Surgical treatment for valvular heart disease: a single centre experience from Sri Lanka

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Abstract

Valvular heart disease (VHD) is an important cause of morbidity and mortality in the world. Anatomically, it affects mostly the left side of the heart (aortic and mitral valves), but the right side (tricuspid and pulmonary valves) can also be involved.

Etiologically, a variety of underlying mechanisms can damage the heart valves and lead to stenosis, regurgitation, or a combination of both. Although rheumatic heart disease (RHD) has been reduced in the world, it remains the commonest cause of VHD in many countries [1]. It affects 33.4 million people worldwide and its long-term effects on heart valves are still seen in developing countries [2]. RHD, predominantly but not exclusively, affects the mitral valve and can often involve multiple valves [3]. In countries such as the USA and UK, age-associated degeneration of the valves has become the major contributor to valve disease [4]. With better living standards, as the longevity of people increases, the diagnosis and referral of diseases improve. Therefore, overall surgical treatment for VHD in the world is increasing [4]. Degeneration of the aortic valve is mainly caused by calcification, and usually causes aortic stenosis [5], whereas degeneration of the mitral valves tends to be myxomatous, and usually causes mitral valve prolapse, which could subsequently lead to mitral regurgitation [6]. Acute infective endocarditis (IE), caused by a highly virulent organism, can deform a previously normal valve, while endothelial damage present in RHD can predispose to subacute bacterial endocarditis. Congenital valvular disease can involve all four valves and can present at any age, but the congenital bicuspid aortic valve is the commonest type and is present in 1% of the world population [8]. Dilatation of the annulus is the key mechanism of functional regurgitation [9]. Coronary artery disease that causes ischemic changes of the mitral papillary muscles can cause ischemic mitral regurgitation [10]. Valve disease is usually progressive, frequently debilitating, and with time, can be life-threatening. While medical management provides an important ancillary treatment, and interventional procedures are important for selected valve diseases, it is surgical therapy that still plays a major role in definitive therapy.

Valvular heart surgeries (VHS) may be in the form of valve repair or valve replacement, the choice depending on the type of valvular lesion, the patient's characteristics, the surgeon's experience and the facilities available at the centre - to name a few. Recently, many modern techniques, including minimally invasive valve surgery [11] and combined surgical and interventional approaches such as Transcatheter Aortic Valve Implantation (TAVI) [12], have become available. However, because of the high costs of these treatment modalities, more traditional surgical options remain the standard of care, especially in parts of the world where resources are limited.

The demography, underlying pathology, aetiology and the outcome of patients undergoing valve surgery have been extensively reviewed in the USA and Europe [4], while data from Sri Lanka is mostly lacking. In this environment, management decisions have been based on “international data” that may not adequately represent local conditions. Therefore, we need to understand the profile of patients undergoing VHS in Sri Lanka, as it will influence our management decisions.

Material and Methods

Ethical clearance to do the study was obtained from the local ethical review committee. Permission to do the study was obtained from the head of the institution. No identification details were published or exposed to anyone other than the investigators of the study.

This is a retrospective descriptive cross-sectional study in a single surgeon-led cardiothoracic unit from August 2010 to April 2020. Operation notes, clinical records including microbiological reports, perfusion records and morbidity-mortality records of all patients who had undergone valve operations during the study period were reviewed. The operations included isolated and multiple valve operations.
valve orifice and minimal calcification. The other aetiologies were degenerative (51; 29.1%), congenital (28; 16%), acute endocarditis (9; 5.1%), ischemic (6; 3.4%) and functional (5; 2.8%). There were 6/175 redo operations in this series.

Subacute bacterial endocarditis had been present in 14/175 (8%) of these patients; thus, a total of 23/175 (13.2%) had endocarditis at some point of their disease. The mitral valve was involved in 16/23 (69.5%) of patients with endocarditis. The commonest organisms involved were of the Genus Streptococcus. These were all native valve endocarditis. There were no patients with prosthetic valve or intracardiac devise endocarditis.

A total of 195 prostheses were used in this series consisting of 178 valves (153/178; 88.8% mechanical valves, 25/178; 14% tissue valves) and 17 rings. The sizes most frequently used were 29 mm for mitral valves, 19 mm for aortic valves and 29 mm for mitral valve rings.

Ten (5.7%) patients had postoperative complications: Reopening for bleeding was the commonest cause of morbidity (5/175; 2.9%). All were resolved successfully.

The overall in-hospital mortality was 15/175 (8.6 %) (Table 1). The mortality of the most frequently performed (60/175; 34.2% %) valve replacement surgery, mitral valve replacement, was 8.3 % and that of the most frequently performed (9/26; 34%) valve repair surgery, isolated MV repair, was zero. It is noteworthy that one third (5/15) of those who died had endocarditis. The endocarditis group had a high mortality 5/23 (23%), especially for those with fungal endocarditis as both patients with candida endocarditis died. Elective valve surgery carried a mortality rate of 5.7% (8/141) while that of non-elective surgery was 20.6% (7/34). There were no deaths (0/6) in the small group of redo operations.

All patients in this unit routinely undergo a post-operative echocardiogram before discharge. Accordingly, 2/136 (1.5%) patients who were discharged following valve replacements had mild paravalvular leaks that were managed conservatively. The postoperative valve functions of 134/136 (98.5%) of valve replacements and 100% of valve repairs were good. It is the unit’s protocol that all patients after VHS are prescribed

Table 1. The case load and mortality of valvular heart surgery

| Type of Surgery                      | Number of Patients | Deaths |
|--------------------------------------|--------------------|--------|
| Valve replacement                    | 149 (85.1%)        | 13 (8.7%)|
| Valve repair                         | 21 (12%)           | 1 (4.8%)|
| Combined valve replacement and repair| 5 (2.9%)           | 1 (20%) |
| Total                                | 175 (100%)         | 15 (8.6%)|

Results

During the study period, a total of 175 patients had undergone VHS which constituted 15.7% (175/1115) of the total workload of this unit. The mean age of patients was 51.5 years (range 6-76 years). There were 105 (60%) males and 70 (40%) females. There were no referrals of pregnant females for valve surgery in this series.

The majority (151/175; 86.3%) of operations were single valvular heart operations while 21 (12%) were double valve operations and three (1.7%) were triple valve operations. Most (132/175; 75.4%) were isolated valvular procedures while (43/175; 24.6%) were combined valvular procedures.

The protocol in this unit is that all patients above the age of 40 years awaiting VHS should routinely undergo coronary angiography. Accordingly, 35/175 (20.5%) patients were found to have coronary artery disease severe enough to warrant concomitant Coronary Artery Bypass Surgery (CABG). Other procedures that were done concomitantly with the VHS were: four ventricular septal defect closures, two atrial septal defect closures, one aortic root replacement and one pericardiectomy.

The commonest valve involved was the mitral valve (117/175; 66.9 %) followed by the aortic (72/175; 41.1%), tricuspid (10/175; 5.7%) and pulmonary valves (3/175; 1.7%). There were differences in their mean ages: 56 (19-76, SD 11.7) years for aortic valve lesions, 52 (7- 75, SD 13.5) years for mitral valve lesions, 30 (23-37 SD 7.0) years for pulmonary valve lesions and 26.5 (6-56 SD 21.8) years for tricuspid valve lesions.

The commonest hemodynamic pathology was mitral regurgitation (88/175; 50.3%) present alone or in combination with other valvular pathologies followed by mitral stenosis (38; 21.7%). The commonest aetiology was RHD (76; 43.4%) which was diagnosed based on the past medical history of RHD and was confirmed macroscopically during surgery. In the case of the mitral valve, macroscopic findings typically included thickened, shortened and fused chordae tendinea as well as thickened and fibrosed valve leaflets. In the case of the aortic valve, the typical findings were thickened and fibrosed free edges of the leaflets, fused commissures, a classic “fish mouth” appearance of the aortic valve orifice and minimal calcification. The other aetiologies were degenerative (51;29.1%), congenital (28; 16%), acute endocarditis (9; 5.1%), ischemic (6; 3.4%) and functional (5; 2.8%). There were 6/175 redo operations in this series.

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warfarin. This is omitted three months after surgery in those who have had a repair or a tissue valve replacement, while those who have had a mechanical valve will essentially continue warfarin for life.

Six patients have died after discharge due to warfarin-related issues: Two died due to haemorrhage: one was a 14-year-old who died two years after discharge due to massive intracerebral haemorrhage. The other was an adult who died two months after discharge due to massive generalized haemorrhage after taking four tablets of 5mg warfarin instead of the prescribed four tablets of 1mg warfarin. Four patients have died due to possible thrombotic complications after stopping warfarin: two died within the first year: one when a doctor had stopped warfarin for three days to control an ecchymotic patch and another due to four days of vomiting when he most likely vomited his warfarin tablets. Two patients died five years after discharge due to neglecting their medication amidst family conflicts and social problems.

Discussion

VHS is second only to coronary operations in most adult cardiac surgical centres in the world and usually accounts for 20% to 35% of their procedures [13]. As our unit deals with both cardiac and thoracic surgery, VHS accounted for only 15.6% of all operations in our unit and is the third commonest operation next to coronary and thoracic operations.

Rheumatic carditis was the most frequent etiological factor for VHD. According to WHO data published in 2017, the age-adjusted death rate due to rheumatic carditis in Sri Lanka is 1.94 per 100,000 of population and ranks Sri Lanka at number 92 in the world [14].

World data shows that IE is slightly commoner in aortic valves [15]. However, the mitral valve was the commonest valve affected by IE (69.5%) in our series. This is because RHD, a risk factor for IE, predominantly involves the mitral valve and RHD is, by far, the commonest aetiology for VHD in our community. International data shows that most native valve endocarditis is now caused by Streptococcus, Staphylococcus, and Enterococcus [16]. The commonest organisms in our series were Streptococcus and Enterococcus. Fungal endocarditis remains the most serious form of infective endocarditis, with high mortality rates of 44-80% in world series [17] and this dismal prognosis is reflected in our small series as well.

Valve replacement can be done using either a mechanical or tissue valve. In this series, 88.8% of valves used were mechanical. Mechanical valves last a lifetime but have the disadvantage of requiring lifelong anticoagulation, usually with warfarin. Neither tissue valve replacements nor valve repairs require such long-term warfarin for the valve per se (unless the presence of arrhythmia influences this decision).

Warfarin requirement confers disadvantages to patients in many aspects, especially with regards to pregnancy due to its risks of bleeding and teratogenicity. Patients on warfarin need to have their International Normalized Ratio (INR) measured monthly. The INR can change with alcohol and certain types of food and drugs—all of which can be problematic to patients. Our experience with warfarin is that patients' compliance in the long term is not optimal. There are no home INR testing facilities in Sri Lanka and patients need to travel to a hospital for the test and the medication, and the motivation to do so can dwindle over time. Problems have arisen with dosing as the 1mg, 2mg and 5 mg tablets are all white, of the same size and shape, and are not marked on the tablet. The quality of the warfarin tablets is questionable and tends to crumble when trying to break it into parts. Inadvertent massive overdoses have happened occasionally due to confusion in tablet strength. In this series, the death of six patients after discharge is related to such issues. Authorities need to take action to prevent such complications by marking the strength or colour-coding the warfarin tablets as was done in the past.

One way to overcome these problems during surgery is to use a tissue valve instead of a mechanical one, but as tissue valves last only 10-15 years, it is usually recommended for the older age group. As the patients' age at surgery shows an increasing trend, the use of tissue valves is increasing in the world [4]. If a young patient opts for a tissue valve (e.g. wishes to become pregnant and avoid warfarin) the chances are that 10-20 years later, she will need a redo operation. Recent trends in the USA show increasing use of tissue valves even in the 50-60-year age group, but with higher rates of reoperations [18]. Redo operations carries a higher risk than a first-time operation [19]. Despite these problems with warfarin, we use tissue valves only in the above 60-years age group and continue to insert mechanical valves for the younger patients. This is not only to avoid the technical challenges of reoperation but also to avoid an additional operation in an already over-burdened system where the waiting time for any cardiac operation is long.

There has been a strong move in the US and Europe to repair rather than replace valves [20]. Valve repair requires, among many other facilities, the availability of intraoperative transoesophageal echocardiography (TEE), accredited experts to perform it, interpret it and liaise with the surgeon during surgery to ensure a good repair. Our unit does not have TEE, despite yearly efforts by the surgical team to convince the administration to invest in one and highlights how financial issues have a direct impact on therapy in Sri Lanka.
Until TEE is available, we have tried to overcome this problem by performing valve repairs in carefully selected patients with favourable anatomy. The repair is assessed intraoperatively using static water testing, with a low threshold to convert to a replacement on-table should test results be less than ideal. This method has given excellent postoperative echocardiography results and has conferred the advantage of managing selected patients without long term warfarin. However, the zero morbidity and mortality of this small group (9/175; 5.1%) of isolated mitral valve repair patients is perhaps due to our careful selection of uncomplicated patients for repairs. Furthermore, cardiologists refer patients for repairs (as opposed to replacement) earlier - before the onset of complications. Both factors could contribute to a better outcome in the repair group. We continue our efforts to obtain TEE facilities, without which we cannot progress safely with mitral valve repairs.

A large study was done in 2005 of more than 400,000 patients in the Society of Thoracic Surgery (STS) database in the USA over 10 years found an overall mortality of 7.1% [19]. The acute presentation was the most important risk factor to confer high mortality (12.9%) for valve surgery [19]. In this study, the authors urged to refer patients with severe valve lesions under elective and not emergency conditions. Our own unit's mortality reflected a similar trend with 5.7% mortality for routine versus 25% for acute presentations. Therefore, the desirability of early referral and intervention appears to be relevant in present in our setting as well. Given the cost of valve operations (SLR 1-1.3 million) and the added cost of a stormy intensive care stay for compromised patients, fast-tracking valve patients before clinical deterioration should be a topic of discussion between clinicians and administration.

Over time, VHD compromises the myocardial and overall organ functions. Patients who have not undergone surgical correction in time often present late with significant myocardial dysfunction, pulmonary hypertension and cardiac cachexia. Late presentations could be a cause for higher mortality in our setting. However, objective measurements of myocardial compromise such as the ejection fraction, or a complexity scoring were not available in our records. This is a shortcoming in this retrospective study and should be studied in future prospective studies. Furthermore, the long term survival of this cohort merits further study.

Conclusions
This is the first study of baseline data of patients undergoing VHS in a cardiothoracic unit in Sri Lanka. It has established the workload, demography, aetiology, pathology, trends in surgical treatment and outcome of VHS in the local setting which have important differences from those of international studies. This has also highlighted aspects of VHS in Sri Lanka that need to be developed and areas that merit further audit and research.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

References
1. Soler-Soler J, Galve E. Worldwide perspective of valve disease. Heart. 2000 Jun 1;83(6):721-5. http://dx.doi.org/10.1136/heart.83.6.721
2. Huntley GD, Thaden JJ, Nkomo VT. Epidemiology of heart valve disease. In Principles of Heart Valve Engineering 2019 Jan 1 (pp. 41-62). Academic Press. https://doi.org/10.1016/B978-0-12-814661-3.00003-4
3. Seekeler MD, Hoke TR. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. Clinical epidemiology. 2011:3:67 https://dx.doi.org/10.2147%2FCLEP.S12977
4. Dunning J, Gao H, Chambers J, Moat N, Murphy G, Pagano D, Ray S, Roxburgh J, Bridgewater B. Aortic valve surgery: marked increases in volume and significant decreases in mechanical valve use—an analysis of 41,227 patients over 5 years from the Society for Thoracoarterial Surgery in Great Britain and Ireland National database. The Journal of thoracic and cardiovascular surgery. 2011 Oct 1;142(4):776-82. https://doi.org/10.1016/j.jtcvs.2011.04.048
5. Goldbarg SH, Elmariah S, Miller MA, Fuster V. Insights into degenerative aortic valve disease. Journal of the American College of Cardiology. 2007 Sep 25;50(13):1205-13. https://doi.org/10.1016/j.jacc.2007.06.024
6. Hayek E, Gring CN, Griffin BP. Mitral valve prolapse. The Lancet. 2005 Feb 5;365(9458):507-18. https://doi.org/10.1016/S0140-6736(05)17869-6
7. Todd L, Kiefer, Thomas M. Bashore. Infective Endocarditis: A Comprehensive Overview. Reviews in Cardiovascular Medicine, 2012, 13(2-3): 105-120. https://doi.org/10.3909/ricm0633.
8. Nakashishi T, Markwald RR, Baldwin HS, Keller BB, Srivastava D, Yamagishi H. Notch Signaling in Aortic Valve Development and Disease--Etiology and Morphogenesis of Congenital Heart Disease: From Gene Function and Cellular Interaction to Morphology. https://doi.org/10.1007/978-4-431-54628-3_53
9. Muraru D, Guta AC, Ochoa-Jimenez RC, Bartos D, Aruta P, Mihaila S, Popescu BA, Iliecu S, Basso C, Badano LP. Functional regurgitation of atrioventricular valves and atrial fibrillation: an elusive pathophysiological link deserving further attention. Journal of the American Society of Echocardiography. 2020 Jan 1;33(1):42-53. https://doi.org/10.1016/j.echo.2019.08.016/
10. Gimpel D, Cheung M, Bassin L, Jennings S, Weiss B, Akhunji Z, Grant P, Wolfenden H. Operative Results of Mitral Valve Repair and Replacement in Chronic Ischaemic Mitral Valve...
11. Schmitto JD, Mokashi SA, Cohn LH. Minimally-invasive valve surgery. Journal of the American College of Cardiology. 2010 Aug;56(6):455-62. https://doi.org/10.1016/j.jacc.2010.03.053

12. Munkholm-Larsen S, Croce B, Harris R. TAVI: transcatheter aortic valve implantation. Annals of cardiothoracic surgery. 2012 Jul;1(2):263. https://dx.doi.org/10.3978%2Fj.issn.2225-319X.2012.07.09

13. Jung B, Vahanian A. Epidemiology of valvular heart disease in the adult. Nature Reviews Cardiology. 2011 Mar;8(3):162.

14. Kiefer TL, Bashore TM. Infective endocarditis: a comprehensive overview. Reviews in cardiovascular medicine. 2019 Jul 17;13(2-3):105-20. https://doi.org/10.3909/ricm0633

15. Williams JB, Shah AA, Zhang S, Jung SH, Yerokun B, Vemulapalli S, Smith PK, Gammie JS, Gaca JG. Impact of microbiological organism type on surgically managed endocarditis. The Annals of thoracic surgery. 2019 Nov 1;108(5):1325-9. https://doi.org/10.1016/j.athoracsur.2019.04.025

16. Siciliano RF, Gualandro DM, Sejas ON, Ignoto BG, Caramelli B, Mansur AJ, Sampaio RO, Pierrotti LC, Barbosa G, Golebiovski W, Weksler C. Outcomes in patients with fungal endocarditis: A multicenter observational cohort study. International Journal of Infectious Diseases. 2018 Dec 1;77:48-52. https://doi.org/10.1016/j.ijid.2018.09.016

18. Iribarne A, Leavitt BJ, Robich MP, Sardella GL, Gelb DJ, Baribeau YM, McCullough JN, Weldner PW, Clough RA, Ross CS, Malenka DJ. Tissue versus mechanical aortic valve replacement in younger patients: A multicenter analysis. The Journal of thoracic and cardiovascular surgery. 2019 Dec;158(6):1529-38. https://doi.org/10.1016/j.jtcvs.2019.02.076

19. Rankin JS, Hammill BG, Ferguson Jr TB, Glower DD, O’Brien SM, DeLong ER, Peterson ED, Edwards FH. Determinants of operative mortality in valvular heart surgery. The Journal of thoracic and cardiovascular surgery. 2006 Mar 1;131(3):547-57. https://doi.org/10.1016/j.jtcvs.2005.10.041