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Quality of life after Ross procedure in children

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Original Article

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Abstract

Introduction: Health-related quality of life in children who have undergone the Ross procedure has not been well characterised. The aim of this study was to characterise health-related quality of life in this cohort and compare to children with other CHD. *Method:* In this cross sectional, single-centre study, health-related quality of life was assessed in patients who underwent a non-neonatal Ross procedure using the Pediatric Quality of Life Inventory. Ross cohort scores were compared with healthy norms, patients with CHD requiring no surgical intervention or had curative surgery (Severity 2, S2) and patients who were surgically repaired with ≥1 surgical procedure and with significant residual lesion or need for additional surgery (Severity 3, S3). Associations between Pediatric Quality of Life Inventory score and patient factors were also examined. *Results:* 68 patients completed surveys. Nearly one-sixth of patients had overall scores below the cut-off for at-risk status for impaired health-related quality of life. There was no difference in overall health-related quality of life score between the Ross cohort and healthy children ($p = 0.56$) and S2 cohort ($p = 0.97$). Health-related quality of life was significantly higher in the Ross cohort compared to S3 cohort ($p = 0.02$). This difference was driven by a higher psychosocial health-related quality of life in the Ross cohort as compared to S3 cohort ($p = 0.007$). Anxiety scores were significantly worse in the Ross cohort compared to both S2 ($p = 0.001$) and S3 ($p = 0.0017$), respectively. *Conclusion:* Children who have undergone a Ross procedure report health-related quality of life equivalent to CHD not requiring therapy and superior to CHD with residual lesions. Despite these reassuring results, providers should be aware of potential anxiety among Ross patients.

With improved survival following surgery for CHD, there has been a paradigm shift with focus on long-term outcomes including improving the quality of life in children and adults with CHD. Studies have shown that children with a wide range of CHD disease severity, including heart transplant recipients, have good overall health-related quality of life but did perceive lower health-related quality of life as compared to healthy children across all age groups.[1,2] Studies of specific CHD and palliations, however, have been limited in scope to a few lesions and repairs.[3,4]

Aortic valve disease is one of the most common problems encountered by paediatric cardiologists, often making management of the disease complex. In cases where there is at least moderate valvular disease, surgery is often necessary to improve valve function and prevent deterioration of ventricular function and development of heart failure. Multiple surgical options are available including primary valve repair, replacement with an artificial mechanical valve, replacement with a tissue valve, or the Ross procedure. The Ross procedure involves replacement of the diseased aortic valve with the patient's own pulmonary valve or autograft. A pulmonary valve from a human donor, known as an allograft, is then used to replace the patient's own pulmonary valve. Short and long-term survival in patients who undergo Ross procedure is excellent, with a 10-year survival of 93–98% and freedom from operation of 72–75%.[5,6] Health-related quality of life in this group has not been rigorously evaluated. Luciani et al. assessed quality of life in Ross patients using indices such as NYHA class, school grade, employment, and regular and strenuous physical activity.[7] The majority (87%) of late survivors endorsed NYHA Class I symptoms. Although these parameters are informative, they did not use validated measures to truly assess "health-related" quality of life, defined by Varni et al., as a practical and multidimensional assessment of patients and parents consisting of a 23-item core health dimension.[8,9] The core health dimension includes emotional, physical, school, and social function.

Patients who undergo the Ross procedure are a unique subset of patients with CHD as the successful surgical recipient recovers initially from cardiac surgery with minimal or no residual lesion, but will develop residual disease requiring future interventions (i.e. right ventricular-to-pulmonary artery conduit replacement).[5,6,10] While understanding this expected history clearly could affect health-related quality of life, there is currently limited literature regarding health-related quality of life in young patients who undergo non-neonatal Ross procedure.

The primary aim of the study was to assess and compare health-related quality of life as perceived by patients and their parents in children who have undergone a non-neonatal Ross

procedure to healthy children and children with various CHD. The second aim was to examine the relationship between patient factors and health-related quality of life scores.

Method

Patient population

Patients who were 5–25 years of age who underwent a non-neonatal Ross procedure with at least 1-year post-operative follow-up were included in the study. Patients with concomitant simple congenital heart defects such as an atrial septal defect, ventricular septal defect, and patent ductus arteriosus were included. Patients with more severe concomitant CHD (e.g. hypoplastic aortic arch requiring arch construction, atrioventricular canal defect, etc.) were excluded. Patients who underwent a neonatal Ross procedure were also excluded from the study. Neonates most often present with different substrate of disease than older patients with high incidence of complex lesions necessitating more extensive surgery and has been shown to have higher early mortality rate.[11,12]

A review of the Society of Thoracic Surgeons database was conducted to search for patients who had ever undergone a non-neonatal Ross procedure at the University of Michigan Congenital Heart Centre. All patients meeting the inclusion criteria who were alive at follow-up were asked to participate in this cross-sectional study. Patients and/or their parents were contacted by mail using their last known address explaining the study. They could decline further contact by returning a postcard stating these intentions to the investigators. Gift certificates were offered for participating in the research study. Quality of life surveys were then administered prospectively via mail to the cohort of patients and parents. Patient demographic and clinical data were retrieved from the medical record. The study was approved by the institutional review board, and informed consent and child assent were obtained from the participating families.

Measures

Health-related quality of life in children who underwent a non-neonatal Ross procedure was assessed via the Pediatric Quality of Life Inventory including the PedsQL Generic Core 4.0 and Cardiac Module 3.0 Scales. Both encompass parallel self-report and parent proxy report formats. Developmentally appropriate self-report forms included children ages 8–12, 13–17, and 18–25 years. Parent proxy report forms were completed for children age 5–7, 8–12, and 13–17 years of age. Items are reversed-scored from 0 to 100 with higher scores indicating better health-related quality of life.

Pediatric Quality of Life Generic Core Scales have established reliability and validity with a large normative database of healthy children and those with chronic health conditions.[8,9] The brief 23-item PedsQL Generic Core Scale incorporates physical, emotional, social, and school functioning domains. To create a psychosocial health summary score, the mean is computed as the sum of the items divided by the number of items in the emotional, social, and school functioning scales. The PedsQL 3.0 Cardiac Module is also a well-validated survey consisting of 27 items with five scales related to heart problems and symptoms, perceived physical appearance, treatment anxiety, cognitive problems, and communication.[13]

Statistical analysis

Descriptive statistics were generated for demographic information and reported as mean and standard deviation (SD) for continuous variables or percentage (%) for categorical variables. Pediatric Quality of Life generic core and cardiac scores were reported as mean and SD for the Ross cohort. Mean health-related quality of life scores in patients who underwent a Ross procedure was then compared to data from patients with varying degrees of CHD severity from a previous study by Uzark and colleagues.[1] In that study, patients were categorised into cohorts based on disease severity. Severity 1 (S1) were patients that had mild CHD requiring no therapy or were effectively treated non-operatively (e.g. catheter based), Severity 2 (S2) had moderate CHD requiring no surgical intervention or had curative surgery (e.g. ASD, ventricular septal defect), Severity 3 (S3) had surgically treated CHD (> or = to 1 procedure) with significant residual lesion or needed additional surgery. Based on this classification, patients with a Ross procedure would be Severity 3. Pairwise comparisons between Ross and S2, Ross and S3 were made using Wilcoxon rank sum test. Univariate analysis was performed to examine the relationship between patient factors and total health-related quality of life scores. Spearman rank correlation coefficient was computed to assess the relationship between Pediatric Quality of Life scale scores and continuous variables, including demographics such as age at surgery and current age. Individual Psychosocial Summary scores were plotted to determine the frequency of scores >1 SD below population mean, the cut-off score for clinically significant impairment.[14]

Results

Patient characteristics

Of 80 families queried, 68 families completed surveys with an overall response rate of 85%. Thirty-six parents and sixty children who underwent Ross procedure completed the Pediatric Quality of Life Generic Core 4.0 and Cardiac Module 4.0. The median age at time of completion of the survey was 17.4 years with a mean age at surgery of 8.9 years (Table 1). The majority of patients had CHD.

Comparison of health-related quality of life self-report scores between Ross cohort and healthy children

By Pediatric Quality of Life self-report, there were no statistically significant differences in overall health-related quality of life scores between Ross cohort and healthy children with a mean score of 81.08 ± SD 12.78 and 82.87 ±13.16, respectively (Table 2). There were also no significant differences in all other domains encompassing health-related quality of life.

Comparison of health-related quality of life self-report scores between Ross and CHD

There were no statistically significant differences in overall health-related quality of life scores between Ross and S2 cohorts with a mean score of 81.08 ± 12.78 and 86.52 ± 12.46, respectively. Furthermore, there were no significant differences in all other domains encompassing total health-related quality of life between the two cohorts. When comparing the Ross cohort to S3 cohort, total health-related quality of life scores were significantly higher in the Ross cohort with a mean of 81.08 ± 12.78 and 75.36 ± 15.57 ($p = 0.02$), respectively. All domains except for emotional functioning scale were significantly higher/better in the Ross cohort

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Table 1. Patient characteristics (n = 68)

Age	16.4 (5.3)
Age at surgery	8.9 (5.3)
Time since surgery	7.4 (4.4)
Male	49 (72%)
Acquired heart disease	6 (0.1%)

(Table 2). The difference in health-related quality of life scores between the two cohorts appeared to be primarily driven by a higher psychosocial health-related quality of life with a mean score of 80.45 ± 15.63 vs. 73.97 ± 16.76 (p = 0.02), respectively. Nearly 15% of Ross patients reported scores meeting criteria for being "at risk" for psychosocial impairment.

In terms of the Pediatric Quality of Life Cardiac Module self-report scores, anxiety scores were significantly lower/worse in the Ross cohort as compared to both S2 and S3 cohorts, mean score of 68.33 ± 29.43, 83.66 ± 21.03 and 83.57 ± 22.29, respectively (Table 3). Nearly one in six patients reported frequent worry about what will happen to them. Communication was significantly higher/better in S2 group compared to Ross cohort; all other domains encompassing cardiac health-related quality of life were not significantly different between the groups.

Parent–child comparison

By Pediatric Quality of Life parent report, there was no difference in overall score on the Pediatric Quality of Life generic scores (paired t-test, p = 0.77) when compared to patient self-report. Additionally, there were no significant differences noted in any of the individual/summary generic scores including physical (p = 0.19), emotional (p = 0.95), social (p = 0.38), school (p = 0.13), and psychosocial domain (p = 0.92). There were no statistically significant differences in cardiac scale scores including cognitive (p = 0.68) and communication domains (p = 0.96). Patients scored significantly higher than parents did on appearance (p = 0.04) and patient scores for heart problems/symptoms tend to be lower (p = 0.09), but were not statistically different as compared to parent reports.

Correlates with health-related quality of life scores

Associations between Pediatric Quality of Life overall health-related quality of life scores and patient factors were examined using univariate analysis. Although no individual marker was associated with total health-related quality of life score, several trended toward significance (Table 4). Worse health-related quality of life scores were associated with the presence of more patient-reported symptoms (p = 0.09) and longer time since surgery (p = 0.06).

Discussion

Previous studies have evaluated quality of life using functional status alone. Our study is the first to assess "health-related" quality of life in children who underwent a Ross procedure. Health-related quality of life utilises validated measures to represent the patient's perception as related to their health.

The majority of children had good overall health-related quality of life as compared to both healthy children and those with mild to moderate CHD. Patients in the Ross cohort had lower school functioning than patients with milder CHD, but better school functioning than those with moderate CHD in this study. The need for open heart surgery as a neonate or infant increases the risk for neurodevelopmental impairment.[1,15–17] Exclusion of patients with neonatal Ross may have contributed to better school functioning than other patients with moderate CHD who may have had surgery in infancy and were included in the moderate CHD comparison group.

Despite the overall good health-related quality of life in the Ross cohort, the distribution of self-reported psychosocial health-related quality of life scores revealed that nearly 15% of Ross patients reported scores 1 SD below the mean for health-related quality of life for age, meeting the cut-off criteria for "at risk" status for impaired health-related quality of life. Early identification of patients with significantly impaired health-related quality of life can prompt referrals for psychosocial interventions and may influence decisions regarding re-intervention if poor perceived physical quality of life is suggested.

Among cardiac module subscales, Ross patients had significantly lower quality of life scores than the other CHD severity groups, specifically related to anxiety. It is reasonable to infer that Ross patients may be more worried as they will likely require re-intervention and there is uncertainty regarding the timing of future surgery.

There were no differences in overall patient and parent reported total scores on the Pediatric Quality of Life. Patients reported scores were significantly higher than parents on appearance (i.e. embarrassed when others see their body or scar). This has been observed in previous studies.[1] This also suggest that patients themselves may not worry or care about their physical appearance as much as their parents do. Parents may perceive their child as "sicker" or more "fragile" than patients themselves.

As there are various surgical options in patients with aortic valve disease, future research should focus on comparing health-related quality of life of children who underwent a Ross procedure to those with a mechanical aortic valve. Limited data suggest that patients with aortic valve disease requiring a mechanical valve have lower quality of life compared to Ross patients, but due to small sample size, there was less of a difference when patients were matched by age.[18] Therefore, larger studies evaluating health-related quality of life comparing children undergoing non-neonatal Ross procedure and mechanical aortic valve replacement is needed. The need for anticoagulation with a mechanical aortic valve may have a major impact on health-related quality of life, as this has been shown in a small study of children requiring daily warfarin for mechanical mitral valves.[19]

There are several limitations in our study. First, our patient cohort was older with a mean age of 16.4 ± 5.4 years compared to 9.7 ± 4.8 years in the study comparing quality of lifeQOL in CHD.[1] Therefore, scales such as psychosocial and anxiety may be affected by the mean age difference with the Ross cohort averaging in the adolescent age. Second, we did not have data on the type of residual lesions or current clinical state of patient's aortic valves or conduit which may influence their health-related quality of life or proximity to future surgery.

Conclusion

Overall, patients who underwent the Ross procedure reported health-related quality of life nearly equivalent to CHD patients who did not require surgical intervention or had a "curative" repair. Despite having good health-related quality of life in the majority of Ross patients, nearly one in six patients are at risk

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Table 2. PedsQL self-report scores (n = 68)

Score*	Ross	Healthy	S2	S3	Ross vs. Healthy p-value	Ross vs. S2 p-value	Ross vs. S3 p-value
Physical	84.32 (13.09)	86.86 (13.88)	86.52 (12.46)	78.26 (18.17)	0.41	0.29	0.02
Emotional	77.33 (20.84)	78.21(18.64)	79.01 (19.84)	73.61 (19.76)	0.30	0.57	0.22
Social	86.12 (15.31)	84.04 (17.43)	89.09 (15.04)	80.21 (19.75)	0.34	0.19	0.03
School	77.93 (18.47)	79.92 (16.93)	89.58 (13.81)	70.66 (20.69)	0.21	0.0001	0.02
Psychosocial	80.45 (15.63)	80.73 (14.70)	78.08 (13.88)	73.97 (16.76)	0.15	0.32	0.02
Total	81.08 (12.78)	82.87 (13.16)	81.02 (12.26)	75.36 (15.57)	0.56	0.97	0.02

Heart disease severity: S2 = moderate CHD requiring no therapy or surgically corrected (curative); S3 = surgically treated CHD (≥ 1 procedure with significant residual or need for additional surgery). Scores are reported as mean (SD).

Table 3. PedsQL cardiac self-report scores

Score	Ross	S2	S3	Ross vs. S2 p-value	Ross vs. S3 p-value
Heart Symptoms	78.27 (15.27)	80.11 (12.45)	73.10 (17.77)	0.41	0.06
Appearance Score	80.37 (23.61)	82.95 (22.37)	75.22(26.86)	0.49	0.230
Anxiety	68.33 (29.43)	83.66 (21.03)	83.57 (22.29) (28.77)	0.0002	0.0017
Cognitive	74.07 (22.37)	80.12 (18.76)	72.94 (21.61))	0.07	0.75
Communication	72.29 (25.06)	84.50 (20.06)	78.46 (25.40)	0.001	0.14

Scores are reported as mean (SD).

Table 4. Patient factors associated with quality of life scores

	Spearman rank coefficient	p-value
Gender	n/a	0.20
Time since surgery	−0.25	0.06
Age at surgery	0.22	0.10
Age at enrollment	0.04	0.79

for significantly impaired health-related quality of life. Providers should be aware of potential anxiety among Ross patients, especially related to the need for future surgery. Routine assessment of quality of life is essential to inform interventions to improve health outcomes.

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Conflict of interest. None

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committee.

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