St. Jude Medical versus TTK Chitra mechanical heart valves at aortic/mitral position – Comparison of long term results.

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Abbreviations
Ao  Aorta
AF  Atrial Fibrillation
AVR  Aortic valve replacement
BMV  Balloon mitral valvuloplasty
CHVP  Chitra mechanical heart valve prosthesis
CM  Carbomedics
EF  Ejection fraction
FC  Functional class
LA  Left atrium
LVDD  Left ventricular diastolic dimension
LVSD  Left ventricular systolic dimension
MH  Medtronic Hall
MVP  Mitral valve prolapse
MVR  Mitral valve replacement
NYHA  New York Heart Association
PAH  Pulmonary artery hypertension
PVT  Prosthetic valve thrombosis
RF  Rheumatic fever
RHD  Rheumatic heart disease
SCTIMST  Sree Chitra Tirunal Institute for Medical Sciences and Technology
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**Introduction**

Valvular heart disease (VHD) continues to be a major contributor to morbidity and mortality worldwide, especially in the developing nations where chronic rheumatic heart disease (RHD) still accounts for the vast majority of VHD.\(^{(1)}\) In resource limited settings, not all patients requiring cardiac surgery are able to afford it. Hence, there existed a large unmet need for a low cost and efficacious prosthetic heart valve in India. It is to bridge this gap that the TTK Chitra mechanical heart valve prosthesis (CHVP) was developed in the 1980s. The first human implant was done on December 6, 1990 at SCTIMST. It is in widespread use for the past two decades and more than 70,000 implantations have been done so far.\(^{(2)}\)

The CHVP is a monoleaflet, tilting disc design heart valve. A multicentric clinical trial in 2001 reported excellent clinical outcomes with CHVP.\(^{(3)}\) However, literature is still divided on the comparative advantages of a particular heart valve design over others. The oldest generation of heart valves, with a caged ball design are not in wide use anymore. The most commonly used valves currently are those with a bileaflet design. Relative merits and disadvantages between the monoleaflet and bileaflet designs are not very well established as most clinical trials report outcomes from follow up of a single valve type. Few comparative studies suggest that both valve types have similar clinical performance and durability.\(^{(4, 5)}\)
St. Jude Medical bileaflet valve and Medtronic Hall monoleaflet valve were most commonly implanted valves till 2009, when Medtronic stopped production of its monoleaflet valve (6). In this context, the CHVP could offer patients suffering from VHD, comparable clinical outcomes to existing bileaflet and monoleaflet valves at a much lower cost. Comparative clinical outcome data between this monoleaflet valve model and the existing bileaflet valves is not available. We had planned to conduct this study to systematically analyze the outcomes of patients receiving CHVP and compare it to commonly used bileaflet valves.
Review of Literature

Epidemiology of valvular heart disease and valve replacement surgery

Among the non communicable diseases, valvular heart disease is a major contributor to morbidity and mortality. With changing demographic ratios and a rapidly ageing population, the incidence and prevalence of valvular heart disease is expected to increase worldwide. In developing nations, rheumatic heart disease related complications continue to be responsible for majority of valvular heart disease. The number of patients requiring heart valve replacement is projected to increase threefold by 2050, from approximately 2,90,000 in 2003 to over 8,50,000 in 2050 proportionate to an increase in world population with about 22% individuals above the age of 60 years.(7) A large subset of these patients will be rheumatic heart disease patients in third world countries who have limited access to health care.(1)

There are over 15 million patients with rheumatic heart disease worldwide with an estimated 470,000 new cases of rheumatic fever per year, of which 60% (282,000 people) develop structural heart disease as sequelae. Rheumatic heart disease (RHD) accounts for mortality in over 2,33,000 patients each year.(8) With improvement in living conditions and access to health care, rheumatic fever is now uncommon in the developed world, but continues to be a major health care
problem in developing countries where these facilities have not improved.(9) In India, the incidence of rheumatic fever (RF) is estimated to be 0.2-0.75/1000/year in children of the age group 5-15 years.(10-12) With a median incidence of 0.54/1000/year, about 131,000 new patients develop rheumatic fever per year in India. (13) In the late 1970s, prevalence of RF/RHD among school children in India was 2-11 per 1000 with a mean of 6 per 1000.(14) Three decades later, a study from South India conducted in 2002 showed a drastic reduction in the prevalence to 0.68 per 1000 children.(15) However, these studies based on clinical diagnosis of RHD may be underestimating the actual burden of disease. In 2011, a cross-sectional survey utilizing portable echocardiography to identify asymptomatic RHD, reported the prevalence in rural school children aged 5-15 years, residing in North India to be 20.8/1000 (95% CI: 16.9–23.9/1000). The prevalence going by clinical diagnosis was only 0.8/1000 school children.(16) Among the adult population too, the prevalence of RHD in developing nations (123-200 per 100,000 population) is much greater than in developed nations (0.05/100,000).(17) In developing nations, it is estimated that about one in 150 deaths is attributable to rheumatic heart disease.(17) 25%–50% of newly diagnosed RHD cases, deaths and hospitalization due to RHD are from India.(18) 22-50% of all cardiac patients seen in Indian hospitals and 28-45% of all cardiovascular
deaths in hospitals are due to RHD.(19) As a corollary, 50% of heart surgeries performed in our country is for RHD.(20)

Given the limited healthcare resources in developing countries not all VHD patients have access to the treatment they require. In India there are nearly 80 heart centers performing 20,000 heart valve operations per year. Given that India has 1.1 billion inhabitants this implies that per 100,000 inhabitants approximately 1.8 heart valve surgeries take place every year. In contrast, this number is approximately 28 in the Netherlands.(1) For the large number of VHD patients in India, mostly contributed by chronic RHD and belonging to the lower socioeconomic strata, with limited access to health care and finances, RHD accounts for a major proportion of DALYs lost. Hence, a low cost mechanical heart valve prosthesis was a large unmet need in India. It is with the aim of addressing this unmet need that the first indigenously developed low cost mechanical heart valve was pioneered by the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala in the 1980s.

**Prosthetic heart valves**

Hufnagel is credited with earliest heart valve implantation in 1952 and this prototype was implanted in the descending thoracic aorta.(21) Orthotopic heart
valve replacements became feasible in 1960, when cardiopulmonary bypass techniques were established.(22) Prosthetic heart valves have undergone multiple design improvisations since then in pursuit of an ideal heart valve. Harken et al. in 1962 enumerated the prerequisites of an ideal heart valve and these characteristics have been modified since then.(23, 24) Ideally, the heart valve prosthesis should mimic the characteristics of a normal native valve. Excellent hemodynamic parameters, long durability, high resistance to thrombosis and embolism, and ease of implantation are especially important. Unfortunately, these parameters are difficult to meet and such an ideal prosthetic does not exist yet. Of the currently available prosthetic valves, each has its own set of inherent limitations. Broadly, there are two types of prosthetic heart valves: mechanical heart valves (MHVs) and bioprosthetic heart valves (B HVs).

**Mechanical Valves**

Mechanical heart valves are produced using artificial biomaterials like Teflon, Dacron, titanium, cobalt, LTI carbon, Delrin, etc.(25) Mechanical heart valve designs have evolved over time resulting in three types of mechanical heart valves: caged ball, monoleaflet and bileaflet valves.(26)
Caged Ball Valves

The earliest mechanical heart valves were of caged ball design and are no longer implanted. Caged ball mechanical heart valves are made of a three metal arches making a cage and a circular sewing ring at base. Silastic ball kept inside cage moves in opening and closed position during cardiac cycle. This design of mechanical value has shown excellent durability, even over 40 years post surgery. Bulky design of this valve caused problems of interference with other nearby structures while implanting these valves in patients with small left ventricular cavity and aortic annulus. Also incidence of hemolysis was more compared to other valve designs(22).

Monoleaflet Valves

Monoleaflet valves consist of a single disk attached to a metallic ring. Opening of disc produce 2 orifices of different sizes and the opening angle of the tilting disc with respect to the valve annulus ranges from 60° to 80°. Examples include Bjork–Shiley valve, Medtronic Hall valve, Omniscience/Omnicarbon valves, Monostrut valve, Ultracor valve and TTK Chitra valve.

Bileaflet Valves

Bileaflet valves consist of 2 semicircular discs attached to a metallic ring by tiny hinges. Opening of the valve results in three orifices: a central orifice between 2 leaflets and 2 larger semicircular openings lateral to the discs. The leaflets open at
an angle of 75° to 90° relative to the plane of the annular ring. Currently, bileaflet valves are the most widely used type of mechanical prosthesis worldwide. Examples include St. Jude Medical valve, St. Jude Regent valve, Carbomedics valve, Sorin Bicarbon valve, Edwards Mira valve and Medtronic Advantage valve.\(^{(26)}\)

**Bioprosthetic Valves**

Bioprosthetic valves, as the name suggests are made up of bio materials. They are of two main types: Stented and stentless. They are usually made of porcine aortic valves or bovine pericardium fixed in glutaraldehyde and implanted on a metallic or polymer supporting stent. Stentless bioprosthetics were designed to improve hemodynamics and durability. These valves don’t have metallic supporting stent. Advantage of these valves is avoidance of lifelong anticoagulation. Limiting factors for these bioprosthetic valves is limited durability and need for reoperation after around 10 years.

**Bioprosthetic Versus Mechanical Valves**

The decision to choose a bioprosthetic or mechanical heart valve has to individually tailored on a patient-to-patient basis. Apart from patients preference, patient characteristics that favour a mechanical prosthesis over bioprosthesis include: \(^{(26)}\) young age with a long life expectancy, no contraindication for anticoagulation or already on anticoagulation for other indication or known to have
condition predisposing to accelerated bioprosthesis degeneration like hyperparathyroidism and renal insufficiency. Apart from patients preference, bioprosthetic valves are preferable in older patients with high risk of both thrombotic and bleeding risks, in whom bioprosthesis may last longer than patient’s estimated survival, patients with contraindications or non compliance to anticoagulants or women of child bearing age group planning pregnancy. Worldwide, majority of the implanted prosthetic heart valves are mechanical (55%) and rest bioprosthetic. In developed countries, percentages are reversed with biological valves accounting for 55%.(27) Since majority of heart valve replacement in India are for rheumatic valvular heart disease with patients being younger in age, mechanical heart valves are the preferred choice in majority of our patients .(28)

**Comparision of various Mechanical Prosthetic Heart Valves**

**Randomized trials**

In a randomized control trial, the Starr-Edwards valve (Edwards Lifesciences, Irvine, California), a caged-ball valve in use since 1965, was compared with the St. Jude Medical valve (St. Jude Medical, St. Paul, Minnesota), first used in 1977. Survival, event-free survival and other outcomes were similar for both valves in aortic as well as mitral replacements (29).
In another study, the Carbomedics valve (Carbomedics, Austin, Texas) a bileaflet mechanical heart valve was compared with the St. Jude Medical, another bileaflet design. After either mitral or aortic valve replacement, survival and freedom from complications were similar at 10 years (30).

Nonrandomized studies

Follow up studies of up to 40 years have established good outcomes with virtually no structural valve deterioration with the caged-ball design Starr-Edwards valve (31). 20-25 year follow up data is available for the Medtronic-Hall valve (Medtronic, Minneapolis, Minnesota) (32, 33), the Bjork-Shiley valve (Shiley, Irvine, California) and St. Jude Medical valves. (34-36) Thromboembolism and bleeding rates were similar among the various mechanical valves in a review of 70 published studies, encompassing 24,202 valves and 132,519 patient-years of follow-up (37).

Two of the most widely used mechanical heart valves at our centre are St. Jude Medical® Mechanical Heart Valve (SJM; St. Jude Medical Inc.; Minneapolis, Minn) and TTK Chitra heart valve (CHVP; TTK Healthcare, Kazhakootam, Trivandrum, India). Many distinctive design features distinguish SJM from TTK Chitra valve. SJM is a bileaflet mechanical valve with a low profile, made of
pyrolytic carbon. SJM valves are available in sizes of 17–31 (aortic), 17–31 (mitral) with opening diameters of 14.7–26 mm (aortic and mitral) respectively.(38) In the open position, all aortic and mitral SJM bileaflet valves have a height of 8.4–12.2 mm. These valves demonstrated symmetric and relatively nonturbulent flow during in vitro analyses. Mean pressure gradients ranging from 3.0 to 5.2 mm Hg in the aortic position and from 1.4 to 7.0 mm Hg in the mitral position have been recorded in vivo. Regurgitant volumes noted range from 7.6 to 10.6 cm³/stroke in aortic position and 4.3 to 6.4 cm³/stroke in mitral valve.(39) The entire valve including leaflets is made of graphite coated with pyrolytic carbon. Tungsten (5–10 wt.%) is additionally included in the leaflets to make them adequately radio-opaque.(38) Hinges attaching the leaflet to the struts hinge are configured as a butterfly-like depression and with upright pivot guards. The sewing cuff is made of polyester PET or PTFE.(40) The low profile of bileaflet valves make them easier to implant during surgery. St. Jude valve is in use for more than two decades and there are large series with follow-up of 10 or more years.(34-36)

In a study published by Ikonomidis et al (34), 20 years of experience with SJM mechanical valve was reported. The study population included 837 patients (AVR 478, MVR 359) and mean follow up was around 7 years. Operative mortality was
3.6% in AVR and 5.3%) in MVR groups. For AVR, around 57% survived at 10 tears and 26% at 20 years. For MVR, 10 and 20 year actuarial survival was 61% and 39% respectively. There was no episode of structural valve deterioration. In the AVR group, freedom from re-operation was 93% and 90% at 10 and 20 years, 82% and 68% remained free of thromboembolic events; no bleeding was reported in 77% and 66%. Freedom from prosthetic valve endocarditis at 10 and 20 years was 94%. Valve related mortality was also low. Similar good outcomes were reported with mitral valve replacement.

In another study by Kratz et al (35), 456 adult patients who underwent isolated AVR (254) or MVR (202) with the SJM between 1979 to 1990 were followed up for a total of 2073 patient-years (mean 55± 37 months). Early mortality (within 30 days of surgery) was 3.9% in AVR group and 3.5% in MVR group. For AVR actuarial survivorship was 80% at 5 years with a drop to 47% by 10 years. Incidence of thromboembolism was 1.8%/ patient year, and about 67% patients remained free of thromboembolism at 10 years. The mean NYHA functional class improved significantly after surgery (3.1 ± 0.76 to 1.6 ± 0.84, p < 0.0001). In the MVR group, actuarial survivorship was 80% at 5 years and 63% at 10 years. Incidence of thromboembolism was 2.9%/ patient-year. At 10 years, about 77% patients were expected to remain free from thromboembolism. The mean NYHA
functional class improved significantly after surgery (3.4 ±0.63 preoperatively to 1.8 ± 0.91 postoperatively (p < 0.0001). There were no mechanical failures, but 19 patients underwent 22 replacements of a previously implanted St. Jude prosthesis for endocarditis (14), paravalvular leak (41), thrombosis (2), and hemolysis (2). Another study published in 1994 by Fernandez et al (36), followed 1200 patients with SJM. They reported slightly higher early deaths (6.8 % ). The 5-year actuarial survivorship was 75 %. More than 95% were projected to remain free of thromboembolism, bleeding, valve thrombosis, reoperation, endocarditis and paravalvular leak individually at 5 years. 74% and 94% were projected to remain free of any valve related event or valve related mortality at 5 years respectively.

**The TTK Chitra heart valve prosthesis**

The TTK Chitra mechanical heart valve prosthesis (CHVP) was developed at SCTIMST, Trivandrum, India, more than two decades ago. The high cost of existing imported valves and huge demand for prostheses due to high prevalence of chronic rheumatic heart disease motivated the development of TTK Chitra heart valve.(41) The TTK Chitra heart valve (TTK Healthcare, Kazhakoottam, Trivandrum, India) is designed as a single leaflet valve with a tilting disc design and an integrally fabricated cobalt alloy cage. It has an ultra-high molecular weight polyethylene disc, Haynes-25 alloy cage, and a polyester sewing ring. This design
was chosen owing to its superior hydrodynamics and considering the age
distribution of intended recipients, most of whom were young. This concern for
durability was also reflected in the choice of the polymer-metal combination which
was known for its extremely low wear rate. The hydrodynamic performance in
vitro was comparable to that of existing and proven clinical models. On accelerated
lifetime testing, lifetimes over 50 years were demonstrated and pre-clinical trials in
large animals showed the valve to be safe. (41)

In the initial clinical trial of TTK Chitra heart valve (41), 306 patients with
isolated mitral or aortic valve replacements were followed up for a total of 371
patient years (mean 1.37 years). Results of this trial clearly showed that TTK
Chitra valve was safe and comparable to other mechanical valves in clinical use.
There was no structural valve deterioration or paravalvular leak reported.
Linearized rate of late thromboembolism and anticoagulant related bleeding were
6.2%/patient-year and 0.54%/patient-year respectively. Higher rate of
thromboembolism reflects poor socioeconomic background of Indian patients and
hence poor compliance to anticoagulants and irregular monitoring of INR values.
Rate of infective endocarditis was low (0.54%/patient-year), which suggest
resistance of valve to infection. The total actuarial survival estimated at 2 years
after valve implantation was 89.5%. 

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In a multicentric study done in India (3), patients undergoing isolated aortic or mitral mechanical heart valve replacements with TTK Chitra valve (total number =306, AVR= 101, MVR =205) were analyzed. Early operative mortality rate was reported to be 6.9%, which was comparable to studies of other mechanical heart valves. Total follow up duration was 1212 patient-years, including 445 patient-years follow up of AVR patients and 767 patient-years follow up of patients who underwent MVR. Linearized rate of late deaths was 4.3%/pt-yr (2.2%/patient-year in AVR group and 5.5%/ patient year in MVR group). 35 patient had valve related deaths. Prosthetic valve thrombosis was noted in 13 patients, 12 patients of them had MVR. Linearized rates of valve thrombosis was estimated to be 1.6%/patient-year after MVR and 0.2%/patient-year after AVR. 25 patients had embolic episodes with linearized rates of 1.6%/patient-year after AVR and 2.4%/patient-year after MVR. Bleeding events and infective endocarditis were low, consistent with earlier reports of valve replacement with TTK Chitra heart valve (41). Similarly, paravalvular leaks and structural deterioration of valve were not noted on longer follow up. Actuarial survival rates were estimated to be 82.4+/-4.0% for AVR patients and 65.2+/-5.0% for MVR patients at 7 years from valve replacement. Valve thrombus-free and embolism-free survival at 7 years after AVR was estimated to be 98.9+/-1.1% and 94.1+/-1.9% respectively. For
MVR patients, valve thrombosis and embolism free survival at 7 years was 92.3+-2.8% and 82.1+-5.7% respectively. Event free survival at seven years was estimated to be 81.5+-4.1% among AVR patients and 64.2+-5.1% among MVR patients.

In studies conducted at SCTIMST by Namboodiri et al, gradients across TTK Chitra at mitral position and aortic positions were normal for each size of the valve and were comparable to other valves of common use (42, 43). Similar results were obtained from another single centre study (44).

In a single centre study(45), outcomes of 152 Chitra valves implanted between December 1992 and July 1998 were studied. In this study, 65 patients underwent isolated AVR and 64 patients underwent isolated MVR, rest had both aortic and mitral valve replaced. Early mortality reported was very low (0.6%). 4.6% of patients had late mortality. Out of 7 late deaths, 2 patients had prosthetic valve thrombosis and 2 died of complications of infective endocarditis. Cause of death could not be found in rest 3 patients. Surviving 144 patients had a total follow up of 622 patient years. Thromboembolic complication was noted in 11 patients (7.2%) with a linearized rate of 1.8 percent/ patient years. TTK Chitra valve was found to be comparable to other mechanical valves on hemodynamic evaluation.

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Freedom from thromboembolic events and event free survival at 5 years was estimated to be 82% and 78% respectively.

In another single centre study by Malhotra A et al from Bhopal (46), follow up data of 200 patients with 249 TTK Chitra valve replacements was published. There were 122 MVR, 29 AVR and 49 DVR patients, which were followed for a mean duration of 2.5 years. Total follow-up duration was 451 patient-years. Late deaths occurred at a linearized rate of 3.98%±0.92% per patient-year (n=18). Prosthetic valve thrombosis was noted in only 1 MVR patient, producing a linearized rate of 0.36%±0.36% per patient-year. Embolic events after AVR, DVR and MVR were at rate of 2.74%±1.91% per patient-year(n=2), 1.95%±1.36% per patient-year (n=2) and 1.08%±0.62% per patient-year (n=3) respectively. Event free survival at 4 years after MVR, DVR and AVR was 86%±4%, and 89%±6% respectively. Gradients, both peak and mean and velocities across implanted valve was also comparable to other mechanical valves used commonly. They concluded that TTK Chitra valve is comparable to other mechanical heart valves in terms of hemodynamics and complications.
Bileaflet versus monoleaflet valves

Though many studies have reported long term outcomes with a single valve type, cross comparisons between valve types are few. In a study published in 2001, Masters RG et al compared clinical outcomes of SJM, Carbomedics (CM) and Medtronic Hall (MH) valves in patients undergoing isolated MVR or AVR(47). AVR was performed in 953 patients (SJM = 394, MH = 314, CM = 245) and MVR in 591 patients (SJM = 193, MH = 264, CM = 134). Total follow up duration was 3336 patient-years after AVR and 1693 patient-years after MVR. In both AVR and MVR group, even though significantly more MH patients were high risk surgery group because of previous valve surgery (p = 0.001) or higher NYHA class III/IV (p = 0.03), hospital mortality, late survival and other valve related complication with SJM, MH and CM valves was similar.

In a randomized clinical trial comparing SJM (bileaflet) and MH (tilting disc) heart valve, there were no difference between these two designs of mechanical valves in terms of hemodynamics and clinical performance over long term (4). In this trial, 156 patients were randomized to undergo MVR with either the SJM (n = 80) or MH (n = 76) over a period of 12 years. Baseline characteristics were similar between two groups. Early operative mortality was similar between SJM and MH
group, 11.2 % and 13.1% respectively. Late mortality was also comparable between the two mechanical valves (27% with SJM and 22% with MH).

Other randomized trials comparing bileaflet (SJM) and tilting disc (MH) designs of mechanical heart valves suggested similar outcomes (48, 49). In a randomized trial comparing intraoperative and postoperative hemodynamic of bileaflet versus tilting disc designs of mechanical heart valves implanted at aortic position in their optimal orientation, superior hemodynamic performance was observed with tilting disc valves compared with the bileaflet valves. Superior hemodynamics of tilting disc valves was more prominent among valves implanted at smaller aortic annulus (5). Although other randomized trial showed similar clinical and hemodynamic outcomes with both valves in patients with small aortic annulus (50).

Thus, even after decades of use, the literature is inconclusive on the relative merits and demerits of monoleaflet versus bileaflet valve design. The Medtronic Hall (MH) monoleaflet prosthesis production has been stopped by the manufacturer since 2009. The TTK Chitra valve, the design of which closely resembles the MH valve, thus has the potential to provide equivalent results at much lower cost to thousands of patients suffering from valvular heart disease. No comparative study
exists to document the long term performance of TTK Chitra valve in comparison to the commonly used bileaflet valves. This study attempted to bridge this knowledge gap by comparing the long term clinical performance of CHVP with the widely used SJM bileaflet valve in clinical practice.
AIMS

To compare the long term clinical outcome of monoleaflet tilting disc and bileaflet mechanical heart valve prosthesis at aortic or mitral position
OBJECTIVES

To measure clinical and echocardiographic parameters, mortality and adverse events after isolated mitral or aortic valve replacement with TTK Chitra or St. Jude Medical heart valve prosthesis
Methods

Study design

We conducted a single center, retrospective-prospective follow up study to compare the long term outcome of patients undergoing isolated mitral or aortic valve replacement with the indigenously developed tilting disc (CHVP) or commonly used bileaflet valves. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants. As the most commonly used bileaflet valve at our center during the study period was SJM (100%), this was chosen as a standard comparator. Subjects were identified from the hospital electronic medical records system (operation executed section) using keywords “MVR” for mitral valve replacement and “AVR” for aortic valve replacement and “CHVP” for TTK Chitra valve or “SJM” for St. Jude Medical valve. Demographic, clinical and echocardiographic data were collected from the hospital records using a structured proforma (Appendix – I). Follow up data was obtained during scheduled annual review visits in person. Those lost to follow up for more than 12 months were contacted over telephone or post with returned stamped envelope and telephonic interview conducted for collection of follow up data. Consecutive patients who underwent isolated aortic or mitral valve replacement receiving CHVP or SJM mechanical prosthesis from January 2007 to December 2013 were included. Patients undergoing double valve replacement,
redo surgery or other cardiac surgeries concomitantly (eg: coronary artery bypass
graft) were excluded. Follow up duration was calculated as number of days from
surgery to death, valve explantation or till closing date of data collection for
patients whose follow up till closing date was available. For those lost to follow
up, time from surgery to last follow up and status at that time were entered.

Data Collection
Demographic details including age at surgery, gender and socioeconomic status
were collected using a structured proforma. Socioeconomic class was identified
using the hospital classification system (5 tier system). Clinical data regarding
etiology of valve disease, functional class (NYHA), pulmonary artery hypertension
and baseline cardiac rhythm were recorded. 2D transthoracic echocardiography
and doppler evaluation was done in all patients at baseline and on follow up. Left
ventricular ejection fraction, left ventricular dimensions (in systole and diastole),
gradient across the diseased valves, left atrial size and aortic diameter were
documented. For analysis of outcomes we compared these parameters
longitudinally at baseline, 30 days after surgery and at last available follow up.
Data was also collected regarding type of valve implanted, its size, duration of
hospital and intensive care stay after surgery. Therapeutic INR was defined as
between 2.0-3.0 for AVR and 2.5 -3.5 for MVR. Time in therapeutic range
anticoagulation (TTR) was calculated using the traditional formula (Percent of Visits in Range). Aspirin use was also documented. Adverse events were identified from hospital records and interviewing during regular follow up visits or telephonic interview with patient or relative in those lost to follow up. Hospital deaths, late deaths, and valve-related events were defined according to the published guidelines for reporting mortality and morbidity after cardiac valve interventions from the Society of Thoracic Surgeons and American Association of Thoracic Surgery, 2008.(51) Prosthetic valve thrombosis (PVT) was defined as confirmed PVT if there was documentation of increased gradients, thrombus and reduced leaflet movement on echocardiography and/or fluoroscopic evidence of restricted valve movements in and PVT was presumed when there was history suggestive of PVT and patient died after treatment at local hospital, but records are not available for confirmation. Both presumed and confirmed PVT were included in final analysis.

**Outcome variables**

The primary outcome variable was all cause mortality, early deaths and valve related mortality. Secondary outcome variables included adverse events on follow up, cumulative survival, event free survival and clinical and echocardiographic parameters. For event free survival analysis, mortality from any cause and valve related complications were considered as events.
**Statistical analysis**

Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc, Chicago, Illinois, USA, V 16.0 for Windows). Comparisons were done between the valve types in the entire cohort initially followed by subgroup analysis of MVR and AVR. Data was represented as mean or percentage as applicable with SEM/SD as dispersion measure. Continuous variables that were not normally distributed were compared using Mann Whitney U test. Chi square or Fisher’s exact test as applicable was used to compare proportions. For multiple comparisons of ordinal data, Friedman’s test with post hoc Wilcoxon signed-rank test was used. For comparison of continuous variables on follow up, mixed design ANOVA was used with TIME as within-subjects factor and VALVE TYPE as a between-subjects factor. Kaplan-Meier survival analysis with log rank test was used to compare survival durations and event free survival between the groups. Cox proportional hazards model was used to identify independent predictors of mortality or predefined event.
**Results**

Among 1231 medical records screened, 735 subjects met the inclusion-exclusion criteria and were included for analysis (Figure 1). Baseline characteristics of the entire cohort are shown in Table 1. Mean age at surgery was 42.4±12.5 years. More than 6 months follow up was available in 99% of patients and total follow up for the entire cohort was 2836.0 patient-years (SJM: 1865.1 patient-years, CHVP: 971.0 patient-years). There was a male preponderance in the CHVP group (p=0.048), they belonged to lower socioeconomic classes (p=0.000) and were younger in age compared to the SJM group at surgery (p=0.048).

![Figure 1: Patient flow chart](image-url)
Table 1: Baseline characteristics of the entire cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>SJM</th>
<th>CHVP</th>
<th>P-value</th>
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<tr>
<td>Number of patients, n (%)</td>
<td>489 (66.5%)</td>
<td>246 (33.5%)</td>
<td>-</td>
</tr>
<tr>
<td>MVR (n=510)</td>
<td>378 (74.1%)</td>
<td>132 (25.9%)</td>
<td></td>
</tr>
<tr>
<td>AVR (n=225)</td>
<td>111 (49.3%)</td>
<td>114 (50.7%)</td>
<td></td>
</tr>
<tr>
<td>Age at surgery (yrs)</td>
<td>43.0±12.5</td>
<td>41.1±12.5</td>
<td>p=0.050</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>51.2</td>
<td>58.9</td>
<td>p=0.048</td>
</tr>
<tr>
<td>Low socioeconomic status (%)</td>
<td>62.1</td>
<td>89.4</td>
<td>P=0.000</td>
</tr>
</tbody>
</table>

For the entire cohort, estimated cumulative survival after valve replacement was 2773.47 ±41.9 days for the CHVP group and 2576.4±26.6 days for SJM (p=0.864, Figure 2). Estimated cumulative event free survival was also similar (SJM: 2302.1±42.4days, CHVP: 2483.9 ±64.8 days, p=0.393) (Figure 3). There was no significant difference between the groups in all cause mortality (p=0.894), early mortality (p=0.452) and valve related mortality (p=0.681) (Table 2). Major complications like prosthetic valve thrombosis (p=0.155), embolism (p=0.210), hemorrhage (p=0.959), infective endocarditis (p=0.084) and need for reintervention (p=0.102) were similar in both the groups (Table 2).
Figure 2: Estimated cumulative survival entire cohort

Figure 3: Estimated event free survival entire cohort
## Table 2: Mortality and complications entire cohort

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SJM (n=489)</th>
<th>CHVP (n=246)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All cause mortality, n (% ,%/pt-years)</strong></td>
<td>27 (5.5/1.5)</td>
<td>13 (5.3/1.3)</td>
<td>P=0.894</td>
</tr>
<tr>
<td>Early Mortality, n(%)</td>
<td>4 (0.82)</td>
<td>4 (1.62)</td>
<td>0.452</td>
</tr>
<tr>
<td>Valve related mortality, n (%/pt-yrs)</td>
<td>21 (4.3/1.1)</td>
<td>9 (3.7/0.9)</td>
<td>0.681</td>
</tr>
<tr>
<td>PVT, n(% ,%/pt-yrs)</td>
<td>25 (5.1/1.3)</td>
<td>7 (2.9/0.7)</td>
<td>0.155</td>
</tr>
<tr>
<td>Embolism, n(% ,%/pt-yrs)</td>
<td>29 (5.9/1.6)</td>
<td>15 (6.1/1.6)</td>
<td>0.210</td>
</tr>
<tr>
<td>Hemorrhage, n(% ,%/pt-yrs)</td>
<td>19 (3.9/1.0)</td>
<td>8 (3.3/0.8)</td>
<td>0.959</td>
</tr>
<tr>
<td>Infective Endocarditis, n(% ,%/pt-yrs)</td>
<td>10 (2.0/0.5)</td>
<td>1 (0.4/0.1)</td>
<td>0.084</td>
</tr>
<tr>
<td>Reintervention, n(% ,%/pt-yrs)</td>
<td>7 (1.4/0.4)</td>
<td>0 (0.0/0.0)</td>
<td>0.102</td>
</tr>
</tbody>
</table>
None of the baseline factors age at surgery (p=0.695), gender (p=0.464), baseline NYHA functional class (p=0.929), cardiac rhythm (0.999), valve type (p=0.749), anticoagulant used (p=0.705), aspirin use (p=0.988), INR TTR (p=0.191), LA size (p=0.108), EF (p=0.140), gradient across diseased valve (p=0.314), PAH (p=0.307) were predictors of all cause mortality. None of the factors age at surgery (p=0.650), gender (p=0.270), baseline NYHA class (p=0.398), rhythm (p=0.480), valve type (p=0.196), anticoagulant used (p=0.922), aspirin use (p=0.286), INR TTR (p=0.551), LA size (p=0.312), baseline EF (p=0.193), LVSD (p=0.066), gradient (p=0.379), PAH (p=0.563) were independent predictors of an event occurring.

**Mitral valve replacement**

Subgroup analysis of MVR and AVR cohorts were done to further characterize the results. For MVR, total follow up was 1885.6 patient-years. Baseline characteristics are shown in Table 3. Patients in the CHVP group were younger at surgery and belonged to lower socioeconomic status. Rheumatic heart disease was the commonest indication for surgery accounting for 88.5% of all patients undergoing MVR. Baseline functional class, pulmonary artery hypertension and number of patients with atrial fibrillation or flutter were similar between the groups (Table 3). The groups were also matched for left atrial size, mean gradient across
mitral valve, baseline ejection fraction and left ventricular dimensions at baseline (Table 4).

**Table 3: Baseline characteristics of patients undergoing mitral valve replacement**

<table>
<thead>
<tr>
<th>Variable</th>
<th>SJM</th>
<th>CHVP</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients, n (%)</strong></td>
<td>378 (74.1%)</td>
<td>132 (25.9%)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Age at surgery (yrs)</strong></td>
<td>43.5±12.5</td>
<td>39.9±12.0</td>
<td>p=0.004</td>
</tr>
<tr>
<td><strong>Male gender (%)</strong></td>
<td>42.1</td>
<td>39.4</td>
<td>p=0.609</td>
</tr>
<tr>
<td><strong>Low socioeconomic category</strong></td>
<td>63.1</td>
<td>96.2</td>
<td>P=0.000</td>
</tr>
<tr>
<td><strong>Indication for surgery (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RHD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVP</td>
<td>86.0</td>
<td>90.9</td>
<td></td>
</tr>
<tr>
<td>Post BMV MR</td>
<td>10.3</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
<td>Emergency MVR</td>
<td>2.6</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.1</td>
<td>-</td>
<td>P=0.800</td>
</tr>
<tr>
<td><strong>Functional class (%)</strong></td>
<td>47.9/49.2/2.9</td>
<td>46.2/51.5/2.3</td>
<td>p=0.858</td>
</tr>
<tr>
<td><strong>NYHA II/III/IV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAH (%) 0/1/2/3</td>
<td>17.5/32.8/28.0/21</td>
<td>15.9/35.6/28.8/1</td>
<td>p=0.903</td>
</tr>
</tbody>
</table>
Median valve size used for MVR was 27 in both the groups (range, SJM: 17-33, CHVP: 23-31, p=0.944). Perioperative hospital stay (≈11 days, p=0.581) and postoperative intensive care unit stay (≈3 days, p=0.083) were similar in both groups.

During follow up, percentage of time spent in therapeutic range of INR was low in both the groups (SJM: 29.2%±23.0, CHVP: 33.7%±27.1, p=0.381). Warfarin, Acenocoumarol and Phenindione were the anticoagulants used. 27.2% in the SJM group and 30.3% in CHVP group received additional aspirin (p=0.501). Similar improvements in functional status and pulmonary artery hypertension were noted.
at 30 days and on last follow up in both the valve groups (Table 5). Ejection fraction, gradient across mitral valve and left ventricular dimensions improved to a similar extent and on repeated measures analysis, there was no effect of valve type as a between subjects factor on any of the above outcomes, suggesting that improvement in echocardiographic parameters was similar in both the groups and independent of the type of prosthesis.

Table 5: Clinical and echocardiographic outcomes in MVR

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (SJM/CHVP)</th>
<th>30 days</th>
<th>Last visit</th>
<th>Effect of valve type</th>
</tr>
</thead>
<tbody>
<tr>
<td>FC</td>
<td>III</td>
<td>I</td>
<td>I</td>
<td>P=0.000</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>I</td>
<td>I</td>
<td>P=0.000</td>
</tr>
<tr>
<td>PAH</td>
<td>I</td>
<td>0</td>
<td>0</td>
<td>P=0.000</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>0</td>
<td>0</td>
<td>P=0.000</td>
</tr>
<tr>
<td>EF</td>
<td>64.2±8.5/64.2±8.6</td>
<td>61.1±8.2/62.5±8.3</td>
<td>60.6±8.1/62.2±8.0</td>
<td>F=3.064, p=0.081</td>
</tr>
<tr>
<td>Gradient</td>
<td>12.3±6.5/12.6±7.0</td>
<td>5.0±3.1/4.2±1.5</td>
<td>5.9±3.9/4.9±1.8</td>
<td>F=2.638, p=0.105</td>
</tr>
<tr>
<td>LVSD</td>
<td>32.3±7.2/32.5±7.3</td>
<td>31.8±6.4/31.9±6.6</td>
<td>32.0±6.3/31.3±5.7</td>
<td>F=0.053, p=0.819</td>
</tr>
<tr>
<td>LVDD</td>
<td>50.9±10.9/50.1±10.5</td>
<td>46.7±7.2/47.2±7.1</td>
<td>47.1±7.7/47.3±6.5</td>
<td>F=0.001, p=0.970</td>
</tr>
</tbody>
</table>

Adverse events noted during follow up are shown in Figure 4. Incidence of adverse
events per 100 patient years was as follows; PVT, SJM: 1.77%/ pt-year, CHVP: 1.34% per pt-yr, Embolism SJM: 1.99% per pt-yr, CHVP: 2.1% per pt-yr; hemorrhage, SJM: 0.81% per pt-yr, CHVP: 1.15% per pt-yr; IE SJM: 0.44% per pt-yr, CHVP: 0.19% per pt-yr; need for reintervention SJM: 0.52% per pt-yr, CHVP: 0% per pt-yr. There was no difference in the frequency of prosthetic valve thrombosis (p=0.665), peripheral embolism (p=0.110), hemorrhage (p=0.740), infective endocarditis (p=0.683) and need for reintervention (p=0.242) between the two valve types.

![Adverse events graph]

**Figure 4: Adverse events after mitral valve replacement**

All cause mortality was 6.08% (1.76%/pt-yr) for SJM and 8.33% (2.10%/pt-yr) for CHVP (p=0.373). Valve related mortality (SJM: 1.4%/pt-yr, CHVP: 1.34%/pt-yr, p=0.585) and early valve related deaths were also similar for both the valve types (p=0.608) (Figure 5). Estimated cumulative survival (SJM: 2557.43±32.62 days, CHVP: 2706.90±66.26 days, p=0.686) and event free survival
(2245.9.43±51.9 days, CHVP: 2354.2±92.9 days, p=0.992) were similar for both valve types (Figure 6).

![Mortality rate](image)

<table>
<thead>
<tr>
<th></th>
<th>All cause mortality (%)</th>
<th>Early valve related deaths (%)</th>
<th>Valve related mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SJM</td>
<td>6.08</td>
<td>0.79</td>
<td>4.76</td>
</tr>
<tr>
<td>CHVP</td>
<td>8.33</td>
<td>1.51</td>
<td>4.54</td>
</tr>
</tbody>
</table>

**Figure 5: Mortality in MVR**

![Cumulative survival and event free survival](image)

**Figure 6 Estimated cumulative survival and event free survival in MVR**

None of the baseline or treatment factors like age at surgery (p=0.564), gender (p=0.309), baseline NYHA class (p=.921), baseline rhythm (p=0.985) valve type
(p=0.559), anticoagulant used (p=0.596), aspirin use (p=0.936), INR TTR (p=0.114), LA size (p=0.086), EF (p=0.362), LVSD (p=0.083), gradient across mitral valve (p=0.165), PAH (p=0.064) were predictors of all cause mortality. age at surgery (p=0.377), gender (p=0.226), baseline NYHA class (p=0.146), AF (p=0.531), valve type (p=0.636), anticoagulant used (p=0.878), aspirin use (p=0.096), INR TTR (p=0.305), LA size (p=0.531), baseline EF (p=0.443), LVSD (p=0.327), gradient across mitral valve (p=0.211) and PAH (p=0.421) were not independent predictors of an event occurring.

**Aortic valve replacement**

For MVR, total follow up was 950.4 patient-years. Baseline characteristics are shown in Table 6. Patients in the CHVP group belonged to lower socioeconomic classes. Rheumatic heart disease was the commonest indication for surgery accounting for 43.0% of all patients undergoing AVR. Calcific/degenerative aortic valve disease and bicuspid aortic valve were the other common indications. Baseline functional class was similar between the groups majority (98.2%) were in sinus rhythm in both valve groups (Table 3). The groups were also matched for mean gradient across aortic valve, baseline ejection fraction, aortic diameter and left ventricular dimensions at baseline (Table 7).
Table 6: Baseline characteristics of AVR cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>SJM</th>
<th>CHVP</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n (%)</td>
<td>111 (49.3%)</td>
<td>114 (50.7%)</td>
<td>-</td>
</tr>
<tr>
<td>Age at surgery (yrs)</td>
<td>41.1±12.5</td>
<td>42.4±13.0</td>
<td>p=0.482</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>82.0</td>
<td>81.6</td>
<td>p=0.938</td>
</tr>
<tr>
<td>Low socioeconomic status (%)</td>
<td>57.7</td>
<td>81.6</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Etiology of valve damage (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RHD</td>
<td>37.8</td>
<td>48.2</td>
<td></td>
</tr>
<tr>
<td>Calcific/degenerative</td>
<td>33.3</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>19.8</td>
<td>21.9</td>
<td></td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td>3.6</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>5.4</td>
<td>2.6</td>
<td>p=0.386</td>
</tr>
<tr>
<td>Functional class (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA I/II/III</td>
<td>0.9/62.1/36.9</td>
<td>0/60.5/39.5</td>
<td>p=0.564</td>
</tr>
<tr>
<td>NSR (%)</td>
<td>98.2</td>
<td>98.2</td>
<td>P=0.572</td>
</tr>
</tbody>
</table>
Table 7: Baseline echocardiographic parameters in AVR

<table>
<thead>
<tr>
<th>Variable</th>
<th>SJM</th>
<th>CHVP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>62.3±12.1</td>
<td>62.1±10.7</td>
<td>P=0.901</td>
</tr>
<tr>
<td>Aortic valve gradient (mmHg)</td>
<td>41.3±28.0</td>
<td>40.7±27.2</td>
<td>P=0.804</td>
</tr>
<tr>
<td>Aortic diameter (mm)</td>
<td>31.5±6.4</td>
<td>32.0±5.4</td>
<td>P=0.579</td>
</tr>
<tr>
<td>LV systolic dimension (mm)</td>
<td>37.7±11.4</td>
<td>38.1±11.6</td>
<td>P=0.839</td>
</tr>
<tr>
<td>LV diastolic dimension (mm)</td>
<td>58.2±12.4</td>
<td>58.1±13.0</td>
<td>P=0.944</td>
</tr>
</tbody>
</table>

Median valve size used for AVR was 21 (range 17-29) in SJM and 23 (range 17-29) CHVP group (p=0.001). Perioperative hospital stay (≈11 days, p=0.509) and post operative intensive care unit stay (≈ 3 days, p=0.834) were similar in both groups. All patients were on oral anticoagulants. During follow up, percentage of time spent in therapeutic range of INR was significantly lower in the CHVP group (33.3% ±24.3) compared to SJM (SJM-44.7±28.3, p=0.005). 16.2% in the SJM group and 42.1% in CHVP group received additional aspirin (p=0.000).

Similar improvement in functional class was noted at 30 days and on last follow up in both the valve groups (Table 8). Ejection fraction, gradient across aortic valve and left ventricular dimensions improved to a similar extent (Table 8).
Table 8: Clinical and echocardiographic parameters on follow up in AVR cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>30 days</th>
<th>Last visit</th>
<th>Effect of valve type</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA functional class (median)</td>
<td>II</td>
<td>I</td>
<td>I</td>
<td>P=0.000</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>I</td>
<td>I</td>
<td>P=0.000</td>
</tr>
<tr>
<td>NYHA functional class (median)</td>
<td>II</td>
<td>I</td>
<td>I</td>
<td>P=0.000</td>
</tr>
<tr>
<td>EF (%)</td>
<td>62.3±12.1/62.0±10.7</td>
<td>64.6±12.9/62.3±9.4</td>
<td>64.3±12.2/64.6±8.7</td>
<td>F=0.540, p=0.463</td>
</tr>
<tr>
<td>Gradient across aortic valve (mmHg)</td>
<td>41.3±28.0/40.0±26.9</td>
<td>13.9±8.3/13.4±5.5</td>
<td>13.9±7.3/13.6±6.7</td>
<td>F=0.218, p=0.641</td>
</tr>
<tr>
<td>LVSD (mm)</td>
<td>37.7±11.4/38.3±11.6</td>
<td>31.6±9.8/33.2±8.3</td>
<td>30.9±7.3/30.4±6.5</td>
<td>F=0.348, p=0.556</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>58.2±12.4/58.5±12.8</td>
<td>48.4±9.2/49.4±8.3</td>
<td>48.2±7.0/47.8±6.7</td>
<td>F=0.093, p=0.761</td>
</tr>
</tbody>
</table>
On repeated measures analysis, there was no significant effect of valve type as a between subjects factor on any of the above outcomes, suggesting that improvement in echocardiographic parameters was similar in both groups and independent of the type of prosthesis.

Adverse events noted during follow up are shown in Figure 7. Infective endocarditis was more common in the SJM group (3.6% vs 0.0% in CHVP, p=0.041). There was no difference in the frequency of prosthetic valve thrombosis (p=0.493), peripheral embolism (p=0.559), hemorrhage (p=0.225) and need for reintervention (p=0.161) between the two valve types.

![Adverse events](chart.png)

**Figure 7: Adverse events of follow up in AVR**

All cause mortality was 1.8% in both the groups (p=0.979). Valve related mortality (p=0.577) and early valve related deaths (p=0.498) were also similar for both the
valve types (Figure 8). Estimated cumulative survival (SJM: 2603.50±25.57 day, CHVP: 2877.72±35.94 days, p=0.898) and event free survival (SJM: 2395.1±66.9days, CHVP: 2656.9±81.4 days, p=0.691) were similar for both valve types (Figure 9).

Figure 8: Mortality rate on follow up in AVR

Figure 9: Estimated cumulative survival and event free survival in AVR
None among the factors age at surgery (p=0.943), gender (p=0.831), baseline NYHA class (p=0.718), rhythm (p=1.000), valve type (p=0.958), anticoagulant used (p=1.000), aspirin use (p=1.000), INR TTR (p=0.974), LA size (p=0.996), EF (p=0.781), gradient across aortic valve (p=0.942), PAH (p=0.975) were predictors of all cause mortality. Similarly, age at surgery (p=0.727), gender (p=0.746), baseline NYHA class (p=0.284), rhythm (p=1.000), valve type (p=0.446), anticoagulant used (p=0.976), aspirin use (p=0.862), INR TTR (p=0.768), baseline EF (p=0.267), LA size (p=0.782), gradient across aortic valve (p=0.354), LVSD (p=0.779) and PAH (p=0.987) were not independent predictors of an event occurring.
Discussion

Our results suggest comparable long term clinical outcomes between CHVP, an indigenously developed, low cost, single tilting disc valve and SJM, a commonly used bileaflet valve in aortic and mitral positions. These are the two most commonly used mechanical valves at our centre and possibly at other cardiac surgery centres of India and other developing nations, so a comparative study looking at long term outcomes was desired.

Several points merit special consideration while interpreting our results in the light of available literature. Consistent with data from developing nations, our patients undergoing valve replacement were significantly younger and chronic RHD was the etiology in the majority, both for mitral as well as aortic valve disease. Mean age at surgery was 26–29 years in other reports published from India and RHD accounted for 70–90% of valve replacements (44-46). Data from the Western hemisphere, however, usually deals with an older population, in the range of 52-63 years(4, 30, 34, 49). It is known that chronic RHD is not only more prevalent in developing countries with poor socioeconomic status, but that lack of access to healthcare and non compliance to antibiotic prophylaxis in combination with poor living conditions lead to higher recurrence rates of rheumatic fever and more severe valvular damage which presents at younger age compared to the West.
Also, in India mitral valve replacements outnumber aortic valve replacements, the reverse of what is seen in developed nations as RHD affects the mitral valve preferentially compared to degenerative valvular disease more commonly affecting aortic valve. As a consequence, rate of atrial fibrillation overall was also higher in our study, similar to data from other Indian studies, reflecting the higher proportion of mitral valve disease. In the MVR subgroup, frequency of AF at time of surgery was similar in our study (40-75%) as well as other Indian and Western data(30, 45, 46).

Reported rates of early mortality with SJM at mitral and aortic positions are in the range of 3-7%(30, 49). In our study early mortality rate was much lower (1%). This could be due to younger age of our population and because of strict selection criteria resulting in exclusion of redo surgeries, concomitant left heart surgeries and patients with severe LV dysfunction. Moreover, the earlier reports are from about a decade prior and advances in surgical techniques and perioperative care may have contributed to decreased mortality rates. The multicentric clinical study of CHVP reported in 2001 an early mortality of 6.9%, in a population similar to ours and including only isolated aortic or mitral valve replacement(3). A drastic reduction in early mortality to 0.6-1.5% has been reported in recent studies with Chitra valve(44-46). For MVR and AVR subgroups, early mortality was similar to
those reported previously for CHVP (MVR: 1.4-1.6% and AVR: 0-1.1%) (44, 46). In studies reporting outcomes of SJM from the Western hemisphere, early mortality was higher for both MVR (3.2-11.2%) and AVR (3.6-4.8%) likely due to a higher proportion of patients with poor functional class and inclusion of patients undergoing concomitant surgeries (30, 34). Wide variation in the incidence of valve related deaths has also been reported in literature for SJM (1.4-6.25%/pt-yr) again owing to baseline and technical considerations (4, 30). Incidence of various valve related complications were also in the range reported in previous studies of SJM and CHVP.

As surgical expertise, techniques and perioperative –post operative care may differ among centers, valid conclusions about valve performance are better inferred from single center experience of a uniform cohort of patients. In this regard, we report for the first time, comparative data between the SJM and CHVP mechanical prostheses. For the entire cohort, primary outcomes in terms of all cause mortality, early mortality and valve related deaths were comparable between the valve types. On multivariate analysis, valve type was not a significant predictor of mortality or event free survival. These results suggest that both valve designs are equally efficacious in terms of survival as well as freedom from thromboembolism, hemorrhage and infective endocarditis. We did not come across any case of
structural valve deterioration in either valve group.

On subgroup analysis of MVR, patients receiving CHVP were significantly younger and belonged to lower socioeconomic classes, the latter reflecting the lower cost of CHVP. For MVR, similar improvement in functional class and echocardiographic parameters were noted with both valves. Pulmonary artery hypertension also improved to a similar extent. There was no significant difference in all cause mortality or valve related mortality between the two valve types. Estimated cumulative survival and event free survival were also similar. Adverse events were also encountered at similar rates. Incidence of thromboembolism was low in both groups, compared to previous results, in particular the multicentric clinical trial of CHVP which reported a linearized rate of 6.2%/pt-yr for combined thromboembolism(3). This is in spite of the fact that on follow up, patients in both CHVP and SJM groups remained in therapeutic anticoagulation only about one third of the time. The incidence of thromboembolism overall is low with the newer generation of monoleaflet and bileaflet valves, and our results replicate these findings(30, 46, 49). For SJM, its central flow design is thought to reduce risk of thromboembolism. The superior hydrodynamics of the tilting disc design may be responsible for lower rates of thromboembolism in CHVP. In vitro testing demonstrated that low negative pressure gradients and absence of ‘cavitation
effect’ with CHVP might lower the risk of thrombosis, compared to valves with rigid occluders(52). Given the low thrombogenic potential observed, our results may also lend support to the notion of lower intensity anticoagulation with the newer generation of mechanical prosthesis, which merits clinical testing in both tilting disc as well as bileaflet valves in a bid to further reduce hemorrhagic complications(53). Although, age and socioeconomic status were dissimilar at baseline, multivariate analysis suggested that they did not contribute significantly to outcome or event free survival.

In the AVR subgroup, patients receiving CHVP belonged to lower socioeconomic classes as expected. In addition, patients were in therapeutic range INR for significantly shorter periods of time. In spite of these differences, primary outcome variables of mortality and thromboembolism were similar between the valve types. On multivariate analysis, socioeconomic class and time in TTR were not predictors of mortality or event free survival. Importantly, the type of valve, SJM or CHVP was also not an independent predictor of mortality and freedom from events, suggesting equal efficacy of both valve designs for the primary outcome. Secondary outcomes of NYHA class, and echocardiographic parameters improved similarly with both valve types. The only statistically significant difference noted was in the incidence/ frequency of infective endocarditis; this was higher for SJM
valves implanted in the aortic position. Although the number of patients, undergoing aortic valve replacement subsequent to valve damage from infective endocarditis was higher in the SJM group, we found only 1 patient who developed prosthetic valve infective endocarditis after surgery for infective endocarditis related valve damage. In all other patients, prosthetic valve infective endocarditis occurred de novo after surgery. These results are consistent with previous claims of CHVP being resistant to infections(41).

Our study has certain limitations. Firstly, it is not a randomised control trial between the valve groups and thus certain baseline differences were found to exist between the two valve groups, although adjusting for these did not reveal any statistically significant effects. Secondly, being a retrospective-prospective study, it is prone to recall bias on follow up and data from hospital admissions outside could have been missed. Thirdly, although we report the largest follow up series of CHVP so far, sample size may still be inadequate to detect differences, given the low rate of events observed. To definitively rule out any difference in performance between two prostheses, would require some 10,000 patient-years of follow-up with a study size of around 1400 patients in each group(54). Fourth, the TTR calculation was done through traditional methods, as we used hospital INR recorded during 6 monthly-annual visits. We could not apply the Rosendaal
method of TTR estimation as interim 8 weekly INR data was not collected(55). Fifth, due to differences in demographics and strict selection criteria employed, we cannot assume that these results can be generalized to the larger population, especially in Western hemisphere blindly. In spite of these limitations, our study provides convincing evidence of comparability between these two commonly employed valve designs in actual clinical practice settings.
Conclusion

The results of this study indicate that the long term performance of the St. Jude and TTK Chitra mechanical valve prostheses are comparable in terms of clinical benefits, adverse events and mortality. The CHVP offers equivalent results at almost half the cost of an imported SJM valve making the prospect of cardiac surgery available to a large number of deserving patients in resource limited settings.
References


35. Kratz JM, Crawford FA, Jr., Sade RM, Crumbley AJ, Stroud MR. St. Jude


47. Masters RG, Helou J, Pipe AL, Keon WJ. Comparative clinical outcomes with St. Jude Medical, Medtronic Hall and CarboMedics mechanical heart valves.


Appendix – I (PROFORMA)

Code -Age/Sex:
Hospital No.:Contact No.
Address:
Weight:Height:BSA :

Indication of valve replacement:
Cause of valve disease:
Valve replacement done (MVR/ AVR):
Type of valve Used:
Functional class (NYHA I- IV):
   Prior to surgery
   6 months after surgery
   At last follow up
Left ventricular function
   Prior to surgery
   Prior to discharge/ 30 days post surgery
   At last follow up
Cardiac rhythm and conduction abnormalities
   Baseline
   After surgery/ with 30 days of surgery
   Last follow up

Operative characteristics
   CPB time
   Aortic clamp time
   Valve size and type
   Hospital stay

INR (at each follow up)
Aspirin (Y/N)

Echocardiography : Baseline Within 30 days of surgery Last follow up
LA and Ao size
Ejection fraction
EDV
ESV
Gradient across prostheses (Doppler)
Complications (with time after valve replacement)

1. Mortality: related to valve/surgery unrelated (cause) unknown
   30 day
   After 30 days
   Total

2. Thromboembolic complications
   Thrombotic:
   Embolic:
     CNS
     Others

3. Hemorrhagic complications
   CNS
   Others

4. Infections

5. Rhythm or conduction disturbances
   Within 30 days
   After 30 days

6. Dehiscence / paravalvular leaks
7. Redo surgery

Duration of follow up: