Pathophysiology, and diagnosis of valvular heart disease

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Abstract:

In this review we discuss the valvular heart disease, it's pathophysiology and focus on diagnosis. We searched online databases MEDLINE, EMBASE and the Cochrane Library using search terms as Valvurar heart disease, and diagnosis to find studies supporting our review published up to June 2018. People with valvular heart illness are living longer, with much less morbidity, compared to in the past. Advances in surgical methods and a better understanding of timing for surgical treatment make up increased rates of survival. Echocardiography remains the gold requirement for medical diagnosis and periodic analysis of patients with valvular cardiovascular disease. Typically, patients with stenotic valvular lesions could be kept track of scientifically up until signs appear. On the other hand, patients with regurgitant valvular lesions need mindful echocardiographic surveillance for left ventricular function and may call for surgery also if no signs and symptoms exist. Risk aspects for obtained valve diseases consist of age, gender, cigarette usage, hypercholesterolemia, hypertension, and kind II diabetes mellitus.

Introduction:

Valvular heart disease (VHD) is a significant health issue affecting the elderly particularly, with a prevalence of 2.5% in the United States. VHD occurs as a result of congenital defects or as a result of gotten pathology [1].Calcific aortic valve disease (CAVD) is launched as aortic valve sclerosis

(AVSc), which is a light thickening of the valve, to aortic valve stenosis (AVS), which results in serious disability of the valve activity. CAVD is increasingly existing in the maturing populace, getting to epidemic percentages, with approximately one third of individuals aged > 65 years, revealing sub-clinical proof of CAVD, through aortic sclerosis [2].As a huge proportion of the worldwide population is becoming aged, the frequency of acquired forms of VHD is anticipated to rise [3].Age, gender, tobacco use, hypercholesterolemia, rheumatic heart disease and hypertension constitute considerable danger factors of gotten CAVD. Congenital CAVD primarily arises from the disturbed expression of genes that are associated with normal heart valve advancement. Congenital valve abnormalities comprise virtually 50% of the cases of congenital heart defects (CHD) [4].Advancements in the recognition of these defects and in the connected care for babies experiencing CHDs is on the increase, thus enhancing the net occurrence and burden of congenital valve illness [4].Kind II diabetes is taken into consideration an important risk factor for indigenous CAVD [5].The pathogenesis of congenital and obtained CAVD is likely because of the interplay of genetic and ecological influences, despite the fact that the accurate mechanisms are not recognized.

Although the occurrence of VHD is high, restorative strategies for this illness are restricted. The only offered primary medical strategy for valve repair or replacement is surgery as the primary treatment [6], [7].In truth, aortic valve substitute is the second most frequent cardiac surgery adhering to coronary artery bypass grafting [8] CAVD advances to calcific aortic stenosis (CAS), which is one of the most serious kind of the illness. It is exceptionally devastating influencing as numerous as 2% of people > 60 years of age, needing surgery to preclude fatality, once the signs and symptoms end up being obvious [9].CAVD is primarily detected by clinical examination, echocardiography and cardiac catheterization. There are additionally numerous possible

biomarkers that give scientifically valuable information concerning the extent, severity, development and prognostication of CAVD [8].

In this review we discuss the valvular heart disease, it's pathophysiology and focus on diagnosis.

Methodology:

We searched online databases MEDLINE, EMBASE and the Cochrane Library using search terms as Valvurar heart disease, and diagnosis to find studies supporting our review published up to June 2018. Database searches were supplemented by the reference lists obtained from relevant articles.

Discussion:

- **Diagnosis**

The medical diagnosis of valvular cardiovascular disease is a difficult issue in everyday professional practice. There is a broad range of presentation- in many cases murmurs are found accidentally and in others, patients present extremely late with alarming haemodynamic consequences of ignored valve sores that may preclude them from definite surgery. With the decrease in rheumatic cardiovascular disease and the ageing populace in the established world, there has been a modification in the illness patterns of valve lesions over the last few decades. Nowadays western populaces are dealing with greater numbers of degenerative valve disease. In the creating globe, nevertheless, rheumatic cardiovascular disease continues to be an important reason for valve pathology. Sliwa et al., [10] in the Heart of Soweto Study, showed an occurrence of new cases of rheumatic heart problem of 23.5/ 100 000 instances per annum. Clinical evaluation (history and examination) continues to be the cornerstone of evaluating for valve pathology. An

electrocardiogram (ECG) and a chest radiograph (CXR) could give important diagnostic clues to verifying pathology and are viewed as crucial adjuncts to medical assessment. Echocardiography with colour circulation and Doppler (not concentrate evaluated transthoracic echocardiography (FATE) scans) plays a critical function in verifying the medical diagnosis, and evaluating the severity of the valve lesions and concomitant pulmonary hypertension, various other valve lesions and haemodynamic consequences. Invasive examination with cardiac catheterisation is booked for patients in whom there is a disparity between medical searchings for and echocardiography.

- **Mitral stenosis**

What is the pathophysiology behind mitral valve stenosis[11]?

The normal orifice of the mitral valve is 4-5 cm2, and it works as the inlet valve to the left ventricle by essentially producing a typical chamber between the left atrium and left ventricle during diastole. Usually, the mitral valve is a complex device comprised of 2 leaflets that are attached by chordae tendineae to 2 papillary muscular tissues and an annulus. The papillary muscular tissues originate from the wall surfaces of the left ventricle and safeguard the chordae and mitral leaflets, avoiding prolapse of the valve during ventricular systole. Mitral valve stenosis results from any type of congenital or gotten pathologic process that tightens the reliable mitral valve orifice at the supravalvular, valvular, or subvalvular degrees. During ventricular filling, pressures are equivalent in between the two chambers. As the mitral valve orifice narrows in mitral valve stenosis, a pressure slope establishes in between both chambers as a result of the restraint of circulation from the left atrium to the left ventricle. This pressure gradient is transferred to the left ventricle diastolic pressure. This leads to an elevation of left atrial and pulmonary venous pressures. Bigger bronchial veins could trespass on small bronchioles, with succeeding rise in airway resistance. Pulmonary edema happens when pulmonary venous pressure is above plasma oncotic pressure. Pulmonary

artery hypertension occurs with the compensatory vasoconstriction and medial hypertrophy and intimal thickening of the pulmonary arterioles. As the disease advances, the appropriate ventricle falls short and pulmonary blood flow decreases, lowering systemic blood circulation. If the autumn in cardiac outcome is substantial, end-organ failing, shock, and metabolic acidosis could happen. Right ventricular failure results in systemic venous congestion with development of hepatomegaly, ascites, and edema [11].

Diagnosis

Any kind of condition that boosts heart rate, consisting of sepsis, thyroid disease, anaemia, atrial fibrillation (AF) and pregnancy, might precipitate symptoms.When the condition is mild, patients could be asymptomatic at rest and with effort [13].As the stenosis gets worse, dyspnea on effort, orthopnea, and paroxysmal nocturnal dyspnea take place. Increased left atrial pressure may result in hemoptysis as a result of tear between bronchial veins Clinical attributes and special examination findings are explained in Table 1 [12].

Table 1. Clinical and special investigation features of mitral stenosis

History : Exertional dyspnoea Orthopnoea Paroxysmal nocturnal dyspnoea Acute frank pulmonary oedema Haemoptysis Embolism: 20 - 25%, especially cerebral Chest discomfort Hoarseness: Ortner's syndrome	**Special investigations:** **ECG** Usually unremarkable In sinus rhythm, LA enlargement: broad P wave in lead II or a predominantly negative deflection in lead V1 In AF, no comment on LA size can be made **CXR** Normal-sized heart (ventricle) Upper-lobe blood diversion/interstitial oedema Enlarged LA seen by: Straight left heart border Splaying on the coryna Double shadow on the right heart silhouette
Physical findings : Normal character, small volume pulse in severe MS Irregularly irregular pulse: atrial fibrillation JVP may be elevated: prominent cv wave if concomitant significant TR	

Undisplaced, tapping apex beat Loud first heart sound Loud pulmonary component of S2 if pulmonary hypertension Opening snap after S2, if pliable valve The closer to S2, the more severe the MS Low-pitched mid-diastolic murmur Best heard at the apex Longer murmur = more severe MS If patient is in sinus rhythm, presystolic accentuation of the murmur may be audible Pulmonary crepitations at lung bases Other associated valve lesions: mitral regurgitation, tricuspid disease, aortic disease

JVP = jugular venous pressure; TR = tricuspid regurgitation; MS = mitral stenosis; LA = left atrial; AF = atrial fibrillation.

- **Mitral regurgitation**

The pathophysiology of mitral regurgitation[14].

Resembling to aortic regurgitation, mitral regurgitation could establish from occasions that negatively affect leaflet integrity. Mitral regurgitation can develop from distortion of the mitral annulus or from practical or structural abnormalities of the submitral mechanism, consisting of the chordae tendineae and the papillary muscle mass. Patients who provide with extreme acute mitral regurgitation frequently have myocardial infarctions, perivalvular abscesses, or endocarditis as the underlying etiologies. Endocarditis triggers mitral regurgitation via leaflet destruction or through infection and rupture of the chordae muscular tissues. Myocardial ischemia leads to impaired reducing of the papillary muscles, permitting regurgitant flow. Ischemia, especially of the posteromedial papillary muscle mass, which obtains its blood supply from the dominant coronary artery, could lead to infarction of papillary muscle mass and total transection of the papillary muscle head with succeeding regurgitation via the mitral valve. Chronic mitral regurgitation is often due to mitral valve prolapse, rheumatic heart problem, left ventricular dysfunction, and ischemic or nonischemic dilated cardiomyopathy.

Diagnosis

The medical and investigational features of chronic MR are summed up in Table 2 [13]. Signs of seriousness include scientific features of heart failure, pulmonary hypertension, a loud murmur level ≥ 3/6 and presence of a 3rd heart sound in the lack of heart failure. Functional MR is qualified by normal brochures and is additional to a dilated and dysfunctional left ventricle. Echocardiography is required to precisely verify this medical diagnosis and might distinguish ischaemic from non-ischaemic causes [12].

Table 2. Clinical and special investigation features of mitral regurgitation

History	**Physical findings**
Heart failure symptoms (dyspnoea, paroxysmal nocturnal dyspnoea, orthopnoea) Leg swelling	Displaced, volume-loaded apex beat Soft S1 Pan-systolic murmur at apex, radiating to axilla Third heart sound
Special investigations **ECG** Usually unremarkable The presence of abnormal QRS complexes eludes to underlying myocardial pathology rather than primary isolated mitral valve pathology **CXR** Cardiomegaly Upper-lobe blood diversion/interstitial oedema	

- **Aortic stenosis**

Aortic stenosis (AS) is the most common valve lesion in western countries and mainly a disease of the elderly[15].
Common causes of AS include:
• degenerative trileaflet AS
• degenerative bicuspid AS
• rheumatic heart disease – there would usually be concomitant MV
• disease
• other (rare): congenital AS, Paget's disease, end-stage kidney disease, chronic inflammatory diseases.
Explain the pathophysiology of aortic stenosis. Aortic stenosis is the most regular of all valvular irregularities, estimated to occur in 2% of the populace. Reasons of aortic stenosis include both

congenital and obtained etiologies [16].The most usual kind of gotten aortic stenosis is deterioration of previously normal tissue leading to calcification of the cuspal tissue or calcification of congenitally bicuspid shutoffs, which occurs in about 1% of the population. The nidus for calcium and inorganic phosphate ions to crystallize and create hydroxyapatite crystals in the plasma membrane layer of dying cells is suggestive of a senile pathologic mechanism. Typically, it was thought that passive accumulation of hydroxyapatite mineral in the setup of sclerosis leads to calcification. Nevertheless, it is currently understood that active procedures just like those involved atherosclerotic arteries, consisting of inflammation and lipid infiltration, play a considerable role in aortic stenosis.

Diagnosis

The primary symptoms of aortic stenosis include syncope, angina pectoris, and dyspnea [12].Generally, symptoms could be credited to aortic stenosis if the valve location is<1.0 cm2 or if the mean transvalvular slope exceeds 50 mmHg [17].The ordinary time to fatality after the onset of angina, syncope, and dyspnea are 5, 3, and 2 years, respectively. Left ventricular hypertrophy establishes in reaction to the progressive obstruction. Threat variables for degenerative AS resemble those for atherosclerosis, i.e. hypertension, diabetes, dyslipidaemia and smoking cigarettes. Patients are asymptomatic for several years. As soon as signs and symptoms take place, nonetheless, there is a rapid decline in life expectancy [18].Scientific features of AS are displayed in Table 3.

Table 3. Clinical and special investigation features of aortic stenosis[18].

History	**Special investigations**
Exertional dyspnoea Angina Syncope	***ECG*** Left ventricular hypertrophy ***CXR*** Normal-sized heart (ventricle) Aortic calcification Post-stenotic dilatation: especially in bicuspid valves

Physical findings
Small-volume, slow-rising pulses
Narrow pulse pressure JVP normal, unless heart failure or MV disease
Pressure-loaded undisplaced apex beat
Soft or single second heart sound
Crescendo-decrescendo ejection systolic murmur at base of the heart
Radiated to carotids
Longer murmur = more severe
High-pitched widely radiating murmur: Gallavardin effect – can be mistaken for MR
Systolic click in bicuspid valve may be heard

- **Aortic regurgitation**

What is the pathophysiology of aortic regurgitation? Lesions that cause aortic regurgitation develop an orifice that permits regurgitant flow throughout diastole. In acute aortic regurgitation, a rapid increase in left ventricular filling pressures occurs as a result of the sudden increase in left ventricular volume without a rise in left ventricular conformity. Left ventricular stroke volume lowers as the regurgitant fraction increases. Tachycardia shortens the period of diastole and consequently minimizes the regurgitant fraction. Diastolic filling of the ventricle may be endangered if left ventricular pressure exceeds left atrial pressure, leading to premature closure of the mitral valve. Raised systemic blood pressure boosts systemic vascular resistance and could enhance aortic regurgitation [15].

In chronic aortic regurgitation, ventricular renovation happens in reaction to the quantity overload state. Remodeling is identified by boosted fiber length and ultimately enhanced end-diastolic quantity. This leads to boosted diastolic compliance, increased end-diastolic amount, and enhanced stroke volume without increasing filling up pressures substantially [19].Gradually, left ventricular contractility decreases causing boosts in filling up, end-diastolic, and systolic pressures, and to lowered ejection fractions.

Diagnosis

Aortic regurgitation is generally discovered as an incidental finding on echocardiography. In acute aortic regurgitation, the electrocardiogram can appear regular. The chest radiograph usually reveals pulmonary edema with normal heart dimension. The professional assessment searchings for consist of a decrescendo diastolic murmur, expanded pulse pressure, and bounding pulses.

The medical functions are summed up in Table 4. Symptomatic aortic regurgitation needs recommendation for the evaluation for aortic valve substitute. There is no location for clinical therapy outside of it being a bridge to surgery or in those also unwell for surgery [20-22].

Table 4. Clinical and special investigation features of aortic regurgitation

History Long asymptomatic period Dyspnoea Orthopnoea Paroxysmal nocturnal dyspnoea Nocturnal angina	Special investigations ***ECG*** No specific diagnostic changes Occasionally in severe AR-left ventricular hypertrophy, and left axis deviation may be seen ***CXR*** Cardiomegaly Pulmonary congestion
Physical findings Collapsing pulses Wide pulse pressure (difference between systolic and diastolic is >50% of the systolic pressure) Duroziez sign Heart failure signs: elevated JVP, leg swelling, crepitations at lung bases Volume-loaded, displaced apex Early diastolic murmur at base of heart Best heard with patient sitting forward, in end-expiration Longer murmur = more severe A systolic murmur (due to increased flow or concomitant AS) An Austin-Flint murmur (late diastolic apical murmur)	

- **Tricuspid valve disease**

Tricuspid stenosis (TS) is uncommon and typically rheumatic in origin [23].A lot of patients with rheumatic tricuspid valve (TV) condition present with tricuspid regurgitation (TR) or a mix of TR and TS. Isolated rheumatic TS is uncommon, yet generally accompanies MV illness. It is very rare and unusual root causes of blockage to right atrial (RA) emptying consist of congenital tricuspid atresia, RA tumours, carcinoid disorder, endomyocardial fibrosis, TV greeneries, pacemaker leads or extracardiac tumors [23].TS is found at autopsy in 15% of patients with rheumatic heart illness, however is of medical importance in <5%. As holds true with MS, TS is much more usual in ladies. The RA is normally dilated in TS. Clinical and specific examination findings in TS are presented in Table 5.

Table 5. Clinical and special investigation features of tricuspid valve disease

Tricuspid stenosis	Tricuspid regurgitation
History Progressive fatigue, oedema, anorexia Minimal orthopnoea and paroxysmal nocturnal dyspnoea Pulmonary oedema and haemoptysis are rare	**History** Well tolerated in absence of pulmonary hypertension, often asymptomatic Right heart failure (swollen abdomen, swelling of legs and painful, congestive enlargement of liver) Throbbing pulsations in the neck (from elevated JVP) and eyeballs
Physical findings Diastolic rumble at lower left sternal border, increasing in intensity with inspiration Often confused with mitral stenosis Neck vein distention, with prominent a waves Absent right ventricular lift/heave Hepatic pulsation Ascites, peripheral oedema Associated murmurs of mitral and aortic valve disease	**Physical findings** Weight loss, cachexia, cyanosis and jaundice AF is common Elevated JVP with prominent cv waves Venous systolic thrill and murmur in neck Tender hepatomegaly S3 gallop originating from RV Loud P2 and parasternal heave if pulmonary hypertension present Pansystolic murmur of TR
Special investigations ***ECG*** Tall right atrial P waves and no RV hypertrophy ***CXR***	**Special investigations** ***ECG*** Usually nonspecific; incomplete RBBB, Q waves in V1, AF are common ***CXR*** Marked cardiomegaly

Dilated RA without enlarged pulmonary artery segment	

Conclusion:

People with valvular heart illness are living longer, with much less morbidity, compared to in the past. Advances in surgical methods and a better understanding of timing for surgical treatment make up increased rates of survival. Echocardiography remains the gold requirement for medical diagnosis and periodic analysis of patients with valvular cardiovascular disease. Typically, patients with stenotic valvular lesions could be kept track of scientifically up until signs appear. On the other hand, patients with regurgitant valvular lesions need mindful echocardiographic surveillance for left ventricular function and may call for surgery also if no signs and symptoms exist. Risk aspects for obtained valve diseases consist of age, gender, cigarette usage, hypercholesterolemia, hypertension, and kind II diabetes mellitus. In enhancement, a number of hereditary anomalies that create congenital valve diseases have been recognized together with specific SNPs associated with CAVD. In spite of the numerous advances, there is still a lack of pharmacological therapies for the valve diseases and the most extensively approved method is surgery. Current advancements in the recognition of molecular mechanisms included in the advancement and pathogenesis of valvular illness are making a significant effect in our understanding of the heart valve condition.

Reference:

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee: Heart disease and stroke statistics-2013 update: a report from the American Heart Association. Circulation. 2013;127:e6–e245.
2. Rajamannan NM, Evans FJ, Aikawa E, Grande-Allen KJ, Demer LL, Heistad DD, Simmons CA, Masters KS, Mathieu P, O'Brien KD, et al. Calcific aortic valve disease: not

simply a degenerative process: a review and agenda for research from the National Heart and Lung and Blood Institute Aortic Stenosis Working Group. Executive summary: Calcific aortic valve disease-2011 update. Circulation. 2011;124:1783–1791.

3. d'Arcy JL, Prendergast BD, Chambers JB, Ray SG, Bridgewater B. Valvular heart disease: The next cardiac epidemic. Heart. 2011;97:91–93.
4. Le Gloan L, Mercier LA, Dore A, Marcotte F, Ibrahim R, Mongeon FP, Asgar A, Miro J, Poirier N, Khairy P. Recent advances in adult congenital heart disease. Circ J. 2011;75:2287–2295.
5. Katz R, Wong ND, Kronmal R, Takasu J, Shavelle DM, Probstfield JL, Bertoni AG, Budoff MJ, O'Brien KD. Features of the metabolic syndrome and diabetes mellitus as predictors of aortic valve calcification in the Multi-Ethnic Study of Atherosclerosis. Circulation. 2006;113:2113–2119.
6. Itagaki S, Adams DH, Anyanwu AC. Triggers for surgical referral in degenerative mitral valve regurgitation. Circ J. 2013;77:28–34. doi: 10.1253/circj.CJ-12-0972.
7. Maeda K, Kuratani T, Mizote I, Shimamura K, Takeda Y, Torikai K, Nakatani S, Nanto S, Sawa Y. Early experiences of transcatheter aortic valve replacement in Japan. Circ J. 2013;77:359–362. doi: 10.1253/circj.CJ-12-0650.
8. Beckmann E, Grau JB, Sainger R, Poggio P, Ferrari G. Insights into the use of biomarkers in calcific aortic valve disease. J Heart Valve Dis. 2010;19:441–452.
9. Nightingale AK, Horowitz JD. Aortic sclerosis: Not an innocent murmur but a marker of increased cardiovascular risk. Heart. 2005;91:1389–1393.
10. Sliwa K, Carrington M, Mayosi BM, Zigiriadis E, Mvungi R, Stewart S. Incidence and characteristics of newly diagnosed RHD in urban African adults: Insights from the Heart of Soweto Study. Eur Heart J 2010;31:719-727.
11. Braunwald E. Valvular heart disease. In: Braunwald EB, ed. Heart Disease: A Textbook of Cardiovascular Medicine. 5th ed. Philadelphia, PA: W B Saunders, 1997:1007-1076.
12. Carabello B: Modern management of mitral stenosis. Circulation 112:432–437, 2005.
13. Chikwe J, Walther A, Pepper J: The surgical management of mitral valve disease. Br J Cardiol 11:42–48, 2004.
14. Soble JS, Neumann A: Valvular heart disease producing critical illness. In Parrillo JE, Dellinger RP (eds): Critical Care Medicine: Principles of Diagnosis and Management in the Adult, 2nd ed. St. Louis, Mosby, 2002, pp 638–657.
15. Mohler E: Mechanisms of aortic valve calcification. Am J Cardiol 94:1396–1402, 2004.
16. Schoen F: Cardiac valves and valvular pathology: Update on function, disease, repair and replacement. Cardiovasc Pathol 14:189–194, 2005.
17. Lester S, Heilbron B, Gin K: The natural history and rate of progression of aortic stenosis. Chest 113:1109–1114, 1998.
18. Rosenhek R, Zilberszac R, Schemper M, et al. Natural history of very severe aortic stenosis. Circulation 2010;121:151-156.
19. Schoen F: Cardiac valves and valvular pathology: Update on function, disease, repair and replacement. Cardiovasc Pathol 14:189–194, 2005.

20. Vehanian A, Ottavio A, Andreotti F, et al. Guidelines on the management of valvular heart disease. Eur Heart J 2012;33:2451-2496.
21. Nishimura R, Otto C, Bono RO, et al. 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease – a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63(22):e57-e185.
22. Cupido B, Commerford PJ. Valvular heart disease. In: Rosendorff C, ed. Essential Cardiology. 3rd ed. New York: Springer, 2013.
23. Bruce CJ, Connolly HM. Right-sided valve disease deserves a little more respect. Circulation 2009;119(20):2726-2734.