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The Comparison of Postoperative Quality of Life of Children and Adolescents who Underwent Minimally Invasive and Major Surgery for Vesicoureteral Reflux Disease: A Retrospective Cohort Study

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What's known on the subject? and What does the study add?

Since their physical and psychological impacts are considered severe, major surgeries in pediatric urology often receive less attention compared to minor procedures. However, studies investigating long-term quality of life with evenly distributed patient groups based on diagnosis are still lacking. We believe that urologists should take into account not only the surgical procedures, complications, and follow-up challenges but also the psychological consequences associated with these interventions.

Abstract

Objective: We aimed to compare endoscopic subureteric injection with conventional open ureteral reimplantation in vesicoureteral reflux disease (VUR) in terms of long-term postoperative quality of life (QoL) to find potential factors that would predict the psychological outcome.

Materials and Methods: This retrospective cohort was based on data from February 2016-December 2019 on 115 children and adolescents (4-18 years old) who underwent elective surgery due to VUR disease and were hospitalized thereafter. Patients were divided into two groups according to the surgery they underwent, "endoscopic subureteral hyaluronic acid/dextranomer copolymer injection" (n=65), and "open ureteroneocystostomy" (n=50). With their mothers, the patients filled out the Pediatric QoL Questionnaire (PedsQL) remotely 2 to 6 years post-surgery (median 49 months), and the postoperative QoL was compared among the patients with regard to the QoL. Those with congenital or concomitant diseases were excluded.

Results: In VUR, patients undergoing either type of surgery had similar scores in all domains in PedsQL. In other words, postoperative QoL levels did not differ between endoscopic treatment and conventional open ureteral reimplantation. Furthermore, linear regression analysis identified maternal higher education level as the only significant predictor of higher postoperative QoL (estimate: 10.89; 95% confidence interval: 1.54-20.23; p=0.023). Conversely, factors such as surgery type, length of hospital stay, previous surgical experience, and patients' age at the time of the survey were not associated with postoperative long-term QoL.

Conclusion: The less invasive surgical modalities of VUR in the pediatric age group do not provide a significant advantage over open surgeries regarding the long-term postoperative QoL.

Keywords: Endourology, general urology, pediatric urology

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Introduction

The World Health Organization states that being healthy requires a combination of physical, mental, and social well-being beyond the absence of disease or infirmity (1). Quality of life (QoL) is, therefore, a fundamental part of pediatric practice. Many diseases can hinder children from engaging in physical and social activities. Thus, their QoL is frequently reduced because of diseases (2). Moreover, QoL is affected significantly by surgeries. In a cohort of 915 children who underwent many different types of inpatient surgery, such as general surgery, urology, and orthopedics etc., QoL scores declined significantly in 23% of children after one month (3).

The relationship between surgery and the development of a child's QoL and sense of well-being has been explored in pediatric urology. A recent study from our group investigated 151 children and adolescents undergoing different elective urological surgeries, and compared major versus minor surgeries, as well as open versus endourological surgeries (4). In that study, we found high parental preoperative psychiatric symptoms, number of previous surgeries, and female sex were associated with lower postoperative QoL. Schönbucher et al. (5) specifically evaluated the impact of hypospadias surgery in children and adolescents, finding that the severity of the disease was closely linked to lower QoL scores.

Investigating the effect of primary surgeries specific to a disease on QoL may be valuable for deciding surgical strategies. In vesicoureteral reflux disease (VUR), even though open ureteroneocystostomy (UNC) has higher success rates than endoscopic treatment, endoscopic procedures may be preferred to open techniques in reasonable indications, such as due to parental preference, having lower grades of reflux, and mild clinical course (6). We have avoided laparoscopic and robotic-assisted interventions for reflux as their superiority is still questioned and these techniques have not gained wide popularity among pediatric urologists (7). Thus, these techniques have not been preferred in our clinic.

We aimed to explore the differences in VUR surgeries with regards to the postoperative QoL outcome through a cohort that included both minimally invasive and major surgery groups, and to find which factors would predict the outcome.

We hypothesized that more extensive surgery in VUR would affect QoL and psychological well-being adversely in pediatric patients.

Materials and Methods

Patient Selection

All patients and parents gave informed consent before the study's initiation. We included all pediatric patients (under the age of 18) who underwent an elective VUR between February 2016 and December 2019, and spent at least one night in the surgical in-patient ward. Most of the patients were referred to our institution from other cities, as it serves as a tertiary center for pediatric urology. They were hospitalized one day before surgery for anesthesia preparation. Each surgical procedure was performed under general anesthesia.

Children with neurogenic bladder and those over five years old, with apparent bladder-bowel dysfunction, as determined by the Dysfunctional Voiding Scoring System, were excluded from the study.

Twenty patients were excluded from the study due to factors potentially affecting the QoL and psychological well-being. These factors include having moderate or severe intellectual disabilities preventing essential cooperation (n=3), psychiatric disorders, such as attention deficit hyperactivity disorder, tic disorders, and developmental coordination disorder, diagnosed or currently being treated (n=4), and multiple congenital anomalies (n=10). Additionally, patients whose parents have a level of language or education that would hinder cooperation with the surveyor were excluded (n=3).

The perioperative data of the study population and accompanying medical information were obtained from the hospital's electronic data system as well as the patients' written documents in the hospital archive. This retrospective cohort study had approval from the Hacettepe University Non-Interventional Clinical Research Ethics Committee (approval number: GO20/697, date: 25.08.2020).

Outcome Measures

1. Pediatric Quality of Life Questionnaire (PedsQL) 4.0: This questionnaire assesses the health-related QoL levels in children/adolescents aged 2-18 years in three domains: physical, psychosocial, and overall health-related QoL. This form is tailored for each group: 2-4, 5-7, 8-12, and 13-18 years. We used parent-reported and child/adolescent self-reported forms for subjects between 4 and 18 years to evaluate health-related QoL levels. Higher scores demonstrate a higher QoL (8-11). In the literature, this questionnaire's reliability, validity, sensitivity, and responsiveness to meaningful change in health-related QoL in healthy children, and children with acute and chronic health conditions have been proven (12). This is a validated questionnaire that has been adapted for use in the Turkish language (10,11).

2. The Strengths and Difficulties Questionnaire (SDQ): This behavior screening survey was developed to evaluate positive social behaviors and emotional and behavioral problems in children/adolescents aged between 2 and 17 years (13). Twenty-five items are categorized into 5 scales: Emotional symptoms (5 items); conduct problems (5 items); hyperactivity/inattention (5

items); peer relationship problems (5 items); prosocial behavior (5 items). In this study, the questionnaire was filled out by parents. This questionnaire was evaluated by medical professionals and found to be valid and reliable in the Turkish language (14). Higher scores indicate worse behavioral conditions.

An elective VUR surgery was carried out on 173 children and adolescents. After implementing the determined exclusion criteria, 153 patients were eligible for the study. Of these, thirty-eight patients (24.8%) could not be reached following the operation. PedsQL and SDQ were applied to the rest of the patients (n=115), and their mothers postoperatively.

All patients were admitted to the hospital one day before their surgeries, and there were no severe or long-term complications observed post-surgery. The patients were discharged after a complete recovery and made regular visits to clinic for routine follow-ups. The rest of the patients and their mothers were later contacted by phone and asked to complete the questionnaires to determine their long-term psychological well-being. The participants responded to the relevant questionnaire according to their age group.

The patients were divided into two surgical groups for analysis:

a. Endoscopic subureteral injection (ESI) with Hyaluronic Acid/Dextranomer copolymer (65 patients)

b. Open (ureteroneocystostomy) (50 patients).

The impact on the long-term psychological well-being of these surgeries was compared.

Statistical Analysis

The Stats (15) and the onewaytests (16) R packages were used to perform statistical analysis. Descriptive statistics of the participants were given as quantity and percentages; group characteristics were given as mean ± standard deviation or medians and minimum-maximum values according to whether they were normally distributed or not. The patient data were divided into two surgery groups: ESI and UNC. These groups are compared, regarding postoperative sociodemographic and psychological features. To identify between-group differences, nominal variables were compared using the Pearson chi-square test. After the Shapiro-Wilk test was implemented, normally distributed continuous variables were compared with an independent samples t-test, and the Mann-Whitney U test was performed for non-normally distributed data. Following univariate analyses, multiple linear regression models were developed to investigate the combined effects of surgery types and clinically important variables on postoperative long-term QoL scores. P<0.05 was defined as the level of statistical significance.

Results

One hundred and fifteen patients who underwent elective VUR surgery in the study were successfully evaluated with the questionnaires. The median time between the surgery and the psychosocial evaluation, which included the patients and their parents, was 47 months (26-73 months). Table 1 details the baseline characteristics of the participants.

Sociodemographic and Perioperative Features

The ESI group included 65 children/adolescents, while the UNC surgery group consisted of 50 participants. All patients in the UNC group underwent the intravesical approach. The number of females was significantly higher in the ESI group (76.9% *vs.* 52%; p=0.005). Excluding the length of postoperative hospital stays (median; ESI *vs.* UNC: 1 day *vs.* 5 days; p<0.001) and the age during the psychosocial evaluation (median; ESI vs. UNC: 9 years *vs.* 7 years; p=0.046), other sociodemographic features were similar between the surgery groups; such as the time gap between the surgery and psychosocial evaluation, age during the surgery, the proportion of subjects who had previous surgery, and maternal age. These findings are presented in Table 2.

QoL and Psychiatric Symptoms

Both parent-reported and child-reported QoL scores in all domains were comparable between the groups. Furthermore, the ESI and the UNC group had no differences regarding SDQ scores in 5 domains. However, the SDQ emotional problems scores are significantly higher in patients who have undergone UNC surgery (median, ESI *vs.* UNC: 0 *vs.* 1; p=0.007). These results are shown in Table 2.

Linear Regression Analysis

Type of surgery, length of hospital stay, previous surgery experience, patient's age at the time of the survey, and mother's education level were determined as factors that could affect the postoperative QoL scores. These factors were examined with linear regression models. It was found that the patient's mother with a higher education level was the only predictor for higher postoperative long-term QoL scores (estimate: 10.89; 95% confidence interval: 1.54-20.23; p=0.023). These results are presented in Table 3.

Discussion

Current findings revealed that the type of surgery performed made no significant difference in postoperative QoL levels for children with VUR. Moreover, the type of surgery could not be used to predict the pediatric patients' postoperative QoL.

Table 1. Descriptive statistics of the participants.

			n	(%)
Mother's health status	Healthy		93	80.9
	Having a disease requiring medication		22	19.1
Mother's education level	Primary school		17	14.8
	Secondary school		24	20.9
	High school		29	25.2
	University		45	39.1
Family structure	Separated family		5	4.3
	Nuclear family		98	85.2
	Extended family		12	10.4
Mode of presentation	Antenatal hydroureteronephrosis		19	16.7
	Febrile urinary tract infection		74	64.9
	Non-febrile urinary tract infection		7	6.1
	Impairment in kidney functions		9	7.9
	Urinary incontinence		2	1.8
	Unsuccessful reflux surgery		3	2.6
Previous surgeries	Yes		31	27.0
	No		84	73.0
Performed surgeries	Endoscopic procedure	Unilateral	25	21.7
		Bilateral	40	34.7
	Open ureteroneocystostomy	Unilateral	22	19.2
		Bilateral	28	24.4

Table 2. Postoperative sociodemographic and psychological features of the patients in different groups

			ESI (n=65)	UNC (n=50)	p
Between the surgery and psychosocial evaluation (month)			46 (26-73)	51 (26-72)	0.210[a]
Age during the surgery (year)			5.0 (0-13)	3.0 (0-13)	0.117[a]
Age during the psychosocial evaluation (year)			9.0 (2-17)	7.0 (3-16)	0.046[a]
Previous surgeries		Yes	28 (43%)	26 (52%)	0.342[b]
		No	37 (57%)	24 (48%)	
Maternal age (year)			38.56±5.83	37.58±5.58	0.360[c]
Postoperative hospital stays (day)			1.0 (1-7)	5.0 (1-8)	<0.001[a]
Maternal education level	Primary school graduate		9	8	0.763[b]
	Secondary school graduate		13	11	
	High school graduate		19	10	
	University graduate		24	20	
SDQ (emotional symptoms)			0 (0-9)	1.0 (0-7)	0.007[a]
SDQ (conduct problems)			1.0 (0-6)	1.0 (0-7)	0.232[a]
SDQ (hyperactivity/inattention)			3.0 (0-10)	5.0 (0-10)	0.081[a]
SDQ (peer relationship problems)			2.0 (0-9)	2.0 (0-10)	0.512[a]
SDQ (prosocial behaviour)			9.0 (0-10)	8.0 (3-10)	0.250[a]
SDQ (total)			16 (10-30)	17 (9-35)	0.329[a]
PedsQL psychical			75 (0-100)	75 (40-100)	0.843[a]
PedsQL psychosocial			75 (33-100)	77 (27-100)	0.845[a]
PedsQL total score			74.28±14.44	74.61±16.48	0.909[c]
PedsQL psychical-parent reported			59 (25-100)	59 (22-100)	0.927[a]
PedsQL psychosocial-parent reported			72 (33-97)	78 (25-95)	0.117[a]
PedsQL total score-parent reported			67 (47-98)	70 (37-97)	0.305[a]

ESI: Endoscopic subureteral injection, UNC: Open ureteroneocystostomy, SDQ: The strengths and difficulties questionnaire, PedsQL: Pediatric quality of life questionnaire
[a]: Mann-Whitney U test, [b]: Pearson chi-square test, [c]: Student's t-test

Table 3. Linear regression analysis of the total score of PedQL					
Predictors	**Patients having vesicoureteral reflux disease**				
	Estimates	**Standard error**	**Confidence interval**	**Statistic**	**P**
(Intercept)	57.77	6.96	43.97-71.57	8.30	<0.001
Surgery type	-0.75	4.94	-10.55-9.065	-0.15	0.880
Secondary school graduate mother	8.81	5.04	-1.19-18.80	1.75	0.084
High school graduate mother	7.83	4.98	-2.04-17.70	1.57	0.119
University graduate mother	10.98	4.71	1.65-20.32	2.33	0.022
Age during the psychosocial evaluation	0.80	0.43	-0.05-1.65	1.87	0.064
Postoperative hospital stays	0.50	1.10	-1.69-2.69	0.45	0.653
Previous surgery	0.63	3.32	-5.95-7.21	0.19	0.851
PedsQL: Pediatric quality of life questionnaire. In this regression model, the variable representing mothers who graduated from primary school was accepted as a reference, and three dummy variables were developed and used					

However, patients who underwent UNC surgery due to VUR tended to have more significant emotional problems than patients who had an ESI. Besides, the schooling degree of the mother can predict the pediatric patients' postoperative QoL level.

As well as the characteristics of the disease and the patient, the parental preference is also important in decision about making management. Ogan et al. (17) reported that parents of VUR patients prefer antibiotic prophylaxis as initial treatment. As the years on follow-up pass, parents would choose definitive correction, and although ESI is less effective than UNC, they prefer ESI with the idea of being less invasive. Moreover, a latter study showed that antibiotic prophylaxis was preferred as the initial therapy for VUR, in time, given persistent VUR, preferences shifted toward surgery. After a period of time, the preference for open surgery increased, which was perceived as a more durable and permanent solution, and the preference for endoscopic surgery decreased (18). These findings underscore the importance of providing accurate and unbiased data to involve parents in building a management plan. Comparing ESI to UNC, there is no difference in the long-term psychological outcomes. Minimally invasive procedures do not always mean minimal psychological effects, especially in the pediatric age group. Therefore, treatment plans can be developed without considering psychological outcomes, as they seem equivalent.

As in other fields, assessing QoL and psychological well-being is a prominent topic in pediatric urology (4,19-21). QoL is a marker that allows the monitoring of the level of recovery in the postoperative period (19). A recent prospective study from our institution involving 151 pediatric urology patients who underwent either major or minor urological surgeries found the predictive factors for early postoperative QoL (4). However, this study's data were heterogeneous in terms of surgical diversity.

Specific surgeries were evaluated with respect to their effect on postoperative QoL in pediatric urology patients (19,21). This study uniquely compares minor and major surgeries in pediatric urology. Until now, clinicians have generally perceived the long-term negative impact of major surgeries on QoL as greater than that of minor surgeries. This perception is primarily based on the severity of major surgical procedures and the way these surgeries are communicated to patients and their families. However, our results were not in accordance with the interpretation above. The results can be explained by the following: Firstly, all surgeries impair patients' physical integrity regardless of their severity. Even though the endoscopic treatment of VUR is minimally invasive, it may not prevent a deterioration in QoL. Secondly, children who undergo major surgeries suffer from more postoperative pain than those who undergo minor surgeries (22). However, since the median time between the surgery and psychosocial evaluation was relatively long in this study, postoperative pain, recovery-related anxiety, and activity restrictions in patients who underwent UNC surgery had already diminished, leading to an overall improvement in their QoL. In addition to that, in the postoperative period, pediatric patients in the UNC group required regular wound dressing and care, which may negatively impact QoL. However, wound healing and care in the study population were completed before the initiation of this study. Another point to note is that all patients who underwent UNC surgery were discharged with Double J stents. They displayed ureteral stent associated symptoms including pain and urinary side effects until its removal which was carried out under anesthesia 4-6 weeks after the surgery. It likely impaired postoperative QoL; however, its effect would have significantly lessened by the time of the study. Lastly, many parents might have chosen reimplantation, which had a higher success rate, even though the immediate post-operative morbidity may have been higher. It is likely that the patients who underwent open

reimplantation might have had fewer post-operative tests, such as voiding cystourethrography (VCUG), because of high success; those who underwent endoscopic treatment may have had more post-operative tests (like multiple VCUGs) repeated, so this may have reduced the QOL difference between the two groups. However, the morbidity associated with open surgery must not be overlooked, and families should be counseled accordingly.

High SDQ emotional subscale scores demonstrate the risk of suffering from concurrent clinical anxiety and depression (23). In this study, high emotional scores were confirmed in patients who underwent UNC surgery. Patients' history may contribute to these findings since patients who had major surgery frequently experienced more severe symptoms (24). Additionally, having an incision following UNC surgery and the need for observation with a urethral catheter for patients in the surgical in-patient ward may explain the findings.

Mothers are almost always the primary caregivers of their children following discharge from the hospital, and they should be able to thoroughly understand the instructions given to them by physicians in the postoperative period. To illustrate, possible surgical and medical complications must be instantly recognized at home once symptoms develop. Parental attention allows pediatric patients to seek medical consultation before the complications become severe or permanent. Wound care, pain management, and effective administration of medicine prescribed by medical doctors are the other instructions they should follow carefully. An adequate educational level of patients' caregivers is essential to understanding the instructions thoroughly. It may prevent a decrease in QoL scores and maintain psychological well-being in the postoperative period. Therefore, we speculate that the effect of maternal education level is more apparent than was previously considered. Mothers of patients who underwent open surgery might better identify the problems and be more conscious of how to overcome them in the management of the postoperative process. The strong association between maternal education level and postoperative QoL in VUR disease might be attributable to several factors.

The main strength of our study is that the sample of participants is evenly distributed in both surgery groups. QoL and emotional scores were compared among the surgeries, and a unique predictor for higher long-term postoperative QoL in VUR was found.

Study Limitations

This study also has some limitations. This study took place in a tertiary referral hospital where a selected group of patients was treated. The age range of the patients was quite broad. Furthermore, some patients and their parents were not able to be reached in order to participate in the study, which may have resulted in selection bias. Even though both PedsQL and SDQ are very well validated and widely used measures for QoL and psychiatric symptom assessment, they still carry the limitations of subjectivity with self-reported Likert-type scales. Moreover, the variables used in the regression model were defined as clinically meaningful, even though they were not significant in univariate analysis. The majority of children and their families may have forgotten postoperative discomfort, such as incision pain; bladder spasms in the open surgery group; the effects of urethral catheterization; and the inconvenience of prolonged hospitalization due to the time gap between the procedure and the completion of the survey. Lastly, due to the nature of the retrospective cohort, children with an underlying/pre-existing psychiatric disease could not be evaluated or excluded through clinical interview.

Conclusion

Whether being treated for VUR with an endoscopic or open surgery may result in similar long-term postoperative QoL remains a subject of investigation. Pediatric urologists should take into consideration that minimally invasive surgeries, notwithstanding their minority, may have a similar effect on long-term postoperative QoL to that of major surgeries.

Ethics

Ethics Committee Approval: This retrospective cohort study had approval from the Hacettepe University Non-Interventional Clinical Research Ethics Committee (approval number: GO20/697, date: 25.08.2020).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.T., H.S.D., Concept: H.S.D., Design B.H., H.T.Ç., Data Collection or Processing: B.H., M.A., Analysis or Interpretation: M.K., H.T.Ç., Literature Search: B.H., M.A., Writing: B.H., H.T.Ç., S.T., H.S.D.

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