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# Part IV
# Valvular Lesions: Right-Sided Heart Valves

# Chapter 14
# Pulmonic Valve: Pulmonic Regurgitation

**Daniel Eum, Kevin Emmerich, and Connor A. King**

## Key Teaching Points

- Trace or physiologic pulmonary valve regurgitation (PR) can often be found in a normal heart without a pathologic condition or pulmonary hypertension [1].
- Among heart valves, it is the least likely to be affected by acquired disease, and thus, most causes of PR are congenital [1].
- Pathologic pulmonary valve regurgitation is usually caused by dilation of either the pulmonary valve annulus or the pulmonary artery, secondary to pulmonary hypertension, idiopathic pulmonary artery dilation, or connective tissue disease [1].
- Rarely, congenital absence of a pulmonary valve leaflet may cause regurgitation [1].
- Iatrogenic causes include pulmonary valve trauma related to balloon valvuloplasty, pulmonary artery catheters, or surgical repair of congenital heart disease [1].
- Tricuspid regurgitation commonly accompanies pulmonary regurgitation in cases involving right ventricular dilatation.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_14) contains supplementary material, which is available to authorized users.

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A.J. Taylor (ed.), *Learning Cardiac Auscultation: From Essentials to Expert Clinical Interpretation*, DOI 10.1007/978-1-4471-6738-9_14

## Case Description

### *History*

- A 42 year-old asymptomatic man is referred for evaluation of hypertension.
- He denies dyspnea, chest pain, and peripheral edema.
- He has a past medical history of connective tissue disease that evolved into a mixed syndrome with features of lupus, scleroderma, and myositis.
- He is currently on metoprolol, lisinopril, triampterine + hydrochlorothizide (maxzide), methotrexate, etanercept, and rabeprazole.

### *Physical Exam*

- BP: 137/83 mmHg, pulse: 70 bpm and regular.
- No jugular venous distention.
- Lungs are clear to auscultation.
- Abnormal precordial palpation with an RV impulse.
- Palpable pulmonic closure in the second left intercostal space.
- Cardiac Auscultation (Fig. 14.1): Grade 2 diastolic decrescendo murmur along the left sternal border that increases with inspiration (Fig. 14.2). P2 is accentuated.

### *Test Results*

- EKG shows right axis deviation (Fig. 14.3).

## Key Auscultation Features of the Lesion

- Heart sounds relating to pulmonary regurgitation are determined by two factors, the pressure gradient and the degree of regurgitation:

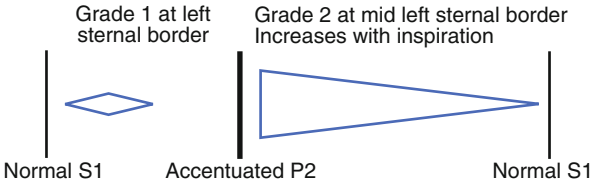


**Fig. 14.1** Typical auscultation features of pulmonic regurgitation including a soft systolic, and decrescendo diastolic murmur which varies with respiration

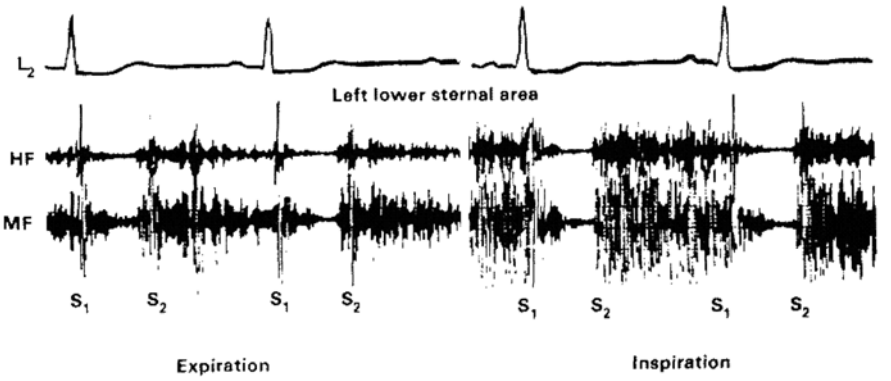


**Fig. 14.2** Diastolic murmur in the left lower sternal area that intensifies with inspiration, indicative of a right-sided murmur of pulmonary regurgitation

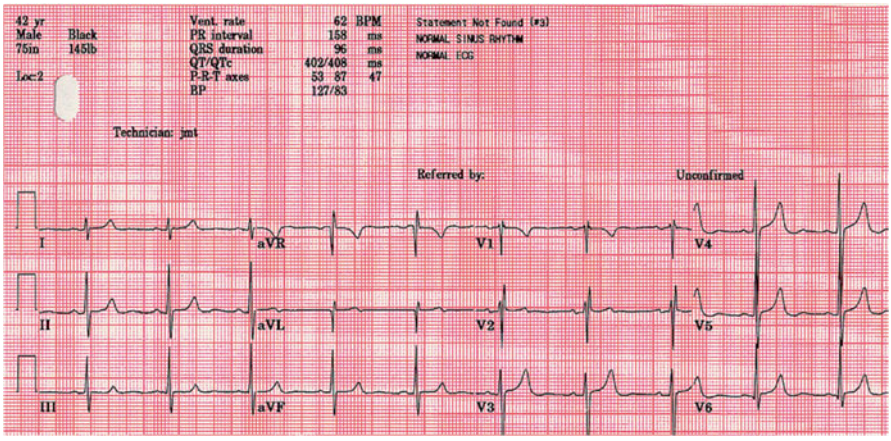


**Fig. 14.3** Electrocardiogram showing right axis deviation, and a right ventricular conduction delay, frequent findings in the setting of pathologic lesions affecting the right side of the heart

- The pressure gradient under which the turbulent flow occurs is determined by the difference between pulmonary diastolic pressure and right ventricular diastolic pressure.
  - The higher frequency the sound, the higher the pressure difference (e.g., the worse the pulmonary hypertension).
  - The PR murmur associated with pulmonary regurgitation secondary to pulmonary hypertension is called a *Graham Steell murmur* (Fig. 14.4).
    - In this case, pressure difference is greatest at S2, and gradually diminishes.
    - This results in a high frequency decrescendo murmur.

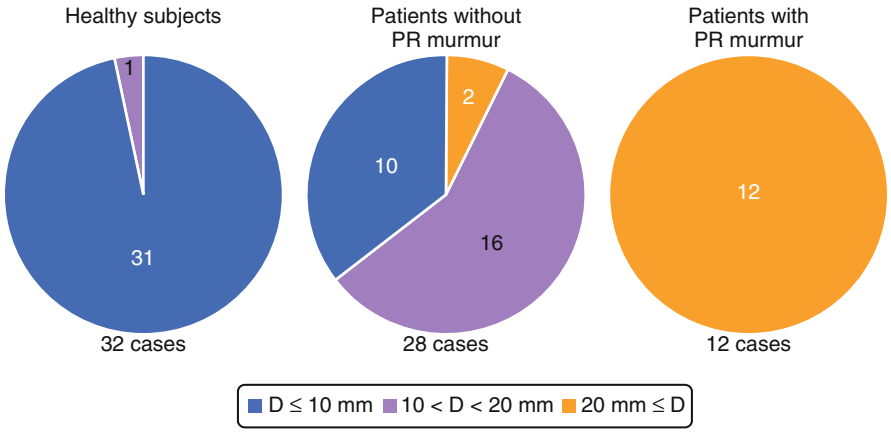


**Fig. 14.4** Compared to healthy patients and patients without a pulmonary regurgitation murmur, the murmur of pulmonary regurgitaton is seen when Doppler evidence of a larger volume and velocity of regurgitation (at least 20 mm on color Doppler) is seen. *D*: right ventricular diastolic pressure (Used with permission from Takao et al. [4])

  - The murmur begins at P2, and sounds similar to aortic regurgitation.
    - A Graham Steell murmur may be differentiated from that of aortic regurgitation by asking the patient to inspire, which increases the amplitude of the murmur.
  - The S2 split may be narrow or wide.
  - The murmur is best heard over the pulmonic area.
  - The P2 may be loud and even palpable at the left second intercostal space.

- Low frequency PR murmur is indicative of more normal levels of pulmonary artery pressure.
  - Initially, during the rapid filling phase, the right ventricular pressure is lower than pulmonary artery pressure. As right ventricular pressure increases with right ventricular filling, the pressure differential decreases.
  - This results in a short crescendo-decrescendo murmur that sounds like a low-frequency rumble.
  - The murmur will start after a brief pause following P2.
  - The S2 split will generally be physiological.
  - The murmur is best heard over the pulmonic area.
  - Note that there may also be an associated ejection systolic murmur due to increased right ventricular stroke volume.
  - Both systolic and diastolic murmurs may be shown to increase in intensity on inspiration.
  - There may be associated pulmonary ejection clicks.

  - Degree of regurgitation.
    - When the degree of regurgitation is severe and long standing, and secondary right ventricular hypertrophy has occurred:
      - Right ventricular diastolic pressure may be increased due to decreased compliance of hypertrophied right ventricle.
        - This can result in rapid deceleration of regurgitant blood from the pulmonary artery in addition to the flow of blood coming through the tricuspid valve during diastole.
          - This may produce a right-sided S3.
    - When the degree of regurgitation is not severe, the above features are not present.
- Auscultation examples of pulmonic regurgitation.
  - Click here to listen to an example of PR, including a pulmonic flow murmur, and to see an image of the phonocardiogram (Video 14.1).

## Auscultation Differential Diagnosis

- All diastolic murmurs should raise suspicion of underlying cardiac pathology.
- In the upper left sternal border, auscultation mimics may include:
  - Eccentric aortic regurgitation murmur.
  - Venous hum.
  - Late stage patent ductus arteriosus as pulmonary hypertension ensues.

## Clinical Clues to the Detection of the Lesion

- The murmur is best heard over left upper sternal border.
- The murmur typically increases with inspiration, although hyperinflation may mask this at LUSB, but not at apex.

## Diagnostic Implications of Auscultation Findings

- A murmur is rarely present with pulmonary artery pressures normal or near normal unless the main pulmonary artery is markedly dilated.

- The murmur is brief and low-pitched with pressures ≤60 mm and high-pitched and blowing when pulmonary pressures exceed 60 mmHg.

## Prognostic Implications of the Auscultation Features

- Most patients with mild degrees of PR have a benign clinical course.
- Chronic severe PR often is well tolerated for many years. However, the RV may dilate and develop systolic dysfunction, analogous to the effect of chronic aortic regurgitation on the left ventricle.
- Severe RV dilation is associated with an increased risk of sudden death related primarily to arrhythmias [2].

## General Statement on Management

- Except in patients with previous surgery for tetralogy of Fallot, PR alone is seldom severe enough to require specific treatment.
- Treatment of the primary condition, such as infective endocarditis, or the lesion responsible for the pulmonary hypertension, such as surgery for mitral valvular disease, often reduces the severity of PR.
- Although no medical therapy has been demonstrated effective in reducing the degree of PR, valve replacement is rarely indicated.
  - Indications for PV replacement include symptoms related to PR, or adverse effects on the RV or RV dilation leading to significant TR.
  - When pulmonic valve replacement is needed, RV volumes and pulmonic regurgitant fraction decreases.
- Prophylaxis against infective endocarditis is not recommended [3].

## Clinical Summary of the Case

Audible PR is often a sign of increased pulmonary artery pressure. In this instance, although overt heart failure is not present, the increased intensity of P2, and the RV impulse suggest pressure and/or volume effects on the right ventricle. An imaging assessment of the valve and of RV size and function is warranted (Fig. 14.5). Pulmonary vascular disease may be the cause, related to autoimmune disease.

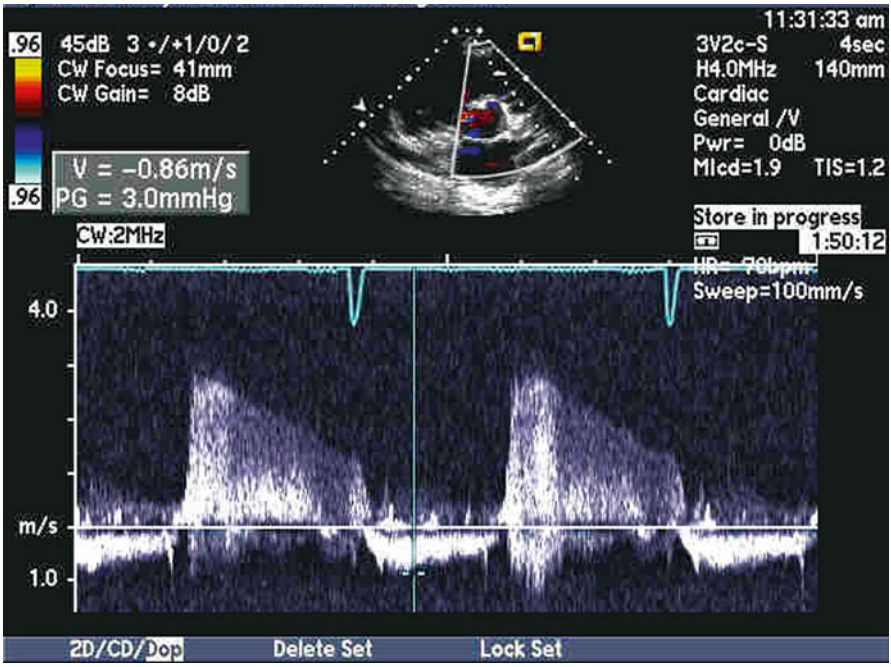


**Fig. 14.5** Doppler echocardiogram showing the diastolic velocity profile of pulmonic regurgitation. This has the same general features of aortic regurgitation, however typically at lower velocities due to the lower pressure in the pulmonary artery. For example, not the peak velocity is approximately 3 m/s. The decreasing velocity profile is consistent with the decrescendo nature of the associated murmur

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# Chapter 15
# Pulmonic Valve: Pulmonic Stenosis

**Amy Fehrmann and Sheelagh M. Pousatis**

## Key Teaching Points

- Pulmonic stenosis is a common form of congenital heart disease.
- Trivial or mild valvular pulmonic stenosis involves peak gradients <50 mmHg and has an excellent prognosis.
- Auscultation of pulmonic stenosis predicts the severity of the lesion.
- Mild forms of pulmonic stenosis by auscultation have clicks present and have a more narrowly split A2/P2 interval.

## Case Description

### *History*

- A 46-year-old woman was diagnosed with mild pulmonic stenosis in childhood and has needed only clinical follow-up.
- She has been asymptomatic with no dyspnea, syncope, or non-cardiac chest pain.
- She is borderline hypertensive, controlled with atenolol, and has a family history of a daughter with a sub-aortic membrane.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_15) contains supplementary material, which is available to authorized users.

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## *Physical Exam*

- On exam, her blood pressure is 130/71 mmHg, pulse regular at 65 bpm, and normal JVP.
- On auscultation (Fig. 15.1), the patient shows a grade 2 crescendo decrescendo murmur at the left sternal border. An ejection click is present. A sharp S2 at the left sternal border that is narrowly split is also present. No diastolic murmurs are present.

## *Test Results*

- Normal EKG (Fig. 15.2).
- Echocardiogram (Fig. 15.3) shows valvular doming and thickening with supravalvular dilation of the left pulmonary artery.

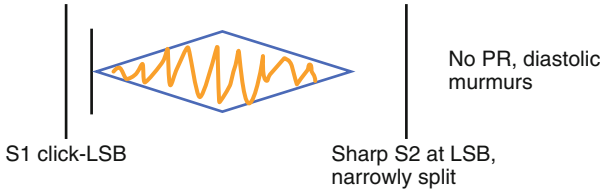



**Fig. 15.1** Auscultation of pulmonic stenosis. Pulmonic stenosis is characterized by an ejection click, crescendo decrescendo murmur loudest at the left sternal border, and sharp, narrowly split S2

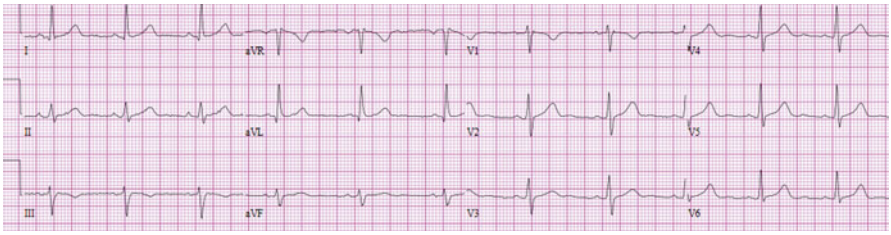



**Fig. 15.2** Normal EKG: normal EKG showing normal sinus rhythm

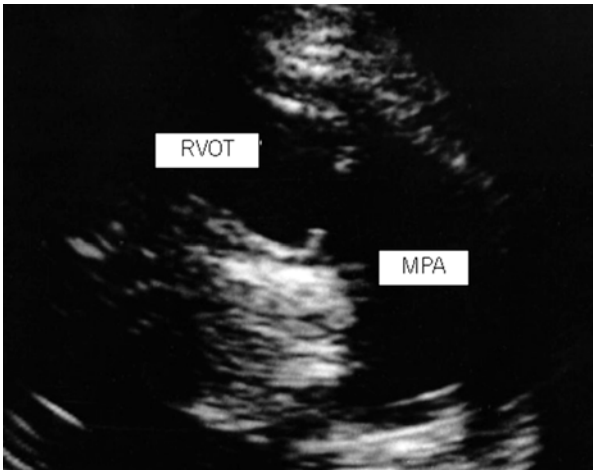



**Fig. 15.3** Pulmonic stenosis echocardiogram: echocardiogram showing valvular doming, and thickened pulmonic valve

## Clinical Basics

### *Anatomy*

- In a normal heart, blood flows from the right ventricle through the pulmonary valve, into the pulmonary artery and into the lungs.
- *Pulmonic valvular stenosis* (Fig. 15.4a, b) occurs when the valve is narrowed and the valve does not open as wide as a normally functioning valve. The valvular cusps can be fused, thickened, or there may be a failure of all three leaflets to form in utero. The result is less blood flow to the lungs, increased pressure in the right side of the heart, and a mid-systolic murmur on auscultation. It is most commonly a congenital condition and can range from trivial to severe.

– Valvular stenosis is the most common form. Stenosis in the pulmonary infundibulum, below the valve, is rare.
– Severity of the lesion is categorized by the peak pressure gradient across the valve:

  - <25 mmHg: trivial.
  - 25–49 mmHg: mild.
  - 50–79 mmHg: moderate.
  - ≥80 mmHg: severe.

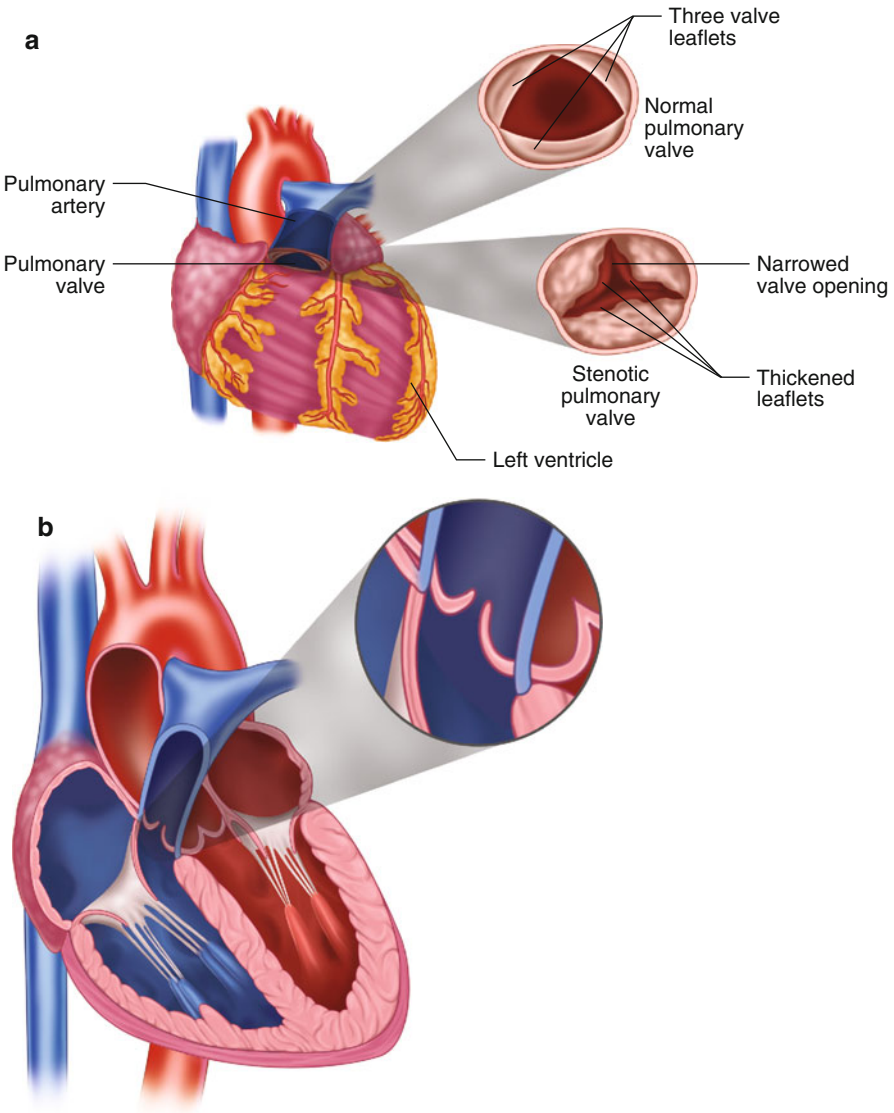



**Fig. 15.4** (**a**, **b**) Pulmonic valvular stenosis: (**a**) Normal pulmonic valve leaflets vs. thickened leaflets with reduced mobility resulting in PS. (**b**) 4-chamber view of the heart showing relationship of the pulmonic valve, affected by PS, to other cardiac structures

- *Pulmonic artery stenosis* is a narrowing of the pulmonary artery that carries blood from the right ventricle to the lungs. It results in a decreased volume of blood reaching the lungs and increased pressure in the right side of the heart.
- Pulmonic stenosis accounts for 10 % of congenital heart disease and is found with an increased prevalence (25 %) in patients with other forms of congenital heart disease.

## *Etiology*

- Congenital heart disease.
  - Isolated pulmonic stenosis.
  - *Multiple Lentigines Syndrome* (formerly called Leopard Syndrome) is an autosomal dominant condition most often caused by a deletion of the PTPN11 gene. Multiple Lentigines Syndrome is characterized by multiple dark skin markings called lentigines, wide-set eyes, abnormal genitalia, growth retardation, deafness, ECG abnormalities, and pulmonic stenosis. It is also associated with cardiomyopathy and coronary heart disease.
  - *Noonan Syndrome* is an autosomal dominant condition that is most commonly caused by a mutation in the PTPN11 gene or, less commonly in the SOS1 gene. It is characterized by short stature, developmental delays, cryptorchidism, inferior pectus excavatum, and congenital heart abnormalities including pulmonic valve stenosis and pulmonary artery stenosis.
  - *Situs Solitus with cardiac dextroversion* is a condition in which the visceral organs are all in the appropriate positions within the body however the heart is located on the right side as opposed to the left and is associated with pulmonic stenosis.
  - *Tetralogy of Fallot* is characterized by ventricular septal defect, a right ventricular outflow obstruction, overriding aorta, and right ventricular hypertrophy. In this condition, the most common pulmonic valve defect is a bicuspid stenotic valve.
- Rheumatic inflammation of the pulmonic valve is a rare occurrence that is usually associated with other valvular abnormalities as well.
- Carcinoid plaque due to malignant carcinoid may cause pulmonic stenosis and can present with flushing, cyanosis, and telangiectasia.

## *Signs and Symptoms*

- Most patients with pulmonic stenosis are asymptomatic, however when present, the most common symptoms are exertional dyspnea, fatigue, palpitations, fainting, cyanosis when severe, and heart failure. A systolic ejection click may be present.
- Pulmonic stenosis is usually diagnosed during routine newborn exams with the detection of the cardiac murmur.
- In a cyanotic patient, the murmur will be softer due to increased blood viscosity and decreased turbulence through the valve.

## Auscultation Differential Diagnosis

- Atrial septal defect- in atrial septal defect, S2 will be split and fixed (unchanged by respiration).

- Aortic stenosis or bicuspid aortic valve, potentially with coarctation- the murmur of PS is usually longer in duration for a given severity of PS, and will be maximal at the LUSB.

## Key Auscultation Features (Fig. 15.5)

- Pulmonic stenosis presents as a systolic murmur, loudest at the second to third intercostal space on the left sternal border that radiates upward and to the right. It is typically louder on inspiration and upon standing.
- A normal S1 will be present.
- An ejection click with an intensity that is inverse to respiration occurs, indicating when the valve reaches the fully open position. This particular feature is unique to pulmonic stenosis.
- The split S2 varies inversely with the intensity of the stenosis.
- If the septum is intact, pulmonic stenosis may cause right ventricular hypertrophy and a right-sided S4 that increases with inspiration.
- The crescendo peak corresponds with stenosis intensity; the later the peak, the more severe the stenosis.
- Auscultation examples of aortic pulmonic stenosis.
  - Click here to listen to an example of a PS murmur and to see an image of the phonocardiogram (Video 15.1).

## Diagnostic Implications

- According to the 1998 study by Danford, et al. [1], pulmonic stenosis is often diagnosed via clinical exam but to ensure the highest sensitivity and specificity of diagnosis, an echocardiogram needs to be done.
  - The study contained 521 individuals under the age of 21 that had previously not been evaluated for murmurs. The physicians preformed a clinical exam and recorded their diagnosis and level of certainty. If no one diagnosis could be decided upon, the physician listed in order of possibility his diagnoses. 62 were found to have pulmonic stenosis post-evaluation via echocardiogram: 29 with mild, 27 with moderate, and 6 with severe. These results were compared to the physicians' results.
  - 31 of the 62 cases listed pulmonic stenosis as the first or only diagnosis, showing a sensitivity of 50 %. If this case is expanded to include patients with pulmonic stenosis that was listed as a second or third choice, the sensitivity rises to 73 %.

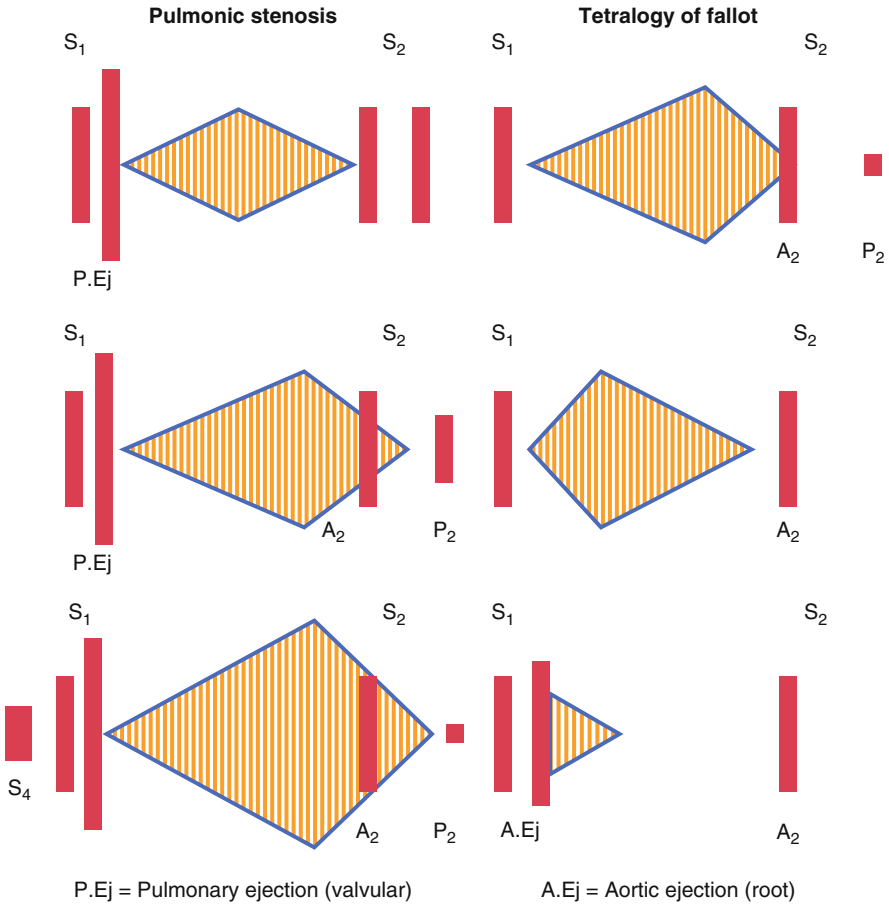



**Fig. 15.5** *Left*: in valvular pulmonic stenosis with intact ventricular septum, *right* ventricular systolic ejection becomes progressively longer, with increasing obstruction to flow. As a result, the murmur becomes longer and louder, enveloping the aortic component of the second heart sound ($A_2$). The pulmonic component ($P_2$) occurs later, and splitting becomes wider but more difficult to hear because $A_2$ is lost in the murmur and $P_2$ becomes progressively fainter and lower pitched. As the pulmonic gradient increases, isometric contraction shortens until the pulmonary valvular ejection sound fuses with the first heart sound ($S_1$). In severe pulmonic stenosis with concentric hypertrophy and decreasing right ventricular compliance, a fourth heart sound appears. *Right*: in tetralogy of Fallot with increasing obstruction at the pulmonic infundibular area, an increasing amount of right ventricular blood is shunted across the silent ventricular septal defect and flow across the obstructed outflow tract decreases. Therefore, with increasing obstruction the murmur becomes shorter, earlier, and fainter. $P_2$ is absent in severe tetralogy of Fallot. A large aortic root receives almost all cardiac output from both ventricular chambers, and the aorta dilates and is accompanied by a root ejection sound that does not vary with respiration (Used with permission from Shaver et al. [2])

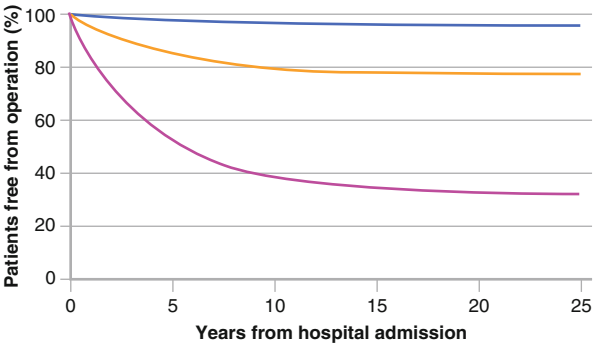
  - 15 of the 459 without pulmonic stenosis were diagnosed with pulmonic stenosis on clinical exam only showing a specificity of 96.8 %. If this case is expanded to include patients with pulmonic stenosis that was listed as a second or third choice, the specificity is lowered to 82.3 %.
  - The ROC curves showed a difference in accuracy of diagnosis depending on the child's age at exam ($p = 0.016$). If the child was under 12 months at exam, the ROC showed $0.806 \pm 0.040$ while diagnosing a child older than 12 months on exam had an accuracy via ROC curves of $0.936 \pm 0.0146$.
  - ECG in addition to exam is more accurate than an exam alone (ROC: $0.875 \pm 0.032$, $0.647 \pm 0.099$, respectively).
- Thrill in the second left intercostal space indicates severe right ventricular outflow tract obstruction.
- If P2 is normal or increased the obstruction is supravalvular.
- Pulmonic stenosis progression is indicated by the systolic ejection murmur lengthening and peaking later in systole, shortening of the interval between S1 and the systolic ejection click, and by a widely split S2 with a disappearing P2.
- A systolic ejection click indicates the pulmonary valve is thin and pliable. The systolic ejection click decreases on inspiration.
- Higher grade stenosis predictive exam features:
  - No click.
  - Longer, louder murmur.
  - Decreased P2.
  - Longer A2/P2 delay.

## Prognostic Implications

The prognosis of trivial to mild PS is excellent, and the lesion generally does not progress in adults. For this reason, using exam to identify diagnostic findings indicating the likely presence of mild PS holds prognostic importance. See Fig. 15.6.

## General Statement on Management

- The treatment modality is selected based on the stage of stenosis present. The stage is obtained depending on the systolic gradient between the right ventricle and the pulmonary artery. See Fig. 15.6. The stages are as follows:
  - Trivial <25 mmHg.
  - Mild 25–49 mmHg.
  - Moderate 50–79 mmHg.
  - Severe ≥80 mmHg.




| | Pressure gradient across stenotic valve (mmHg) | Number of patients | 25-year survival rate (%) |
|---|---|---|---|
| | <25 | 78 | 96.1 |
| | 25–49 | 162 | 77.1 |
| | 50–79 | 60 | 30.9 |

**Fig. 15.6** Medically managed patients with pulmonary stenosis who remain free from surgery (Used with permission from Hayes et al. [3])

- According to the ACC/AHA joint guidelines, the following is recommended for management of pulmonic stenosis.
  - Initial evaluation of pulmonic stenosis should include an ECG and transthoracic Doppler, with a repeat testing every 5–10 years (Class I, level C).
  - Cardiac catheterization is recommended for mild to moderate stenosis and Balloon dilation can be performed if indicated (Class I, level C). Cardiac catheterization should not be done for initial diagnosis (Class III, level C).
  - Balloon valvotomy is recommended in symptomatic patients with mild stenosis and a gradient over 30 mmHg and in asymptomatic patients with a gradient over 40 mmHg (Class I, level C).
  - Balloon valvotomy may be reasonable if the patient is asymptomatic and has a gradient between 30 and 39 mmHg (Class IIb, level C).
  - Balloon valvotomy is not recommended if gradient is less than 30 mmHg and the patient is asymptomatic (Class III, Level C).
  - Asymptomatic patients with mild and trivial stenosis usually need no intervention except minimal clinical follow-ups.

## Clinical Summary of the Case

The patient is asymptomatic, with exam findings indicative of mild PS, with an ejection click, narrow A2-P2 gap, and mid-peaking murmur. Echocardiography confirmed a low gradient, which carries an excellent prognosis.

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# Chapter 16
# Pulmonic Valve: Pulmonary Arterial Hypertension

**Samantha L. Kass, K. Elizabeth Madison, Marsiyana M. Henricus, and Christine K. Chan**

## Key Teaching Points

- Pulmonary hypertension has many causes. In primary pulmonary hypertension, irreversible and idiopathic pulmonary hypertension progresses to more severe stages, characterized by a grossly dilated right ventricle and histologically, by intimal fibrosis and medial thickening of the pulmonary arterioles.
- The signs and symptoms of pulmonary arterial hypertension (PAH) may remain clinically silent until progression to a more advanced stage of the disease which correlates with a worse prognosis.
- Auscultation can be a crucial tool in diagnosing patients with PAH in the earlier stages before significant clinical symptoms arise.
- Prevailing auscultation features include:
  - Increased intensity of P2.
  - Very narrow physiological splitting of S2 or a single S2 may be heard.
  - Late wide splitting of S2.
  - Vibratory S1.
  - Short midsystolic murmur after the ejection click.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_16) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- A 30-year-old white female presents to her primary care physician with progressive fatigue, dizziness, and shortness of breath over the past 6 months. She had an uncomplicated pregnancy, no history of spontaneous abortions, and no other symptoms of other connective disorders.

### *Physical Examination*

- On physical exam, the patient has a BP 105/70 mmHg, HR 110 bpm, BMI 28 kg/m$^2$, and is afebrile.
- Her cardiac exam shows regular rate and rhythm. Jugular venous pressure (JVP) is normal but a slightly accentuated V-wave is present. Palpation of the parasternal area reveals a soft palpable impulse.
- On auscultation, the patient has a normal S1 with no murmurs. The S2 is increased in intensity along the middle of the upper left sternal border. No S3 or S4 heart sounds are present.
- The remainder of the exam is normal.

### *Test Results*

- EKG shows a right bundle branch block with a right axis deviation (Fig. 16.1), and echocardiography shows an enlarged right ventricle with a TR jet (Fig. 16.2).

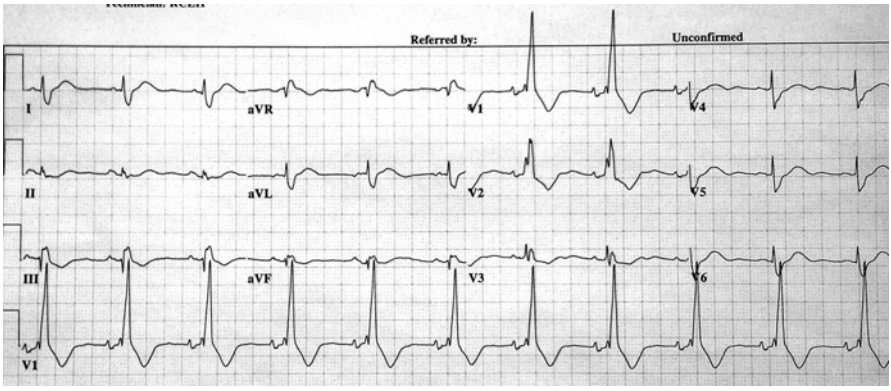


**Fig. 16.1** Echocardiogram. Echocardiogram (apical 4 chamber view) shows an enlarged right ventricle with significant tricuspid regurgitation

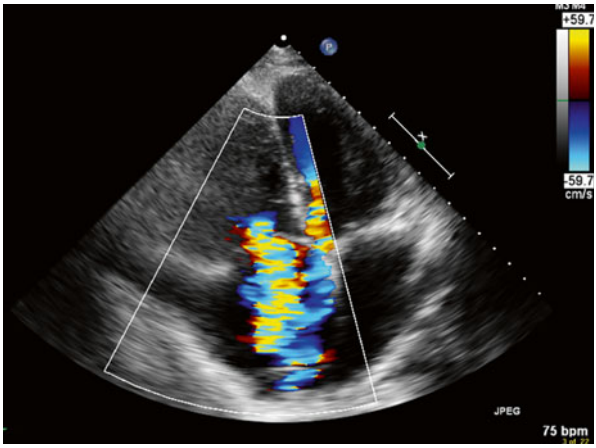


**Fig. 16.2** Electrocardiogram. Electrocardiography shows a right bundle branch block with a right axis deviation

## Clinical Basics

### *Normal Anatomy*

- The right side of the heart receives deoxygenated blood from the body and pumps this blood to the lungs for re-oxygenation.
- The blood receives oxygen via gas exchange through blood vessels that course throughout the lungs. Thus, the integrity of these blood vessels is vital in proper functioning of the cardiovascular system.
- Because of these functions, the pressure in the pulmonary arteries is lower than in the systemic arteries; at rest, pulmonary artery pressure should be between 10 and 20 mmHg, however this number varies based on a variety of factors, including age and weight. As individuals age, pulmonary artery pressure can be considered normal even in the range of 30–39 mmHg.
- When pulmonary artery pressure rises above 40 mmHg, this is a definitive sign of pulmonary hypertension [1].

### *Definitions*

- PAH results as a function of increased arterial resistance. This can be associated with a variety of causes, among them lung diseases with affect oxygenation and vascular diseases, which affect vessel tension (Fig. 16.3a, b).
- In the setting of PAH, the right ventricle must work harder to pump against the increasing arterial pressure. As opposed to the thick-walled left ventricle, the right ventricle has a thin wall and does not adapt to acute changes in pressure very well. It is more equipped to handle abundant volume than excessive pressure. Over time, this causes hypertrophy and symptoms associated with right-sided heart failure (Fig. 16.4).

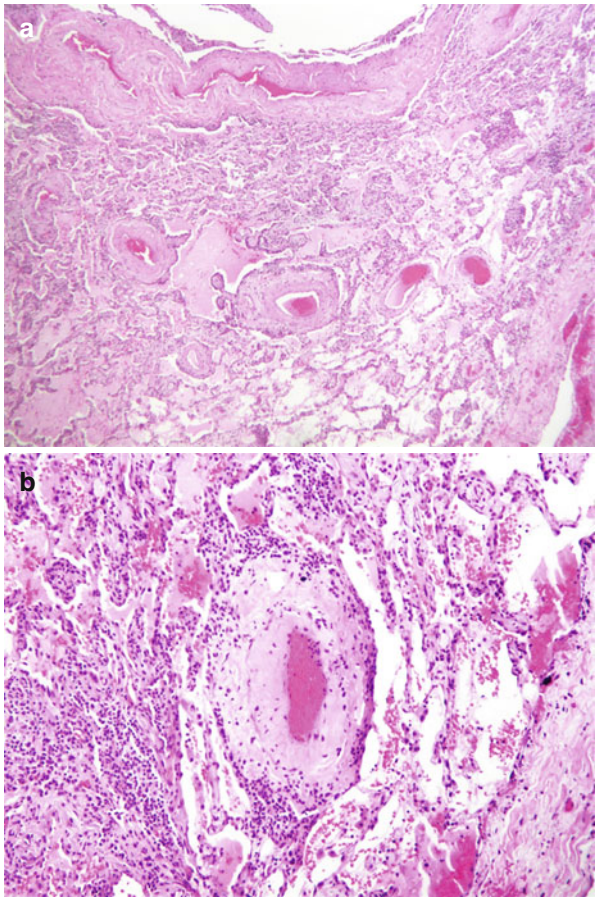


**Fig. 16.3** (**a**, **b**) Vascular changes seen in pulmonary hypertension. (**a**) Generalized thickening of vessels of the lung in a case of pulmonary hypertension, magnification 4×. (**b**) Marked medial wall thickening of a pulmonary vessel in a case of pulmonary hypertension secondary to chronic obstructive pulmonary disease, magnification 10×. (**a**, **b** Courtesy of Dr. Deepu Alex and Dr. Mary A. Furlong, Georgetown University, Department of Pathology)

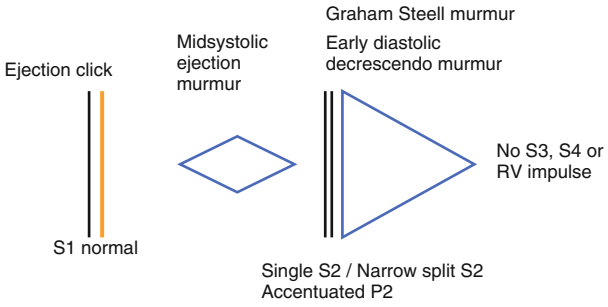


**Fig. 16.4** Auscultation Features of Pulmonary Hypertension. The schematic portrays the auscultation features that have been affiliated with PAH. Common findings include an ejection click, midsystolic ejection murmur, and an early diastolic decrescendo murmur. Additionally, there is a narrow or single (rare) S2 due to the accentuated P2

### *Etiology*

- Pulmonary hypertension can be a sequelae of a variety of conditions.
- However, idiopathic pulmonary arterial hypertension (IPAH) exists when an underlying cause cannot be identified.
- Potential etiologies.
  - Genetic – familial pulmonary hypertension is caused by a mutation in BMPR2 [2].
  - Drugs and toxins.
  - Connective tissue diseases - these include Systemic Sclerosis, Rheumatoid Arthritis, and Systemic Lupus Erythematosus.
  - Human Immunodeficiency Virus.
  - Portopulmonary hypertension.
  - Congenital heart disease.
  - Sleep apnea.
  - Chronic thromboembolic disease.
  - Chronic advanced lung disease.

### *Signs and Symptoms*

- Fatigue.
- Dyspnea.
- Dizziness.
- Syncope.
- Bilateral lower extremity edema.
- Cyanosis.
- Chest pain.
- Tachycardia/palpitations.

### *Prevalence*

- In the USA, 500–1,000 new cases of primary pulmonary hypertension are diagnosed each year [3].

## Key Auscultation Features of the Lesion (Fig. 16.3)

- Increased intensity of the pulmonic component of the second heart sound, P2.
  - The most common cause of an increased P2 sound is pulmonary hypertension of any etiology [4].

  - The increased intensity of P2 may exceed, or be increased although still overall softer than A2.

- Very narrow physiological splitting of S2 due to the early occurrence of P2.
  - A2 and P2 may still be faintly heard as two distinct sounds upon expiration.
- A single S2 may be heard but it must be noted that a truly single S2 is rare.
  - Fusion of A2 and P2 without inspiratory splitting may occur.
  - May be due to a soft pulmonic element.
  - A single S2 is rare in healthy infants, children adults, and even in elderly although advanced age increases the likelihood of hearing a single S2 during both respiratory phases.
  - Lung hyperinflation is the most prevalent cause of inability to hear the pulmonic closure.
  - Emphysema, obesity or pericardial effusion may obscure the auscultation or ability to record the P2.
- A late wide splitting of S2 due to conduction disturbances results from the presence of right ventricular failure, subsequently leading to delayed right ventricular ejection.
- A diastolic murmur that sounds high-pitched and blowing can result from pathologic pulmonary regurgitation associated with hypertension.
  - There may be few cases of normal pulmonic regurgitation in thin individuals.
- Sustained parasternal or subxiphoid impulse may be present and signify right ventricular enlargement or overload.
- Elevated JVP due to tricuspid incompetence.
  - A single outward systolic movement occurs concurrently with the carotid pulse and diminishes in the early diastole phase, after S2.
- With respect to primary pulmonary hypertension or IPAH, unique auscultation features may include.
  - Vibratory S1.
  - A short midsystolic murmur after the ejection click.
- Auscultation example of pulmonary hypertension.
  - Click here to listen to an example of heart sounds in pulmonary hypertension and to view an image of the phonocardiogram (Video 16.1).

## Auscultation Differential Diagnosis

- There are not many clinical syndromes that can resemble primary pulmonary hypertension, however it is unequivocally important to be aware its presence.

- Pulmonary stenosis associated with an ejection murmur.
  - Pulmonary ejection click heard in the left second intercostal space.
  - Frequently, accompanied by a palpable thrill.
  - It can mainly be differentiated from primary pulmonary hypertension by its wide S2 split and increased P2 intensity.
- As noted before, an accentuated physiologic P2 can be heard in young and thin individuals.

## Diagnostic Implications of Auscultation Features (Table 16.1)

- A high index of suspicion is a necessity when diagnosing PAH given that its symptoms are common to other disorders. PAH should be considered in the differential if a patient presents with exertion, fatigue or exercise limitation and

**Table 16.1** Relevant physical examination findings for PAH: signs and implications

| Inspection | |
|---|---|
| Signs | Implications |
| Left parasternal lift | High right ventricular pressure and hypertrophy |
| Jugular venous distension | Right ventricular dysfunction and/or tricuspid regurgitation |
| Peripheral edema and ascites | |
| Low blood pressure, diminished pulse pressure and cool extremities | Reduced cardiac output, peripheral vasoconstriction |
| Palpation | |
| Hepatomegaly | Right ventricular dysfunction and/or tricuspid regurgitation |
| Pulsatile liver | |
| Hepatojugular reflux | High central venous pressure |
| Auscultation | |
| Accentuated pulmonary component of S2 audible at apex (over 90 %) | High pulmonary pressure increases force of pulmonic valve closure |
| Early systolic click | Sudden interruption of opening of pulmonary valve into high-pressure artery |
| Midsystolic ejection murmur | Turbulent transvalvular pulmonary outflow |
| Right ventricular S4 (38 %) | High right ventricular pressure and hypertrophy present |
| Increased jugular “a” wave | Poor right ventricular compliance |
| Holosystolic murmur increasing with inspiration | Tricuspid regurgitation |
| Increased jugular v waves | |
| Diastolic murmur | Pulmonary regurgitation |
| Right ventricular S3 (23 %) | Right ventricular dysfunction |

Source: McLaughlin et al. [8]

a family history of PAH. Symptoms at rest are usually only noticed in severe PAH [5].

- An ejection click is due to stiffened pulmonary valve cusps caused by high pressure in the pulmonary artery and a dilated pulmonary artery root [6]. This occurs later in systole as opposed to with the first heart sound in pulmonary valve stenosis [7].
- A narrowly split S2 due to an early loud P2 is heard in early pulmonary hypertension, while the split widens in late pulmonary hypertension due to right ventricular failure [6].
- Moderate to severe PAH signs include holosystolic murmur that increases with inspiration (due to tricuspid regurgitation), diastolic murmur (due to pulmonary regurgitation) and increased jugular v waves [8].
- Signs of advanced PAH with right ventricular failure include right ventricular S3 (in 23 %), high right arterial (RA) pressure as seen by jugular venous distention (JVD), low blood pressure, diminished pulse pressure, hepatomegaly, ascites and peripheral edema [8, 9].
- Suspected PAH with auscultation findings of systolic murmurs, diastolic murmurs, opening snaps or gallops could be indications of an underlying heart or valvular disease contributing to PAH [8].
- Once PAH is confirmed, other diagnostic methods can be used:
  - Doppler transthoracic echocardiography is first used as a noninvasive evaluation of right ventricular pressure, pulmonary artery pressure, right ventricular function in addition to structural morphology [10].
  - Echocardiographic signs that are significant for PAH include elevated pulmonary artery pressure, a systolic pressure greater than 40 mmHg, tricuspid regurgitation as well as right atrial and right ventricular enlargement, flattening of the intraventricular septum, pericardial effusion and patent foramen ovale [9]. This method is also useful in elucidating causes of PAH such as increased left-atrial pressure, mitral and aortic valvular disease, cardiomyopathy and constrictive pericarditis.
  - Right-heart catheterization is used to diagnose the type of pulmonary hypertension by detecting the degree of hemodynamic impairment as well as prognostic information. This method is used to measure pulmonary-artery pressure, estimate pulmonary vascular resistance, determine cardiac output, evaluate left-right shunt, determine the response to short acting vasoactive agents, and assist with the titration of long-term vasodilators. Increased pulmonary vascular resistance with normal wedge pressure (Levine) would be consistent with PAH. Additionally, this method can help to elucidate any structural abnormalities such as tricuspid regurgitation, a finding in PAH.
  - EKG is noninvasive but a limited test for PAH since many of the diagnostic findings occur as late onset. It provides evidence of right ventricular hypertrophy, right atrial enlargement, right axis deviation, right ventricular strain and right bundle branch block which are all consistent with PAH [9].
  - Checking the conditions of the lungs.

- Pulmonary function tests will evaluate dyspnea. Common findings include a decreased diffusion capacity in addition to mild restriction [11, 12].
- Ventilation-perfusion lung scans can detect segmental or subsegmental perfusion unmatched defects suggestive of a chronic thromboembolic disease.
- Imaging studies such as X-ray and CT scan have been used to visually assess the pulmonary disease. X-ray is useful in excluding other pulmonary diseases deciphering secondary causes of pulmonary hypertension. Certain diagnostic findings such as enlargement of the central pulmonary arteries, decreased capacity of the peripheral pulmonary vessels and cardiomegaly are seen later in the disease. CT provides visualization of pulmonary vasculature, pulmonary parenchyma and mediastinal structures. A pulmonary artery diameter greater than 29 mm is suggestive of pulmonary hypertension [13]. A thrombus may be visualized within the pulmonary arteries in the case of chronic thromboembolic pulmonary hypertension.

– Evaluation of etiology includes a full laboratory work up that requires studies such as serum chemistries, thyroid-function tests, liver-function tests, and complete blood count. Screening for connective tissue diseases are also conducted along with an HIV test [9]. Many of the tests are directly confirmatory such as hyperuricemia, which is common in those with Idiopathic Pulmonary Arterial Hypertension [14]. Elevated brain natriuretic peptide in right ventricular pressure overload correlates with severity of right ventricular dysfunction [15].

## Prognostic Implications of the Auscultation Features

- The estimated median survival of IPAH without treatment is 2.8 years with a 1-year survival of 68 %, a 3-year survival of 48 % and a 5-year survival rate of 34 % [16].
- The prognosis of PAH is based on multiple factors and underlying conditions. The goal of medical care and treatment is to lower mortality risk by improving the functional classes of patients to increase survival (Fig. 16.5a–d and Table 16.2) [17].
- Classification of stages of PAH utilizes the World Health Organization Functional Class (WHO FC) system which was adapted from New York Heart Association functional system of symptoms from no limitation in class I to symptoms at rest in class IV (Fig. 16.5a) [17].

  – Stable WHO FC class I/II symptoms have a 5-year survival rate of 90 %.
  – Deterioration from WHO FC I/II to III/IV results in a decrease in 5-year survival to 66 %.
  – Consistent severe symptoms of WHO FC III/IV result in a 5-year survival of 34 %.
  – However, recovery of symptoms from WHO FC III/IV to I/II improves the 5-year survival to 76 %.

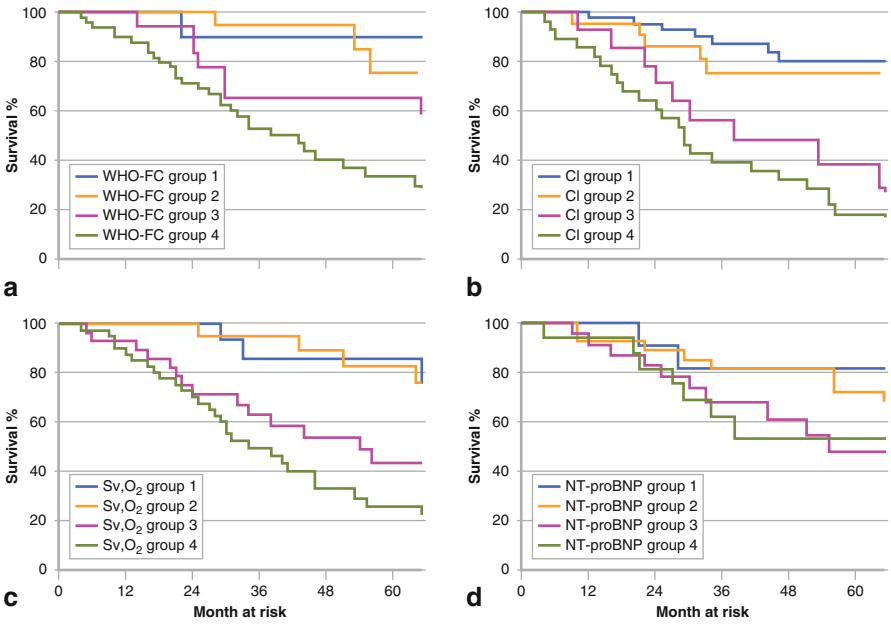


**Fig. 16.5** (**a**–**d**) Prognostic Implications for PAH. The graphs portray Kaplan-Meier estimates of transplant-free survival according to (**a**) WHO; (**b**) cardiac index; (**c**) mix-venous oxygen saturation ($S_v$, $O_2$); and (**d**) N-terminal pro-brain natriuretic peptide. Group 1 maintains stable levels at baseline and follow-up and group 2 begins at a stable baseline and deteriorates at follow-up. Group 3 starts at an unstable level but improves at follow-up while group 4 maintains unstable levels at baseline and at follow-up (Used with permission from Nickel et al. [17])

**Table 16.2** Criteria for categorizing patients as stable/satisfactory or unstable/deteriorating

| | Stable/satisfactory | | Unstable/deteriorating | |
|---|---|---|---|---|
| | Group 1 | Group 2 | Group 3 | Group 4 |
| WHO functional class | I–II at baseline and at follow-up | III–IV at baseline, I–II at follow-up | I-II at baseline, III–IV at follow-up | III–IV at baseline and at follow-up |
| Cardiac index | ≥2.5 L·min$^{-1}$·m$^{-2}$ at baseline and at follow-up | <2.5 L·min$^{-1}$·m$^{-2}$ at baseline, but ≥2.5 L·min$^{-1}$·m$^{-2}$ at follow-up | ≥2.5 L·min$^{-1}$·m$^{-2}$ at baseline, but <2.5 L·min$^{-1}$·m$^{-2}$ at follow-up | <2.5 L·min$^{-1}$·m$^{-2}$ at baseline and at follow-up |
| $Sv_1o_2$ | ≥65 % at baseline and at follow-up | <65 % at baseline, but ≥65 % at follow-up | ≥65 % at baseline, but <65 % at follow-up | <65 % at baseline and at follow-up |
| NT-proBNP | <1,800 ng·L$^{-1}$ at baseline and at follow-up | ≥1,800 ng·L$^{-1}$ at baseline, but ng·L$^{-1}$ at follow-up <1,800 | <1,800 ng·L$^{-1}$ at baseline but ≥1,800 ng·L$^{-1}$ at follow-up | ≥1,800 ng·L$^{-1}$ at baseline and at follow-up |

Used with permission from Nickel et al. [17]
*WHO* World Health Organization, *$Sv_1o_2$* mixed-venous oxygen saturation, *NT* proBNP: N-terminal pro-brain natriuretic peptide

- Pulmonary arterial systolic pressure (PASP) is a critical factor in the diagnosis of PAH.
  - A PASP <50 mmHg is indicative of a higher survival rate, while there is a 6 fold increased risk of mortality with a PASP >50 mmHg [18, 19]. Although PASP was determined to increase in the general population with age, the rise in PASP was more severe in combination with a clinically evident cardiopulmonary disease such as PAH [18].
  - Currently, there are very few non-invasive ways to estimate PASP such as echocardiography, which can also detect pericardial effusion, right-atrial enlargement interventricular septal distortion, and increased pulmonary systolic pressure [20].
- Other favorable prognostic factors:
  - No or gradual progression of symptoms [5].
  - No evidence of right ventricular heart failure (no evidence of widened S2 split, S3 sound, JVD, peripheral edema, hepatomegaly) [8].
  - RA pressure less than 10 mmHg and therefore improved or nonexistent JVD has a median survival of 46 months [21].
  - Cardiac index higher than 2.5 L/min/$m^2$ has a 5-year survival of 80 % (Fig. 16.5b) [5, 17].
  - No/little limitation of physical activity characteristic of WHO FC I/II [22].
  - Maximal oxygen consumption (peak VO2) greater than 10.4 mL/kg/min [22]. determined by exercise testing in IPAH patients had a better 1-year survival [8].
  - Stable mixed-venous oxygen saturation ($SvO_2$) of >65 % or improved $SvO_2$ to >65 % had a 5-year survival of more than 80 % (Fig. 16.5c) [17].
  - Low level of N-terminal pro-brain natriuretic peptide (NT-proBNP) has a 5-year survival of 82 % (Fig. 16.5d) [17].
- Other poor prognostic factors:
  - Rapid progression of symptoms [22].
  - High RA pressure seen with worsening JVD has a median survival of 1 month if ≥20 months [21].
  - Clinical signs of right heart failure (widened S2 split, S3 sound, JVD, peripheral edema, hepatomegaly, ascites) [5].
  - Right ventricular enlargement.
  - Pericardial effusion [22].
  - Deteriorating cardiac index <2.5 L/min/$m^2$ or consistently low cardiac index has a 5-year survival of 39 % and 18 %, respectively (Fig. 16.5b) [17].
  - Significantly elevated brain natriuretic peptide (BNP) has a 5-year survival of 53 % (Fig. 16.5d) [17].
  - A diminished exercise capacity characteristic of WHO FC III/IV [22].
  - Peak VO2 less than 10.4 mL/kg/min [5].
  - Progressively decreasing $SvO_2$ and consistently low $SvO_2$ of <65 % has a 5-year survival rate of 44 % and 26 %, respectively (Fig. 16.5c) [17].

## Statement on Management

- The ACC/AHA includes general recommendations as well as treatment suggestions. General recommendations include addition of consistent low level aerobic exercise (Class I-C), a sodium restricted diet, and possibly supplemental oxygen on commercial aircrafts (Class IIa-C). Pregnancy is also contraindicated (Class I-C) [1, 23].
- Warfarin anticoagulation titirated to INR of 1.5–2.5 is recommended in all patients without contraindication (Class IIa-C) and diuretics should be utilized to manage right heart failure (Class I C). Oxygen should also be used to maintain an oxygen saturation rate of greater than 90 % (Class I-C) [8, 23].
- Select patients with a positive acute vasodilator response may respond to calcium channel blockers and should be monitored closely (Class I-C), but if there is no improvement, an alternative therapy should be administered instead. A positive response is defined as a mean pulmonary-artery pressure decrease of greater than 10 mmHg to a mean less than 40 mmHg with an increase of maintenance of cardiac output [8, 23, 24].
- Oral phosphodiesterase type-5 inhibitors and endothelin receptor antagonists are first line drugs (Class I-A) recommended for treatment of IPAH in patients with no positive acute vasodilator response. They have been shown to improve exercise capacity in PAH patients [8, 23].
- First line treatment for high risk patients includes IV prostanoids, either epoprostenol (Class I-A) or treprostinil (IIa-C). Epoprostenol is the only therapy that has been shown to improve survival [8, 23].
- Inadequate response can be countered by combination therapy, and lung transplantation and/or balloon atrial septostomy are last resort options for progression in spite of aggressive medical treatment (Class I-C) [8, 23].

## Clinical Summary of the Case

In this symptomatic patient, exam suggests PAH based upon the findings of an increased P2 and RV impulse, but importantly there is not evidence of right heart failure. The absence of murmurs or gallops suggests against severe PAH. Quantitative assessment of pressure level can assist in the prognostic assessment. The absence of right heart failure is a favorable sign.

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# Chapter 17
# Tricuspid Valve: Tricuspid Regurgitation

**Laura Felder, Kathryn S. King, and Naudereh Noori**

## Key Teaching Points

- Auscultatory findings of Tricuspid Regurgitation (TR) correlate to murmur grade and range from none, to an early systolic murmur, to a holosystolic murmur. Mild TR can be a clinically insignificant finding in normal individuals.
- Tricuspid regurgitation is typically associated with a holosystolic parasternal murmur that increases in intensity with inspiration (Carvallo's sign) but decreases in intensity with handgrip maneuvers. Other auscultatory features include positive Mueller maneuver and decreased intensity with Valsalva maneuver.
- TR may be distinguished from mitral regurgitation which is associated with a holosystolic apical murmur that decreases in intensity on inspiration, and increases in intensity with handgrip maneuvers.
- Echocardiography is a useful clinical tool to assess both the severity of regurgitation and cardiac architecture. Audible tricuspid regurgitation murmurs are typically associated with more severe regurgitation.
- TR with pulmonary hypertension, right ventricular dysfunction, or more severe regurgitation are associated with worse prognosis and often necessitate surgical intervention.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_17) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- A 76 year old man is admitted with congestive heart failure, dyspnea, and edema following recent right popliteal-tibial bypass.
- His past medical history is significant for two-vessel coronary artery disease with an ejection fraction of 17 % and multiple perfusion defects, in addition to insulin-dependent diabetes mellitus retinopathy. He smokes two packs of cigarettes per day.
- Current medications include aspirin 325 mg/day, carvedilol 6.25 mg bid, ramipril 2.5 mg/day, pravastatin 20 mg qhs, clopidogrel 75 mg/day, furosemide and digoxin.

### *Physical Examination*

- Physical exam shows BP of 146/73 mmHg, and regular heart rate of 63 bpm.
- Jugular venous pressure (JVP) is markedly elevated, with a mild V wave.
- Chest and abdominal examination reveal bilateral crackles upon auscultation.
- Cardiac exam reveals quiet precordial palpation with no impulses.
- Auscultation is significant for a grade 3 left lower sternal border (LLSB) epigastric murmur with a normal S1 and S2. The murmur increases upon inspiration. See Fig. 17.1.
- The liver is non-pulsatile.

### *Test Results*

- Electrocardiogram demonstrates sinus rhythm, with a rightward axis, and RSR' pattern suggestive of incomplete RBBB (Fig. 17.2).
- Echocardiogram (Fig. 17.3a, b) showed a severely depressed ejection fraction (EF) and right ventricular enlargement (RVE) with decreased right ventricular ejection fraction (RVEF). Due to RVE, there was incomplete coaptation of the

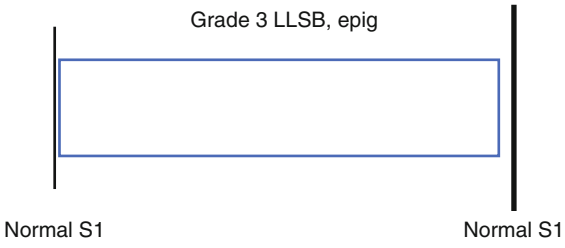


**Fig. 17.1** Case tricuspid regurgitation auscultation diagram. Auscultation demonstrated a holosystolic murmur with a normal S2 heard at the lower left sternal border

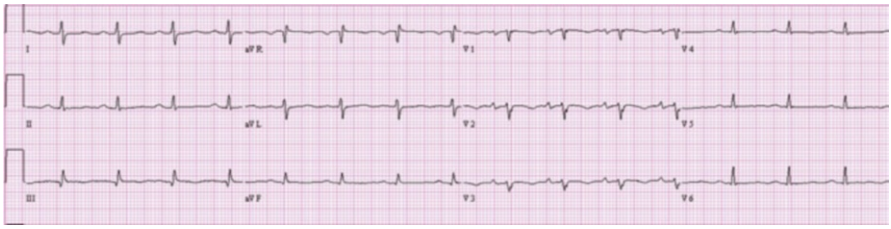

**Fig. 17.2** 12-lead echocardiogram showing an incomplete right bundle branch block pattern with rightward axis

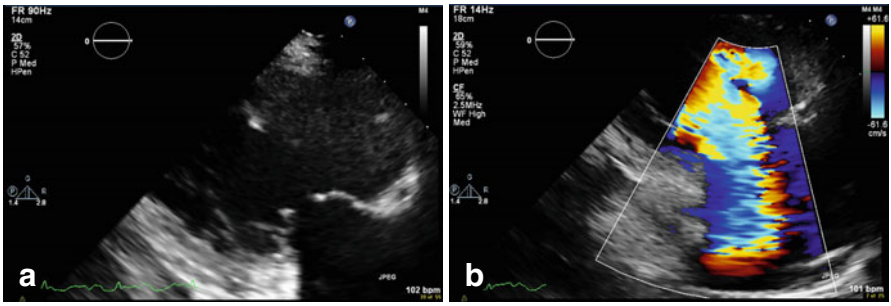


**Fig. 17.3** (**a**, **b**) Case echocardiograms. (**a**) 2-dimensional echocardiogram of the tricuspid valve in systole showing significant leaflet separation (malcoaptation) in systole. (**b**) Color-Doppler echocardiogram in the same projection showing severe tricuspid regurgitation through the separated valve leaflets

valve leaflets and severe tricuspid regurgitation (TR) with a peak velocity of 3.4 m/s. The IVC demonstrated dilation without respiratory collapse. Right ventricular systolic pressure (RVSP) is estimated to be 60–65 mmHg.

## Clinical Basics [1]

### *Normal Anatomy*

- The tricuspid valve is composed of three leaflets: septal, anterosuperior, and inferior leaflets (Fig. 17.4).

### *Definitions*

- Tricuspid regurgitation is defined by retrograde blood flow from the right ventricle to the right atrium due to an insufficient valve.

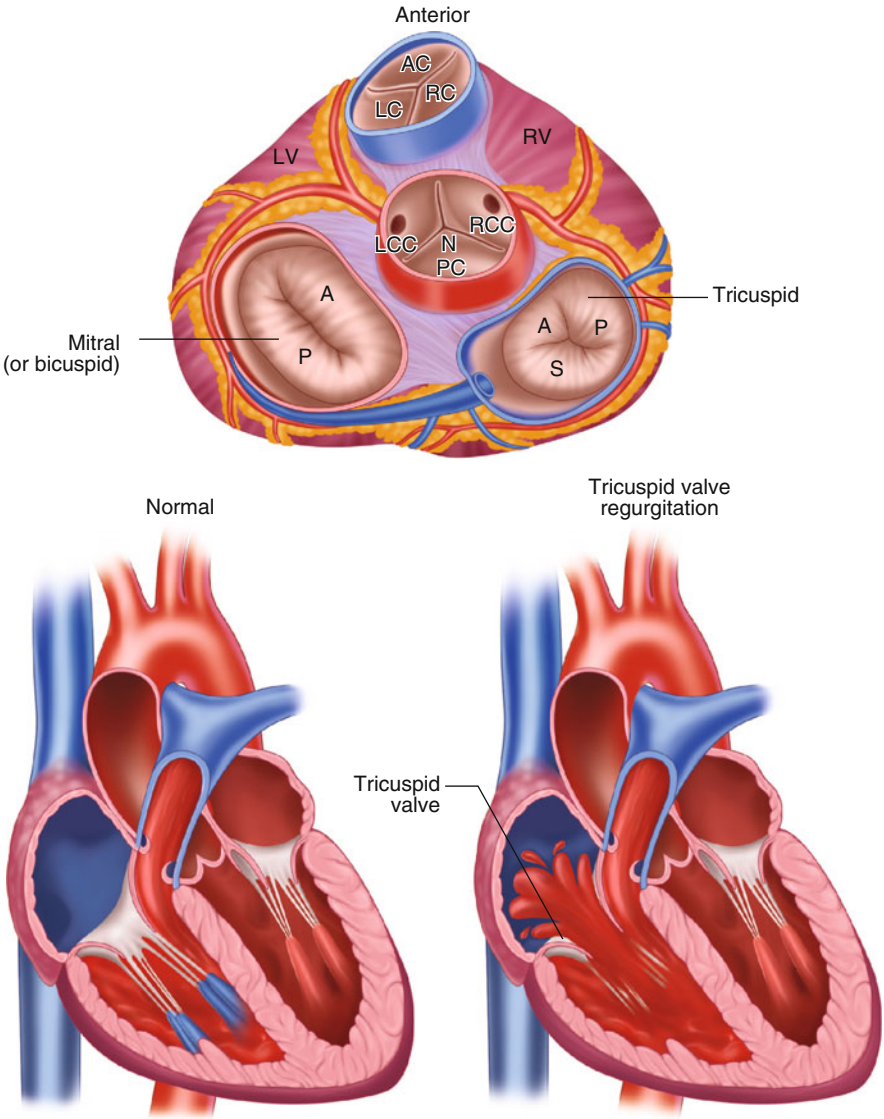


**Fig. 17.4** Normal anatomy of tricuspid valve. Tricuspid valve is made up of three leaflets connected to the tricuspid annulus. In tricuspid regurgitation blood will flow from the right ventricle into the right atrium due to insufficiency of the valve. The insufficiency can be due to a direct insult to the valve itself (congenital abnormalities, infective endocarditis) or secondary to right ventricular dilation and annulus dilation

## *Etiology* (*Table 17.1*)

- It can occur from primary valvular pathologies or secondary to increased RVSP, generally greater than 55 mmHg.
- The most common cause of TR is left sided heart failure, which results in increased right ventricular volumes and subsequent functional TR.
- Causes of functional, or secondary, TR also include:
  - pulmonary hypertension (congenital or acquired).
  - right ventricular failure or infarction.
  - The annulus of the valve, located in the right atrium, is commonly dilated in response to large pressures or volumes entering the heart and can be another secondary cause of regurgitation.
- Intrinsic valvular disease leading to primary TR is much less common but can result from a variety of pathologies. Primary causes include:
  - congenital valve abnormalities.
  - disorders or trauma leading to papillary muscle dysfunction.
  - valve prolapse.
  - ruptured valve.

## *Signs and Symptoms*

- The signs and symptoms of TR vary depending on the severity of the insufficiency but can include ascites, cyanosis, jaundice, hepatomegaly, edema, fatigue, and dyspnea.

**Table 17.1** Primary and secondary causes of tricuspid regurgitation

| Primary causes of TR | Secondary causes of TR |
|---|---|
| Congenital valve abnormalities – Ebstein anomaly, Malpositioned TV annulus | Pulmonary hypertension |
| Rheumatic heart disease | Right ventricular failure |
| Carcinoid heart disease | Right ventricular infarction |
| Endomyocardial fibrosis | Congenital pulmonary hypertension |
| Traumatic valve injury | Left sided heart failure |
| Infective endocarditis | |
| Dilated cardiomyopathy | |
| Papillary muscle dysfunction or valve prolapse | |
| Myxomatous leaflets | |
| Malpositioned TV annulus | |

- Other clinical findings may be a systolic wave in the venous pulse, jugular venous distention with large v waves, an impulse in the right ventricle, systolic pulsations in the eyeballs and pulsations in the neck.
- A systolic murmur is often heard on auscultation and is an important clinical finding and useful diagnostic and prognostic marker.
  - TR is generally heard best at the left lower sternal border but may also be loudest in the epigastrium or right upper sternal border.

### *Prevalence*

- Mild TR is quite prevalent and in a study of patients with an average age of 52 only 10 % of patients with mild TR on echocardiography were found to have a corresponding murmur [1]. This is likely clinically insignificant but conversely, auscultatory findings in patients with TR on echocardiogram suggest clinically significant moderate or severe TR that may require treatment. This is much less prevalent.

## Key Auscultation Features [2]

- A murmur is present in only about ¼ of patients with echocardiographic TR, however in a majority of those with grade 3 or 4 TR.
- TR auscultatory findings vary depending on the severity of the insufficiency.
- Mild TR will present with an early systolic murmur, while more severe TR will present with a holosystolic murmur (Fig. 17.5).
  - TR is additionally associated with a Carvallo's Sign, a holosystolic murmur that becomes louder with inspiration at the LLSB.
- With TR, S3 also increases on inspiration, and the murmur remains louder on held inspiration.
- If pulmonary HTN is associated with the TR, then P2 accentuation will be present on auscultation, as well as a high pitched S3 at the fourth intercostal space.
- The P2 will increase with increased venous return, such as with standing, exercise, or leg raising. The P2 will decrease following Valsalva and return to pre-maneuver levels within 1 s. This contrasts with MR, which takes three or more seconds to return to pre-maneuver levels.
- Auscultation example of tricuspid regurgitation.
  - Click here to listen to an example of a TR murmur and to view an image of the phonocardiogram (Video 17.1).

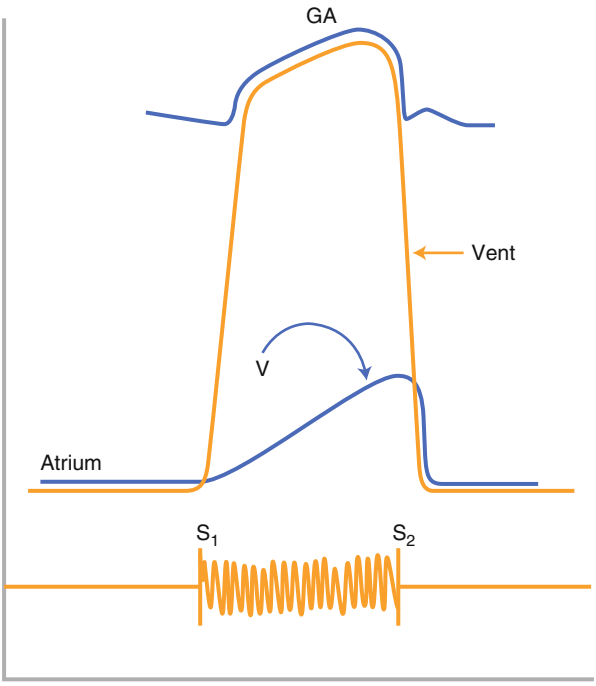


**Fig. 17.5** Cardiac pressure diagram. The pressure gradient between the right atrium and ventricle is relatively stable throughout systole resulting in a holosystolic murmur. The v wave represents atrial filling during systole and includes a regurgitant volume due to tricuspid valve insufficiency

## Auscultation Differential Diagnosis [2]

- TR can present with variable auscultatory findings depending on the severity of valvular insufficiency. Less severe pathology may present without auscultatory findings, or as a murmur limited to early systole, whereas more severe pathology may present with a holosystolic murmur.
- The differential of a holosystolic murmur includes mitral regurgitation (MR), and ventral septal defects.
  - MR is distinguished from TR as its murmur presents loudest at the apex.
  - Other causes of systolic murmurs include aortic valve stenosis or sclerosis, pulmonary valve stenosis, dilation of the pulmonary or aortic root, and increased blood flow across the semilunar valves.
  - Mid-systolic murmur can also be clinically insignificant with no underlying pathology.

## Diagnostic Implications of the Auscultation Features

When considering a diagnosis of TR the auscultation features can have important diagnostic implications. Specific auscultation features can help distinguish between mitral and tricuspid regurgitation, assess the severity of the regurgitation, and assess for pulmonary hypertension:

- The presence of a TR murmur, favors that a more severe grade of TR is present.
- TR is distinguished from MR by a parasternal murmur that increases in intensity on inspiration but does not increase in intensity with handgrip maneuvers. However, severe TR may not be associated with increased murmur intensity on inspiration.
- In contrast, MR is associated with an apical murmur that decreases in intensity on inspiration, and increases in intensity with handgrip maneuvers.
- A high-pitched, pansystolic parasternal murmur is often associated with pulmonary hypertension while the absence of pulmonary hypertension is associated with a low intensity murmur occurring in the first half of systole (Table 17.2). In this case, other findings of pulmonary hypertension may be present (increased P2, parasternal impulse) [2].
- An echocardiogram should be performed to further characterize the severity of regurgitation and right ventricular function.
  - Several studies [1, 3, 4] have demonstrated the presence of TR on echocardiography without corresponding auscultation findings.
    - A 1989 study by Rahko et al. [1] found that only 28 % of patients with TR on echocardiography had a corresponding murmur on physical exam. Severity of regurgitation, however, was associated with a higher incidence of auscultation findings. Eighty-six percent of patients with severe TR demonstrated an audible murmur on exam compared to 10 % with mild TR.
- Despite these findings, it is important to note that annular dilation and right ventricular dysfunction are often associated with less audible murmurs. This further indicates the need for echo studies not only to assess the severity of the murmur but also to detect other cardiac abnormalities that could be contributing to the regurgitation.

**Table 17.2** Auscultation features of mitral valve and tricuspid valve regurgitation

| | TR | MR |
|---|---|---|
| Holosystolic murmur | Yes | Yes |
| Murmur location | Parasternal | Apical |
| Valsalva maneuver | P2 returns to pre-maneuver levels within 1 s | P2 returns to pre-maneuver levels in three or more seconds |
| Increase with handgrip | No | Yes |
| Increase with inspiration | Yes | No |

## Prognostic Implications of the Auscultation Features

- The prognosis of TR is generally related to the severity of regurgitation, the presence of pulmonary hypertension, and the degree of right ventricular hypertension.
- A 2010 study by Lee et al. found higher mortality rates among patients who underwent medical treatment without surgery. The mortality rate was highest amongst those with more severe TR, pulmonary hypertension, and RV systolic dysfunction. Therefore, surgery should be strongly considered in these cases [5].
- TR prognosis can also be correlated to vena contracta width (VCW), the smallest diameter of regurgitant valvular flow. A greater valvular insufficiency will result in a greater VCW. A 2011 study conducted by Yang et al. that measured vena contracta width on echocardiography associated more adverse outcomes with a VCW >7mm [6]. Therefore, even in cases of isolated TR, surgical procedures may be indicated in the presence of large VCWs.

## General Statement on Management

- The management of TR is dependent on the etiology and severity of regurgitation. Other factors such as pulmonary hypertension and right ventricular dysfunction can also affect management [2, 5].
- Generally, TR in the absence of pulmonary hypertension and annulus dilation does not necessitate surgical intervention. TR secondary to mitral valve disease without annulus dilation often resolves following mitral valve surgery as a result of declining pulmonary vascular pressure.
- Surgical intervention should be considered for TR secondary to annular dilation, particularly annular dilation >30 mm. This can arise from a variety of causes including mitral valve disease, pulmonary hypertension, and right ventricular failure. The degree of surgical intervention in these patients varies according to the severity of TR: mild regurgitation with annular dilation can often be successfully treated with a suture annuloplasty of the posterior annulus, while severe regurgitation with annular dilation requires valvotomy with ring annuloplasty. See Fig. 17.6.
- Primary TR will require valve replacement if regurgitation is severe. Other factors such as pulmonary hypertension and right ventricular dysfunction must also be taken into account, and are associated with better survival when the TR is surgically treated [5].
- Tricuspid endocarditis (seen in IV drug users) in patients without associated pulmonary hypertension and unsuccessful antibiotic therapy should be treated with excision of the infected tissue without immediate replacement of the valve. The valve should be replaced following antibiotic therapy and full treatment of the infection to avoid re-infection of the valve. Patients without pulmonary hypertension will generally fare well without the valve throughout the antibiotic treatment but the valve does ultimately need to be replaced to avoid right ventricular dysfunction.

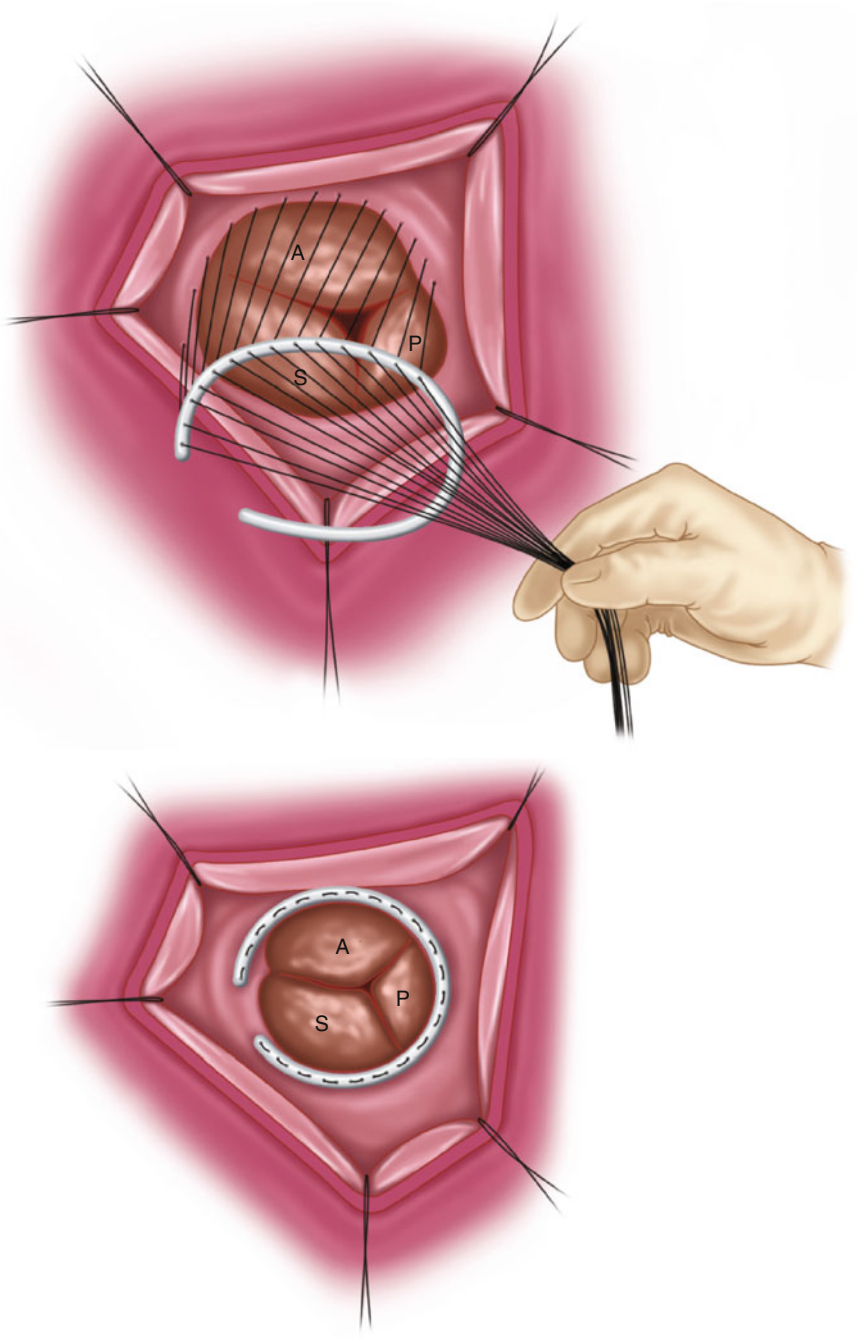


**Fig. 17.6** Surgical implantation of an annuloplasty ring for tricuspid regurgitation. *Top*: sutures are placed by the surgeon around the tricuspid valve. *Bottom*: a circular "ring" is sewn in place. The annuloplasty device pulls the leaflets together to improve coaptation and diminish valve regurgitation

## Clinical Summary of the Case

In this case, the audible detection of TR by itself suggests more severe TR is present. Auscultation findings do not suggest prognostically adverse findings, such as pulmonary hypertension or RV dysfunction; however, the finding of increased JVP does suggest volume overload and a degree of clinical decompensation.

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# Part V
# Other Auscultation

# Chapter 18
# The S3 Gallop

**Cara Sweeney and Blake Choplin**

## Abbreviations

| | |
|---|---|
| ACC/AHA | American College of Cardiology/American Heart Association |
| ACE | Angiotensin-converting enzyme |
| AV valves | Atrioventricular valves |
| BMI | Body mass index |
| CHF | Congestive heart failure |
| EDV | End-diastolic volume |
| EF | Ejection fraction |
| HF | Heart failure |
| LV | Left ventricular |
| LVEDP | Left ventricular end diastolic pressure |
| LVEF | Left ventricular ejection fraction |
| LVH | Left ventricular hypertrophy |
| NSAID | Non-steroidal anti-inflammatory drug |
| PMI | Point of maximum impulse |
| PW Doppler | Pulsed and continuous wave Doppler |
| S1 | First heart sound |
| S2 | Second heart sound |
| S3 | Third heart sound |
| S4 | Fourth heart sound |
| SOB | Shortness of breath |

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_18) contains supplementary material, which is available to authorized users.

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## Key Teaching Points

- An S3 is a low frequency sound at the cardiac apex.
- The sound of an S3 arises from rapid deceleration of fluid as it impacts the ventricular wall during passive filling.
- Auscultation must be done in a quiet environment and accentuated by positioning in the left lateral decubitus position and maneuvers increasing venous return and atrioventricular flow.
- A pathologic S3 is specific for heart failure and indicates a worse prognosis.
- The significance of an S3 should be based on case history and clinical suspicion.

## Case Description

### *History*

The patient is a 76 year-old male presenting with fatigue for 3 months. He says chores are becoming more difficult. In the past, he mowed his lawn, but he recently had to hire a teenager in the neighborhood to do the yard work.

- He complains of shortness of breath upon exertion. He denies dyspnea at rest, but endorses orthopnea. About a month ago, he started using an extra pillow at night. He denies any episodes of nocturnal paroxysmal dyspnea.
- His past medical history is significant for a posterior myocardial infarction 2 years ago, and he recovered to baseline. The patient's past medical history is otherwise unremarkable.
- Medications include a beta-blocker, carvedilol, and a daily aspirin.

### *Physical Examination*

- Vital signs: Heart rate 100 beats per minute. Blood pressure 110/88 mmHg.
- Chest shows faint bibasilar rales.
- Cardiac exam shows a regular rate and rhythm.
- The apical point of maximum impulse (PMI) was found 5 cm lateral to the midclavicular line.
- The S1 and S2 were normal.
- No murmurs or rubs were found.
- An S3 was heard in the left lateral decubitus position.
- No clubbing or edema was found in his extremities.
- The rest of his physical exam was unremarkable.

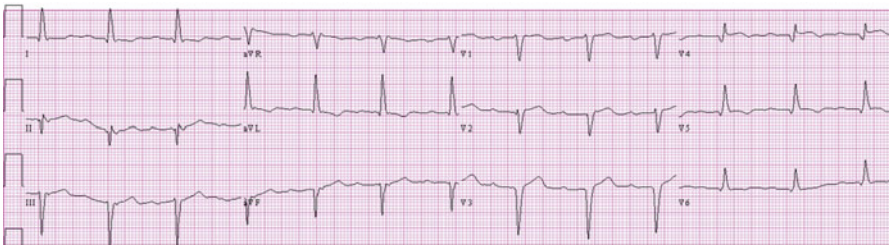

**Fig. 18.1** A representative EKG significant for Q waves in the lateral precordial leads and an ST elevation in V4

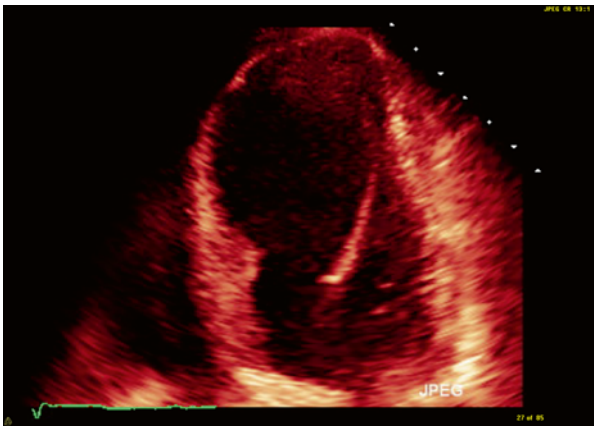


**Fig. 18.2** Left ventricular aneurysm on an echocardiogram

### *Test Results*

- An EKG (Fig. 18.1) was significant for Q waves 3 mm wide in leads V3-V5. ST elevation in V4 suggested an LV aneurysm.
- An echocardiogram (Fig. 18.2) was consistent with finding of an LV aneurysm. Ejection fraction was 23 %.

## Clinical Basics

### *Normal Anatomy*

- A normal cardiac exam is limited to an S1 and S2 heart sounds, with S2 split on inspiration.

## *Definitions*

- A ventricular gallop sound is an extra heart sound. There are two types of gallop sounds, S3 and S4.
- S3 gallop is a low frequency, early to mid-diastolic sound.
- In the normal heart during normal sinus rhythm, diastolic filling of the ventricle across the atrioventricular valves occurs in two phases, early and atrial filling. There are characterized by Doppler echocardiography:
  - E wave is the characteristic wave seen on Doppler related to passive filling of the ventricle.
  - A wave is active filling with atrial systole seen on Doppler.
  - E and A waves representing mitral flow in a healthy heart (E>A). E wave is classically greater than A wave since passive filling encompasses 80 %. In conditions that limit ventricular compliance two abnormalities are possible:
    - reversal – in which the A wave is greater than the E wave. This indicates slow filling caused by older age, hypertension, left ventricular hypertrophy (LVH), or diastolic dysfunction.
    - exaggeration of normal – a tall, thin E wave with a small or absent A wave. This indicates restrictive cardiomyopathy, constrictive pericarditis, or infiltrative cardiac disease [1–3].

## *Etiology*

- There are two phases of ventricular filling. To start the first phase, ventricular blood pressure drops sufficiently to allow the opening of the AV valves. Blood rapidly flows from the atrium to the ventricles comprising 80 % of filling. The recipient ventricle actively relaxes to accommodate the increased volume. The rapid deceleration of blood as it hits the ventricles can produce a protodiastolic sounds called S3. S3 can be physiologic in children and young adults or pathologic. In pathologic cases, the ventricles are stiff due to heart failure or structural heart disease [1]. See Fig. 18.3.
- The sound is heard after the E wave (ventricular filling) due to rapid E wave deceleration due to a non-compliant heart. All heart beats cause these oscillations, but only some have the correct frequency and intensity to be as audible as an S3 [1, 2]. At increased heart rates, the timing of the S3 relative to the start of the next cardiac cycle shortens, leading to a characteristic heart sounds of "buh-buh-buh, buh-buh-buh." See Fig. 18.4.
- E wave deceleration results in loss of fluid kinetic energy and cardiohemic oscillations. Differences can be seen in this between pathologic and physiologic S3. See Fig. 18.5.
  - Physiologic S3 arise from higher E wave velocities.
  - Pathology S3 arise from steeper E wave deceleration [2].

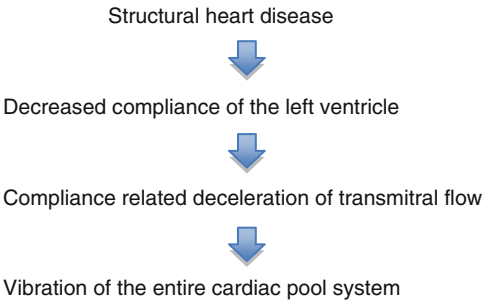


**Fig. 18.3** Progression of structural heart disease that leads to the development of the third heart sound

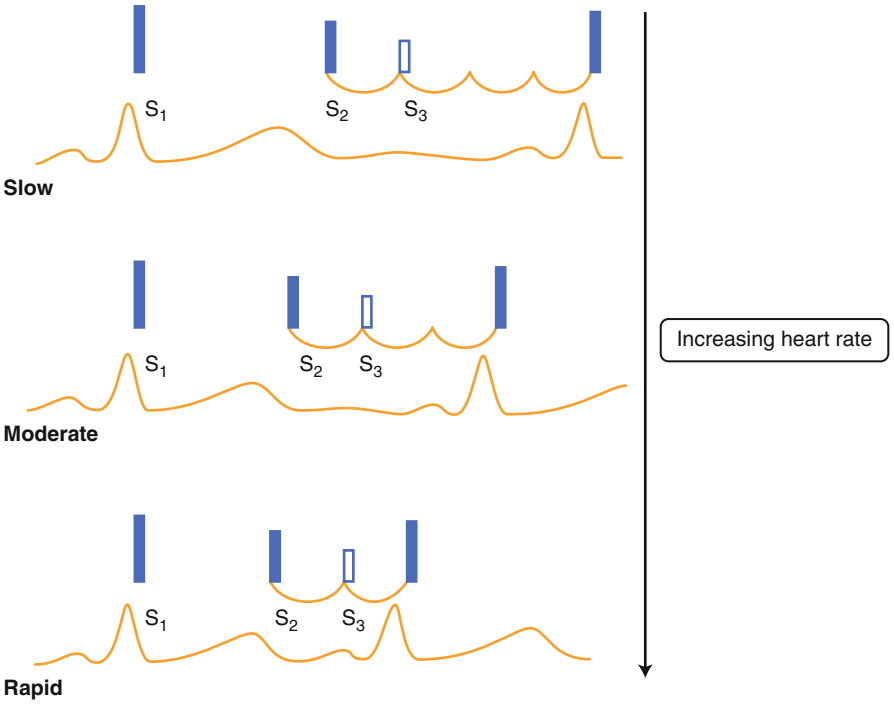


**Fig. 18.4** Multiple oscillations in the cardiac blood pool, including the S3 sound in early diastole. At increased heart rates, the timing of the S3 relative to the start of the next cardiac cycle shortens, leading to a characteristic heart sounds of "buh-buh-buh, buh-buh-buh"

## *Signs and Symptoms*

- Common cardiac findings associated with an S3 include:
  - High left atrial pressure.
  - Noncompliant left ventricle.
  - Restrictive filling characteristics.
  - Reduced LV systolic function (also in diastolic dysfunction).
  - When present, valvular disease is more likely to be severe [3].

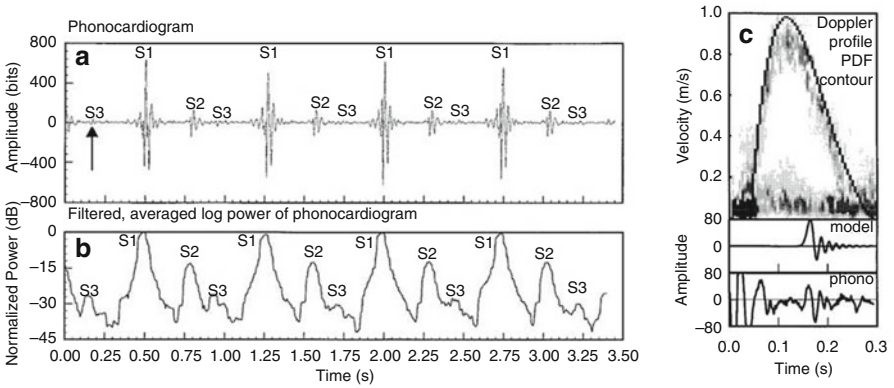


**Fig. 18.5** (**a**) Several consecutive beats of the phonocardiogram from a volunteer without an audible $S_3$. For the untrained observer, $S_3$ features are difficult to discern from baseline noise. (**b**) Filtered, averaged log power of the phonocardiogram above. Note clear $S_3$ feature for each cardiac cycle, although no $S_3$ could be heard. (**c**) Simultaneous Doppler profile, E-wave contour, phonocardiogram, and model-predicted $S_3$ for the heartbeat in **a** indicated by the *arrow*. E-wave parameters: $x_o = -11.2 \pm 0.6$ cm, $c = 12.6 \pm 1.9$ g/s, and $k = 214 \pm 7$ g/s$^2$. $S_3$ model parameters: $C = 50$ g/s, $\mu/S = 0.5$ %, and $\Delta x = 0.2$ cm. *PDF* indicates parameterized diastolic filling (Used with permission from Manson et al. [2])

## *Prevalence*

- Physiologic S3 is uncommon after 35–40 years of age [1].
- Pathologic S3:
  - In the SOLVD treatment trial, 23.9 % of those with established CHF and EF < 35 % had an S3 heart sound.
  - Weak correlation to non-ischemic cardiomyopathy, lower EF, class 3 or 4 CHF [4].

## Key Auscultation Findings

- Examine the patient in a quiet environment because an S3 is a low intensity sound and is easily obscured by extraneous room sounds.
- Examination in the left lateral decubitus position should accentuate the sound.
- Have the patient temporarily suspend their respiration and listen over the left ventricular apex [1].
- Should be a soft, low frequency sound best heard with the bell.
- Sound should be heard during early-mid diastole (.13–.16 s after S2) with a timing that is relatively unaffected by heart rate.
  - Note: The A2-S3 interval can shorten in conditions that shorten IVR and very high heart rates.

- S3 is a localized finding on the exam, and is heard usually in a discrete area (does not radiate widely) [5].
- S3 can be further accentuated by increasing venous return or increasing flow across the AV valve:
  - Increasing venous return can be achieved by passively lifting the patient's legs while they are in a supine position.
  - Increase AV flow by having the patient exercise (e.g., stair climbing) to increase venous flow return and accelerate the heart rate [1].
- Auscultation example of an S3 gallop.
  - Click here to listen to an example of an S3; also soft Still's murmur: Echo is within normal limits. A phonocardiogram is also shown (Video 18.1).
  - Click here to listen to examples of several patients with an S3 gallop, including a 60 year old woman with ventricular gallop, as described by Dr. W. Proctor Harvey (Video 18.2).

## Auscultation Differential Diagnosis

S3 can be heard both in normal young adults and in the setting of heart failure. Physical exam findings can help distinguish between physiologic S2, right-sided S3, and left-sided S3. Right-sided S3 is accompanied by the constellation of findings classically seen in right-sided heart failure: hepatosplenomegaly, peripheral edema, pleural effusions, and ascites. In contrast, patients with left-sided S3 typically have the pulmonary congestion symptoms seen in left-sided heart failure.

Other murmurs commonly confused with S3 are an opening snap of the mitral valve, pericardial knock, atrial myxoma, and atrial septal defect. They can be distinguished by paying attention to location, quality, associated ausculatory findings, and other physical exams findings. See Table 18.1 for further details. Table 18.1 contains a presentation of possible diagnosis that should be included in the differential for a patient who has a third heart sound.

## Diagnostic Implications of the Auscultation Features

### *Physiologic S3*

- The S3 heart sound should be considered within the clinical context. For example, in the case of younger individuals this finding may not be an indication of disease. It can present in patients with a lower BMI and heart rate. Additionally, it will correlate with higher peak early diastolic transmitral velocity and higher acceleration of early diastolic velocity. A physiologic S3 disappears with age as left ventricle function alters [2].

**Table 18.1** Differential diagnoses for the detection of the third heart sound

| Clinical disease | Specific findings |
|---|---|
| Physiologic S3 | Best heard in apex. Very low pitch. Normal heart in a young person |
| Right sided S3 | Best heard in apex. Very low pitch. Right sided heart Failure - Hepatosplenomegaly, peripheral edema, pleural effusions, ascites, congestion of the kidney |
| Left sided S3 | Best heard in apex. Very low pitch. Left-side Heart Failure – rales, fatigue, orthopnea, nocturnal paroxysmal dyspnea, shortness of breath on exertion |
| | Structural heart disease – myocardial and valvular |
| Opening snap – mitral valve | Best heard at lower left sternal border or apex. Medium to High Pitch. Interval short for A2>OS (>100 ms) than A2-S3 (usually 120 ms). Ancillary findings: sharp, S1 accentuated, diastolic murmur/rumble, timing variable |
| Pericardial knock: constriction | Best heard in apex. Medium to high pitch. May occur with shorter interval from S2. Usually loud and palpable. Associated jugular venous findings of constriction |
| Atrial septal defect | Fixed Split S2. Does not vary on inspiration |
| Atrial myxoma | Best heard at apex. Low pitch. Mass on echo. Sound varies in timing and intensity with position. Associated loud S1. Diastolic murmur may be heard |

Data from: Bonow et al. [1], Silverman [5]

- In a study of 1329 asymptomatic individuals with an age range of 18–94, an S3 heart sound was detected in 10 % of subjects (95 % CI, 2.4–5.0 %), with the highest percentage of positive findings in individuals under the age of 30 [6].

## *Pathologic S3*

- The S3 heart sound often will present in patients with high left atrial pressure, a noncompliant left ventricle, reduced left ventricular function, and more severe valvular disease [3].
- **Conditions associated with pathologic S3.**
  - **Ventricular dysfunction/Heart Failure.**
    - In established congestive heart failure with an ejection fraction of less than 35 %, S3 was found to appear in 23.9 % of 2479 patients. In the same study, data revealed weak correlations with non-ischemic cardiomyopathy, lower ejection fraction and class three or four congestive heart failure [4].
    - In a study of 90 patients receiving left-sided heart catheterization S3 was specific for a left ventricular end-diastolic pressure (LVEDP) of greater than 15 mmHg, a left ventricular ejection fraction less than 50 %, and a B-type natriuretic peptide levels greater than 100 pg/ml.
    - Accuracy for detecting abnormal hemodynamics:

  - For detection of an LVEDP > 15 mmHg the sensitivity was 41 (26–58) and the specificity was 92 (80–98).
  - Left ventricular ejection fraction less than 50 % the sensitivity was 52 (31–73) while the specificity was 87 (76–94).
  - B-type natriuretic peptide concentration > 100 pg/ml the sensitivity was 32 (20–46) and the specificity was 92 (78–98) [7, 8].

- **Valvular defects**
  - Aortic stenosis.
    - The presence of a third heart sound in the setting of aortic stenosis is indicative of increased left atrial pressure, reduced left ventricular ejection fraction and increased left ventricular end-diastolic volume. In 448 patients, 50 had an S3 and were found to have a left atrial pressure of 18.6 mmHg (± 10.3), which was significantly different from the average of those without a third heart sound, 12.1 mmHg (± 6.5); p-value < 0.001. The left ventricular ejection fraction in the S3 group of 40 patients was 38 % (± 15.2) while the 300 individuals without an S3 had an ejection fraction of 55.9 (± 14.7); p-value < 0.001. Similarly, 40 of 341 patients had an average end-diastolic volume of 138.8 ml/m$^2$ (± 52.6). Patients without an S3 had a volume of 104.7 (± 38.5); p-value < 0.001 [9].
  - Aortic regurgitation.
    - S3 may be found in aortic regurgitation (AR), both acute and chronic [10]. In a sample of 121 patients with aortic regurgitation, 14 had a positive S3, a finding indicative of more severe AR and lower ejection fraction. The regurgitant fraction in those with an S3 was 51 % (± 13) while those without had a regurgitant fraction of 36 % (± 15), which was a significant difference (p = 0.001). In the same study, the ejection fraction (EF) of those with an S3 was 49 % (± 12) while those without an S3 had an EF of 64 % (± 8), giving a p-value of 0.001 [3].
  - Tricuspid and Mitral regurgitation.
    - A detectable third heart sound on the left lower sternal border in the setting of tricuspid regurgitation is associated with severe valvular insufficiency [1, 11].
    - In a study of 176 older adults, the presence of an S3 heart sound in individuals with mitral regurgitation was related to an increase in end-diastolic volume (EDV) and regurgitant fraction. Those with an S3 had an EDV of 136 ml/m$^2$ while patients without an S3 had a volume of 101 ml/m$^2$ (p < 0.001). In addition, regurgitant fraction in patients with an S3 was 92 %, while individuals without an S3 heart sound had a fraction of 55 % (p < 0.001) [12].

- Miscellaneous.
  - High output states.
  - In both thyrotoxicosis and pregnancy, more rapid filling of ventricles and increased compliance. These may produce an S3 heart sound, but do not correlate with cardiac dysfunction [1, 10, 13].
- Septal defects.
  - An S3 heart sound may be found in the setting of a septal defect. With a ventricular septal defect, the sound indicates increased flow across the mitral valve. In an atrial septal defect, the sound correlates with more flow over the tricuspid valve [10, 13].
- Restrictive cardiomyopathy.
  - A third heart sound may often be heard in the presence of restrictive cardiomyopathy. For example, in a study of 26 patients receiving treatment for constrictive pericarditis, 24 had an S3 [14]. The third heart sound will become louder as the patient inspires and is correlated with the y descent of the jugular venous pulse [10]. In this setting the third heart sound is higher pitched and occurs earlier thus it may be called a pericardial knock to differentiate it from the sound heard in other conditions [1, 10, 13].

## Prognostic Implications of the Auscultation Features

- Since S3 can be physiologic and pathologic, the prognostic implications are based on clinical suspicion. In individuals older than 40, it is more likely to be pathologic [1].
- Although not all patients with heart failure have an audible early diastolic gallop, an S3 can aid with the assessment of patient prognosis, such as progression of heart failure. In comparison to patients without S3, patients with S3 had a significantly higher risk for death from all causes with a relative risk of 1.35, confidence interval 1.17–1.55, and $P<0.001$. Combining the risk for death or hospitalization for heart failure the relative risk was 1.42 with a confidence interval from 1.46 to 1.97 and $P<0.001$ [4].

## Statement on Management

Although an S3 itself does not mandate any specific changes to management, the association with left ventricular dysfunction, higher filling pressures, worse valvular regurgitation, and a poor prognosis, should direct the clinician to evidence-based therapies to improve patient compensation and outcomes.

## *Heart Failure* [15]

- For patients with heart failure with current or previous symptoms, diuretics and salt restriction are indicated for patients with evidence of fluid retention. Bisoprolol, carvedilol, or sustained release metoprolol succinate are recommended for all stable patients as they are proven to reduce mortality. ACE inhibitors are recommended for all patients with symptoms of HF and reduced LVEF unless contraindicated. If contraindicated, angiotensin II receptor blockers are improved for the treatment of HF. Drugs that adversely affect the clinical status of HF patients, such as NSAIDS, calcium blockers, and some anti-arrhythmics, should be avoided.

## *Valvular Defects* [16]

- Aortic stenosis.
  - There is no strong indication for medical or surgical intervention in patients with asymptomatic aortic stenosis. As symptoms develop and become moderate to severe, physicians should consider aortic valve replacement, especially in the setting of a left ventricular ejection fraction less than 50 % or severe valve calcification.
- Aortic regurgitation.
  - For acute severe aortic regurgitation nitroprusside and surgical treatment are preferred. In chronic aortic regurgitation patients are recommended to receive vasodilator therapy and, if they are a good surgical candidate, aortic valve replacement.
- Tricuspid regurgitation.
  - Regurgitation of the tricuspid valve presenting with an S3 heart sound will likely require valve replacement.
- Mitral regurgitation.
  - Patients with acute severe mitral regurgitation may be treated medically with nitroprusside to reduce regurgitation and subsequently receive valve replacement. The treatment for chronic mitral regurgitation depends on the patient's presentation. There is no preferred therapy for asymptomatic patients. In the setting of symptomatic chronic mitral regurgitation with preserved left ventricular function, a surgical approach is the best treatment. Finally, in patients with symptomatic chronic mitral regurgitation with reduced left ventricular function, ACE inhibitors, beta blockers and biventricular pacemakers have demonstrated efficacy in reducing the severity of regurgitation.

## Clinical Summary of the Case

In this case, the patient presents with heart failure symptoms, and the electrocardiogram suggests an interval anterior myocardial infarction. The S3 present on exam makes the presence of significant LV systolic function, and high filling pressures more likely, and could indicate a worse prognosis from heart failure.

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# Chapter 19
# The S4 Gallop

**Kurt Yaeger, Mark Norton, and Sanjai Jalaj**

## Key Teaching Points

- S4 is a presystolic heart sound commonly associated with reduced ventricular compliance.
- Auscultation of an S4 is characterized by a low frequency sound, best heard at the apex with the stethoscope bell, with the patient in the left lateral decubitus position.
- S4 can be found in healthy individuals, but is also associated with left ventricular hypertrophy, ischemic heart disease, and aortic stenosis.
- Differential heart sounds include S3 and split S1.
- Since S4 may be associated with underlying pathology, further cardiac workup is necessitated.

## Case Description

### *History*

- A 74 year old male with a history of hypertension presented for a routine physical. A pacemaker had been placed for sick sinus syndrome.
- His medications include 50 mg losartan and 25 mg chlorthalidone per day.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_19) contains supplementary material, which is available to authorized users.

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## *Physical Examination*

- Vital signs: Heart rate 80 beats per minute, RR 15 breaths per minute, Blood pressure 145/95 mmHg.
- On auscultation of the left ventricular apex, an additional heart sound can be heard prior to S1, suggestive of an S4 gallop.

## *Test Results*

- On EKG (Fig. 19.1), the waveforms of the precordial leads are suggestive of left ventricular hypertrophy.
- Echocardiogram (Fig. 19.2) shows left ventricular hypertrophy, with a wall thickness of 1.3–1.5 cm.

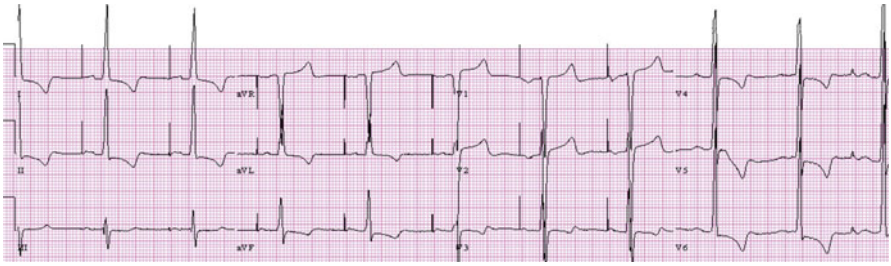


**Fig. 19.1** This 12 lead EKG tracing demonstrates a heart in normal sinus rhythm. There is possible inferolateral ischemia demonstrated by the T wave inversions in II, III, and AVF and V4-V6. Note the particularly tall QRS complexes in V4-V6 indicating left ventricular hypertrophy. Such hypertrophy can result in the S4 heart sound

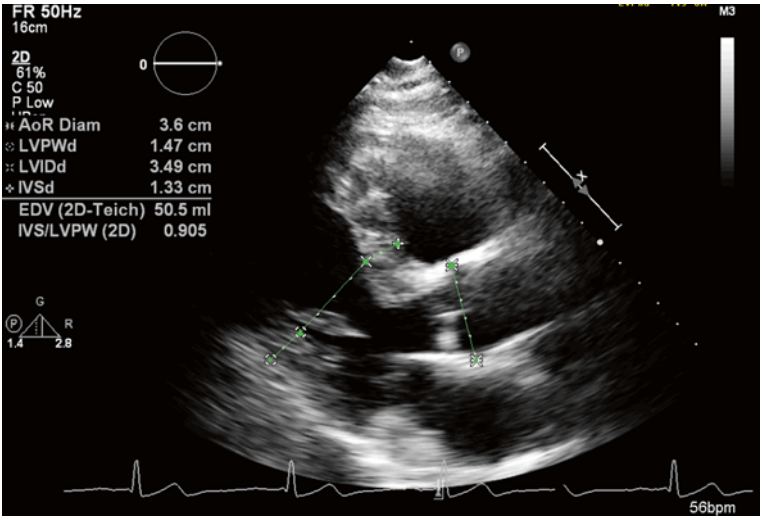


**Fig. 19.2** This is an echocardiogram displaying the ventricles of the heart. Note the thickened ventricular walls consistent with the S4 heart sound and EKG findings

## Clinical Basics

### *Pathophysiology of S4*

- End diastolic ventricular filling normally occurs as the atria contract to provide extra stretch to the ventricles. Stiffening of the ventricles, caused by ventricular hypertrophy, infarction, or fibrosis, reflexively evokes a more vigorous atrial contraction in order to overcome this reduced ventricular compliance. The S4 gallop occurs as the accelerated column of blood decelerates against the stiff ventricular walls. See Fig. 19.3.
- The conditions required for S4 formation include:
  - Reduced ventricular compliance.
  - Healthy atrium.
  - Regular sinus rhythm.
  - The absence of atrioventricular (AV) valve dysfunction.
- Certain pathologies associated with reduced ventricular compliance, and therefore the possible presence of an S4 gallop include:
  - Left ventricular hypertrophy (LVH), as caused by hypertension or left ventricular outflow tract (LVOT) obstruction.
  - Right ventricular hypertrophy (RVH), as caused by pulmonary hypertension or right ventricular outflow tract (RVOT) obstruction.
  - Ischemic heart disease.
  - Aortic stenosis.

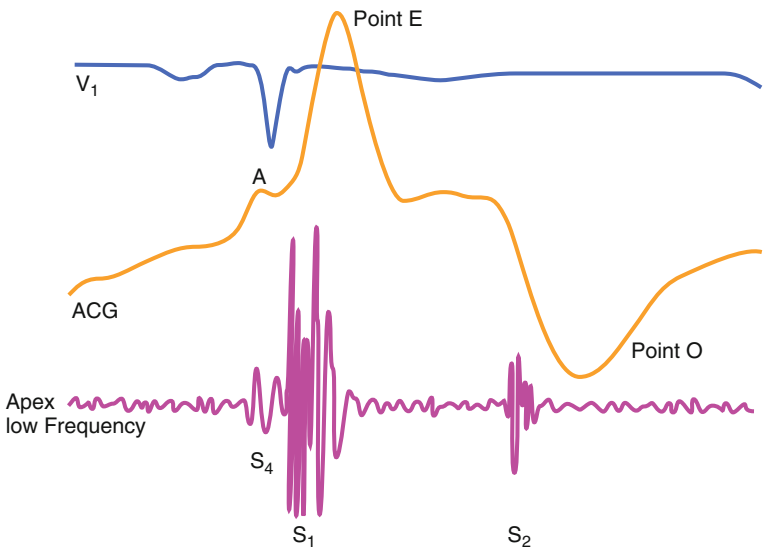


**Fig. 19.3** The diagram illustrates the presystolic nature of an S4 as well as its proximity to S1. It is subtle low frequency sound

- An S4 may also be heard in older patients with age-related ventricular hypertrophy or in well-trained athletes with physiologic ventricular hypertrophy.

## *Key Auscultation Features*

- The S4 gallop is a low frequency (10–50 Hz), presystolic heart sound best detected at the left ventricular apex.
  - Use the bell of the stethoscope.
  - Accentuate the S4 by placing the patient in the left lateral decubitus position.
  - Increased heart rate will shorten the PR interval and cause the S4-S1 interval to shorten and possibly merge (Fig. 19.4).
- S4 typically occurs 160 ms after initiation of P wave, and occurs 55 ms before peak atrial inflow, at the onset of the "a" wave [1].
- A right sided S4 can be heard best at the left sternal border between the 3rd and 5th intercostal spaces, and at the epigastric area when the patient is supine. It is commonly more audible during inspiration.
- Auscultation examples of an S4 gallop.
  - Click here to listen to an example of an S4 gallop. Phonocardiogram is also shown; it is not ideal but audio is excellent (Video 19.1).
  - Click here to listen to an atrial (S4) gallop, as described by Dr. W. Proctor Harvey (Video 19.2).

## *Auscultation Differential Diagnosis*

The following heart sounds may mimic an S4 gallop:

- S3 gallop.
  - S3 and S4 are both low frequency heart sounds heard after S2. However, while S3 is heard closer to S2, S4 is more proximal to S1. This pattern results in a different cadence.

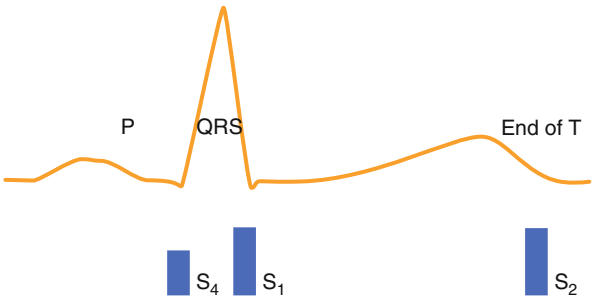


**Fig. 19.4** The diagram illustrates how an S4 is heard while conduction of a ventricular impulse is occurring, but before contraction itself. Hence it is presystolic

- Split S1.
  - The M1 component of a split S1 can be differentiated from S4 by the following criteria:
    - S4 is lower frequency and can be better heard the stethoscope bell.
      - S4 tends to diminish from the apex.
      - S4 is sensitive to blood volume changes (standing will cause S4 to diminish).

## *Diagnostic Implications of the Auscultation Features*

- Routine examination will reveal S4 in up to 50 % of cases by phonocardiogram and up to 30 % of cases by auscultation [2].
- The presence of S4 is associated with higher blood pressure, but is not associated with other cardiovascular risk factors, including coronary artery disease [2].
- However, since S4 is present in up to 50 % of adults, it is of little use in screening apparently healthy, middle-aged patients [2].
- The sensitivity and specificity of an S4 for reduced left ventricular ejection fraction (LVEF) are 43 and 72 %, respectively. The presence of S3 represents a more specific (85 %) marker of left ventricle dysfunction, compared to S4 [3].

## *Prognostic Implications of the Auscultation Features*

- A longer S4-S1 interval is more likely associated with a less compliant left ventricle [4]. See Fig. 19.5.
- The length of S4-S1 interval tends to shorten (from 100 to approximately 75 ms) with improvement of congestive heart failure [4].

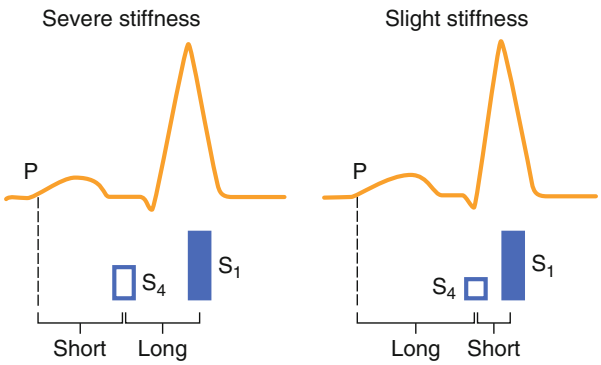


**Fig. 19.5** A stiffer ventricle will have a longer more distinct interval between S4 and S1. A short and subtle interval between S4 and S1 indicates a less stiff ventricular wall

### *Statement on Management*

- Since S4 may indicate underlying ventricular pathology, further cardiologic follow up is necessary. If the patient is symptomatic, treat the underlying condition.
- However, treating an S4 alone is not indicated, since it does not definitively represent a pathological condition.

## Clinical Summary of the Case

Many points in this case speak to the presence of hypertension leading to myocardial noncompliance from left ventricular hypertrophy. The presystolic S4 gallop physiologically correlates to a stiff myocardium, leading to attention to blood pressure treatment and control. Age-related myocardial changes may also contribute to the S4 physiology in this case.

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# Chapter 20
# Pericardial Constriction

**Michael C. Mariorenzi, Amy Matson, and Katherine Unverferth**

## Key Teaching Points

- Constrictive pericarditis (CP) is an uncommon condition; however, it should be considered in certain at-risk populations in patients who present with signs of systemic and pulmonary congestion.
- At-risk populations include patients who have undergone chest radiation or cardiothoracic surgery, as well as patients who have had previous pericardial infections or tuberculosis.
- The typical clinical findings of CP include an early diastolic pericardial knock, systemic and pulmonary congestion, Kussmaul's sign, elevated jugular venous pressure, and pulsus paradoxus. The diagnosis of CP is confirmed by the presence of a septal shift of the interventricular septum on echocardiography and by changes in flow velocities with respiration seen on Doppler echocardiography.
- The pericardial knock is an early diastolic sound caused by a rapid cessation of filling of the ventricular chambers due to the rigid pericardium constricting the heart. On auscultation, the pericardial knock may sound similar to an S3, a split S2, the opening snap of mitral stenosis, and the tumor plop of atrial myxoma.
- The pericardial knock can be distinguished from other diastolic heart sounds by its early timing and loud snapping quality. It is best heard over the left sternal border and is accentuated by maneuvers that increase preload or increase afterload.
- Prognostic implications of cardiac auscultation associated with CP include the timing and intensity of the pericardial knock, well as the presence of a holosystolic

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tricuspid regurgitation murmur or a widely split S2. Delayed timing and a lower intensity of the pericardial knock are associated with a more favorable outcome, whereas the presence of a superimposed holosystolic tricuspid regurgitation murmur or high pulmonary artery pressure as indicated by the presence of a widened S2 are associated with an unfavorable prognosis.
- Etiology is also an important prognostic factor, with post-radiation CP having lower survival rates.
- The definitive treatment for CP is pericardiectomy.

## Case Presentation

### *History*

- A 42 year old African American man presented 6 months ago with clinically diagnosed "pericarditis" and was treated with NSAIDs at an outside facility.
- In the past month he has experienced worsening dyspnea on exertion with decreased run times and mild edema.
- He has no relevant past medical history. The patient currently takes NSAIDs.

### *Physical Exam*

- Vital signs: HR 104 bpm, irregular, respirations 28 per minute, BP 128/70 mmHg.
- Middle aged man, no acute distress.
- Palpation- no abnormal impulses.
- S1 normal.
- S2 normal.
- Diastolic filling sound.
- 2/6 holosystolic murmur noted along the right and left sternal border.
- No friction rub.
- JVP 15–20 cm, no inspiratory fall in pressure.
- Chest- clear to auscultation.
- Severe edema (3–4+) is present in the lower extremities to the thighs.

### *Test Results [1]*

- ECG (Fig. 20.1). EKG findings of patients with constrictive pericarditis are generally non-specific but they can have low voltage QRS due to the thickened pericardium.
- Chest CT (Fig. 20.2). CT scan of the chest in a patient with constrictive pericarditis demonstrates a thickened pericardium.

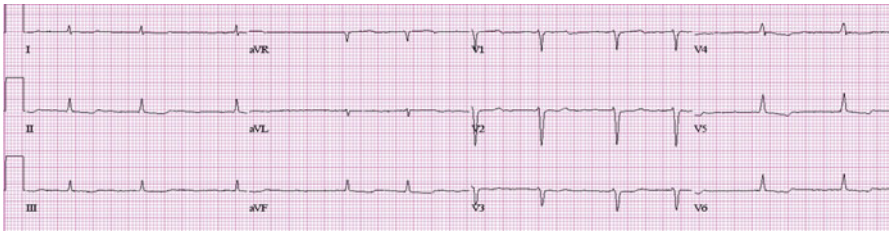


**Fig. 20.1** EKG demonstrating sinus rhythm and low voltage QRS consistent with pericardial thickening

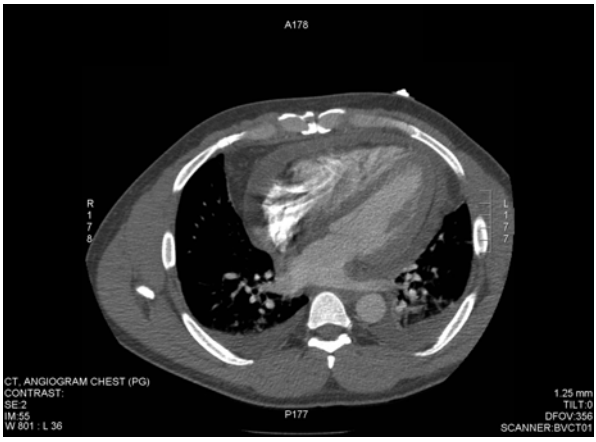


**Fig. 20.2** A thickened pericardium was identified on computed tomography of the chest

- Hemodynamics (Fig. 20.3). In the right atrial pressure tracing, a deep diastolic Y descent is present. Kussmaul's sign is present, seen as the rise in RA pressure with inspiration.

## Clinical Basics

### *Normal Anatomy*

- The normal pericardium has a limiting effect on cardiac volume and amplifies the diastolic interaction by transmitting intracavitary filling pressures to adjacent chambers [2].

### *Definition*

- CP is the end stage of an inflammatory condition in the pericardium that leads to adhesion of the visceral and parietal peritoneum, calcification and dense fibrosis [2].

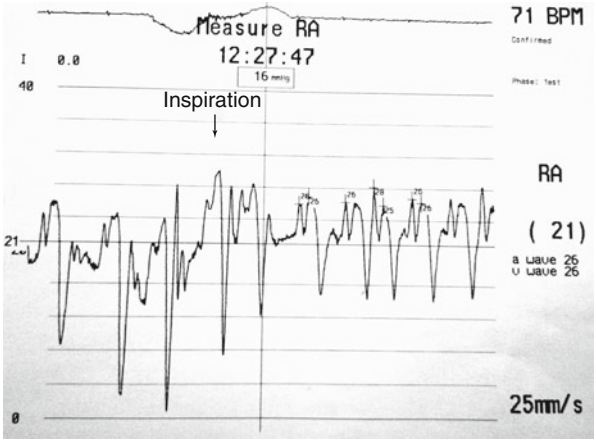


**Fig. 20.3** CP presents with elevated JVP with rapid collapsing diastolic Y descent with or without an X wave descent. In the right atrial pressure tracing, a deep diastolic Y descent is present. Kussmaul's sign is present, seen as the rise in RA pressure with inspiration. The systolic X descent may create an M or W pattern

- This leads to restriction of the myocardium and prevents adequate ventricular filling leading to elevated diastolic pressures in all four chambers [1].

## *Etiology*

- Previously, the major cause of CP was tuberculosis [1]. However, recent studies have indicated that idiopathic, prior surgery and irradiation therapy account for the majority of cases in the developed world.
- More recently, the cause of CP in 163 patients who underwent pericardiectomy was determined [3].
  - 46 % – viral or idiopathic.
  - 37 % – post surgical.
  - 9 % – secondary to mediastinal irradiation.
  - 8 % – Miscellaneous: tuberculosis, rheumatoid arthritis, systemic lupus erythematosus, prior chest trauma, Wegener's granulomatosis, or purulent pericarditis.

## *Signs and Symptoms*

- A common presentation of CP is right sided heart failure [1].
- A preoperative analysis of 135 patients who were diagnosed with CP (Table 20.1) revealed the following clinical characteristics [4].
- Common signs and symptoms include:
  - *NYHA grade III–IV heart failure.*
  - *Elevated JVP.*
  - *Peripheral edema.*

**Table 20.1** Clinical characteristics of patients with CP

| 1985–1995 cohort (n = 135) | | |
|---|---|---|
| Characteristics | No. or value | % |
| Age, years | | |
| Mean | 56 ± 16 | |
| Median | 61 | |
| Range | Nov-78 | |
| Male | 103 | 76 |
| Symptom duration, month | | |
| Median | 11.7 | |
| Range | 0.1–349 | |
| NYHA class | | |
| I–II | 40 | 30 |
| III–IV | 93 | 69 |
| Indeterminate | 2 | 1 |
| Elevated JVP | 119 | 93 |
| Peripheral edema | 103 | 76 |
| Hepatomegaly | 71 | 53 |
| Pericardial knock or S3 | 63 | 47 |
| Ascites | 50 | 37 |
| Pleural effusion | 47 | 35 |
| Kussmaul's sign | 28 | 21 |
| Pulsus peradoxus | 25 | 19 |
| Pericardial rub | 22 | 16 |
| Known CAD | 26 | 20 |
| Diuretic use | 68 | 50 |
| Atrial arrhythmia | 22 | 16 |
| Low QRS voltage | 37 | 27 |
| Pericardial calcification | 34 | 25 |

Used with permission from Ling et al. [4]
*JVP* indicates jugular venous pressure, *CAD* coronary artery disease

  - *Hepatomegaly.*
  - *Pericardial knock or S2.*

- Less common findings include:
  - *Ascites.*
  - *Pleural effusion.*
  - *Kussmaul's sign* – inspiratory increase in venous pressure indicative of the loss of right-sided venous return on inspiration [2].
  - *Pericardial calcification* – in severe cases causing a lack of cardiac impulse change on different body positions [2].
  - *Low QRS voltage* on ECG.
  - *Pulsus paradoxus* – a decrease in systolic BP during inspiration due to a lack of decreased intrathoracic pressure transmission to the left side of the heart [2].

### *Prevalence*

- CP is a relatively rare disease.
- Approximately 9 % of patients diagnosed with acute pericarditis from any cause will progress to constrictive pericarditis [5].

## Key Auscultation Findings

- The characteristic auscultation finding associated with constrictive pericarditis is the early diastolic pericardial knock. This sound occurs during diastole following the second heart sound due to an abrupt halting of rapid ventricular filling by the rigid pericardium.
  - Features of the pericardial knock:
    - The pericardial knock typically occurs 0.06–0.12 s after S2 and exhibits a loud snapping quality [6].
    - It is best heard over the left sternal border and can be accentuated with maneuvers that increase preload (e.g., squatting or increasing blood volume) or increase the afterload (e.g., isometric handgrip or phenylephrine injection) [7].
    - The sound will be diminished with maneuvers that decrease preload (e.g., straining phase of the Valsalva, nitroglycerin or standing) [7].
- CP is frequently accompanied by moderate or severe TR.
- Auscultation examples of a pericardial knock.
  - Click here to listen to examples of several patients with pericardial knock sounds, as described by Dr. W. Proctor Harvey (Video 20.1).
  - As a precursor condition, patients may have a history of pericarditis. The characteristic sound of a pericardial friction rub is illustrated by the following example. Click here to listen to a rub in polyserositis: multiple rubs with respiration variation; a phonocardiogram is also available for view (Video 20.2).

## Auscultation Differential Diagnosis

Other auscultation findings may resemble the pericardial knock and these need to be considered when establishing a differential diagnosis. These findings include an S3 heart sound, the opening snap of mitral stenosis, the ‘tumor plop” of atrial myxoma, and the presence of a split S2. The timing of these auscultation findings are demonstrated in Fig. 20.4.

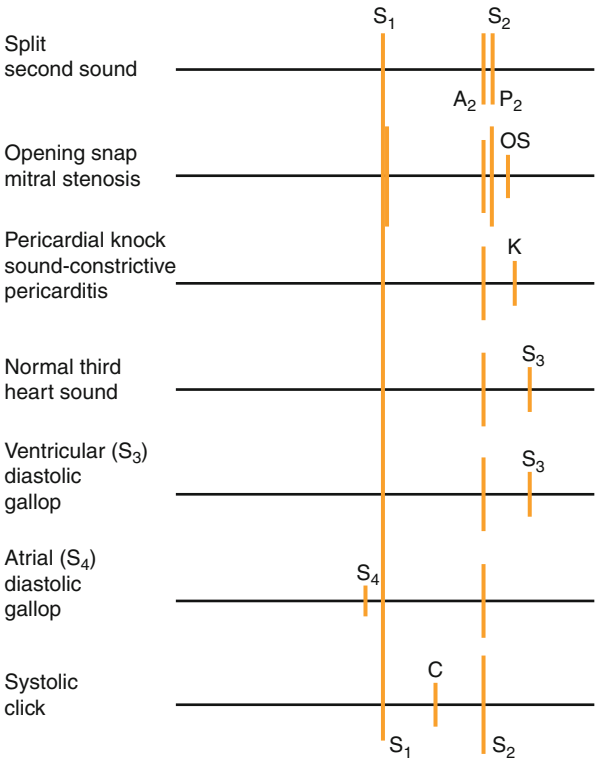


**Fig. 20.4** Comparison of diastolic heart sounds. Typically the pericardial knock (K) occurs slightly later than a split S2 or the opening snap of mitral stenosis and earlier in diastole than S3 or S4. In the clinical setting, however, the timing may vary from patient to patient (Modified with permission. Original published in Harvey [11]. Copyrighted by Laennec Publishing, Inc. All rights reserved)

- Features of an S3:

  Typically, an S3 occurs later in diastole than the pericardial knock. It is lower in pitch and may sound like a "thud" or "boom." It is best heard with the bell of the stethoscope at the apex of the heart while the patient is in the left lateral decubitus position [7].

- Features of an opening snap:

  The opening snap of mitral stenosis may occurs at the same time as the pericardial knock, however it is rarely later than 0.1 s after S2. It is usually high in frequency and is described as a short "clicking" sound. It is best heard using the diaphragm of the stethoscope and is loudest between the apex and the left lower sternal border. When the opening snap is loud, it radiates to the apex and the pulmonic area where it may be mistaken for the pulmonic component of a split S2 [7].

- Features of the "tumor plop" of atrial myxoma:

  The sound of atrial myxoma that occurs in early diastole is described as a "tumor plop" and can also occur at the same time as pericardial knock. It is a loud sound that is best heard over the lower left sternal border, making it difficult to distinguish from pericardial knock.

- Features of a split S2:

  Splitting of S2 can be described as normal inspiratory changes, wide splitting, or fixed splitting. All of these types of splitting will result in a delayed second component of S2 that could resemble a pericardial knock. However, this would typically occur at the very beginning of diastole earlier than a pericardial knock. It is best heard at the 2nd and 3rd left intercostal space [7].

## Diagnostic Implications of Auscultation Features

- The diagnosis of CP can be difficult because symptoms, clinical presentation, and physical exam can mimic many other conditions including but not limited to.
  - congestive heart failure.
  - cardiac tamponade.
  - restrictive cardiomyopathy.
  - liver cirrhosis.
  - any cardiac condition resulting in low cardiac output.
- Differentiating CP from these conditions using auscultation findings and physical exam alone can be difficult. In a cohort of patients with CP at the Mayo Clinic from 1985 to 1995, elevated JVP was found in 93 %, peripheral edema was found in 76 %, hepatomegaly was found in 53 %. Only 47 % of patients had a pericardial knock or S3 and no other clinical characteristics were present in more than 50 % of patients [4]. Therefore, the physical exam is non-specific and on its own cannot confirm the diagnosis of CP.
- Etiology of CP.
  - A very important diagnostic clue is the etiology of CP. A physician should consider CP when the patient has a certain clinical history that predisposes them to developing CP. In the same Mayo Clinic cohort, the cause of CP was idiopathic in 45 %, post-surgical in 24 %, post-pericarditis in 22 %, post-radiation in 17 %, arthritic disease in 10 %, post-infectious in 4 %, and the remaining causes were non-specific. Therefore, in a patient who has had pericarditis, undergone chest irradiation, or had prior cardiothoracic surgery the physician should consider CP in the differential diagnosis for the above listed symptoms. In other cohorts, prior infection with tuberculosis has also been an important risk factor for CP. In an otherwise healthy patient with none of the above historical features, CP might not be an important consideration [8].
- Confirming the diagnosis of CP.
  - Definitive diagnosis of CP can only be determined with echocardiography and heart catheterization.
  - With echocardiography there is a septal notch, ventricular septal shift change with respiration, increased pericardial thickness, and finally moderate biatrial enlargement.

- In the Mayo Clinic Cohort, abnormal septal motion was seen in 49 %, increased pericardial thickness in 37 %, and atrial enlargement was seen in 61 % of patients. The use of Doppler echocardiography is also very important for confirming the diagnosis of CP.
- A variation in the early diastolic filling velocity is reciprocal with respiration and this finding has a sensitivity of 85 % and a specificity of 90 %.
- In addition, cardiac MRI can be especially important for differentiating CP from restrictive cardiomyopathy. In a small cohort of patients, cardiac MRI had a sensitivity of 88 % and specificity of 100 % [8].

## Prognostic Implications of Auscultation

- There are certain features on auscultation that have implications for prognosis in a patient with constrictive pericarditis. These features include the timing and intensity of the pericardial knock, the presence of holosystolic murmur of tricuspid regurgitation, and widening of S2.
- Timing of the pericardial knock:
  - The definitive treatment for constrictive pericarditis is pericardiectomy. Following surgery, a more delayed pericardial knock corresponded with a successful surgery and good prognosis. In *one study*, following pericardiectomy the timing of the sound increased to an average of 0.17 s after S2 [9].
- Intensity of the pericardial knock:
  - Following pericardiectomy, a decrease in intensity of the pericardial knock corresponded with a fall in jugular venous pressure and better prognosis. Patients that did not have a decrease in intensity of the pericardial knock had jugular venous pressures that remained elevated [9].
- Holosystolic murmur of tricuspid regurgitation:
  - Tricuspid regurgitation can be a superimposed condition in patients with constrictive pericarditis, which further exacerbates venous pressure elevations. In a study of patients undergoing pericardiectomy for CP at Mayo Clinic, those with moderate or severe tricuspid regurgitation had a 5-year survival of 47 % versus 87 % in those without moderate or severe tricuspid regurgitation [10]. Therefore, the presence of the holosystolic murmur of tricuspid regurgitation in patients with CP has been shown to be indicative of a worse prognosis.
- Widened S2:
  - A high pulmonary artery systolic pressure can be observed in certain patients with CP. On auscultation, this would be detected as a widened S2. Using Cox proportional hazard analyses, Bertog et al. found that high pulmonary artery systolic pressure is an independent predictor of decreased mortality in patients with CP. The high pulmonary artery systolic pressure may reflect the severity of constriction, concomitant myocardial dysfunction, or pulmonary pathology [3].

- In addition to auscultation features, a very important predictor of prognosis is the etiology of CP. In patients with idiopathic CP the 7-year Kaplan-Meier survival is 88 %, compared to 27 % in patients with radiation-induced CP. Moreover, patients with post-surgical CP had a 7-year Kaplan-Meier survival of 66 % [3].
- Several other independent predictors of mortality and prognosis have been found that are not auscultation features. These include advanced age, impaired renal function, low serum sodium, and reduced left ventricular ejection fraction [3,7].

## Management and Treatment of CP

### *Pericardiectomy*

- The definitive treatment for CP is pericardiectomy aimed at resecting the diseased pericardium as completely as possible. However, not all patients are good candidates for pericardiectomy, specifically patients with calcified adhesions or presence of myocardial fibrosis. The mortality rate of this procedure is 6 % [6].

### *Medical Management*

- In addition to pericardiectomy, patients with CP can be medically managed with diuretics, dietary changes including salt restriction, and treatment of any underlying medical conditions that may be exacerbating symptoms.

## Clinical Summary of the Case

In this case, recurrent pericarditis has led to exam and hemodynamic findings of constrictive pericarditis. Supportive evidence is the thickened pericardium as shown on CT of the chest. The presence of an early diastolic filling sound, known as the pericardial knock, in the setting of normal LV systolic function on echocardiography can be a clue to the diagnosis. Kussmaul sign is typical, and should be easily detected in the neck, leading one to suspect that a pericardial process accounts for the elevated central venous pressures. The finding of a TR murmur in this instance is common in CP, and is an ominous finding, portending a worse prognosis.

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# Chapter 21
# Prosthetic Heart Valves

**Christine K. Chan, Marsiyana M. Henricus, George S. Ibrahim, and Omar Z. Maniya**

## Key Teaching Points

- Prosthetic heart valves have characteristic auscultation profiles; the mitral valve provides characteristic examples of key auscultation features.
- Basic features of a mitral valve mechanical prosthesis include a prosthetic closing click of S1, a normal S2, and then an opening click.
- Antegrade flow murmurs are common in the setting of prosthetic heart valves because a normal prosthetic valve does not provide a fully physiologic valve area and turbulence is created by valve components.
  - Regurgitant murmurs are not expected as part of normal prosthetic valve physiology.
- The diagnosis of prosthetic valve malfunction may be suspected in the setting of abnormal auscultation findings that vary with the valve type. This may include loss of typical opening and closing sounds, which may point to valve thrombosis or the development of a new murmur indicative of valve dysfunction or leak.
- Prognosis.
  - Serial auscultation for valvular click intensity may not be the best way to find PV dysfunction however this is not well studied.
  - Integrated approach incorporating clinical status, murmurs, and a confirmatory doppler is recommended.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_21) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- A 69-year-old white female is admitted for evaluation of chest pain with a history of rheumatic heart disease.
- The patient had a closed commissurotomy in 1955. In 1991, her mitral valve area was found to be 1 $cm^2$ in addition to mild pulmonary hypertension and aortic regurgitation. At that time, the patient underwent a 27 mm St. Jude mechanical mitral valve prosthetic replacement, and a saphenous vein graft to her left anterior descending artery was performed.
- Past medical history is significant for atrial fibrillation and diabetes mellitus.
- Medications include furosemide, atorvastatin, warfarin, metformin, metoprolol, ramipril.

### *Physical Examination*

- On physical exam, the patient BP is 145/84 mmHg and HR is 71 bpm.
- There is a normal jugular venous pressure with an accentuated venous wave. The patient was noted to have lymphedema and a chronic stasis change in her lower extremities. In addition, the patient had a mild left parasternal impulse.
- On auscultation (Fig. 21.1):
  - A loud, crisp mitral closing click and a 2/6 grade murmur was heard from the right upper sternal border to the base of the neck.
  - A crisp mitral opening click was present at the left sternal border, and at the right sternal border it was a grade 1/4 murmur.
  - A normal A2 was present with no mitral diastolic murmur.

### *Test Results*

Echocardiogram results:

- LV ejection fraction 60 %.
- Mild left atrial enlargement (46 mm).

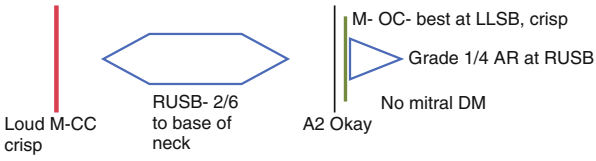


**Fig. 21.1** Cardiac auscltation findings for a 60 year old female presenting with chest pain and a history of rheumatic heart disease

- Grade 2 aortic regurgitation with mild valve thickening.
- Prosthetic mitral valve with peak velocity of 1.3 m/s (Fig. 21.2).
  - Prosthetic closure velocity noted.

## Clinical Basics

### *Definitions*

- Prosthetic heart valves are classified as mechanical or biological:

A. Mechanical valves (Fig. 21.3).

- Primarily made of carbon alloys.
- Manufactured using industrial materials.
- Design is bileaflet or tilting disk [1].

B. Biological valves.

- Primarily made of material from living tissue.
- Includes porcine aortic valves, valves produced from bovine pericardium, homografts (valves from other human beings), and autografts (valves from the patient) [1].

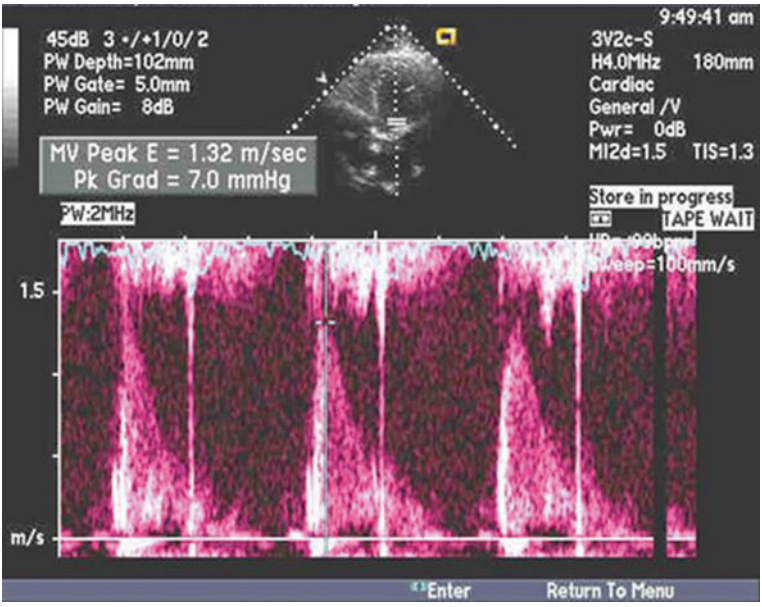


**Fig. 21.2** Echocardiogram of 69 year old female revealing a prosthetic mitral valve with peak velocity of 1.3 m/s


**Fig. 21.3** Common mechanical heart valves: (**a**) Ball in cage design. (**b**) Bileaflet tilting disc. (**c**) Tilting disc

## *Prevalence of Implanted Valves*

- 60 % carbon alloys with a tilting disk or bileaflet design [1].
- 40 % bioprosthetic valves [1].

## *Complications of Prosthetic Heart Valves*

- Thromboembolism.
- Infective endocarditis.

- Valve leaflet failure: uncommon.
- Late complications include pannus formation with or without valve dysfunction.

## Key Auscultation Features

- Mechanical valves have auscultation characteristics including.
  - Flow murmurs.
    - Because even normally functioning prosthetic valves have a pressure gradient across them associated with flow acceleration.
      - The "normal" prosthetic valve does not provide a normal valve orifice area:
        - Normal mitral valve area is 4–6 $cm^2$.
        - Prosthetic MVA (depends on type and size):
          - Starr-Edwards Caged Ball (1.4–2.6 $cm^2$).
          - St. Jude Bileaflet (1.0–2.03 $cm^2$).
          - Bjork-Shiley Tilting Disc (1.72–2.2 $cm^2$).
  - Opening and closing sounds created by mechanical valve components.
- Auscultation examples of prosthetic heart valves.
  - Click here to listen to an example of an auscultation in a patient with aortic valve replacement with a St. Jude valve and view an image of the phonocardiogram (Video 21.1).
  - Click here to listen to examples of several patients with prosthetic valves, as described by Dr. W. Proctor Harvey (Video 21.2).

## Auscultation Differential Diagnosis

- Mechanical valves produce very audible opening and closing clicks, to the extent of not needing a stethoscope. Many patients with prosthetic valves hear their own valve clicks.
- Mechanical heart valves have different auscultation sounds that are dependent on the following:
  - Type of valve used.
  - Position of the valve.
  - If the functioning of the valve is normal.
  - In MV mechanical valves, the heart sound sequence simulates mitral stenosis.

  - Basic Features:
    - S1: prosthetic closing click.
    - S2: should be normal.
  - May be followed by opening click.

- Auscultation differences among prostheses in the mitral valve position (Fig. 21.4); Aortic valve findings are shown in Fig. 21.5.

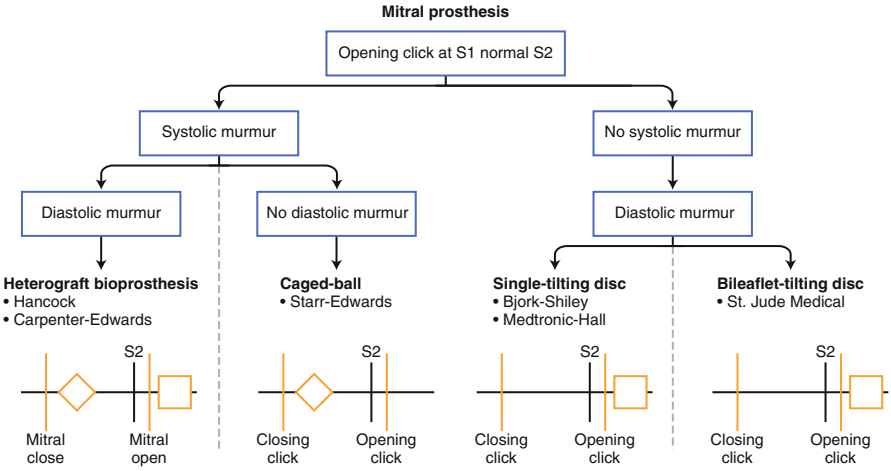


**Fig. 21.4** Typical cardiac auscultation findings for a variety of common mitral prostheses

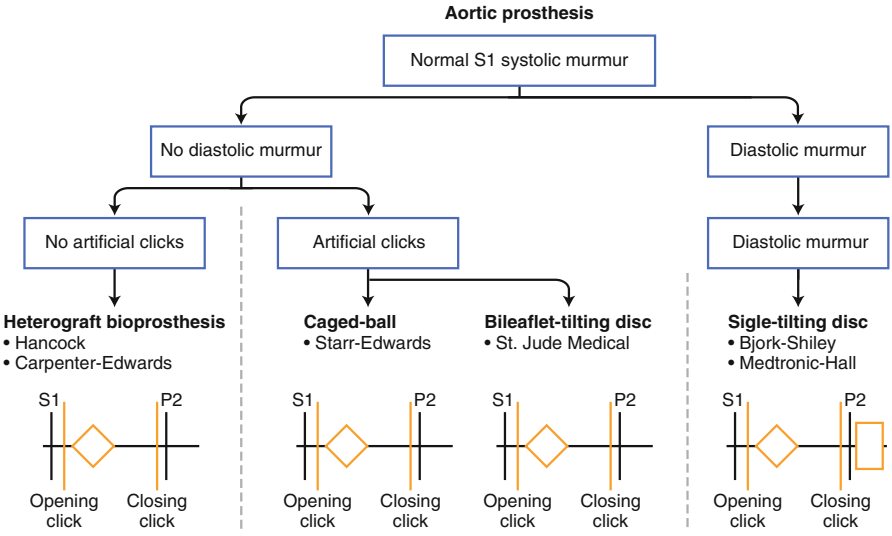


**Fig. 21.5** Typical cardiac auscultation findings for a variety of common aortic prostheses

- Ball-in-cage Valves.
  - With normal valve and ventricular function, the Ball-in-cage valve produces the loudest and most distinguishing opening and closing clicks in any position.
  - A more prominent opening click than closing click.
  - A 2–3/6 systolic ejection murmur is heard.
  - No diastolic murmur is heard.
- Single Tilting Disc Valves.
  - An opening click in the mitral position is rarely heard.
  - A 2/6 systolic ejection murmur is heard.
  - A 1–2/6 diastolic rumble is typically heard.
- Porcine Valves.
  - An opening click is audible 50 % of the time.
  - A 1–2/6 apical systolic ejection murmur is heard 50 % of the time.
  - A diastolic rumble 1/2–2/3.
- Bileaflet Valves.
  - A closing click is very audible while the opening click is typically not heard.
  - Diastolic rumbling murmur may be heard.

## Clinical Clues to the Detection of the Lesion

- All prosthetic valves have gradients, so murmurs in the *forward* flow direction are common.
  - Regurgitant murmurs are not expected.
- Exercising the patient may accentuate a diastolic murmur.
  - Leads to increase in heart rate and blood flow, which increases the gradient, thereby facilitating murmur auscultation.
- Decrease or disappearance of the prosthetic closing sound may represent development of thrombus or fibrous pannus ingrowth.
  - Closing sound should generally be the loudest sound.
- A soft diastolic rumble can occur with MV prosthesis.
  - Should not be loud.
  - New diastolic murmur or change may be significant.

## Diagnostic Implications of the Auscultation Features

### *Testing for Valve Thrombosis*

- Reduction of opening and closing click could point to thrombosis.
- Differences in the valve types: mechanical valves tend to have greater problems than biological valves [2].
- Antithrombotic Therapy.
  - Typically required for mechanical valves but not bioprosthetic valves.

### *What Development of New Murmur May Signify*

- Valve dysfunction.
  - Systolic or diastolic murmur.
- Paravalvular leak.

### *Structural Deterioration*

- Mechanical valves can last 20–30 years.
- 10–20 % human aortic homograft prostheses fail in 10–15 years.
- 30–35 % porcine heterograft prostheses fail within 10–15 years.

### *Development of Infection: Endocarditis*

- Studies conducted proved that antibiotic prophylaxis before invasive surgical procedures prevented endocarditis [3].

### *Evaluation of Valve Function, Infection, Conduction Disturbance, or Myocardial Infarction*

- Interval history and physical examination key signs:
  - Subtle symptoms of heart failure or neurologic events.
  - Abnormal auscultation findings that vary with the valve type this may include loss of typical opening and closing sounds, which may point to valve thrombosis or the development of a new murmur indicative of valve dysfunction or leak [1].

- Transthoracic Doppler Echocardiogram:
  - A baseline study of velocities should be conducted to evaluate the function of prosthetic valves after valve implantation, since this can vary from patient to patient. This baseline can be compared to subsequent visits to measure valvular or paravalvular regurgitation and transvalvular pressure gradients. Valve degeneration is a concern of those with bioprosthetic valves. It is suggested that studies be conducted after 3–5 years [2].
- Cinefluoroscopy:
  - This can be used to assess disk and poppet motion in mechanical valves in patients where auscultatory change is evident.
- Blood tests are used to assess the presence of infection and to ensure electrolyte and metabolic balances:
  - CBC, creatinine, electrolytes, lactate dehydrogenase, INR.
  - Lactate dehydrogenase is mildly elevated due to hemolysis from trauma induced by prosthetic valve.

## Prognostic Implications of the Auscultation Features

- When clinical status of the patient changes, an increase of suspicion is necessary.
  - Be vigilant for changes over time from serial auscultation:
    - Valve sounds and character of opening and closing clicks.
    - Watch for new and changing murmurs.
- Acute Valve Dysfunction.
  - Structural Failure (Early complication after surgery).
    - Paravalvular leaks detected via TEE.
    - Incidence ranges from 18–48 % of those with mitral of aortic prosthesis.
    - However these do not tend to progress over a 2–5 years follow-up [2].
  - Early endocarditis [4].
    - Contamination of the valve during or soon after surgery.
    - Caused by staphylococci or gram negative rods [4].
    - Poor prognosis and the risk is still substantial with antibiotic prophylaxis during surgery [4].
- Chronic Valve Dysfunction.
  - Late structural failure (Long term outcomes).
    - The risk is low with most mechanical valves, which can last 20–30 years.
    - The risk is higher for human aortic homograft where 10–20 % failed in 10–15 years as well as porcine heterograft where 30–35 % have failed in

10–15 years (higher in the mitral position rather than in the aortic position) [2, 5–10].

- Contributing factors leading to structural failure leading to valvular regurgitation:
  - Mechanical stress.
  - Immunologic rejection.
  - Endocarditis.
  - Cusp tear.
- Prognosis varies with age for bioprosthetics:
  - At 15 years the rate of failure varied from 15 % with <65 years old to 9 % with >65 yrs old [10].
  - For aortic valves a study revealed at 15 years it varied from 63 % for 40–49 years old and 10 % with those >70 years old [11].
  - These findings are attributed to the decreased activity seen in older patients resulting in less mechanical deterioration.

– Late endocarditis.

- Contamination of the valve secondary to bacteremia [12].
- Better prognosis than early endocarditis [4].

– Valve obstruction.

- Pannus formation.
  - Idiopathic abnormal fibrovascular or granulation tissue layer formation.
  - Arises from the ventricular aspect of the prosthesis resulting in stenosis or outflow obstruction [13].
  - Formed by collagen and elastic fibrous tissue accompanied by endothelial cells, chronic inflammatory cell infiltration and myofibroblasts [14].
  - Detected via echocardiography.
  - More common in aortic valves.
  - Treatment is via surgical excision with or without valve replacement.
  - May be connected to an increase in transforming growth factor beta, which increases fibrosis and scar formation [15].
- Prosthetic valve thrombosis.
  - Occurs equally in bioprosthetic and mechanical valves.
  - Annual incidence 0.03–5.7 % and higher in mitral prostheses and/or therapeutic anticoagulants [2, 16–18].
  - Diagnosed via transthoracic doppler echocardiography, TEE, or cinefluoroscopy to asses valve motion and clots.
  - Treatment: surgery and thrombolytic therapy (streptokinase, urokinase and recombinant tissue-type plasminogen activator) [19].

- Systemic embolization.
  - Result of valve thrombosis or vegetations.
  - Common in those with atrial fibrillation [20].
  - Tested via transesophageal echocardiography.
  - Occurs 0.7–1.0 %/patient - year with mechanical valves and treated with warfarin [21, 22].
  - 2.2 %/patient-year with aspirin and 4.0 %/patient-year with no anticoagulation.
  - 45 % in mechanical valves (Starr Edwards valves that were not treated with anticoagulants) v. 13 % bioprostheses at 5 years [23].
- Bleeding.
  - Greater risk with mechanical valves because they are thrombogenic and chronic anticoagulation as opposed to bioprosthetic valve recipients that receive short-term anticoagulants.
  - Veterans Affairs Cooperative Study, 575 patients with mechanical or bioprosthetic valves [6].
  - 11 year probability of bleeding was greater in the mechanical valves 42 % v. 26 % in bioprostheses [6].
- Hemolytic Anemia.
  - A result of mechanical damage and seen more often with mechanical valves.
  - Associated with rapid acceleration and deceleration of the regurgitant jet and high peak shear rates [2].
  - Tends to be severe in 15 % of the cases that include ball cage and bileaflet valve models [2].
  - Can be a result of porcine valve failure [2].
  - Signs and Symptoms: anemia, heart failure, jaundice, dark urine, increase in serum lactate dehydrogenase, new murmur [2].
  - Treatment: iron replacement, transfusion or recombinant human erythropoietin.

## General Statement on Management [24]

### *Mechanical Heart Valves*

- First Post-Operative Outpatient Visit 2–4 weeks after discharge.
  - History.
  - Physical.
  - Transthoracic doppler echocardiogram only if a baseline echo was not obtained prior to discharge.
  - Additional testing as indicated.

- Annual Follow-Up Visits.
  - Echocardiography only if there is a change in clinical status.

### *Porcine Heterograft Valves*

- First Post-Operative Outpatient Visit 2–4 weeks after discharge.
  - History.
  - Physical.
  - Transthoracic doppler echocardiogram only if a baseline echo was not obtained prior to discharge.
  - Additional testing as indicated.
- Annual Follow-Up Visits.
  - Echocardiography only if there is a change in clinical status.
  - Annual echocardiogram after 5 years, even in if there is no change in clinical status, may be considered.

## Clinical Summary of the Case

This case presents with findings of a normally functioning mitral prosthetic valve with a normal closing and opening clicks. Opening clicks are not as common with St. Jude mitral valves. The findings are best heard at the left lower sternal border. Important is the exclusion of murmurs suggesting prosthetic valve malfunction. Continued clinical follow up is recommended. Regular echocardiographic exams are not indicated.

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# Chapter 22
# The Clinical Assessment of Ejection Fraction and Hemodynamics in Congestive Heart Failure

**Elizabeth Harkin**

## Abbreviations

| | |
|---|---|
| BNP | B-type natriuretic protein |
| CAD | Coronary artery disease |
| CHF | Congestive heart failure |
| ECG | Electrocardiogram |
| Echo | Echocardiogram |
| JVD | Jugular venous distention |
| JVP | Jugular venous pressure |
| LBBB | Left bundle branch block |
| MI | Myocardial infarction |
| PCWP | Pulmonary capillary wedge pressure |

## Key Teaching Points

- History of reduced cardiac output, myocardial infarction (MI), orthopnea, dyspnea, hepatic congestion, coronary artery disease (CAD), and long standing hypertension warrant clinical consideration of congestive heart failure (CHF).
- Physical exam variables most indicative of CHF include jugular venous distention (JVD), a positive abdominal jugular reflex, rales, edema, and a narrow pulse pressure.

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- Tests results associated with CHF with reduced left ventricular ejection fraction (LVEF) include a B-type natriuretic protein (BNP) greater than 150 pg/ml, an abnormal electrocardiogram (ECG) including either anterior Q waves, left bundle branch block (LBBB), or a QRS complex greater than .10 s, a chest x-ray indicative of cardiomegaly and pulmonary congestion.
- Findings on auscultation include an S3 gallop, sustained left ventricular apex beat, and displacement of cardiac apical pulsation.
- Once the diagnosis of CHF is established it is important to differentiate between systolic and diastolic heart failure. Heart failure with preserved LVEF, above 40 %, may be predicted by diastolic blood pressure >105 mmHg, absence of JVD, and impaired left ventricular relaxation.
- Medication management and specialized interventions should follow ACCF/AHA Heart Failure Guidelines and Staging.
- Variables predictive of patient outcomes include S3 gallop, hypotension, JVD, LVEF, and ECG abnormalities.

## Case Description

### *History*

- A 74 year old man presents with complaints of worsening shortness of breath, especially while lying down, decreased exercise tolerance, fatigue, ankle swelling, and loss of appetite.
- He suffered an MI 6 years ago with an uncomplicated course since that time.
- He has hypertension, sleep apnea, and takes an occasional NSAID for arthritic pain.
- Current medications include captopril 25 mg twice daily, metoprolol 100 mg once daily, 81 mg aspirin once daily, and atorvastatin 20 mg once daily.

### *Physical Examination*

- On physical examination his blood pressure is 119/92 supine and 117/90 standing. Heart rate is 80 bpm both supine and standing. His skin is warm.
- The jugular venous pressure is elevated. An abdominal jugular test is also positive with a significant fall in the JVP after release of right upper quadrant compression.
- He has an early diastolic S3 gallop grade II/VI heard over the cardiac apex in the left later decubitus position and a large apical pulse.
- He has diminished peripheral pulses, 1+ ankle edema. Ascites is noted.
- Auscultation of the lungs shows normal breath sounds, without rales.

### *Testing*

- ECG shows an old anterior wall MI, LBBB, and left ventricular hypertrophy.
- Chest x-ray shows cardiomegaly and pulmonary congestion. Echo demonstrates a LVEF of 40 %, increased left ventricular size and wall thickness, and right ventricular systolic dysfunction.

## Clinical Basics

### *History*

- Previous MIs contribute to ventricular dysfunction.
  - In patients with a previous MI, a prior anterior MI is highly correlated with reduced LVEF [1].
- A past medical history positive for CAD, valvular heart disease, hypertension, hypercholesterolemia, peripheral vascular disease, diabetes mellitus, sleep apnea, rheumatic fever, anemia, and exposure to cardiotoxic medications is associated with CHF [2].
- Signs of low cardiac output include fatigue, weight loss, cyanosis, cool extremities, orthopnea, and dyspnea.
  - Absence of dyspnea makes heart failure unlikely, with a sensitivity of 95 % [1].
- A social history positive for substance abuse, smoking, and international travel increases a patient's risk for CHF.
- Indicators of hepatic congestion from right ventricular dysfunction include nausea, abdominal pain, and ascites.

### *Physical Exam Variables Most Predictive of Reduced LVEF*

- Cardiovascular indicators include tachycardia, hypotension, diminished peripheral pulses, arterial bruits, and a narrow pulse pressure, and JVD [3].
  - The presence of JVD, displaced cardiac apical pulsation, or gallop rhythm suggests heart failure with 95 % specificity [4].
  - A pulse pressure less than 25 % of systolic BP correlates with a cardiac index less than 2.2 L/min/$m^2$ with 91 % sensitivity and 83 % specificity [5].
  - The presence of JVD has a sensitivity of 81 %, specificity of 80 %, and predictive accuracy of 81 % for elevation of pulmonary capillary wedge pressure (PCWP) above 18 mmHg [6].

- The presence of rales suggests high filling pressures due to left ventricular dysfunction.
- Indicators of hepatic congestion from right ventricular dysfunction include nausea, abdominal pain, ascites, and hepatomegaly.
- Systemic indicators of CHF include dependent edema, muscle wasting, abnormal deep tendon reflexes, and thyromegaly.

### *Test Results*

- A BNP level greater than 150 pg/ml has a specificity of 83 % for the diagnosis of heart failure [7].
- Chest radiographic findings most predictive of reduced LVEF include cardiomegaly and pulmonary venous congestion with a sensitivity of 71 % and specificity of 92 % [1].
- A normal ECG, without anterior Q waves or LBBB, has a sensitivity of 94 % and a specificity of 61 % for the diagnosis of heart failure [1].
- A completely normal ECG with no history of previous MI was associated with a LVEF above 50 % in 95 % of patients [8].
- A completely normal ECG combined with normal chest x-ray rules out heart failure with a sensitivity above 95 % [9].
- Echo findings correlating with mortality in heart failure include: left ventricular end diastolic volume, stroke volume, mitral and tricuspid insufficiency, right ventricular systolic dysfunction, impaired peak early-to late-mitral diastolic flow ratios, impaired peak early-diastolic mitral filling velocity to peak early diastolic mitral annular velocity [10].
  - The combination of a mitral E/E' >15, left atrial area >20 cm, and deceleration time <140 ms was predictive of a PCWP >15 with a 92 % sensitivity and 85 % specificity [11].
  - Echocardiography is the first line method for assessment of cardiac function, physiology, and noninvasive hemodynamics.

## Key Auscultation Features

- S3 gallop characteristics.
  - Occurs early in diastole.
  - It is heard best with the bell over cardiac apex with patient in left lateral decubitus position.
  - Low pitch.
  - Follows a "Ken-tuc-key" cadence.
  - Indicates supple ventricle and rapid filling in child or young adult (<20 years).

- In an adult, it indicates disease and increased ventricular filling.
- An abnormal apical beat can provide clues to left ventricular enlargement (when displaced laterally) and left ventricular dysfunction (when sustained).

## Diagnostic Implications of the Auscultation Features

- Clinical clues to the detection of heart failure, particular with reduced LVEF:
  - Orthopnea.
  - S3 gallop.
  - Rales.
  - Abnormal ECG with anterior Q waves or LBBB.
  - Abnormal x-ray demonstrating pulmonary congestion and cardiomegaly.
- The presence of pulmonary rales and S3 gallop on physical exam is associated with significantly higher right-sided pressures and PCWP and a lower cardiac index and left ventricular ejection fraction [6].
- In systolic dysfunction, JVD and the abdominal jugular test can be used to estimated intracardiac filling pressures (PCWP). See Fig. 22.1.
- In the setting of heart failure, it is important to differentiate between heart failure with either preserved or reduced systolic function (also referred to as diastolic and systolic heart failure).

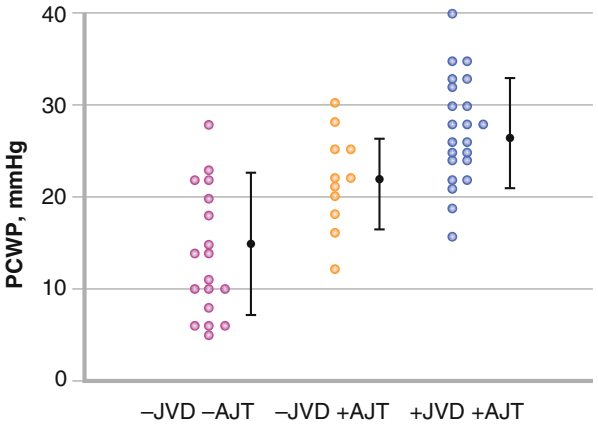


**Fig. 22.1** Pulmonary capillary wedge pressure (PCWP) measurements are reported in relation to the clinical presence (+) or absence (–) of jugular venous distension (*JVD*) and the presence of a positive (+) or negative (–) abdominojugular test (*AJT*). *Purple circles* = patients without elevated jugular venous pressure and a negative abdominojugular test; *Yellow circles* = patients without elevated jugular venous pressure but with a positive abdominojugular test; *blue circles* = patients with evidence of both elevated jugular venous pressure at rest in addition to a positive abdominojugular test (Used with permission from Butman [6])

  - Diastolic heart failure is characterized by a LVEF above 50 %, elevated left atrial pressures, elevated left end diastolic pressure, impaired left ventricular relaxation, and decreased compliance [12].
  - The combination of diastolic blood pressure ≥105 mmHg and the absence of JVD has high specificity and 100 % positive predictive value in identifying diastolic heart failure at the bedside [11].

## Prognostic Implications of the Auscultation Features

- The 1 year life expectancy of advanced heart failure patients is only 62 % [13].
- The prognosis is similar for heart failure with preserved and reduced ejection fraction. The 5 year mortality rate is 65 % for patients with preserved ejection fraction and 68 % for patients with a reduced ejection fraction [14].
- Each 10 % reduction in ejection fraction is associated with a 39 % increase in the risk of mortality in patients with an ejection fraction below 45 % [15].
- The presence of clinical variables such as a previous acute MI, anterior acute MI, congestion on chest x-ray, and creatine kinase >1000 were predictive of a stepwise decrease in LVEF and an increase in the proportion of patients with a reduced LVEF [16].
- The presence of an S3 gallop is indicative of excess morbidity and mortality (42 % increase in hospitalization and 15 % increase in death) [17]. The presence of elevated JVP is also associated with similar increased risks.
- There is a 35 % increase in relative risk of death for each 100 pg/ml increase in BNP from baseline [18].
- Each 1 g/dL reduction in hemoglobin has been associated with a 20 % adjusted increase in risk of death [19, 20].
- Persistently elevated levels of high sensitivity troponin T are associated with a twofold increase in mortality risk [21].
- The cumulative 1 and 2 year survival rates of patients with a $VO_2$ above 14 ml/kg/min) are 94 % and 84 % which is equivalent to post cardiac transplant survival rates [22].

## Statement on Management

- Medication management and timing of specialized interventions should follow the 2009 ACCF/AHA Heart Failure Guidelines.
  - Stage A recommendations include treatment of hypertension and lipid disorders, smoking cessation, control of metabolic syndrome, regular exercise, discouragement of alcohol and illicit drug use, and drug therapy using an ACEI or ARB in appropriate patients.

  - Stage B recommendations include all of Stage A guidelines in addition to treatment with a beta blocker in appropriate patients and the placement of implantable defibrillators in selected patients.
  - Stage C recommendations include all Stage A and B measures in addition to dietary salt restriction, treatment of fluid retention with diuretics, and adjunct aldosterone antagonists, digitalis, and hydralazine or nitrate in selected patients. Biventricular pacing and implantable defibrillators should also be considered in selected patients.
  - Stage D therapy goals include recommendations for Stage A, B, and C in addition to heart transplantation, chronic inotropes, permanent mechanical support, experimental surgery or drugs, and supportive end of life care.

- In patient post-MI, 35 % can be reliably predicted to have and ejection fraction less than or equal to 40 %, with anterior MIs having the highest incidence of reduced LVEF [1].
- In patients with CAD, a normal electrocardiography and the absence of cardiomegaly establishes an extremely high likelihood of normal EF.
- In patients previously diagnosed with CHF, assessment of LVEF, S3 gallop, BNP, hemoglobin, troponin, and $VO_2$ can help predict survival outcomes.

## Clinical Summary of the Case

This patient with a history of prior myocardial infarction presents with symptoms and signs of congestive heart failure. In the setting of left ventricular systolic dysfunction, the presence of elevated JVP, even in the setting of a clear chest exam, indicates high intracardiac filling pressures. The narrow pulse pressure, (27 mmHg [119/92 mmHg], or 23 % suggests that cardiac index is abnormally low. Prognosis is reduced in the setting of poor hemodynamics in chronic systolic dysfunction, therefore tailored management of congestive heart failure with diuresis, afterload reduction, and further assessment of cardiac performance is warranted.

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# Part VI
# Congenital Heart Disease

# Chapter 23
# The Innocent Murmur

**Christine M. Kim and Ryan Hubbard**

## Key Teaching Points

- The term "innocent murmur" is used when conditions that lead to the production of the murmur are entirely benign and free of significant organic abnormalities.
- The murmurs are generally caused by turbulence as a result of normal or rapid flow.
- The murmur may be entirely systolic and occasionally continuous; very rarely it may be mid-diastolic.
- Recognizing individuals with innocent murmurs by auscultation can avoid unnecessary testing.

## Case Description

### *History and Physical*

- A healthy 4-year-old girl presents for a routine physical examination.
- Upon auscultation, it is found that the child has a low frequency early systolic ejection murmur best heard at the lower left sternal border extending to the cardiac apex. [1] See Fig. 23.1.
- This murmur is diagnosed as a Still's murmur (innocent murmur) [1]. No further testing is ordered.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_23) contains supplementary material, which is available to authorized users.

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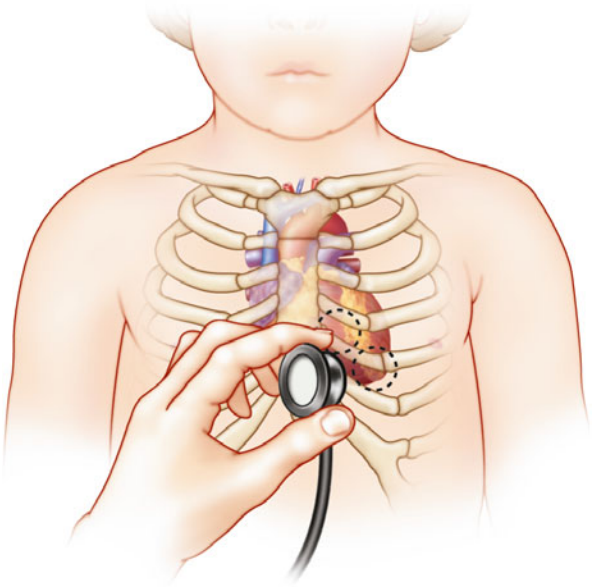

**Fig. 23.1** Still's murmurs are generally Grade 1–3 early systolic murmurs heard best by placing the bell of the stethoscope between the lower left sternal border and the apex of the heart. They have been described as vibratory or musical in quality with a low to medium pitch. They can be heard loudest when the child is supine and will decrease in intensity when the child stands. Still's murmurs are most commonly heard in children under the age of 7 and are benign findings

## Clinical Basics

### *Begin by Obtaining a Good History and Physical*

#### Historical Clues

- Exclude that there is a family history of cardiac congenital anomalies because individuals with an affected relative are more likely to have congenital heart disease [2].
- Exclude any abnormalities in the birth and prenatal hx [3].
  - Examples:
    - Intrauterine insult.
    - Low birth weight.
    - Postnatal poor feeding.
    - Maternal diabetes mellitus.

### General Examination

- Dysmorphic features should be identified, as should any abnormalities within the general cardiovascular examination.
  - Examples:
    - Down's syndrome.
    - Tachycardic at rest.
    - Weak femoral pulse.
    - Full pulses.
    - Precordial bulge of chest wall.

## Key Auscultation Features

- Focus on each sound individually initially.
- Innocent murmurs arise from turbulent ejection, and tend to be short in duration, low in intensity and poorly transmitted across the precordium.
- Specific auscultation features:
  - Low frequency.
  - Early systolic ejection murmur, crescendo-decrescendo.
  - Best heard at left lower sternal border extending to the cardiac apex. See Fig. 23.1.
  - Usually noted after infancy and has peak incidence in 3–7 year olds.
  - Displays vibratory or buzzing quality.
  - Vary with positioning, and best appreciated with bell of stethoscope while patient is supine.
  - Intensity reduced by Valsalva maneuver.
- Features of murmurs associated with cardiac abnormalities.
  - Unusually loud murmurs.
  - Diastolic or pansystolic, or late systolic murmurs.
  - Associated with any other cardiac abnormality.
- Adults may also have benign systolic ejection murmurs.
  - Characteristics.
    - Occurs mostly in adults over 50 years old; relatively common.
    - Can arise from turbulent flow, such as that created by an angulated septum (sigmoid septum) seen on echo with hypertrophy at proximal septum due to co-existing hypertension.
    - Murmurs are ejection in type and generally short duration with early peak.
    - May be musical and humming or vibratory.

  - Diminish in intensity when standing because of decreased venous return and may actually disappear.
  - Also diminish in intensity during strain phase of Valsalva maneuver.
  - Not associated with ejection clicks.

- Auscultation examples of an innocent murmur (Still's murmur).
  - Click here to listen to an example of Still's murmur and to view an image of the phonocardiogram (Video 23.1).

## Auscultation Differential Diagnosis

### *Hypertrophic Obstructive Cardiomyopathy* [2]

- Distinguish from Still's murmur by Valsalva maneuver.
- HOCM murmur intensifies, Still's murmur reduces.
- LVH on EKG.

### *Small VSD*

- Early systolic murmur, best heard in 3rd intercostal space on left.
- Pansystolic.

### *Physiological Pulmonary Systolic Ejection Murmur (PPPS)* [2]

- Early systolic crescendo-decrescendo sound.
- Best heard with diaphragm in left 2nd intercostal space.
- Usually grade II in intensity with little radiation.
- Louder when patients lie supine or during inspiration or exercise.

### *Atrial Septal Defect*

- Grade II or III systolic ejection murmur.
- Best hear at left 2nd intercostal space.
- Prominent right ventricular impulse.
- Loud second component of first heart sound.
- Fixed and widely split 2nd heart sound.
- EKG shows right conduction delay with right axis deviation or ventricular hypertrophy.

### *Pulmonary Stenosis*

- Commonly associated with a click or thrill or wider radiation.

### *Supraclavicular Arterial Bruit* [2]

- Harsh, early systolic murmur.
- Best heard with bell above clavicles on right.
- Louder when patient is sitting.
- Intensity reduced when hyperextending patients shoulders with elbows bent.
- Heard particularly well mid childhood.
- Resultant from turbulence in brachiocephalic or carotid arteries.

### *Aortic Valve Stenosis*

- May have thrill in suprasternal notch.
- Will also likely have an associated click.
- Tends to be loudest below right clavicle and not diminished by shoulder hyperextension.

### *Venous Hum* [2]

- High frequency, soft, blowing, continuous murmur.
- Heard best while patient is sitting.
- Commonly noted between 3 and 8 years old.
- Can be bilateral, but most prominent on right side of sternum.
  - Intensified by rotating patient's head to contralateral side while listening with bell in supraclavicular space.
- Digital compression of ipsilateral internal jugular vein will reduce or eliminate murmur when listening at same position.
- Hum much quieter when patient in supine position.

### *Patent Ductus Arteriosus*

- Cannot be diminished or obliterated by laying supine or compressing internal jugular vein.
- Diastolic component is low pitched and decrescendo.

- Murmur truly continuous.
- Frequently associated with bounding pulses and hyper dynamic left cardiac impulse.

### *Innocent Peripheral Pulmonary Stenosis* [2]

- Occurs mostly in newborns or premature infants.
- Due to dilated main pulmonary artery branches to smaller lateral vessels at sharp angles creates turbulence and an audible sound.
- Short mid diastolic ejection murmur of medium pitch and intensity.
- Heard in pulmonic area in systole, but equally loud when auscultated in axillae.
- Frequently follows child's breath sounds (must auscultate axilla).
- Should radiate widely and disappear in a few months.

## Diagnostic Implications of the Auscultation Features

Pathologic causes of murmurs may be associated with identifiable abnormalities on ancillary cardiac studies such as electrocardiography, chest radiograph, or echocardiography. Normal findings on these examinations make a significant cause of a murmur less likely.

## Statement on Management and Clinical Summary of the Case

The murmur in this young patient consistent with an innocent murmur does not need further evaluation.

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# Chapter 24
# Atrial Septal Defect

**John E. Nolan III, Tarina C. Parpia, and Katherine A. Sanchez-Maldonado**

## Key Teaching Points

- Auscultatory findings of Atrial Septal Defect (ASD) include a wide, fixed split S2 and a systolic murmur from increased pulmonary flow.
- In more severe cases, an S3 murmur and signs of right heart failure and pulmonary hypertension can be noted.
- On electrocardiography, the "Crochetage sign" is characterized by peaked P waves and an incomplete or complete right bundle branch block (RBBB) pattern in the inferior leads.
- Echocardiography demonstrates right-sided heart enlargement and left to right flow across the atrial septal defect, that can vary depending on the degree of defect present.
- A large ASD may require surgical intervention, but a small ASD may be asymptomatic. Prognosis depends on size, the involvement of atrial dysrhythmias, the presence of pulmonary hypertension, and right ventricular failure or dilation.

## Case Description

### *History*

- A 24 year-old patient is referred to a cardiologist for an abnormal EKG and extra beats on routine physical.

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**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_24) contains supplementary material, which is available to authorized users.

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- He is otherwise asymptomatic. He denies dyspnea and cyanosis, though he does experience occasional palpitations.
- His past medical history is unremarkable and he is on no medications.
- His family history is positive for a sister that had an ASD that was recognized and repaired in childhood.

## *Physical Exam*

- Blood pressure of 116/71 mmHg. Pulse is regular at 54 bpm.
- There are no obvious limb abnormalities, though he is double jointed (a trait he shares with his sister).
- JVP and A/V waves are normal.
- Mild RV impulse noted at the lower left sternal border.
- Cardiac auscultation (Fig. 24.1).
  - Grade 1 crescendo-decrescendo systolic murmur.
  - Fixed, split S2 heard at the RUSB.
  - An S3 gallop was noted at the lower left sternal border.

## *Test Results*

- His electrocardiogram showed a right axis RBBB (Fig. 24.2).
- Chest radiography showed a prominent pulmonary artery and mild right ventricular enlargement (Fig. 24.3a, b).

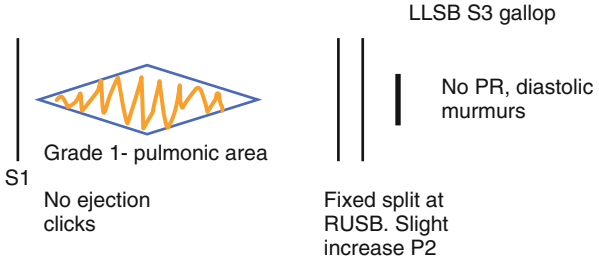


**Fig. 24.1** Typical crescendo-decrescendo systolic murmur of an ASD

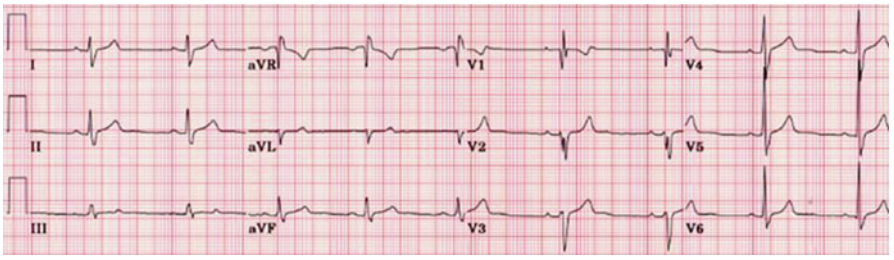


**Fig. 24.2** Right bundle branch block (RBBB) on electrocardiogram

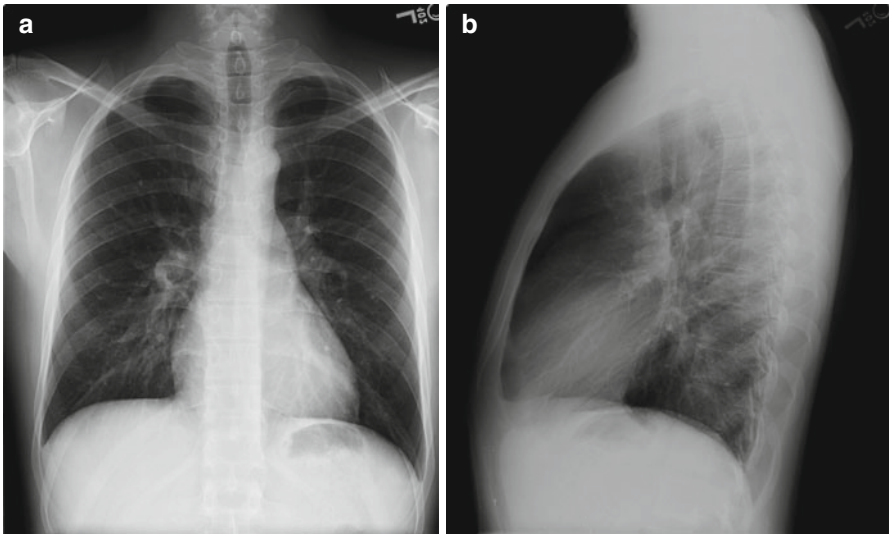


**Fig. 24.3** (**a**, **b**) Prominent pulmonary artery and right ventricular enlargement. (**a**) PA chest radiograph. (**b**) Lateral chest radiograph

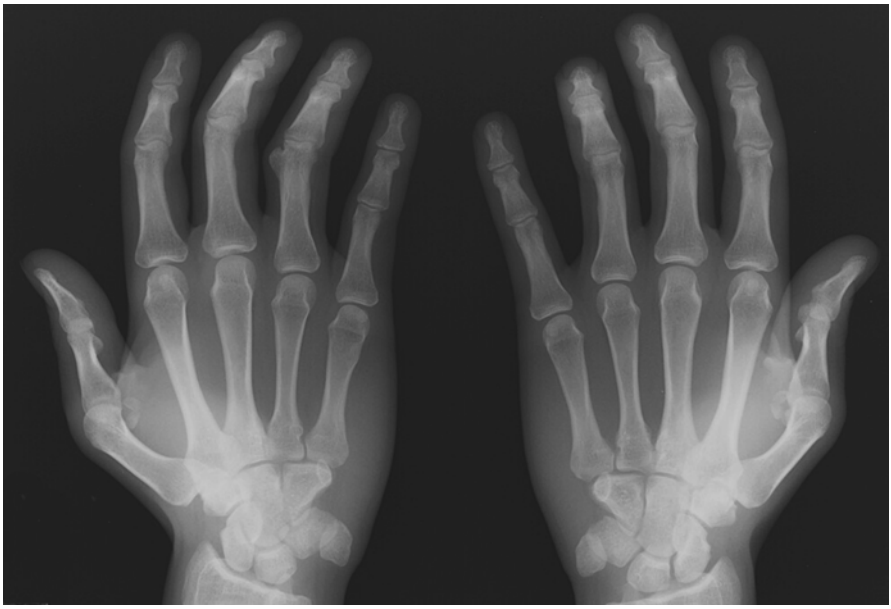

**Fig. 24.4** Mild thenar abnormalities of the hands

- Hand x-rays show mild thenar abnormalities, but grossly radiographically normal (Fig. 24.4).
- Echocardiography showed right atrial and right ventricular enlargement (Fig. 24.5). There was also left to right flow across the atrial septum. A Doppler

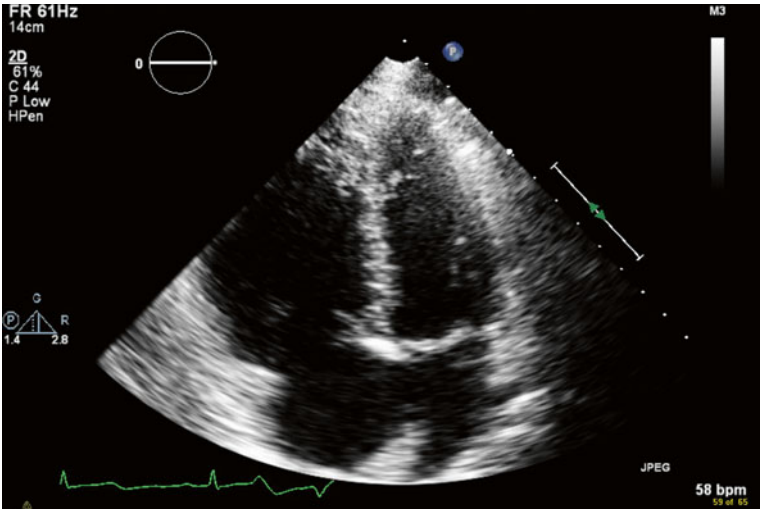


**Fig. 24.5** Echocardiography demonstrating right atrial and right ventricular enlargement

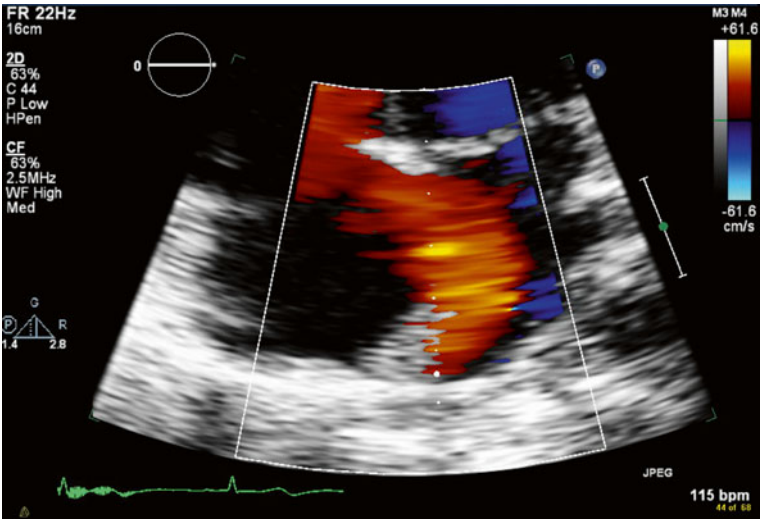


**Fig. 24.6** Left to right flow on Doppler echocardiogram

demonstrated that the left to right flow begins in mid systole and continues to early diastole at a rate of 1 m/s (Fig. 24.6).

- A right heart catheterization showed normal right heart pressures, a pulmonary artery pressure of 24/10 mmHg, and an increased ratio of pulmonary to systemic flow (Qp/Qs) of 2.6:1.

## Clinical Basics

### *Definition*

There are four subtypes of ASD, in decreasing order of frequency (Fig. 24.7):

- Secundum- the most common and arising in the fossa ovalis.
- Primum ASD is often associated with mitral regurgitation.
- Sinus venosus ASD is associated with an anomalous pulmonary venous return.
- Coronary sinus type (uncommon).

### *Symptoms of ASD*

Symptoms of ASD range from asymptomatic to palpitations, dyspnea, and fatigue. Palpitations are a common symptom in patients with ASD and are often secondary to the right ventricular impulse seen with volume overload.

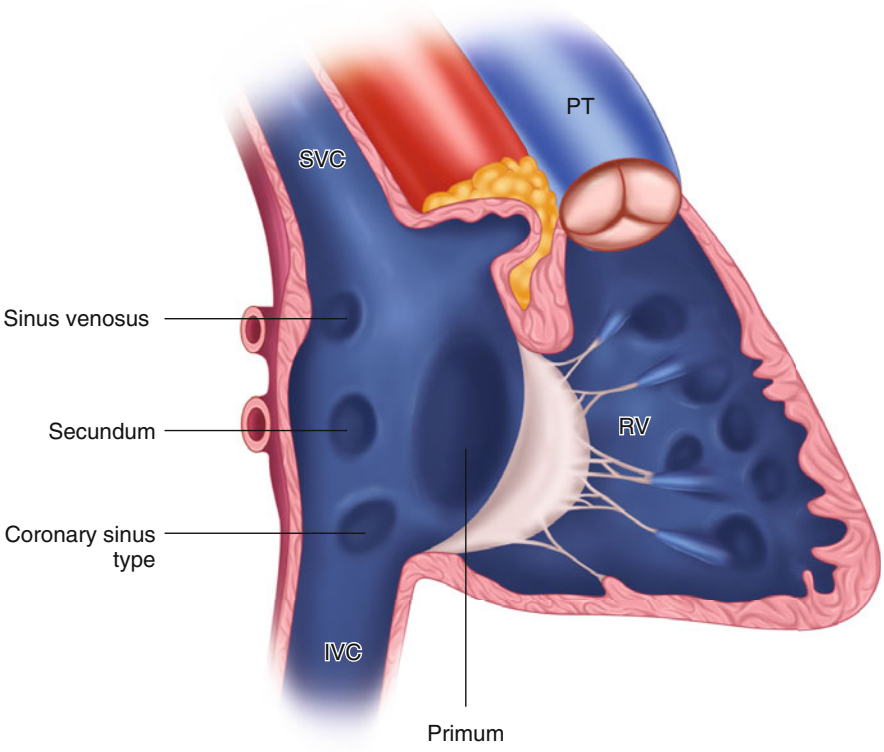


**Fig. 24.7** Location of atrial septal defects

### *Prevalence*

- This defect is the third most common form of congenital heart disease.
- Clinical syndromes associated with ASD include:
  - Hand-Heart syndrome. There can be mild upper limb thenar and carpal functional abnormalities that can appear normal on radiograph. ASD is the most common cardiac finding associated with hand-heart syndrome in 70 % of cases. There may be a genetic basis to this syndrome, but it is heterogeneous with variable penetration.
  - Holt-Oram syndrome is another associated clinical finding of ASD. It is an autosomal dominant disease associated with limb and cardiac abnormalities.

## Key Auscultation Features

- The major auscultation feature of ASD is a fixed, split S2 heart sound.
- The P2 component is typically separated from the A2 component by 30–90 ms.
  - The splitting is not a correlate of the severity of increased pulmonary flow.
  - True fixed splitting must be confirmed in the upright position.
- Other features include a possible split S1, and an ejection sound that may occur with pulmonary artery enlargement.
- A systolic murmur that reflects the pulmonary flow in the LUSB, a right ventricular S3 heard at the LLSB, and a diastolic rumble across the tricuspid valve in high flow states.
- Other clinical findings include an accented V wave on examination of the jugular venous pulse. This V wave reflects the augmented right atrial filling during systole along with tricuspid regurgitation.
- There can also be a pulmonary artery impulse due to pulmonary artery enlargement, or a pulmonic closure sound that indicates a degree of pulmonary hypertension.
  - A pulmonary flow murmur coupled to a fixed, split S2, confirmed in the upright position, distinguishes other pulmonary hypertensive causes from ASD.
  - Some ASDs can have very slight respiratory variations.
  - When pulmonary hypertension develops, and ASD flow drops, the fixed split S2 may disappear (Fig. 24.8).
- Auscultation examples of atrial septal defects.
  - Click here to listen to an example of a wide fixed split S2 in ASD and view an image of the phonocardiogram (Video 24.1).
  - Click here to listen to examples of an ASD with wide splitting of the second sound, as described by Dr. W. Proctor Harvey (Video 24.2).

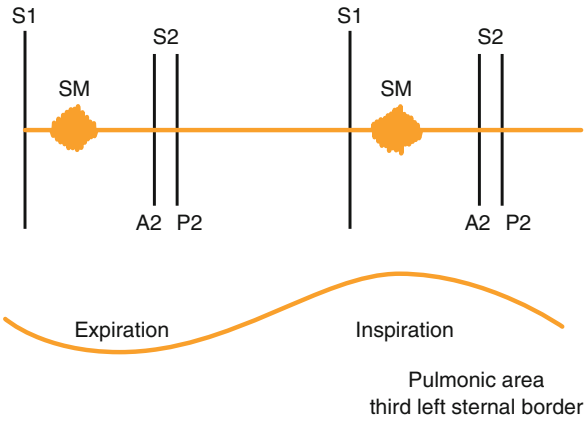


**Fig. 24.8** Atrial septal defects: "fixed" splitting (Modified with permission and courtesy of W. Proctor Harvey, MD, MACC, Jules Bedynek, MD, and David Canfield. Originals published by Laennec Publishing Inc., Fairfield, NJ, and copyrighted by Laennec Publishing, Inc. All rights reserved)

- Click here to listen to examples of an ASD with pulmonary hypertension, as described by Dr. W. Proctor Harvey (Video 24.3).

## Auscultation Differential Diagnosis

- The finding of fixed splitting of the S2 heart sound is unique and pathognomic for ASD, and aided by a concomitant pulmonic flow murmur.
  - Differential diagnosis includes.
    - Bundle branch block with congestive heart failure.
    - Pulmonic stenosis.
    - Anomalous pulmonary vein.
    - An opening snap of mitral stenosis.
- Other associated findings such as the crescendo-decrescendo murmur and the S3 gallop can be due to pulmonary hypertension from other etiologies such as heart failure or primary pulmonary hypertension.

## Diagnostic Implications of the Auscultation Features

- The auscultation exam itself is not predictive of the severity of the septal defect.
- Palpation clues can indicate higher volumes of RV flow.
  - An RV impulse at the left lower sternal border signifies volume overload.
  - A discrete pulmonary artery impulse at the left upper sterna border can be identified in cases with pulmonary artery enlargement.

  - Increased intensity of the pulmonary valve closure sound can signify pulmonary hypertension.

- Contrast-enhanced trans-esophageal echocardiogram (TEE) is considered the gold standard for confirming an ASD [1]. TEE may be enhanced with maneuvers that increase right-to-left shunt such as Valsalva or coughing [2]. If both leftward bulging of the atrial septum and dense contrast filling of the region of the right atrium adjacent to the atrial septum are present, TEE has been shown to have a sensitivity of 95 % [3].

## Prognostic Implications of the Auscultation Features

- Exam findings suggestive of high flow can suggest an adverse prognosis.
  - The size of the defect is the most important predictor for spontaneous closure in children diagnosed with ASD [4].
  - The degree of left to right flow dictates the severity of long-term complications such as pulmonary hypertension or congestive heart failure.
- The age of repair and pulmonary hypertension are important prognostic factors (Fig. 24.9) [5].

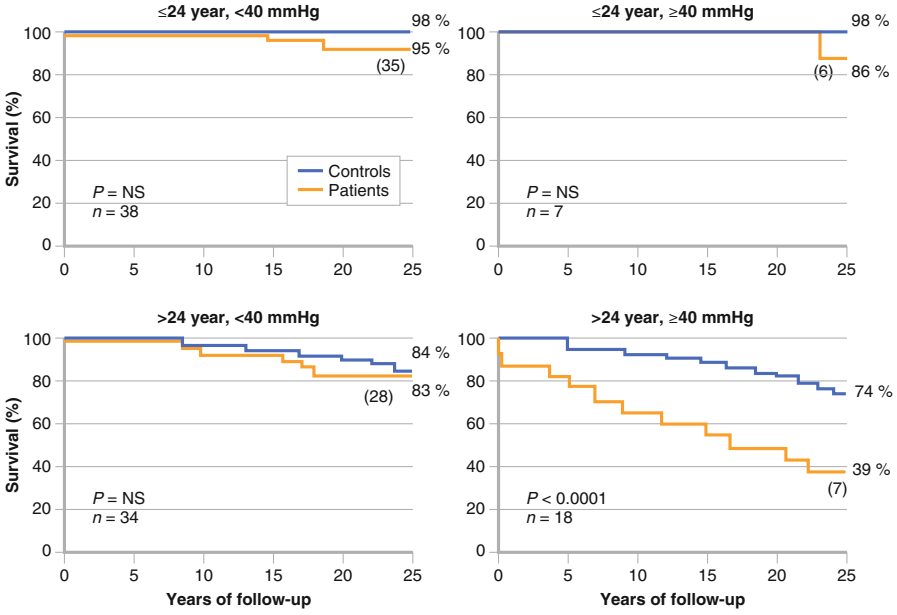


**Fig. 24.9** Long-term survival of patients surviving the peri-operative period, according to age at operate and main pulmonary artery systolic pressure before operation (Used with permission from Murphy et al. [5])

## Statement on Management

- According to ACC/AHA Guidelines, patients with shunts less than 5 mm in diameter with no significant evidence of RV overload (indicated by size on echocardiogram) require no medical therapy. Patients will generally remain asymptomatic throughout life but should be routinely followed.
  - At follow-up, symptoms, including arrhythmias and paradoxical embolic events, should be considered.
  - Repeat echocardiograms are indicated every 2–3 years to monitor changes in RV size, function and pulmonary pressure. In the absence of paradoxical emboli, closure is unnecessary.
- Closure is considered for larger defects (defined as ASDs with diameters greater than 5 mm) with evidence of RV overload. This may prevent the development of atrial arrhythmias, tricuspid regurgitation, right-to-left shunting, CHF, PVD, decreased exercise tolerance and pregnancy-associated embolic events [6].

## Clinical Summary of the Case

The patient presents with a classic ASD, including a fixed split S2, a flow murmur, and exam findings of RV enlargement. The chance occurrence of two children in the same family having an ASD is unlikely, and the possibility exists of a heart-hand syndrome. Exam suggests a large ASD with RV impulse and a right sided S3. With a Qp:Qs of 2.6:1, repair is indicated. Late outcomes are anticipated to be excellent given age at repair <25 years and normal PA pressures.

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# Chapter 25
# Ventricular Septal Defect

**Leonel E. Ampie and Suliman EL-Amin**

## Key Teaching Points

- Physical exam findings suggesting a VSD include a holosystolic murmur at LSB with possible palpable thrill.
- The murmur of a VSD is correlated to size, gradient, and location of the defect.
- Small VSDs are easily identified via physical examination as opposed to the large VSDs. These abnormalities may not require surgery, only bacterial endocarditis prophylaxis.
- Large VSDs commonly present with an S3 gallop, minimal variation, constant quality, and no thrills.
- Physical exam provides clues to diagnosis and defect size, but echocardiography provides confirmation.
- The prognosis after repair of an uncomplicated VSD is favorable.

## Case Description

### *History*

- The patient is an asymptomatic 38 year old male. His wife notices an audible murmur with an occasional thrill while placing her ear on his chest.

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_25) contains supplementary material, which is available to authorized users.

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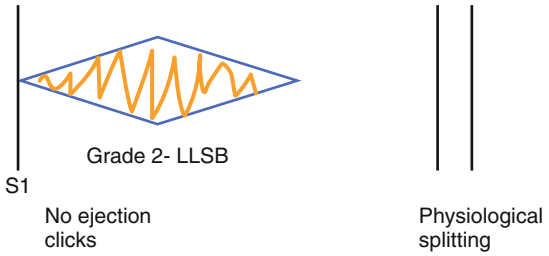


**Fig. 25.1** Grade 2 LLSB crescendo/decrescendo murmur after S1

- He denies any prior history of a murmur during childhood.
- He denies a family history of congenital heart disease.

### *Physical Exam*

- Vital signs normal.
- Chest is clear to auscultation.
  - Jugular venous pulse is normal with normal A and V waves.
  - A grade 2 LLSB crescendo/decrescendo murmur **is** noted after S1 (Fig. 25.1).
- The murmur increases to grade 4 with exertion.
- No ejection clicks noted.
- No diastolic murmurs are present.

### *Test Results*

An electrocardiogram is normal.

## Clinical Basics

### *Normal Anatomy*

Ventricular septum components include the following:

- Muscular septum: muscular trabeculae, muscular outlet and muscular inlet.
- Membranous septum.

## *Definitions*

VSD is a ventricular septal opening caused by improper septal formation (Fig. 25.2a, b).

## *Etiology*

Subtypes of VSD are classified by location:

- Muscular = apical most common (prevalent in neonates).
- Perimembranous = majority of VSD cases (extends into muscular septum).
- Outlet = 5–7 % (approx. 30 % in Far East).
- Inlet (endocardial cushion) = 5–8 %.

## *Signs and Symptoms*

- Signs and symptoms are determined by patient age, size of lesion, and location.
- Adults are primarily asymptomatic, especially with small defects.
- The most common symptom of a VSD is dyspnea.

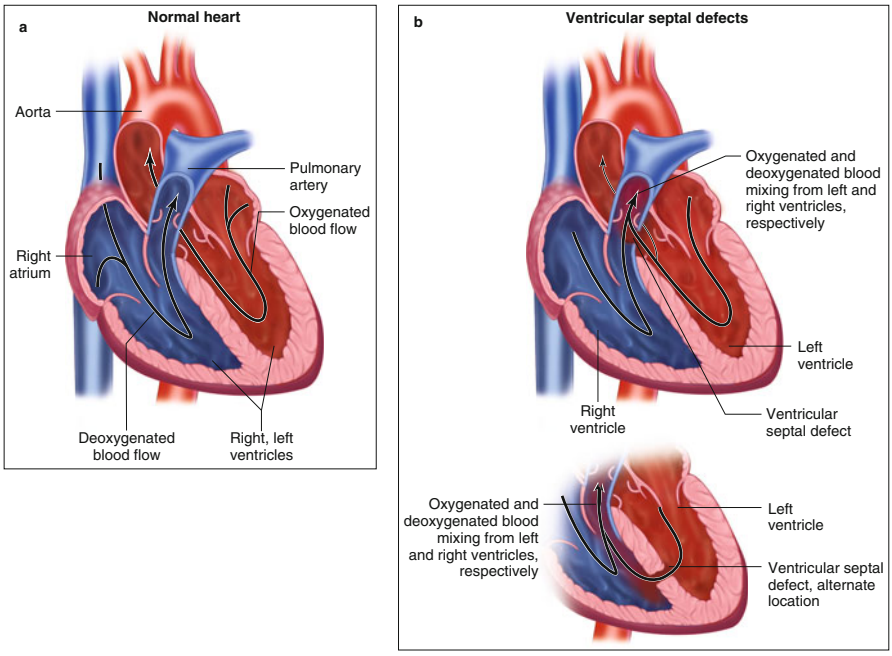


**Fig. 25.2** (**a**) Normal heart anatomy. (**b**) Heart anatomy with ventricular septal defects

### *Prevalence*

VSD is the most common congenital heart defect in adults (20 % of CHD as a solitary lesion) [1].

## Key Auscultation Features of VSD

- Normal S1 and S2 should be present.
  - If S2 is split and/or loud, consider that pulmonary hypertension may be present.
- Systolic murmur.
  - Louder with isometric hand grip and transient arterial occlusion (TAO) [2].
    - TAO: Inflate cuffs on both arms to 20–40 mmHg above peak systolic pressure for 20 s.
  - Small VSD's are the loudest and usually includes thrills [3].
  - The murmur of a VSD begins in early systole and extends through S2.
    - Mid-lower LSB (Infundibular defects heard best at upper LSB).
    - Radiates along LSB or to back.
    - Intensity may vary as the defect changes during contraction with the muscular VSD.
- Diastolic murmur.
  - Diastolic decrescendo murmurs are heard in patients with aortic insufficiency as a complication of the VSD.
  - Noted best at the LSB when the patient is sitting/leaning forward.
  - Large VSDs will have a diastolic rumble at the apex from high flow across the mitral valve [3].
- No extracardiac sounds should be present with a VSD.
- Murmurs may not appear at birth due to equal pressures across the ventricles [3].
- Auscultation examples of a VSD:
  - Click here to listen to a VSD murmur in a 15-year-old boy, as described by Dr. W. Proctor Harvey (Video 25.1).
  - Click here to listen to auscultation findings in a large VSD: harsh holosystolic murmur and soft mid-diastolic rumble; an image of the phonocardiogram is also present (Video 25.2).
  - Click here to listen to auscultation findings in a small VSD: high-pitched short SEM; an image of the phonocardiogram is also present (Video 25.3).

## Clinical Clues to Detect the Lesion

### *Clues to Location*

- Small outlet VSD: second left intercostal space and can radiate into the suprasternal notch.
- Small muscular VSD: short in duration, cuts off in mid-systole (systolic contraction of septal musculature closes the defect).
- Muscular VSD in apical septum may be heard best towards apex.

### *Clues to Size*

#### Small VSD

- No exam findings of LV volume load or pulmonary hypertension.
- Usually normal exam other than murmur.

#### Moderate VSD

- Size 50 % of aortic valve orifice.
- Pansystolic murmur, usually without signs of RV volume or pressure overload. Chamber enlargement (left atrium, left ventricle) common.
- S2 split, P2 usually normal.

#### Large VSD

- Size approximates aortic valve orifice.
- Abnormal palpation showing signs of RV overload.
- Findings of pulmonary hypertension: S2 narrow/single.
- Murmur: Decrescendo or atypically soft as gradient between the RV and LV may be minimal.
- EKG: RV hypertrophy should be present.

## Differential Diagnosis of a VSD Murmur

- Any harsh systolic murmur could be confused for VSD. Because VSDs are less common than acquired valvular lesions (such as aortic stenosis, or mitral regurgitation), recognizing a VSD requires a high degree of suspicion.

  - Consider the patient. If the patient is relatively young, and otherwise healthy, VSD becomes a more likely possibility among systolic murmurs.
- Mitral regurgitation: classic radiation to the axilla should not occur with a VSD.
  - Eccentric MR murmurs may radiate to the parasternal area, particularly with posterior leaflet abnormalities.
- Aortic stenosis: Usually more crescendo/decrescendo in quality. The A2 should be abnormal in AS, and the AS murmur will not increase with afterload maneuvers.
- Pulmonic stenosis: May have ejection clicks, unlike VSD. May have abnormal RV findings (parasternal impulse) making it easy to confuse with VSD.

## Diagnostic Implications of the Auscultation Features

### *Murmur Quality Variations* (Fig. 25.3)

Depending on the magnitude of the septal defect, the murmur quality varies due to differences in pressure gradients.

### *Estimating Pressure Gradients* (Table 25.1)

Murmur "pitch" via echo can help predict gradient severity.

- The "inching" technique can be utilized to predict gradient severity.
- It involves incrementally moving the stethoscope to the point of highest frequency.
- 63 % of gradients predicted to within 10 mmHg; R = 0.76 for gradients <60 [3].

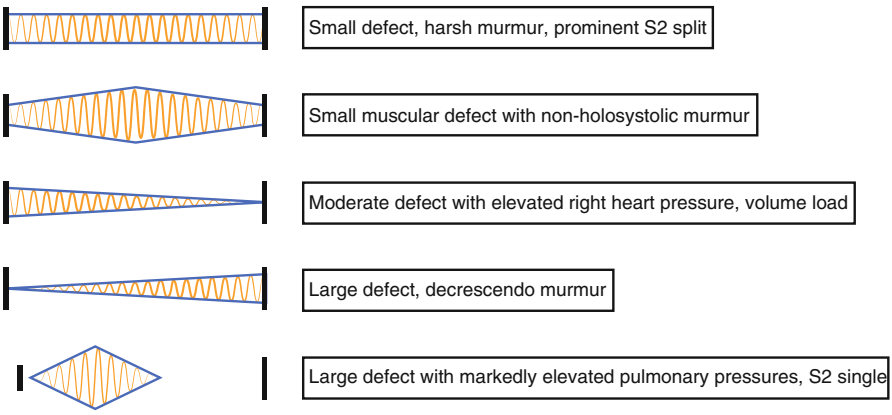


**Fig. 25.3** Cardiac murmurs produced by differing VSD size defects

**Table 25.1** Estimation of pressure gradients by auscultation

| Murmur's frequencies | Estimated pressure gradient (mmHg) |
|---|---|
| All low frequencies | <10 |
| Low with some medium | ~15 |
| Little low with mostly medium | ~20 |
| Primarily medium frequencies | ~25 |
| Trace high frequencies | ~30 |
| Mild high frequencies | ~35 |
| "Easily heard" high frequencies | ~40 |
| Prominent high frequencies | ~50 |
| "Considerable" high frequencies | 55–60 |

Used with permission from Phoon [10]

## *Confirmatory Testing in VSD*

### EKG

- Highly dependent on size/location.
- Small VSD: Normal.
- Exception: LAD with inlet VSD.
- Moderate VSD:
- LV volume load findings, e.g., LAE, LVH.
- Large VSD:
- Biventricular hypertrophy findings.
- 66 % of patients may have normal results at ECG and up to 8 % of patients may be concurrently in sinus rhythm [4].
- With severe VSD and Eisenmenger's syndrome development, patients may present with right atrial enlargement, ventricular hypertrophy, and right-axis deviation findings on ECG.

### Chest X-Ray

- Pulmonary vascularity and cardiac silhouettes appear normal in small VSD.
- Cardiomegaly may be noted in those that progress to Eisenmenger's syndrome.

### Echocardiography

- Parasternal views are most productive to distinguish among different locations for VSD (Fig. 25.4a, b).

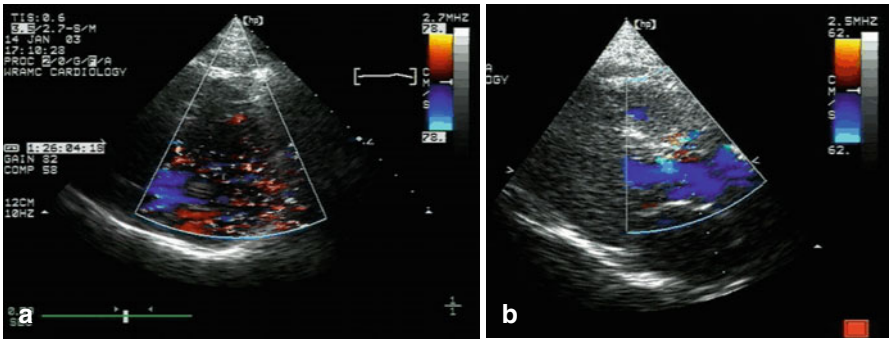


**Fig. 25.4** (**a**) Muscular VSD. (**b**) Perimembranous VSD

## Prognostic Implications of the Auscultation Features

- Dependent on size and subsequent defects that precipitate as a result.
  - Small uncorrected VSD 95.5 % at 8 year follow-up (mean age 30) [5].
- Unclosed defects may lead to Eisenmenger's syndrome, heart failure, arrhythmias, aortic regurgitation, and pulmonary hypertension.
- Small VSDs predisposes to endocarditis due to the turbulent flow [6].
- Young patients: spontaneous closures of the VSD may result in up to 60 % of patients [7].
  - Spontaneous closure results in muscular defects or membranous defects.
- Closure is more common in women with muscular/membranous defects [7].
- A mean pressure less than 20 mmHg carries an excellent prognosis [8].
- Large VSDs should be close in the first year in life.
  - If untreated, will lead to pulmonary over-circulation resulting in heart failure [9].

## Clinical Summary of the Case

The patient presents with a classic, small muscular VSD characterized by a short, intense murmur at the left lower sternal border that has an inducible intensity. This type of VSD is less common than a perimembranous VSD. Findings in this case, typical for small muscular VSD, are limited to the murmur. These can be difficult to define echocardiographically. Late outcomes are highly favorable, left unrepaired. Endocarditis prophylaxis may be considered.

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# Chapter 26
# Patent Ductus Arteriosus

**Brynn Connor, Victoria Eng, Meghan C. Kusko, and Kathryn Maselli**

## Key Teaching Points

- Patent ductus arteriosus (PDA) is a congenital heart defect where the ductus arteriosus maintains a shunt between the left pulmonary artery and the aorta. This can lead to pulmonary complications, endarteritis, and heart failure.
- PDA classically presents with a continuous crescendo-decrescendo murmur described as "machinery-like." This is only truly continuous in patients with large shunts; premature infants may present with a purely systolic murmur.
- Soft, but audible murmurs may be asymptomatic. Louder murmurs may be indicative of a larger PDA; if left untreated, this may lead to persistent elevation in pulmonary vascular resistance.
- Elevated pulmonary vascular resistance may precipitate Eisenmenger's syndrome, whereby shunting is reversed and patients experience a subsequent cyanotic presentation. In the adult, this presents as pulmonary hypertension.
- Doppler echocardiography is the gold standard for visualizing the degree of shunting through the PDA.
- Decision to treat should be based upon a combination of clinical signs and echocardiographic parameters. Treatment options include pharmacological closure in infants, catheterization, or surgical ligation [1].

**Electronic supplementary material** The online version of this chapter (doi:10.1007/978-1-4471-6738-9_26) contains supplementary material, which is available to authorized users.

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## Case Description

### *History*

- A 38 year-old woman was referred due to the chief complaint of intermittent, atypical left-sided chest pain.
- In 1994, a non-specific heart murmur was detected, and echocardiography was reported as showing nonspecific findings.
- In the late 1990s, repeat echocardiography revealed a PDA. No specific management was undertaken.

### *Physical Exam*

- Her physical exam revealed a blood pressure of 120/70 mmHg and a pulse of 70 beats per minute.
- A subtle, dull impulse was noted at the RUSB, and the P2 was intermittently palpable. There were no abnormal LV findings.
- The chest was clear to auscultation.
- Cardiac auscultation revealed a "machinery-like" crescendo-decrescendo murmur at the left upper sternal border, specifically in the second and third intercostal spaces (Fig. 26.1).

### *Test Results*

- Echocardiography showed PA enlargement, LA/LV volume overload, and a wall hugging color flow jet at the bifurcation coursing down to the pulmonic valve (Fig. 26.2).
- Doppler showed a continuous, high velocity jet exceeding up to 4 m/s (Fig. 26.3). Mild pulmonary hypertension was present.

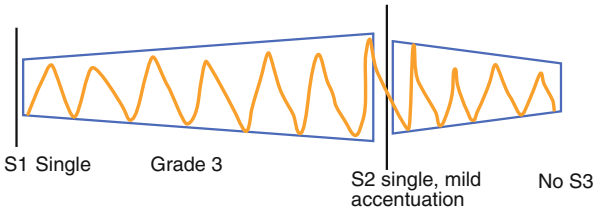


**Fig. 26.1** Schematic of the PDA murmur. Between S1 and S2, the murmur gradually becomes more audible. In contrast, between S2 and S1, the murmur gradually becomes less audible. These findings are consistent with the classic crescendo-decrescendo murmur found in PDA

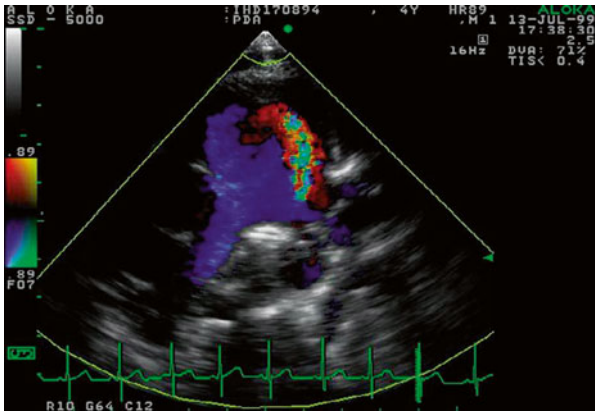


**Fig. 26.2** Echocardiographic findings of a PDA: a color flow jet at the bifurcation coursing down to the pulmonic valve

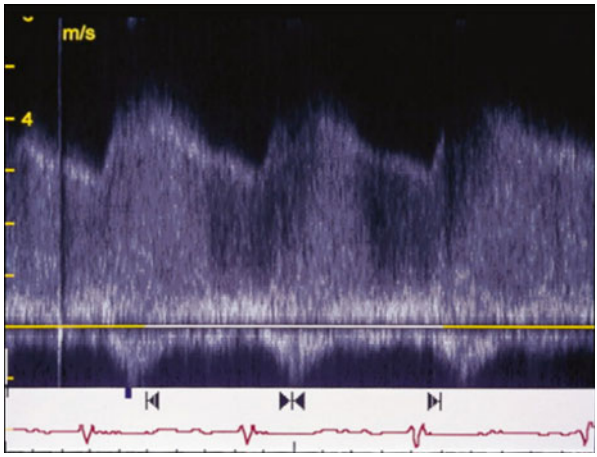


**Fig. 26.3** Doppler of PDA

## Clinical Basics

### *Normal Ductal Anatomy* (Fig. 26.4)

- The ductus arteriosus leaves the main pulmonary artery at its junction with the left pulmonary artery and continues posteriorly to reach the descending aorta about 5–10 mm distal to the origin of the left subclavian artery.
- It functions to divert up to 55 % of the cardiac output of the right ventricle away from the high resistance pulmonary circulation to the low resistance umbilical-placental circulation.
- Its patency is physiologically preserved in the neonatal period due to low P02, local prostaglandins, and local nitric oxide release [2].

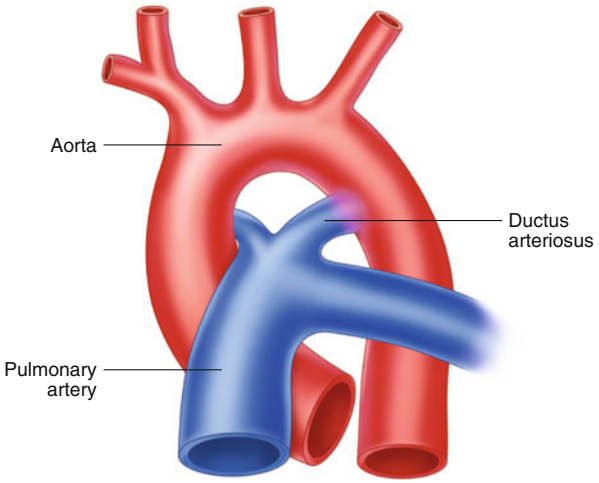


**Fig. 26.4** During embryogenesis and in PDA, the ductus arteriosus joins the pulmonary circulation to the systemic circulation via a direct connection between the pulmonary artery and the aorta

## *Functional Closure* [2]

- Typically occurs within 24 h of birth.
- Physiologic mechanisms include: (1) smooth muscle constriction, (2) reduced pulmonary vascular resistance due to lung expansion (3) increasing oxygen tension (4) reduced prostaglandin levels.

## *Anatomic Closure* [2]

- Typically occurs within 2–3 weeks of birth to form the ligamentum arteriosum.
- Physiologic mechanisms include: (1) medial hypoxia (2) smooth muscle cell death (3) endothelial cell proliferation stimulated by hypoxic induced growth factor release (4) intimal thickening and fibrosis.

## *Differential Diagnosis for Patency*

- Premature birth.
- High altitude.
- Congenital Rubella.

- Concurrent Congenital Heart Disease: In patients with other CHDs, about 15 % also present with PDA [2].
  - Coarctation of the Aorta.
    - PDA is observed in 2/3 of patients.
    - However, the presence of a large PDA can lower the accuracy of diagnosis of a coarctation, leading to significant morbidity and mortality [3].
    - The blood pressure differential normally observed between the upper and lower limbs is partially alleviated by the ductal shunt.
    - Echocardiographic Doppler diagnosis is diminished due to the amelioration of high velocity flow across the coarctation by the ductus [4].
- Interrupted aortic arch.
  - Presence of PDA is essential for systemic perfusion.
  - The absence of a PDA is associated with a 90 % mortality rate in the first month without surgical correction [5].
- Hypoplastic Left Heart Syndrome.
  - Systemic perfusion is dependent on a PDA and ASD.
  - Mortality approaches 95 % within the first month if the ductus does not remain patent.
- Transposition of the Great Arteries [6].
  - PDA is observed in 2/3 of patients.
  - Patency is essential for survival in the pre-operative period, with a 60 % mortality rate in the first 6 months.

## *PDA Morphological Classification* (Fig. 26.5a–e)

- The different morphological variants of a PDA have been categorized according to the Krichenko system of angiographic classification.
- Angiographic classification is the current basis for determining whether the patent ductus can be closed via catheterization.
- Referring to Fig. 26.5a–e:
  - Type A or Conical: well defined aortic ampulla and constriction near the pulmonary artery end.
  - Type B or Window: wide and short ductus that yields no demarcation between the aortic and pulmonary end.
  - Type C or Tubular: long tubular duct without constriction.
  - Type D or Complex: multiple constrictions.
  - Type E or Elongated: long with remote constriction from the anterior edge of the trachea.

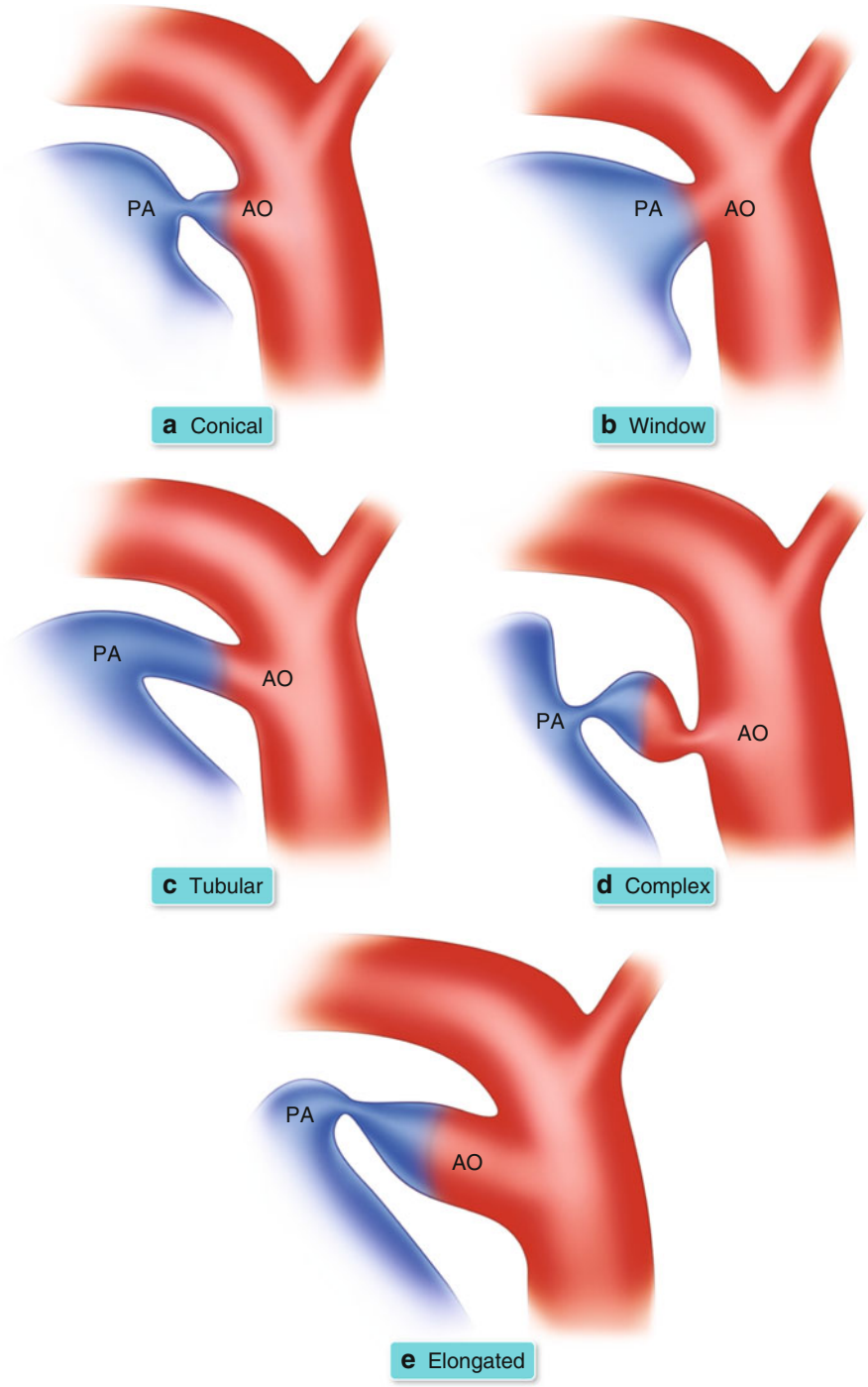


**Fig. 26.5** (**a**–**e**) Illustration of morphological classification of PDA according to principles in Krichenko et al. [16]

## *Etiology*

- Hypothesized to be partial replacement of the smooth muscle cells in the media of the ductus by collagen and elastic fibers [2].
- Most well-known cause of PDA is premature birth.
- While there appears to be no clear genetic cause, the following genetic abnormalities have been associated with PDA [7]:
  - Trisomy 21.
  - 4p syndrome, also known as *Wolf–Hirschhorn syndrome (WHS), Pitt-Rogers-Danks syndrome (PRDS), or Pitt syndrome.*
  - Carpenter's syndrome.
  - Holt-Oram syndrome.
  - incontinentia pigmenti.
  - Char syndrome.
- Genetic influences in PDA appear to be inherited in an autosomal recessive pattern with incomplete penetrance. Siblings have a 3 % rate of concordance in PDA [7].

## *Natural History*

- The natural history of PDA can include long-term, morbidity-free survival.
- For those over the age of 20, infective endocarditis is the most common adverse event, followed by left ventricular consequences, then right ventricular abnormalities.

## *Signs and Symptoms*

- The findings on imaging and laboratory analysis show wide variation in concordance with the degree of shunting present.
- The determined size and magnitude of the shunt can then be utilized to better elucidate the natural course and likely symptomatology of an unrepaired shunt.
- Physical exam findings:
  - Hyperdynamic precordium.
  - Bounding pulses.
  - Wide pulse pressure >20 mmHg.
  - Tachycardia.
  - Chest.

    - Clear to auscultation.
    - Chest X-Ray.
        - Small Shunt – normal chest x-ray.
        - Large Shunt:
            - Left atrial and ventricular enlargement.
            - Increased pulmonary vascular markings in older children and adults.
- Cardiac palpation may reveal:
    - Subtle dull impulse at right upper sternal border
    - Intermittent, palpable P2

### *Prevalence*

- The frequency of PDA ranges from 1 in 2000 to as high as 1 in 500 births and comprises 5–10 % of congenital heart diseases [2].
- Appears to be a female predilection.

## Key Auscultation Features

- "Machinery-like," crescendo-decrescendo murmur at left upper sternal border, in the second and third intercostal spaces [8].
- The continuous murmur of PDA peaks at or just before S2.
    - Earlier peak indicates greater PDA flow.
- The murmur will be loudest at the 2nd left intercostal space, greater than the first intercostal space.
- Other features include that S2 may be paradoxically split, and a diastolic mitral murmur may be audible from high flow across the mitral valve.
- Variations:
    - In premature infants, the murmur is primarily systolic; continuous murmurs are rarely heard [8].
    - With increasing size of shunt (usually in older patients), the murmur becomes louder and more prolonged, extending into diastole [8].
    - Auscultation examples of PDA.
        - Click here to listen to an example of a PDA with a long diastolic component, continuous murmur, and view an image of the phonocardiogram (Video 26.1).
        - Click here to listen to an example of a PDA with a short diastolic component, more typical of PDA, and view an image of the phonocardiogram (Video 26.2).

## Clinical Clues to the Detection of the Lesion

When detected, other findings can be helpful:

- EKG [7]:
  - Small shunts – normal.
  - Moderate-large shunts – left ventricular hypertrophy, left atrial enlargement, sinus tachycardia.
- Echocardiography [7]**:** Echocardiography *is* the gold standard for definitive diagnosis.
  - Findings.
    - General: pulmonary artery enlargement, left atrial and left ventricular overload.
    - Shunt Size.
      - Small shunt:
        - Normal sized chambers.
        - Left to right shunting at origin of the left pulmonary artery.
      - Moderate-large shunt:
        - Enlarged left atrium and ventricle.
        - Left to right shunting at origin of the left pulmonary artery.
- Shunt Direction.
  - Bidirectional: right to left in early systole and left to right in late systole due to high pulmonary vascular resistance and pulmonary hypertension.
  - Left to right: decreased pulmonary vascular resistance, peaks in late systole resulting in pulsatile pattern.
    - Can be correlated with retrograde diastolic flow in the descending aorta.
  - Restrictive PDA: pulsatility is absent, correlates with closing or insignificant PDA.
- Analysis should include:
  - Measurement of chamber sizes and functionality.
  - 2D imaging of the ductus anatomy.
    - Look at ratio of the PDA at its smallest diameter to the left pulmonary artery diameter. This ratio is used to classify the PDA as small, moderate, or large [1] and is the *strongest predictor of spontaneous closure.*
    - Disadvantage: does not reveal the direction of shunting.
  - Color Doppler to elucidate shunt directionality and degree of constriction (ductal diameter).

    - A color jet of greater than 1.6 mm correlates with a significant left to right shunt in neonates.
    - Disadvantage: overestimation of the smallest ductal diameter.
  - Echo provides the following determinations [9]:
    - Ductus patency, identified as a notable color flow jet entering the pulmonary trunk near the origin of the left pulmonary artery.
    - The direction and velocity of the shunt in which:
      - Low pulmonary vascular resistance: shunt will be from left to right.
      - High pulmonary vascular resistance: shunt will be from right to left.
      - Systemic vascular resistance ~ pulmonary vascular resistance: shunt will be bidirectional, right to left followed by left to right.
      - Significance of the shunt on the systemic and pulmonary circulations includes and the finding of a left atrium:aorta ratio >2 as a reliable marker of a hemodynamically significant shunt [2].
  - Pulsed Doppler (Fig. 26.3) can be used to assess the pattern and velocity of the shunt, and disturbances to diastolic blood flow on either side of the duct [9].
- Labs: circulating B-type natriuretic peptide, secreted by ventricles under hemodynamic stress or CHF, can be a sensitive and specific indicator of hemodynamically significant PDA that requires treatment.
  - Levels between 70 and 100 pg/mL have been used to diagnose symptomatic PDA.

## Auscultation Differential Diagnosis

- Venous hum.
- AV fistula.
- Arteriovenous malformation.
- Subclavian arterial stenosis.
- Aortic coarctation with large subcostal collaterals.
- AP window, which is lower along left sternal border.
- Ruptured sinus of valsalva aneurysm.
- Coronary cameral fistula.
- VSD complicated by AR.

## Diagnostic Implications of the Auscultation Findings

- Pulmonary Resistance and Auscultation.
  - Normal Pulmonary Resistance: continuous flow through the PDA and a continuous murmur will be heard, indicating a restrictive defect.

  - Increasing Pulmonary Resistance: diastolic flow will begin decreasing, leaving only the systolic murmur.
  - High pulmonary resistance: PDA murmur can disappear (typically seen in pulmonary hypertension).

- Premature infants with PDA will not present with the classic continuous murmur but will have a systolic only murmur.
- As size of shunt increases, the murmur gets louder and extends into diastole.
- The murmur is only truly continuous in patients with large shunts (may also have bounding peripheral pulses).
- PDA can be silent, especially in premature infants.
- Clinical signs are specific but early, sensitive diagnosis can be aided by imaging [1].

## Prognostic Implications of the Auscultation Findings

- Size of the duct is the major factor driving prognosis.
  - Small PDAs typically have a small but audible murmur which may be continuous.
  - Larger PDAs will have a louder, continuous machinery-like murmur.
  - Diastolic murmur at apex indicates a larger shunt.
  - Increased pulse pressure indicates a larger shunt.
  - Larger PDAs may lead to CHF or pulmonary hypertension.
  - Disappearance of murmur indicates reversal of shunt and development of Eisenmenger's syndrome.
- Typically patients with a small PDA will have a small but audible murmur [7].
  - Usually asymptomatic.
  - Can present in childhood or adulthood.
- Adults with a small PDA and minimal reactive pulmonary hypertension and myocardial changes have a normal life expectancy.
- In infants with an audible murmur and a symptomatic left to right shunt through the PDA:
  - Treatment with indomethacin to close the ductus has a good prognosis with no significant association with neurodevelopmental impairment [10].
  - Surgical ligation of the duct also has a good prognosis, although studies have shown an increased association with chronic lung disease [10].
- Large to moderate PDAs will present with a louder, continuous machinery-like murmur.
  - A diastolic murmur at the apex, prominent left ventricular impulse, and increased pulse pressure can all indicate a larger PDA [7].
- In both children and adults, a larger PDA can lead to CHF or pulmonary hypertension if untreated due to pulmonary overcirculation and left volume heart overload [11].

- If untreated, the mortality rate due to PDA is 20 % by age 20 years, 42 % by age 45 years, and 60 % by age 60 years.
- If the PDA is unrepaired, in some cases, the original left to right shunt can increase the flow through the pulmonary vasculature to the point of pulmonary hypertension.
  - This increased pulmonary resistance places an increased pressure on the right side of the heart, which can actually reverse the shunt into a right to left shunt.
  - This is known as *reverse ductus or Eisenmenger phenomenon* (Fig. 26.6a–c).

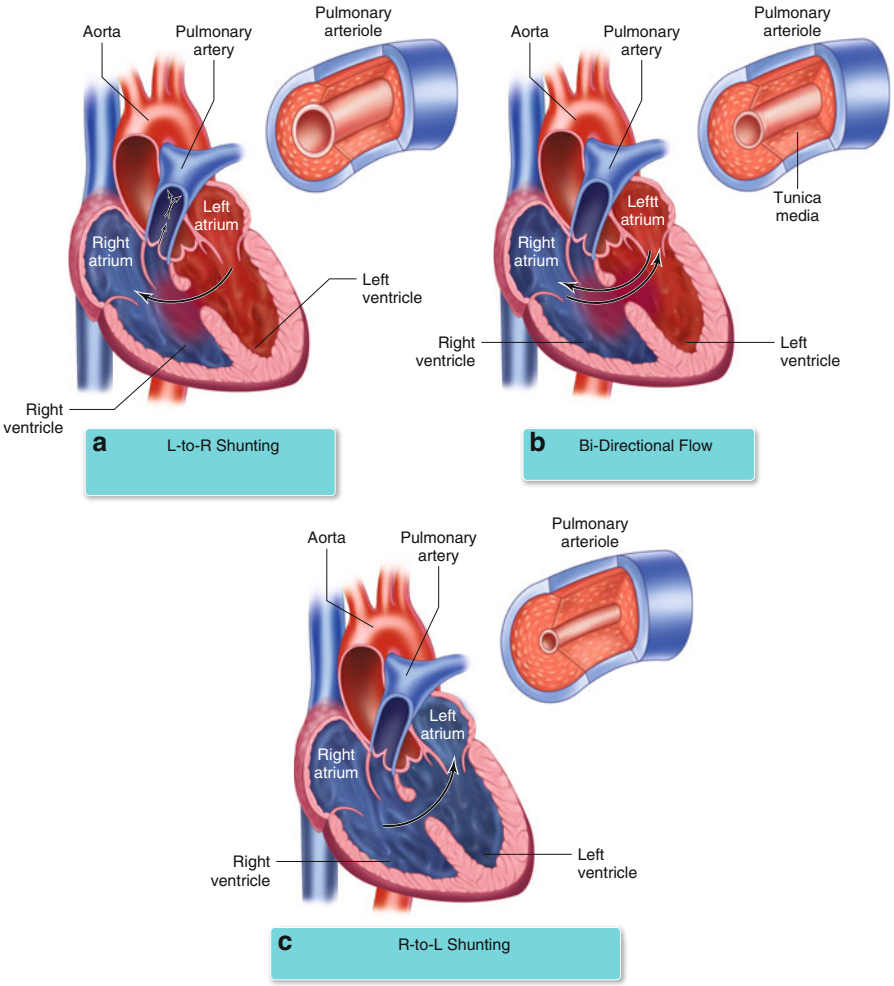


**Fig. 26.6** (**a**–**c**) Eisenmenger's syndrome can occur with an ASD, VSD, PDA, or other complex defects. Initially, flow through the defect occurs in a left-to-right direction (**a**: L-to-R shunting). Over time, pulmonary vascular resistance increases as a result of increased flow through the pulmonary vasculature due to the defect (**b**: bi-directional flow). Eventually, increased pulmonary resistance can cause the flow of blood to change from left-to-right flow to right-to-left, leading to the development of Eisenmenger's syndrome and cyanosis (**c**: R-to-L shunting)

  - The classic physical findings of reverse ductus are reversed or bidirectional shunt, which can be seen on an echocardiogram, and differential clubbing and cyanosis.
    - On echocardiography, the reversed shunt will deliver deoxygenated blood from the pulmonary artery to the aorta, instead of from the aorta to the pulmonary artery via the PDA as seen previously. Because the PDA joins the aorta and pulmonary artery distal to the left subclavian artery, the upper limbs will not be affected but the lower limbs will show clubbing and cyanosis as seen in Fig. 26.7a–d [11].
  - At this point, the murmur caused by the PDA will no longer be heard [7].
- Disappearance of the murmur and development of Eisenmenger's syndrome has a good short-term prognosis but markedly reduces life expectancy and quality of life [12].
  - Survival rates at 30, 40, and 55 years of age are 77, 70, and 55 % and overall life expectancy is reduced by 20 years [13].
  - In patients with a large PDA and pulmonary hypertension, the most important determinant of prognosis is whether the pulmonary hypertension is reversible.
  - In patients with reversible pulmonary hypertension, ligation of the PDA is beneficial [14].
  - By the time Eisenmenger's syndrome develops, however, pulmonary hypertension is irreversible.
- In older patients with a PDA, duct size is one of the most important prognostic factors.
  - Most patients who survive past 60 years-old without repair have a luminal diameter of 6 mm or less [15].
- In infants, the most important factor for predicting a hemodynamically significant PDA is diameter [2]:
  - Diameter >1.5 mm predicts a significant PDA.
    - 81 % sensitivity.
    - 85 % specificity.
- As patients with a PDA age, there is a progressive increase in heart size, even with a small ductus [15].

## Treatment

- Ductus closure is indicated for any child or adult who is symptomatic from significant left-to-right shunting through the PDA.
- In asymptomatic patients, closure is indicated for patients with significant left-to-right shunting and left heart enlargement as this will reduce the risk of further complications [7].

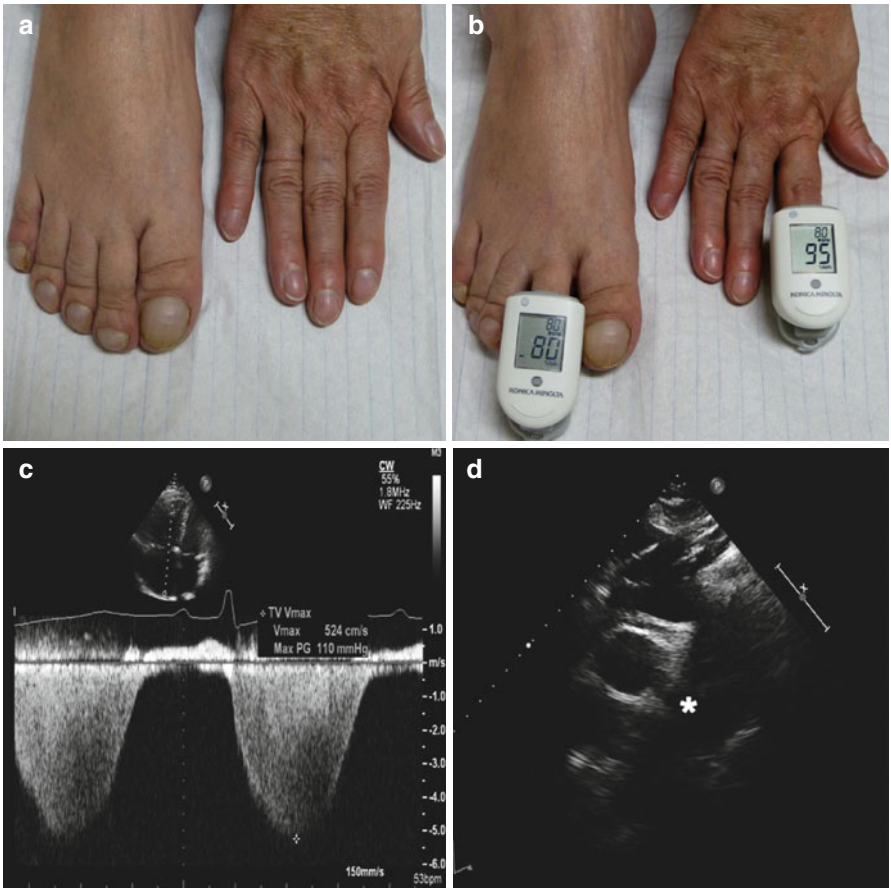


**Fig. 26.7** (**a**–**d**) 52-year-old woman was seen at the outpatient clinic for adults with congenital heart disease. Cardiac auscultation revealed a single and loud S2 and a soft pansystolic murmur of tricuspid regurgitation. On clinical examination, clubbing of the toes was noted and cyanosis was present only in the lower half of the body, whereas her fingers did not present evidence of clubbing or cyanosis (**a**). Using the same pulse oxymeter model simultaneously at her fingers and her toes while breathing room air, differential cyanosis ($SO_2$ toes 80 %, $SO_2$ fingers 95 %) could be confirmed (**b**). On 10 L $O_2$ via nasal cannula $SO_2$ on the lower extremities remained unchanged, whereas $SO_2$ increased in the upper extremities. Echocardiographically, a suprasystemic right ventricular systolic pressure was measured (estimated systolic pulmonary arterial pressure 120 mmHg) with an arm-cuff blood pressure measurement of 115/83 mmHg (**c**). As clinically suspected, a large patent ductus arteriosus (PDA) was found (marked with *asterisk* in **d**) (Used with permission from Moccetti et al. [17])

- Therapeutic catheterization is the treatment of choice and is highly effective with a success rate of greater than 90 % (Fig. 26.8a–e).
  - In transcatheter occlusion, a catheter is advanced across the ductus and a coil is positioned to occlude the duct [7].
  - If the duct has unfavorable anatomy such as large size or torturous path, catheterization may not be possible and the duct must be closed by surgical ligation [8].

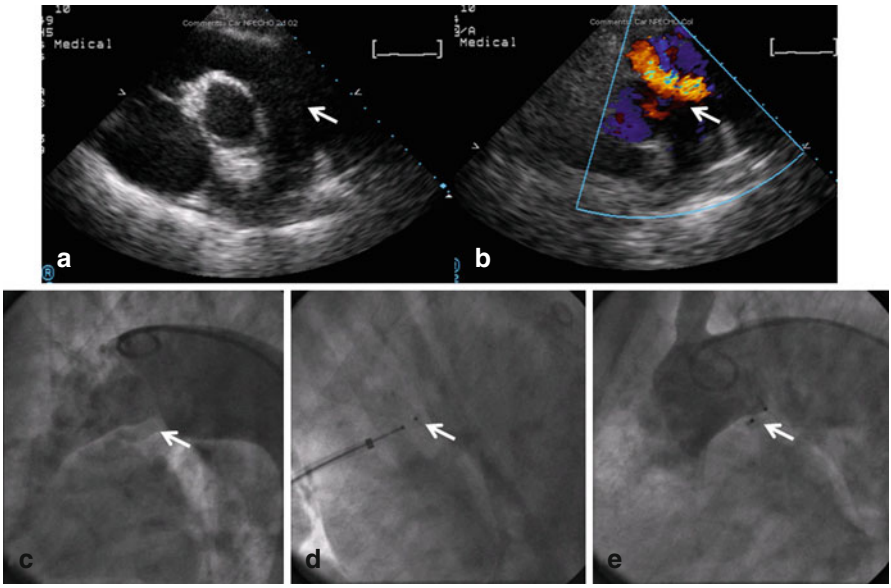


**Fig. 26.8** (**a**–**e**) Patent ductus arteriosus (PDA) pre- and post-percutaneous closure. *White arrow* identifies findings. (**a**) Echocardiogram showing pulmonary artery dilation. (**b**) High velocity color jet into the left pulmonary artery. (**c**) Aortography showing aorta-pulmonary artery shunt. (**d**) Placement of percutaneous delivery of an Amplatzer occluder. (**e**) Post-occlusion aortagram showing closure of the PDA

- Extremely premature infants with PDA are placed on ventilation and pharmacological therapy rather than surgery/catheterization as the standard of care.
  - Indomethacin or ibuprofen is given to close the PDA.
  - These are COX inhibitors that lead to reduced synthesis of prostaglandins and falling levels of prostaglandins are what drives closure of the PDA.
- Patients with a symptomatic PDA will usually improve after treatment with diuretics and digoxin to treat their congestive heart failure [7].
  - These patients may also benefit from treatment with an angiotensin-converting enzyme inhibitor to reduce afterload.
  - Medical therapy for CHF is typically short term until the PDA can be closed by catheterization.
  - Patients with significant symptoms and cardiomegaly may require long-term treatment [7].
- Prophylaxis for infective endocarditis is recommended for all patients with PDA until 6 months after closure.
- Patients with PDA and pulmonary vascular disease may benefit from pulmonary vasodilating agents such as chronic oxygen, PGI2, calcium channel blockers, endothelin antagonists, and phosphodiesterase type 5 inhibitors, although there

are no systematic studies on the benefit of these agents in patients with PDAs and high pulmonary vascular resistance [7].
- If pulmonary vascular resistance decreases, these patients may undergo closure of the PDA.

## General Statement on Management

- Definitive diagnosis should be based on visualization with imaging techniques and demonstrating shunting across the defect (with or without LV volume overload).
- For an uncomplicated PDA, diagnostic cardiac catheterization is not recommended with adequate non-invasive imaging.
- Maximal exercise testing is not recommended for PDA with significant PAH.
- Diagnostic workup includes determining the presence and size of the PDA; the functional effect of the shunt on the left atrium, left ventricle, and pulmonary circulation; and any associated lesions.
- For small PDA without LV volume overload, routine follow up is recommended every 3–5 years.
- Endocarditis prophylaxis is not recommended for those with a repaired PDA and no residual shunt.
- Surgical closure (percutaneous or surgically) is indicated with LA and/or LV enlargement, if PAH is present, or if there is a net left to right shunt; also indicated with prior endocarditis.
- Careful evaluation and consultation is needed before selecting surgical closure for patients with a significantly calcified PDA.
- Surgical repair is indicated when the PDA is too large for device closure or the duct is tortuous (precludes device closure).
- Small PDAs can be closed via catheter device.
- PDA closure is reasonable for patients with PAH with a net left-right shunt.
- PDA is not recommended for patients with PAH and a net right-left shunt.

## Clinical Summary of the Case

In this case, PDA presents with a continuous machinery murmur indicative of a restrictive defect. The exam suggesting increased pulmonary pressure is concerning. The patient's chest pain may be related to mild pulmonary hypertension, or the high flow. The fact that the patient has not lost the diastolic murmur is an important finding indicating that PVR has not risen too much. However, sizing of the PDA, and coil closure is indicated due to the mild pulmonary hypertension, and apparent symptoms.

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