Evaluation of TTK Chitra heart valve prosthesis in pediatric patients

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Abstract
This report highlights the outcome of valve replacement using TTK Chitra heart mechanical valve in a subgroup of pediatric patients. This cohort of 27 pediatric patients with implantations during January 2006 to December 2018 was followed up prospectively. The cohort consisted of 12 aortic valve replacement (AVR), 14 mitral valve replacement (MVR), and 1 double valve replacement (DVR) patients. Total follow-up was 254 patient-years (AVR = 107, MVR = 136, DVR = 11) being 90% complete. The results show that the survival rates and event-free rates were satisfactory. Despite many reservations due to the high risk involved, the long-term benefits of having a durable valve replacement seem to outweigh the risks and offer acceptable long-term survival.

Keywords TTK Chitra heart valve (TTKCHV) · Mechanical heart valve · Rheumatic heart disease · Pediatric

Introduction
The TTK Chitra™ heart valve (TTKCHV) developed by the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum [1], and manufactured by TTK Healthcare Limited is used in a large number of centers dealing with rheumatic heart disease (RHD) [2]. A number of clinical studies that have been published over the last 25 years clearly show the valve to be as good, if not better, than many of the currently imported mechanical valve models [3–5]. However, there are no detailed studies reporting on the use of this valve in pediatric patients (≤ 18 years). This report summarizes the long-term clinical and hemodynamic performance of TTKCHV and survival in pediatric patients.

Methodology
There were 27 pediatric patients (less than or equal to 18 years) consisting of 12 aortic valve replacements (AVR), 14 mitral valve replacements (MVR), and one double valve replacement (DVR).

This pediatric cohort was evaluated as part of the retrospective-prospective, single-center, single-arm, observational study that covered 476 patients implanted with TTKCHV from 1 January 2006 to 31 December 2018 at a major tertiary university hospital in South India. The study was conducted in full conformance with the principles of the “Declaration of Helsinki” (as amended at the 56th WMA General Assembly, Tokyo, Japan, 2008). The institutional ethics committee approval was obtained before initiating the study.

Patient medical history and demographic characteristics were collected retrospectively from the medical records for all 27 patients. Prospective data collection included a one-time detailed follow-up. Informed consent was obtained from the guardians of all nine pediatric patients, who consented for the detailed follow-up. Blood investigations, New York Heart Association (NYHA) functional class assessment, hemodynamic performance, and any event post valve implantation were recorded. Ten patients who were not willing to visit the hospital due to the coronavirus infectious disease (COVID-19) pandemic were contacted over phone and clinical information was collected using a questionnaire. The
follow-up method of pediatric patients was the same as that followed for the long-term evaluation of the TTKCHV study.

Continuous variables were reported as mean ± standard deviation, and categorical variables were represented as percentages. The actuarial curves were calculated by the Kaplan–Meier technique using the R—R Studio statistical analysis package. Linearized rates were expressed as percent/patient-year (%/py) with ± 1 standard error, which has been computed by the Greenwood formula.

**Study endpoints**

Long-term clinical and hemodynamic performance of TTKCHV in pediatric patients and actuarial survival.

**Results**

The mean age of the entire cohort was $12.8 \pm 4.78$ years at the time of surgery. The youngest was a 5.5-month-old male MVR patient, and the oldest were 18-year-old patients (Table 1). There were four patients in the age group 0 to 4 years, with an average weight of 12 kg (range: 3.3 to 22 kg). Nine patients were in the age group 10 to 13 years, with an average weight of 34.04 kg (range: 23.6 to 44 kg). Fourteen patients were in the age group 14 years to 18 years with an average weight of 42.02 kg (range: 25.3 to 55 kg).

During the follow-up, 19 (70.4%) patients were confirmed alive, 5 (18.5%) were confirmed dead, and 3 (11.1%) were lost to follow-up. Nine patients (47%) attended the follow-up clinic while for the rest 10 patients (53%) data was collected through telephonic discussions. Twelve AVR patients had a total 107 patient-years of follow-up; 14 MVR patients had a total 136 patient-years, and the 1 DVR had 11 years of follow-up. The total follow-up was 254 patient-years with a mean of 9.4 years; 90% of patients were followed up with a maximum follow-up of 15.3 years for an 18-year-old MVR patient.

The youngest patient was a 5.5-month-old male baby with congenital heart defects (double outlet right ventricle, large peri-membranous ventricular septal defect, severe infundibular pulmonic stenosis, dysplastic mitral valve and severe mitral valve regurgitation in congestive heart failure and complete heart block) underwent intra-cardiac repair and mitral valve repair. On postoperative day 1, he underwent MVR with 17-mm TTK Chitra aortic valve for recurrent severe mitral regurgitation (MR). The boy was 3 years old at the time of this latest follow-up and was doing well. He had undergone a permanent pacemaker implantation (PPI) along with valve replacement. The main valve disease etiology and valvular lesions of the pediatric group are shown in Table 2. In this group, size distribution values of aortic valves are 21.4% (3) in 17 mm, 7.1% (1) in 19 mm, 35.7% (5) in 21 mm, 14.3% (2) in 23 mm, and 14% (3) in 25 mm. Mitral valve sizes used are 14.3% (2) in 25 mm, 50% (7) in 27 mm, 14.3% (2) in 29 mm, and 21.4% (3) in 31 mm. The mean international normalized ratio (INR) value during follow-up was $2.10 \pm 0.76$.

**Mortality**

Procedural mortality (30 days from procedure or discharge from hospital whichever is longer) [6] was nil.

| Study details | AVR | MVR | DVR | Overall |
|---------------|-----|-----|-----|---------|
| Total number of patients | 12 | 14 | 1 | 27 |
| Age (mean ± SD) | $11.8 \pm 4.97$ | $13.4 \pm 4.61$ | 18 | $12.8 \pm 4.78$ |
| Age range (min.:max.), years | (2y:18y) | (0y 5 m:18y) | 18y | (0y 5 m:18y) |
| Male, n (%) | 7 (58%) | 7 (50%) | 1 | 15 (55.5%) |
| Female, n (%) | 5 (42%) | 7 (50%) | 0 | 12 (44.4%) |
| Weight (mean ± SD), kg | 31.14 ± 11.7 | 36.9 ± 12.03 | 52.3 | 34.9 ± 10.18 |
| Weight range (min.:max.), kg | (11:51.4) | (3.3:55) | - | (3.3:55) |
| Patient follow-up status | | | | |
| Attended the follow-up clinic | 6 | 2 | 1 | 9 |
| Confirmed alive — did not attend follow-up clinic | 4 | 6 | 0 | 10 |
| Confirmed dead | 1 | 4 | 0 | 5 |
| Lost to follow-up | 1 | 2 | 0 | 3 |
| Early mortality | 0 | 0 | 0 | 0 |
| Follow-up detail in patient-years — pediatric | | | | |
| Actual follow-up (patient-years) | 107 | 136 | 11 | 254 |
| Percentage of patients followed up (%) | 91 | 80 | 100 | 86 |

AVR aortic valve replacement, MVR mitral valve replacement, DVR double valve replacement, n number of patients, SD standard deviation, min. minimum, max. maximum
Late mortality (after discharge and 30 days of valve implantation): Late deaths occurred in five patients (1.96% patient-year (py)) consisting of 1 AVR (0.93% py) and 4 MVR (2.9% py). Two MVR pediatric patients had sudden cardiac death after 13 years of implantation; one patient had a sudden death after 3 years of valve replacement while the reason for death for another patient could not be ascertained and was considered under the valve-related category for analysis, one AVR patient died after 10.5 years of valve replacement. This patient had Takayasu arteritis and encountered multiple episodes of persistent polymorphic ventricular tachycardia (VT) since June 2008. Automatic implantable cardioverter defibrillator (AICD) implantation was suggested but did not proceed due to the family’s decision.

Valve-related complications

Five valve-related late serious adverse events occurred (Table 3). A 2-year-old AVR patient implanted with a 17-mm valve had high gradients after 7 years of implantation and underwent aortic root enlargement using Konno procedure for severe patient-prosthesis mismatch. The valve was replaced with a 21-mm valve of a different make.

A 12-year-old AVR patient had two events. Initially, he presented with dyspnea on exertion and was diagnosed to have moderate paravalvular leak through the anterior margin of the valve after 1 year of implantation. The leak was closed with a patent ductus arteriosus (PDA) device. After 4 years of PDA device closure, this patient developed a residual leak to the right and anterior to the device and again underwent device closure of the residual defect.

Pannus growth was observed in a 16-year-old MVR patient after 10 years of implantation, which led to the replacement of the valve. A 10-year-old MVR patient died unexpectedly after 7 years of surgery; reasons for the death could not be established.

Improvement in functional class

Preoperatively, 25 (92.5%) pediatric patients were in the NYHA class II and 2 (7.4%) patients in class III. The clinical follow-up assessed that out of the 19 alive patients, 18 (95%) patients moved up to class I and 1 (5%) patient to class II.

Survival

The actuarial survival rates for pediatric patients are shown in Fig. 1. The mean survival time in overall survival analysis was 8.55 ± 4.75 years. Actuarial survival curves indicate a 95.8% survival rate at 3 years, 90.8% survival at 7 years, 84.7% at 10 years, and 63.6% at 15 years. The event-free survival rates for TTKCHV pediatric patients at 5 years, 10 years, and 15 years from serious valve-related morbidity and mortality were 91.9%, 78.9%, and 42.4%.

Discussion

Congenital and RHD were the commonest valve pathology encountered in pediatric population in this study. Despite improvements in diagnostic workup, surgical timing, and expertise in pediatric valve repair techniques, valve replacements were unavoidable in few patients. Valve replacements were offered only if the lesions are not amenable to repair because valve replacements in children have higher

Table 2  Etiology and valvular lesions

| Etiology                  | AVR N=12 | MVR N=14 | DVR N=1 | Total N=27 |
|---------------------------|----------|----------|---------|------------|
| No. of patients           |          |          |         |            |
| Rheumatic heart disease   | 4        | 11       | 1       | 16         |
| Congenital heart disease  | 7        | 1        | 0       | 8          |
| Degenerative              | 1        | 2        | 0       | 3          |

Valvular lesions

|                  | AVR N=12 | MVR N=14 | DVR N=1 | Total N=27 |
|-------------------|----------|----------|---------|------------|
| No. of patients   |          |          |         |            |
| Mitral stenosis   | 0        | 0        | 0       | 0          |
| Mitral regurgitation | 5      | 12       | 0       | 17         |
| Mixed mitral valve lesion | 0 | 1 | 1 | 2 |
| Aortic stenosis   | 0        | 0        | 0       | 0          |
| Aortic insufficiency | 10     | 2        | 1       | 13         |
| Mixed aortic valve lesion | 2 | 0 | 0 | 2 |

AVR aortic valve replacement, MVR mitral valve replacement, DVR double valve replacement, N number of patients

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Table 3  Details of valve-related adverse events — pediatric population

| Valve-related SAEs — pediatric | AVR (N=12) | MVR (N=14) | Total | Linearized rates (% py) |
|--------------------------------|------------|------------|-------|-------------------------|
| Inappropriate valve size       | 1          | 0          | 1     | 0.39                    |
| Major paravalvular leak        | 2          | 0          | 2     | 0.78                    |
| Unexpected death               | 0          | 1          | 1     | 0.39                    |
| Pannus overgrowth              | 0          | 1          | 1     | 0.39                    |
| Total                          | 3          | 2          | 5     |                          |

SAEs severe adverse events, AVR aortic valve replacement, MVR mitral valve replacement, DVR double valve replacement, N number of patients, py patient-years

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perioperative mortality and poor long-term results compared to adults [4, 5, 7, 8].

Optimal valve substitute in children would be one that’s available in different sizes, durable with excellent durable hemodynamic profile, has growth potential, and associated with minimal thromboembolism risk thus not requiring anticoagulation. No valve substitute currently offers all these qualities. Mechanical valve replacement has the advantage of availability even in small sizes, but is limited by the need for anticoagulation and potential for development of patient-prosthesis mismatch with somatic growth [9].

However, it was gratifying to note that the 30-day mortality was nil in our cohort with acceptable long-term survival. The survival rates were comparable to earlier published studies (Table 4) [10–14].

Table 4 Total actuarial survival comparison of TTKCHV with other valves in pediatric population

| Study/valve                                      | Mean age (years) | No. of patients | Actuarial survival (%) |
|-------------------------------------------------|------------------|-----------------|------------------------|
|                                                 |                  |                 | 3–5 years   | 5–8 years   | 10–12 years | 15–17 years |
| TTKCHV (this study)                             | 12.8 ± 4.78      | 27              | 95.8        | 90.8        | 84.7        | 63.6        |
| Tiete AR, et al.[10] (St. Jude Medical valve), 2006 | 7.2 ± 5.2        | 27              | 92.6        | 92.6        | -           | -           |
| el Makhlouf A, et al.[11] (Starr-Edwards, Bjork-Shiley, Hancock valves), 1987 | 12               | 273             | 86          | 75          | -           | -           |
| Antunes MJ, et al.[12] (Medtronic Hall and St. Jude valves), 1989 | 15.3 ± 4.0       | 352             | -           | 76          | -           | -           |
| Atik FA, et al.[13] (St. Jude, Carbomedics, Omnicarbon, Sorin valves), 1999 | 10               | 18              | 92.5        | 92.5        | 92.5        | 92.5        |
| Iyer KS, et al.[14] (Bjork-Shiley valve), 1984 | (6 to 20 years) | AV 50            | 89.2        | 89.2        | -           | -           |
|                                                 |                  | MVR 61           | 81.0        | 81.0        | -           | -           |
|                                                 |                  | DVR 25           | 81.8        | 81.8        | -           | -           |

TTKCHV TTK Chitra heart valve
This study on the use of the TTKCHV in the pediatric patients clearly highlights the benefits of the valve in this vulnerable group. The long-term survival of these patients justifies using this valve, when native valve is not amenable for repair.

Conclusion

Use of the valve in the pediatric patient group offers acceptable long-term survival.

Limitations

This is a single-center study and results were confined to data of only 27 patients. Echocardiography data and blood parameters were collected only for 9 patients who visited for follow-up. Functional status was evaluated for only 19 patients who were followed up at the site or through telephonic discussion.

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Declarations

Ethics approval Institutional ethics committee approved the study on 20 May 2019 with IEC no-IEC-AIMS-2019-CVTS-085.

Informed consent Informed consent was obtained from all individual consenting participants included in the study.

Conflict of interest Dr. G. S. Bhuvaneshwar reports receiving consultation fees from TTK Healthcare Limited on guidance provided for the company’s post-market clinical studies. The remaining authors have no conflicts of interest to declare.

Statement of human and animal rights All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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