Mitral valve disease: clinical features focusing on auscultatory findings including auscultation of mitral valve prolapse

Abbreviations

AF: atrial fibrillation

AR: aortic regurgitation

AS: aortic stenosis

HCM: hypertrophic cardiomyopathy

LA: left atrium

LV: left ventricle

MVP: mitral valve prolapse

MR: mitral regurgitation

MS: mitral stenosis

OS: opening snap

TR: tricuspid regurgitation

VSD: ventricular septal defect

Introduction

The mitral valve allows unidirectional unobstructed blood flow from the left atrium to the left ventricle. A normal competent valve may allow a trivial amount of flow in the reverse direction, but anything more than a trace of regurgitation is considered pathologic [1]. Several acquired and congenital conditions can affect the mitral valve, leading to mitral stenosis (MS) or mitral regurgitation (MR) or a combination of both.

In this article, the standard auscultatory technique will be briefly mentioned and then the typical auscultatory findings of mitral stenosis and mitral regurgitation will be described. The associated haemodynamics will be explained. The relevant differential diagnosis of different sounds and murmurs and the way to differentiate them will also be described. The auscultatory findings are of significant value in the evaluation of mitral valve pathologies but these need to be considered along with history and other physical findings and investigations in diagnosing and treating these conditions.

Methods of auscultation

A thorough and systematic auscultation is needed to avoid missing any subtle signs of mitral valve disease. The patient should be auscultated in three positions - supine, sitting, and left lateral. Both the bell and the diaphragm of the stethoscope should be used. All of the five classic areas are auscultated - mitral area (area over the apical impulse), tricuspid area (left parasternal line, 5th intercostal space), pulmonary area (left parasternal line, 2nd intercostal space), aortic area (right parasternal line, 2nd intercostal space), and accessory aortic area (left parasternal line, 3rd intercostal space) [2]. The stethoscope should be moved from one area to another by a small movement rather than jumping from one to the other. Auscultation should also be extended to the relevant adjoining areas to appreciate the radiation of the murmurs. Finally, dynamic auscultation is performed to note the changes of sounds and murmurs with respiration, after ectopic beat and with some specific manoeuvres.

Mitral stenosis

Most cases of mitral stenosis are caused by rheumatic heart disease. The prevalence varies from 1 in 100,000 in Europe and North America to 35/100,000 in Africa. Approximately 25% of rheumatic heart disease patients will have isolated MS and 40% will have a combination of MS and MR. Thirty-eight percent (38%) of MS patients will also have other valve involvement [3] and hence, during auscultation of MS, it is quite important to look for signs of other valvular disease.

Some of the signs of mitral stenosis are very subtle and hence physical examination, particularly auscultation, should be carried out in a quiet setting in a systematic way. Co-existent atrial fibrillation, which develops in about 40% of patients [4], makes it difficult for clinicians to detect the auscultatory signs of mitral stenosis, more so if the ventricular rate is high. Auscultatory signs are subjective and there are no data in terms of the sensitivity, specificity and predictive value of these signs in diagnosing mitral stenosis [2].

Before proceeding to auscultation, mitral facies (plethoric cheeks with bluish patches), tapping apex and apical diastolic thrill may suggest the presence of mitral stenosis. The jugular venous pulse may show prominent ‘a’ wave and there may be a right ventricular (RV) heave in the presence of pulmonary hypertension.

The first heart sound (S1) is typically loud due to the rapidity with which RV pressure rises (dP/dt) at the time of mitral valve closure (because of high pressure in the left atrium, the left ventricle [LV] needs to reach a higher pressure before it can close the mitral valve and hence LV pressure has more time to accelerate) [5] and the wide closing excursion of the leaflets. The wide closing excursion of the leaflets happens because the transmitral gradient keeps the valve wide open at the end of diastole rather than allowing the valve to go to a semi-closed position as happens normally without mitral stenosis. The intensity of the first heart sound is reduced if the valve is thickened and calcified. The presence of a loud S1 suggests that the patient may be a likely candidate for balloon mitral valvuloplasty [2]. With the development of atrial fibrillation, the intensity of the S1 will vary depending upon the RR intervals with a louder S1 audible in shorter cycles.

The nature of the second heart sound (S2) depends upon the severity of pulmonary hypertension. Initially, the intensity of P2 increases as pulmonary artery pressure increases. As pulmonary artery pressure increases further, splitting of the S2 narrows as P2 becomes earlier and then S2 becomes single and loud with further increase in pulmonary artery pressure.

The opening snap (OS) of the mitral stenosis is a high-pitched early diastolic sound due to sudden tensing of the valve leaflets and subvalvular apparatus at the end of the opening excursion. The OS occurs 40-120 milliseconds after A2. The A2-OS interval varies inversely with the severity of mitral stenosis. An A2-OS interval of less than 70 milliseconds usually suggests severe MS and an A2-OS interval of more than 100 milliseconds usually indicates mild MS [2]. In the presence of AF, the A2-OS interval varies directly with the length of the previous RR interval. Because of its higher pitch, the OS can be heard over a wider area over the precordium than mid-diastolic rumble. It can be heard at the left sternal border and even at the base of the heart. An OS is a much higher pitched sound than S3 which is also localised to the apex only. A loud P2 may simulate the OS but normally P2 is not heard at the aortic area unless there is severe pulmonary hypertension. A crisp OS suggests a pliable valve and hence is probably suitable for balloon mitral valvuloplasty.

The classic mid-diastolic low-pitched rumbling murmur of mitral stenosis with pre-systolic accentuation is best audible at the apex, in the left lateral position with the bell of the stethoscope. Pre-systolic accentuation usually means the presence of atrial contraction and hence sinus rhythm, but it may persist in AF following short diastoles [6]. The duration of the murmur is directly proportional to the severity of mitral stenosis, but the intensity of the murmur is not. The murmur can be heard provided the atrioventricular gradient remains above 3 mmHg [3]. Because diastolic mean gradient is directly related to heart rate, the manoeuvres that increase heart rate can help to detect an otherwise faint murmur.

Other auscultatory features depend upon the severity of pulmonary hypertension and associated valve lesions. Pulmonary artery dilatation due to severe pulmonary hypertension can cause a non-valvular pulmonic ejection sound which decreases with inspiration unlike any other right-sided event in the heart. A pansystolic murmur of tricuspid regurgitation (TR) may be audible in severe MS with pulmonary hypertension and may be confused with associated mitral regurgitation. The murmur of TR is better audible left parasternally in the 4th intercostal space, the intensity increases with inspiration and there will be an associated large v wave in the jugular venous pulse. A high-pitched decrescendo diastolic murmur may (rarely) be audible along the left sternal border because of functional pulmonary regurgitation (Graham Steell murmur) in severe pulmonary hypertension, but more commonly this murmur indicates associated aortic regurgitation. A left-sided S3 rules out significant mitral stenosis in mixed mitral valve disease.

Mitral stenosis is very rare in the developed world. In older patients, a diastolic rumble is most likely due to mitral annular calcification and 90% of patients with a diastolic apical murmur will have no evidence of MS on echocardiography [3]. Any condition which gives rise to increased flow across a non-stenotic mitral valve such as severe mitral regurgitation or a large ventricular septal defect can cause a short diastolic murmur. Left atrial myxoma can cause a diastolic murmur and a tumour plop may resemble the OS and can mimic MS. Hypertrophic cardiomyopathy can cause a diastolic rumble due to early diastolic flow into a

hypertrophied stiff left ventricle. A mid-diastolic rumble, the Austin Flint murmur, can be heard in aortic regurgitation when an eccentric jet of AR hits the anterior leaflet of the mitral valve causing it to reverberate generating an apical rumble. There is also some suggestion that this murmur may not be due to reverberation of the anterior leaflet and may actually be due to an AR jet preventing the mitral valve from opening fully [5]. Amyl nitrate inhalation has been used in the past to differentiate between the two. A diastolic murmur mimicking MS can also be heard in cor triatriatum sinister, a rare congenital abnormality where the LA is divided into two chambers usually by a thick fibromuscular septum, but in this case S1 will not be loud and there will be no OS [7].

Mitral regurgitation

The mitral valve apparatus consists of mitral annulus, valve leaflets, chordae tendineae and papillary muscles. Abnormalities of one or a combination of these structures can cause MR. MR is commonly caused by mitral valve prolapse, ischaemic heart disease, cardiomyopathy, infective endocarditis, rheumatic heart disease and annular calcification. Acute MR is usually caused by papillary muscle dysfunction/rupture, rupture of the chordae tendineae either spontaneous or against a background of myxomatous degeneration, infective endocarditis and prosthetic valve dysfunction [8].

As mentioned before, the examinational findings of mitral regurgitation will depend upon the severity and aetiology as well as the chronicity of the development of MR.

A significant MR will cause a sharp carotid upstroke, and a downward and outwardly displaced brisk hyperdynamic apical impulse. Expansion of the large left atrium during systole may cause a late systolic thrust in the parasternal region and this may mimic right ventricular enlargement.

If MR is caused by defective leaflets, the S1 is usually soft. The S2 can be widely split because of earlier A2 due to shortened LV ejection as well as reduced resistance to LV ejection. The P2 is louder if there is significant pulmonary hypertension. The increase in diastolic flow across the mitral orifice during the rapid filling phase may produce S3. An S4 can be heard in MR of recent onset and in ischaemic or functional MR in sinus rhythm [5].

Single or multiple non-ejection systolic clicks can be heard if the cause of MR is mitral valve prolapse (described in detail later in the mitral valve prolapse [MVP] section).

The systolic murmur is the most important auscultatory finding. In severe MR, the systolic murmur starts immediately after a soft S1 and may continue beyond A2 as the pressure difference between LV and LA persists even after aortic valve closure. The holosystolic murmur of MR is blowing, high-pitched and best audible at the apex with radiation to the left axillary and infrascapular area. The murmur can radiate anteriorly towards the left parasternal area in case of mitral valve prolapse with involvement of the posterior leaflet. There is weak correlation between the intensity of the murmur and the severity of MR. In patients with severe MR due to LV dilatation, acute myocardial infarction, paraprosthetic valvular regurgitation and in patients with severe emphysema, obesity and chest deformity, the systolic murmur may be very faint or even not audible [3]. Murmurs of shorter duration usually correspond to mild MR. It may be early systolic in functional MR and late systolic in

MVP or papillary muscle dysfunction. The late systolic murmur of papillary muscle dysfunction may become holosystolic during acute ischaemia and may disappear when ischaemia is relieved. In MVP, the late systolic murmur is usually preceded by mid/late systolic clicks, and the response of the clicks and murmur to different manoeuvres can distinguish MR due to MVP from other causes.

A low-pitched diastolic murmur may be heard at the apex following S3 in severe MR because of increased flow across the mitral inflow in the absence of any mitral stenosis.

An acute MR will produce only a short early systolic murmur, making the diagnosis clinically challenging. This happens because a large v wave is generated in a non-compliant left atrium and LA and LV pressure essentially equalise in systole removing any reverse gradient across the mitral valve after the early part of systole. A left-sided S4 is usually heard. An abrupt rise in LA pressure leads to pulmonary oedema and increased pulmonary vascular resistance and even right heart failure. Pulmonary hypertension can cause a loud P2, and rarely a large v wave in the pulmonary artery pressure pulse in acute severe MR can prematurely close the pulmonary valve leading to paradoxical splitting of the S2.

The MR murmur should be differentiated from the systolic murmurs of aortic stenosis (AS), TR and ventricular septal defect (VSD). The intensity of the aortic stenosis murmur increases after a premature beat or in the beat after a long cycle length in AF. This helps in differentiating AS from MR, particularly in older patients where the AS murmur may be prominent in the apex (Gallavardin effect). The systolic murmur of AS increases in the beat following a premature beat because of the combined effect of increased LV filling and post extra-systolic potentiation of ventricular contraction. The intensity of the MR murmur does not change after a premature beat, can decrease (papillary muscle dysfunction) or become shorter after a premature beat (MVP).

The holosystolic murmur of a VSD may resemble MR but the former is usually loudest at the left sternal border and can be accompanied by parasternal thrill. The murmur of TR may appear in the differential diagnosis but is usually best heard at the left sternal border. Its intensity increases during inspiration and it is associated with prominent v wave and y descent in the jugular venous pulse.

Dynamic auscultation helps to differentiate MR from other systolic murmurs. It also helps differentiating MVP from other causes of MR. The holosystolic murmur of MR does not vary much with respiration. Sudden standing diminishes the murmur and squatting increases the murmur. The late systolic murmur of MVP behaves in another way, decreasing after squatting and increasing with standing (mechanism and haemodynamics explained in the MVP section). The holosystolic murmur of MR is reduced during the strain phase of the Valsalva manoeuvre. The holosystolic murmur of MR will increase with hand grip compared to the murmur of AS and hypertrophic cardiomyopathy, both of which will reduce with hand grip.

In patients with mixed rheumatic mitral valve disease, careful auscultation may help to find the predominant lesion. A loud S1, a prominent OS with a short A2-OS interval and a short systolic murmur favour predominant MS, whereas an S3 and soft S1 favour predominant MR.

Mitral valve prolapse

Mitral valve prolapse (MVP) is the leading cause of significant MR in developed countries [9]. MVP, or degenerative mitral valve disease as it is sometimes called in a broader sense, is defined by a spectrum of mitral valve lesions involving one or more components of the mitral valve apparatus. It can vary from simple chordal rupture with prolapse of an isolated segment of the posterior leaflet (P2) in an otherwise normal valve to multi-segment prolapse affecting one or both leaflets in a valve with significantly excess tissue and a larger annulus [2]. As expected, on auscultation MVP produces some characteristic but at the same time varied features.

The characteristic auscultatory feature of MVP is a mid-systolic click, a high-pitched sound. It results from sudden tensing of the mitral valve apparatus as the leaflets prolapse into the left atrium in systole. Multiple clicks can be heard as different parts of the mitral leaflets prolapse at different times of systole. The loudness and timing of the clicks can vary according to left ventricular volume and contractility. Compared to aortic ejection click which occurs with the beginning of the carotid pulse upstroke, the clicks of MVP happen after the beginning of the upstroke. The clicks are often but not always followed by a mid or late systolic murmur. The duration of the murmur usually corresponds with the severity of MR. When the murmur is restricted only to the later part of the systole, the MR is not severe but, as the MR progresses, the systolic murmur becomes holosystolic.

There can be significant variation in physical findings in MVP from patient to patient as well as in the same patient at different times. Some patients can present with both mid-systolic click and murmur, others with either one of them. The same patient can have only a click at one time and a murmur at another time, both on another occasion and no abnormality at another time [3]. Mid-systolic click can happen in tricuspid valve prolapse and also in atrial septal aneurysm. Dynamic auscultation is quite useful to establish the diagnosis of MVP. The mitral valve starts to prolapse when the LV systolic volume reaches a specific point below which the valve leaflets cannot coapt. At this point the click occurs and MR and hence murmur starts. Anything that decreases the left ventricular volume such as decreased venous return, tachycardia, increased myocardial contractility or reduced afterload will cause the mitral valve leaflets to prolapse earlier in systole, and systolic click and murmur will move towards the first sound and the murmur will become longer. On the other hand, when LV volume is increased because of increased venous return, increased afterload, decreased myocardial contractility and bradycardia, the onset of click and murmur will be delayed.

The change in intensity of murmur after a premature beat helps in differentiating MVP murmur from that of hypertrophic cardiomyopathy (HCM). The intensity and duration of HCM murmur increases after a premature ventricular beat compared to MVP murmur where the intensity decreases or remains unchanged.

Table 1. Response of mitral valve prolapse murmur to different interventions [10].

Intervention	Change in murmur (timing, duration and intensity)

Positional changes:	Earlier, longer and louder
Standing	Later, softer, may disappear
Squatting	
Post PVC	Shorter
Valsalva	Longer and louder
Amyl nitrate inhalation	Biphasic, softer and then louder than control

Conclusion

Mitral valve disease is a common condition that all cardiologists encounter in their day-to-day practice. A careful auscultation can go a long way to diagnose and assess the severity of mitral valve disease and to differentiate it from similar cardiac conditions. However, auscultatory findings should only be used in combination with symptoms and other physical findings and results of imaging and other investigation results to diagnose and treat mitral valve disease.

For general information on the management of valvular heart disease including MS, please refer to the “2017 ESC/EACTS Guidelines for the management of valvular heart disease” [11].

Notes to editor

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