

Valvular Heart Diseases - A Review

Khawaja Tahir Mahmood¹, Mashal Anees², Ayesha Asghar²

¹Drug Testing Lab Lahore, ²Department of Pharmacy, Lahore College for Women University

Abstract

Prevalence of valvular heart diseases (VHD) and the way such patients are managed in health care vicinity, patients for the type of VHD, their causes, risk factors associated with the disease, symptoms, surgical interventions of the patients, pre and post-operative care and the drug therapy given are reviewed. VHD may be congenital or acquired that may be either due to valvular stenosis or valvular insufficiency. Young patients are more in number, reason being some of them carry the disease since childhood as a congenital anomaly. As poverty brings so much other problems, VHD also prevails in such population. Mitral valve is the high risk valve for developing the disease. RHD is the leading factor in prevalence of disease and a lot of patients develop the disease even after surgical intervention at some stage of their lives. This happens either due to some abnormality in patients' valve physiology or in case of valve replaced by mechanical valve, anticoagulation therapy non-compliance is a key factor. Pharmacist, being an important member of healthcare team, plays most important role in drug therapy management and in a broader sense, in increasing patient compliance which is ultimately good for patient's healthy life.

Key words: International normalized ratio, mitral valve, palpitations, rheumatic heart disease, and valvular heart disease.

INTRODUCTION

Diseases of the hearts valves include a diverse group of acquired and congenital lesions. Some of these occur in isolation and others occur in association with other heart diseases. Deformed cardiac valves may cause disease by two major mechanisms. First, they impose a major hemodynamic burden on the cardiac chambers by causing obstruction (stenosis) or regurgitation (incompetence) or sometimes a combination of two. Second, the abdominal valves are more susceptible to infection and thus predispose patients to infective endocarditis and its many complications. With the possible exception of infective endocarditis and carcinoid heart disease, lesions of the tricuspid and pulmonic valves are much less common. Major causes of acquired heart valve disease include mitral valve stenosis, mitral regurgitation, aortic stenosis or aortic regurgitation.

Valvular heart disease (VHD) encompasses a number of common cardiovascular conditions that account for 10% to 20% of all cardiac surgical procedures. A better understanding of the natural history coupled

with the major advances in diagnostic imaging, interventional cardiology, and surgical approaches have resulted in accurate diagnosis and appropriate selection of patients for therapeutic interventions. A thorough understanding of the various valvular disorders is important to aid in the management of patients with VHD. Appropriate work-up for patients with VHD includes a thorough history for evaluation of causes and symptoms, accurate assessment of the severity of the valvular abnormality by examination, appropriate diagnostic testing, and accurate quantification of the severity of valve dysfunction and therapeutic interventions, if necessary. Role of the therapeutic interventions vs the natural history of the disease in the assessment of outcomes is important [1].

PREVALENCE

No difference in the frequency of moderate or severe valve disease between men and women exists but women are less often diagnosed than are men. Prevalence increased with age, in 18—44 year olds to 75 years and older group [2].

CAUSES OF VHD

VHD mainly results from rheumatic fever. Rheumatic fever is a preventable disease, but the combination of a lack of resources, lack of infrastructure, political, social and economic instability, poverty, overcrowding, malnutrition and lack of political will contributes to the persistence of a high burden of rheumatic fever, rheumatic VHDs and infective endocarditis [3].

TYPES OF VHD

Significant valvular heart disease includes mitral or aortic stenosis severity, moderate or severe mitral regurgitation, moderate or severe aortic regurgitation and moderate or severe tricuspid regurgitation. Mitral regurgitation and aortic regurgitation are the most frequent valve diseases. Valvular disease is higher in individuals, with mitral regurgitation and aortic regurgitation as the most frequent valve diseases (49% and 28% respectively). The left ventricular (LV) dimensions function and the presence and severity of heart valvular disease is evaluated by echocardiography [4]. Aortic regurgitation (AR) is characterized by diastolic reflux of blood from the aorta into the left ventricle (LV). Acute AR typically causes severe pulmonary edema and hypotension and is a surgical emergency. Chronic severe AR causes combined LV volume and pressure overload. It is accompanied by systolic hypertension and wide pulse pressure, which account for peripheral physical findings, such as bounding pulses [5].

DIAGNOSTIC PROCEDURES

The accuracy of exercise testing was assessed in predicting symptom onset within 12 months in patients with asymptomatic aortic stenosis and to establish the criteria that define a positive test. Assessment on the basis of Specific Activity Scale (SAS) classification, transthoracic

echocardiography, and treadmill exercise testing using the modified Bruce protocol shows a significant proportion of patients with apparently asymptomatic aortic stenosis experience limiting symptoms on treadmill exercise testing. The subsequent development of spontaneous symptoms is strongly related to the severity of stenosis and to limiting symptoms on exercise testing, but less so to an abnormal blood pressure response or ST segment depression [6].

Echocardiography remains the gold standard for diagnosis and periodic assessment of patients with valvular heart disease [7]. An ultrasonic Doppler instrument has been used for determining velocities in normal and diseased heart valves. A method is described for identifying the different heart valves, based on their relation to one another as well as the form of the velocity curve. The pressure drop across the mitral valve can be determined from the maximum velocity and the mean velocity can be used to determine the degree of aortic insufficiency. Recordings of mean and maximum velocities can give an indication of the form of the whole spectrum, thus making complete frequency analysis unnecessary for most purposes [8].

The ejection fraction is probably the most useful of the readily obtainable, single hemodynamic measurements in assessing the import of deranged left ventricular function on the outlook for patients undergoing cardiac surgery [9].

MANAGEMENT OF VHD

VHDs can be managed either by appropriate drug therapy or surgically.

Medication

Patient may be prescribed medications to treat symptoms and to lessen the chance of further valve damage. Some medications may be stopped after patient had valve surgery to correct their problem. Other

medications may need to be taken for whole life. Medications used are Diuretics, Anti arrhythmic medications, Vasodilators, ACE inhibitors, Beta blockers, Anticoagulants and Antithrombotic agents. Treatment may be with medication but often (depending on the severity) involves valve repair or replacement (insertion of an artificial heart valve). Drug therapy plays a key role in the management of valvular heart disease, though in many cases it does not alter its course or delay the need for surgery. The importance of drug therapy lies in stabilizing the patient's condition when the disease is due to abnormal valve structure, and in treating the underlying condition when the condition is due to a functional abnormality. Drug therapy also lowers the risk of bacterial endocarditis and rheumatic fever [10].

For patients with rheumatic mitral valve disease and atrial fibrillation (AF), or a history of previous systemic embolism, long-term oral anticoagulant (OAC) therapy (target international normalized ratio [INR], 2.5; range, 2.0 to 3.0) is recommended. For patients with rheumatic mitral valve disease with AF or a history of systemic embolism who suffer systemic embolism while receiving OACs at a therapeutic INR, we recommend adding aspirin, 75 to 100 mg/d. For those patients unable to take aspirin, adding dipyridamole, 400 mg/d, or clopidogrel is recommended. In patients with MVP and documented but unexplained TIAs, recommend long-term aspirin therapy, 50 to 162 mg/d. For all patients with mechanical prosthetic heart valves, recommend vitamin K antagonists. For patients with bioprosthetic valves, we recommend vitamin K antagonists with a target INR of 2.5 (range, 2.0 to 3.0) for the first 3 months after valve insertion in the mitral position and in the aortic position. For patients with bioprosthetic valves who are in sinus rhythm and do not have AF, we

recommend long-term (> 3 months) therapy with aspirin, 75 to 100 mg/d [11].

Prognosis

Only the extent of valve calcification is an independent predictor of outcome, whereas age, sex, and the presence or absence of coronary artery disease, hypertension, diabetes, and hypercholesterolemia are not. The presence of moderate or severe valvular calcification, together with a rapid increase in aortic-jet velocity, identifies patients with a very poor prognosis [12].

Surgical intervention

In patients with aortic stenosis who develop the classic symptoms of angina, syncope, or dyspnea, prompt aortic valve surgery should be performed to prevent sudden death. Thus, aortic valve replacement should be performed within 30 days after symptoms develop. Asymptomatic patients with severe aortic stenosis can be managed medically, but such management has taken on a more active investigative strategy. All such patients should undergo exercise testing if they can exercise. If unexpectedly poor exercise tolerance is demonstrated or if there is exercise-induced hypotension or ventricular arrhythmia, aortic valve replacement seems wise, although benefit in this group is not absolutely proven [13].

Balloon valvuloplasty is an effective intermediate palliation for aortic stenosis and is an acceptable alternative to surgical valvotomy [14]. Open valvotomy remains the gold standard in the management of AS in neonates, infants and older children. It is associated with low operative mortality and provides lengthy freedom from recurrent AS and regurgitation [15].

A percutaneously implanted heart valve (PHV) composed of 3 bovine pericardial leaflets mounted within a balloon-expandable stent was developed. Nonsurgical implantation of a prosthetic heart valve can be successfully

achieved with immediate and midterm hemodynamic and clinical improvement. After further device modifications, additional durability tests, and confirmatory clinical implantations, PHV might become an important therapeutic alternative for the treatment of selected patients with nonsurgical aortic stenosis [16].

Many patients with chronic severe AR may remain clinically compensated for years with normal LV function and no symptoms. These patients do not require surgery but can be followed carefully for the onset of symptoms or LV dilation/dysfunction. Surgery should be considered before the LV ejection fraction falls below 55%. The primary role of medical therapy with vasodilators is to delay the need for surgery in asymptomatic patients with normal LV function or to treat patients in whom surgery is not an option. The goal of vasodilator therapy is to achieve a significant decrease in systolic arterial pressure. Future therapies may focus on molecular mechanisms to prevent adverse LV remodelling and fibrosis [17].

VHD AND PREGNANCY

Association between valvular heart disease (VHD) and maternal and fetal outcome is important. Available information regarding outcome of pregnancy in women with VHD is limited to either anecdotal reports or small series of patients without an appropriate control. A better understanding of the effects of valvular abnormalities on pregnancy outcome is of value for risk assessment and the design of a therapeutic plan. Women with VHD had a significantly higher incidence of congestive heart failure (38%), arrhythmias (15%), initiation or increase of cardiac medications (41%), and hospitalizations (35%). Moreover, VHD also had an effect on fetal outcome, resulting in an increased preterm delivery, intrauterine

growth retardation and a reduced birth weight. Increased maternal morbidity and unfavourable fetal outcome were seen mostly in patients with moderate and severe mitral stenosis (MS) and AS. Despite high maternal morbidity, mortality is rare [18]. Pregnant patients with mechanical valves require careful attention to ensure maternal survival. Congenital submitral aneurysms are a unique cause of mitral regurgitation [19].

DRUGS INDUCED VHD

The appetite suppressants fenfluramine and dexfenfluramine, the dopamine agonists pergolide and cabergoline, and more recently, the recreational drug ecstasy (3, 4 methylenedioxymethamphetamine; MDMA), their drug dose and treatment duration affect both the risk of developing the disease and its severity. The natural history of the disease remains unclear, although regression of valvular lesions after the end of treatment has been reported. Interference with serotonin metabolism and its associated receptors and transporter gene seems a likely mechanism for development of the drug-induced valvular heart disease. Physicians need to balance the benefits of continued therapy with these drugs against possible risks [20].

We consider patients taking dopamine agonists for Parkinson's disease (pergolide, patients; cabergoline, and non-ergot-derived dopamine agonists). Clinically important regurgitation (moderate to severe, grade 3 to 4) in any valve was found with significantly greater frequency in patients taking pergolide or cabergoline but not in patients taking non-ergot-derived dopamine agonists. The relative risk for moderate or severe valve regurgitation in the pergolide group was higher for mitral regurgitation, then for aortic regurgitation and for tricuspid regurgitation corresponding relative risks in the cabergoline group. It should

be considered in evaluating the risk–benefit ratio of treatment with ergot derivatives [21].

VHD ASSOCIATED WITH CABG

Management of asymptomatic mild aortic stenosis at the time of coronary artery bypass grafting (CABG) remains controversial. Patients requiring aortic valve replacement (AVR) subsequent to CABG and their operative morbidity and mortality should be compared. Patients having AVR subsequent to CABG had a significantly prolonged aortic cross-clamp time and global myocardial ischemic time and incurred a twofold increase in operative mortality. The operative mortality and morbidity of a second operation for AVR is high, but there is no significant difference in survival at 10 years. In at least a portion of patients having mild aortic stenosis at the time of CABG there will be progression of the stenosis necessitating reoperation at a later date [22]. CABG should be performed for obstruction of major epicardial arteries even without ischemic symptoms in patients having aortic valve replacement (AVR) for aortic stenosis (AS), there has been little or no consideration of whether "mild-to-moderate" AS should be treated by valve repair or AVR at the time of CABG. Serious consideration of AVR should be entertained for patients with any degree of aortic valve obstruction who must undergo CABG surgery [23].

Percutaneous aortic valve replacement represents an endovascular alternative to conventional open heart surgery without the need for sternotomy, aortotomy, or cardiopulmonary bypass. Percutaneous Transarterial Aortic Valve Replacement is done in selected High-Risk Patients with Aortic Stenosis [24].

CONCLUSION

Valvular heart disease is a leading cause of morbidity and mortality. Valvular disease

ranks among the major cardiovascular afflictions. Significant valvular heart disease includes any mitral or aortic stenosis severity, moderate or severe mitral regurgitation, moderate or severe aortic regurgitation and moderate or severe tricuspid regurgitation. Valve problems may be congenital or acquired. Treatment may be with medication but often involves valve repair or replacement. Symptoms of valve diseases include shortness of breath and/or difficulty in breathing, weakness or dizziness, discomfort in chest, palpitations, edema, wheezing after limited physical exertion, chest pain, fatigue, dizziness or fainting, fever (with bacterial endocarditis) and rapid weight gain. Diagnosis of heart valves includes listening heart sounds and diagnostic tests like echocardiography, cardiac catheterization, magnetic resonance imaging (MRI), stress testing to measure blood pressure, heart rate, ECG changes and breathing rates during exercise. Three goals of treatment for heart valve disease: protecting valve from further damage, lessening symptoms and repairing or replacing valves. Rheumatic heart disease and infective endocarditis are important factors towards occurrence of valvular heart disease. Valves can be repaired or replaced. Tissue valves are preferred as they do not require life-long use of anticoagulants. But as far as wear and tear is concerned, mechanical valves are more advantageous. Heart valves may also be repaired by other procedures such as percutaneous balloon valvotomy.

RECOMMENDATIONS

- International Normalized Ratio (INR) level should be monitored carefully after valve replacement or valve repair. Use of heparin to adjust INR range should be monitored regularly by health care professionals.

- Anticoagulant therapy should be carefully monitored. Pharmacist should play his role by increasing patient compliance to anticoagulant especially in patients with mechanical valve replacement.
- Individuals at higher risk of endocarditis must be identified properly. Higher risk patients have prosthetic heart valves, history of endocarditis leading to high morbidity and mortality.
- Patient should be informed about the treatment of oral or dental procedures the initial amoxicillin dose is reduced to 2 g, a follow-up antibiotic dose is no longer recommended, and erythromycin is no longer recommended for penicillin-allergic individuals.
- Heart patients should have a complete physical exam and get an accurate assessment of current physical health.
- Pharmacist consultation should be encouraged for heart patients follow up. People with valvular heart problems may experience changes in their prothrombin time.
- Doctor while choosing the type of prosthesis for a valve replacement, the patient must be involved in the decision and needs to be educated with regard to issues such as the prevention of endocarditis and use of anticoagulation therapy.
- Pharmacist should provide pharmaceutical care to the patients with VHDs to improve their quality of life.

REFERENCES

- [1]. Kameswari Maganti, Vera H. Rigolin, Maurice Enriquez Sarano, and Robert O. Bonow, Valvular Heart Disease: Diagnosis and Management, *Mayo Foundation for Medical Education and research*, 2007, 356; 39-46
- [2]. Vuyisile T Nkomo, Prof Julius M Gardin, Prof Thomas N Skelton, Prof John S Gottdiener, Christopher G Scott, Prof Maurice Enriquez-Sarano, Burden of valvular heart diseases: a population-based study, *The Lancet*, 2006, 368(9540);1005-1011
- [3]. Vuyisile T Nkomo, Epidemiology and prevention of valvular heart diseases and infective endocarditis in Africa, *Mayo Clinic, Heart*, 2007, 93; 1510-1519
- [4]. Thomas van Bommel, Victoria Delgado, Jeroen J Bax, Jacobijn Gussekloo, Gerard J Blauw, Rudi G Westendorp and Eduard R Holman, Impact of valvular heart disease on activities of daily living of nonagenarians: the Leiden 85-plus study a population based study, *BMC Geriatrics*, 2010, 10; 17
- [5]. Raffi Bekeredjian, Paul A. Grayburn, Aortic Regurgitation, *Baylor University Medical Center*, 2005, 112; 125-134
- [6]. Paul Das, Helen Rimington and John Chambers, Exercise testing to stratify risk in aortic stenosis, *Eur Heart J*, 2005, 26 (13):1309-1313
- [7]. Bhandari Suman, Subramanyem K., Trehan N, Valvular heart disease: Diagnosis and management, *Journal of Association of Physicians of India*, 2007, 55; 575-584
- [8]. A. O. Brubakk, A. J. Angelsen and I. Hatle, transcutaneous Doppler ultrasound, *Cardiovasc Res*, 1977, 11 (5): 461-469
- [9]. Peter F. Coh, Richard Gorlin, Lawrence H. Cohn, and John J. Collins, Left ventricular ejection fraction as a prognostic guide in surgical treatment of coronary and valvular heart disease, *Am J Cardiol*, 1974, 34(2), 136-141
- [10]. E Hayek, B P Griffin, Current medical management of valvular heart disease, *Cleve Clin J Med*, 2001, 68; 881-887
- [11]. Deeb N. Salem, Paul D. Stein, Amin Al-Ahmad, Henry I. Bussey, Dieter Horstkotte, Nancy Miller, and Stephen G. Pauker, Antithrombotic Therapy in Valvular Heart Disease Native and Prosthetic, *CHEST*, 2004, 126 (3); 457S-482S
- [12]. Raphael Rosenhek, Thomas Binder, Gerold Porenta, Irene Lang, Günther Christ, Michael Schemper, Gerald Maurer, and Helmut Baumgartner, Predictors of

- Outcome in Severe, Asymptomatic Aortic Stenosis, *NEJM*, 2000, 343(9);611-617
- [13]. Blase A. Carabello, Evaluation and Management of Patients with Aortic Stenosis, *American Heart Association Circulation*, 2002, 105; 1746-1750
- [14]. Micheal A. Kuhn, Larry A. Latson, John P. Cheatham, Scott E. Fletcher, Cynthia Foreman, Management of pediatric patients with isolated valvular aortic stenosis by balloon aortic valvuloplasty, 1998, 39; 55-61
- [15]. Christos Alexiou, Qiang Chen, Stephen M. Langley, Anthony P. Salmon, Barry R. Keeton, Marcus P. Haw, James L. Monro, Is there still a place for open surgical valvotomy in the management of aortic stenosis in children? The view from Southampton, *Eur J Cardiothorac Surg*, 2001, 20; 239-246
- [16]. Alain Cribier, Helene Eltchaninoff, Assaf Bash, Nicolas Borenstein, Christophe Tron, Fabrice Bauer, Genevieve Derumeaux, Frederic Anselme, François Laborde, Martin B. Leon, Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis, *American Heart Association Circulation*, 2002, 106; 3006
- [17]. Raffi Bekeredjian, Paul A. Grayburn, Aortic Regurgitation, *Baylor University Medical Center*, 2005, 112; 125-134
- [18]. Afshan Hameed, Ilyas S. Karaalp, Padmini P. Tummala Omar R. Wani, Menahem Canetti, Mohammed W. Akhter, Murphy Goodwin, Natalia Zapadinsky, and Uri Elkayam, The effect of valvular heart disease on maternal and fetal outcome of pregnancy, *J Am Coll Cardiol*, 2001; 37; 893-899
- [19]. Mohammed Rafique Essop, Vuyisile T. Nkomo, Rheumatic and Nonrheumatic Valvular Heart Disease Epidemiology, Management, and Prevention in Africa, *American Heart Association Circulation*.2005, 112; 3584-3591
- [20]. Sanjeev Bhattacharyya, Drug-induced fibrotic valvular heart disease, *The Lancet*, 2009, 374; 577 – 585
- [21]. Renzo Zanettini, Angelo Antonini, Gemma Gatto, Rosa Gentile, Silvana Tesei, and Gianni Pezzoli, Valvular Heart Disease and the Use of Dopamine Agonists for Parkinson's Disease, *Engl J Med*, 2007, 356;1676-1680
- [22]. Andrew C. Fiore, Marc T. Swartz, Keith S. Naunheim, Debra A. Moroney, David A. Canvasser, Lawrence R. McBride, Pamela S. Peigh, George C. Kaiser, Vallee L. Willman, Management of Asymptomatic Mild Aortic Stenosis During Coronary. *Ann Thorac Surg*, 1996, 61; 1693-1697
- [23]. John J. Collins Jr., Sary F. Aranki, Management of Mild Aortic Stenosis during Coronary Artery Bypass Graft Surgery, *J Card Surg*, 1994, 9; 145-147
- [24]. John G. Webb, Sanjeevan Pasupati, Karin Humphries, Christopher Thompson, Lukas Altwegg, Robert Moss, Ajay Sinhal, Ronald G. Carere, Brad Munt, Donald Ricci, Jian Ye, Anson Cheung, Sam V. Lichtenstein, Percutaneous Transarterial Aortic Valve Replacement in Selected High-Risk Patients With Aortic Stenosis, *American Heart Association Circulation*, 2007, 116; 755-763