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Investigation of the Frequency of Vesicoureteral Reflux (Vur) and the Effect of Regular Follow-up on the Progression to End-stage Renal Disease İn Patients With Spina Bifida

Cumali Berkan Unal

berkanunal42@gmail.com

Sağlık Bilimleri Üniversitesi

Fatma Saraç

Sağlık Bilimleri Üniversitesi

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Abstract

Objective

In this study, we aimed to investigate the frequency of vesicoureteral reflux (VUR) in patients with spina bifida and neurogenic bladder, as well as the effect of regular follow-up and clean intermittent catheterization (CIC) on the progression to end-stage renal disease (ESRD).

Materials and Methods

The study was conducted retrospectively by reviewing the medical records of patients with a diagnosis of spina bifida followed up and treated in our hospital's Pediatric Surgery clinic. The patients' medical files were examined for biochemical urea-creatinine values, radiological voiding cystourethrography (VCUG) results, static renal scintigraphy (DMSA) results, urodynamic findings, initiated and ongoing treatments, and surgical interventions.

Results

A total of 236 patients diagnosed with spina bifida were included in the study. According to VCUG results, 34.7% of the patients had vesicoureteral reflux. 13.1% of the patients had chronic kidney disease (CKD). Among those with CKD, 45.2% were regularly followed up, while 95.1% of those without CKD were regularly followed up. A statistically significant difference was found between the two groups regarding regular follow-up ($X2 = 66.340$; $p < 0.001$). The regular follow-up rate was lower in patients with CKD compared to those without CKD. In addition, 32.3% of the CKD patients and 88.8% of the non-CKD patients received regular CIC. A statistically significant difference was also found between the two groups regarding regular CIC application ($X2 = 56.717$; $p < 0.001$). The regular CIC rate was lower in patients with CKD compared to those without CKD.

Conclusion

Our study suggests that regular follow-up and clean intermittent catheterization (CIC) in patients with spina bifida can reduce the progression to chronic kidney disease compared to those who do not undergo regular follow-up or CIC. Initiating CIC at an appropriate time from the neonatal period can prevent nephrological/urological complications and, consequently, the progression to chronic kidney disease.

Introduction

Spina bifida (SB) is a congenital anomaly that occurs when the spinal cord and spine fail to close during the fetal period due to a defect in the neural tube development. It is one of the most complex congenital

anomalies that can be encountered in human life.

Genetic and environmental factors are effective in the development of neural tube defects (NTDs). Important risk factors include maternal folate deficiency, diabetes, obesity, exposure to excessive heat (e.g., fever, sauna) or certain medications (e.g., carbamazepine, valproic acid, methotrexate) in early pregnancy, and a family history of pregnancies with NTDs.

Spina Bifida is not just a spinal defect. It is the most common congenital anomaly that causes permanent damage. It is a complex syndrome that can cause abnormalities and dysfunction in many organs and systems, including the musculoskeletal system, gastrointestinal system, genitourinary system, central and peripheral nervous systems. It requires the long-term follow-up and collaboration of multiple medical specialties. Pediatric surgery is one of them. As indicators of impaired bladder and bowel functions, neurogenic bladder, vesicoureteral reflux (VUR), urinary incontinence (UI), recurrent urinary tract infections and chronic renal failure (CRF), constipation, encopresis and fecal incontinence are significant causes of morbidity. In patients with SB, bladder continence is 40–85%, bowel continence is 50–85%, and combined bladder and bowel continence is 25%. CRF is the leading cause of mortality after the first year of life. Although awareness and care about SB are increasing, it is difficult to predict which patients will develop chronic kidney disease (CKD) and/or require urological surgery; or which patients will require surgical procedures for adequate bowel evacuation. In our study, we aimed to investigate the effect of regular follow-up and regular clean intermittent catheterization on the progression to end-stage renal disease (ESRD) in patients with spina bifida and neurogenic bladder.

MATERIALS AND METHODS

2.1. RESEARCH METHOD

Our study is a retrospective clinical study. In our study, demographic data, urodynamic imaging, voiding cystourethrography (VCUG), Static Renal Scintigraphy (DMSA), biochemical results, applied surgical treatments, and the final status of the patients who were followed up in our hospital were investigated retrospectively.

2.2. SELECTION OF PATIENT AND CONTROL GROUPS

236 patients of both genders who were followed up and treated in our clinic and diagnosed with spina bifida were included in the study. We aimed to examine pediatric cases in our study. Since the child age limits in our country are determined as 0–18 years old, this age range was selected.

Including criteria for the study; being between 0–18 years old, patients diagnosed with spina bifida and followed up in pediatric surgery were included in the study. Exclusion criteria for the study; Patients who were over 18 years of age and lost follow-up were not included in the study.

2.3. ETHICS COMMITTEE APPROVAL

This study was applied to Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee and received ethics committee approval on 22.02.2023 with the decision number 2023-76.

2.4. STATISTICAL ANALYSIS

The data obtained in the study were analyzed with SPSS version 25.0 package program. The distribution of the data is shown with descriptive analysis parameters (mean, median, standard deviation, minimum, maximum, frequency, percentage). The Kolmogorov-Smirnov test was used to analyze whether the data were normally distributed. In the comparison of continuous variables between two independent groups, the Mann Whitney U Test was used because the data did not comply with the normal distribution. Chi-Square tests (Pearson Chi-Square Test, Fisher Exact Test, Fisher Freeman Halton Exact Test) were used in comparisons made between categorical variables. Data analysis was examined at a 95% confidence interval (p = 0.05).

RESULTS

The general clinical characteristics of the patients included in the study were evaluated (Table 3.1). According to the results obtained; the mean age of the patients was 12.03 ± 4.55 years, the mean age at presentation was 3.35 ± 4.27 years and the mean birth weight was 2974.94 ± 609.04 g.

Table 3.1
General Clinical Characteristics of Patients

	X ± SS	**M (Min - Max)**
Age (Years)	12,03 ± 4,55	12,0 (3–18)
Age of Application (Years)	3,35 ± 4,27	1,0 (0–17)
Birth Weight (gr)	2974,94 ± 609,04	3000,0 (640–4250)
	N	**%**
Gender		
Male	118	50,0
Female	118	50,0
Total	**236**	**100**

It was determined that 50% of the patients were male and 50% were female.

Table 3.2
Distribution of Patients' Urinary System Findings and Pathologies

	N	%
Chronic Renal Failure		
Yes	31	13,1
No	205	86,9
Hydronephrosis		
Yes	65	27,5
No	171	72,5
Renal Agenesis		
Yes	14	5,9
No	222	94,1
Renal Agenesis Side		
Right Agnesia	10	4,2
Left Agnesia	4	1,7
Renal Atrophy		
Yes	27	11,4
No	209	88,6
Renal Atrophy Side		
Right Atrophy	12	5,1
Left Atrophy	15	6,4
Urinary System Stone		
Yes	36	15,3
No	200	84,7
Bladder Trabeculation		
Yes	133	56,4
No	103	43,6
Horseshoe Kidney		
UV: Ureterovesical, PUV: Posterior Urethral Valve, UP: Ureteropelvic Stenosis		

	N	%
Chronic Renal Failure		
Yes	19	8,1
No	217	91,9
Urinary System Pathologies		
Urinary System Stone	36	15,3
Ureterovesical Junction Stasis (UV Stasis)	12	5,1
Inguinal Hernia	11	4,7
Penoscrotal Hypospadias	7	3,0
Neurogenic Bladder	6	2,5
Undescended Testis	6	2,5
Bladder Diverticulum	5	2,1
Renal Rotation Anomaly	5	2,1
Dual System	5	2,1
Posterior Urethral Valve (PUV)	4	1,7
Crossed Renal Ectopia	3	1,3
Unspecified Hypospadias	3	1,3
Urachal Cyst	2	0,8
Ureterocele	2	0,8
Cloca Anomaly	2	0,8
Hydrocele	2	0,8
Ureteropelvic Junction Stasis (UP Stasis)	1	0,4
Accessory Scrotum	1	0,4
Epispadias	1	0,4
Hemametrotocolpos	1	0,4
Anorectal Malformations		
Yes	34	14,4
UV: Ureterovesical, PUV: Posterior Urethral Valve, UP: Ureteropelvic Stenosis		

	N	%
Chronic Renal Failure		
No	202	85,6
Anorectal Malformations		
Without Fistula	14	5,9
Vestibular Fistula	7	3,0
Urethral Fistula	6	2,5
Rectovesical Fistula	3	1,3
Rectal Fistula	2	0,8
Perianal Fistula	1	0,4
Vesical Fistula	1	0,4
Urinary System Infection		
Yes	202	85,6
No	34	14,4
Residual Urine		
Yes	147	62,3
No	29	12,3
Total	**236**	**100**
UV: Ureterovesical, PUV: Posterior Urethral Valve, UP: Ureteropelvic Stenosis		

The urinary system and pathologies of the patients included in the study were evaluated (Table 3.2). According to the results obtained; It was determined that 13.1% of the patients had chronic renal failure. It was determined that 27.5% of the patients had hydronephrosis. It was determined that 2.9% of the patients had renal agnesia, 4.2% had right renal agnesia, and 1.7% had left renal agnesia. It was determined that 11.4% of the patients had renal atrophy, 5.1% had right renal atrophy, and 6.4% had left renal atrophy. It was determined that 15.3% of the patients had urinary system stones, 56.4% had bladder trabeculation, and 8.1% had horseshoe kidney. Among the pathologies found in the patients, urinary system stones were found to be the first with a rate of 15.3%, UV stasis was found to be the second with a rate of 5.1% and inguinal hernia was found to be the third with a rate of 4.7%.

Anal atresia was found in 14.4% of the patients, anal atresia without fistula was found in 5.9%, vestibular fistula was found in 3%, urethral fistula was found in 2.5%, rectovesical fistula was found in 1.3%, rectal fistula was found in 0.8%, perianal fistula was found in 0.4% and vesical fistula was found in 0.4%.

Urinary system infection was found in 85.6% of the patients. Residual urine was found in 62.3% of the patients.

Table 3.3
VCUG (Voiding Cystourethrography-Urination Film) Test Results of Patients

	N	%
VUR		
Yes	82	34,7
No	154	65,3
VUR Side		
Right VUR	20	8,5
Left VUR	32	13,6
Bilateral VUR	30	12,7
VUR Grade		
Grade 1	6	2,5
Grade 2	12	5,1
Grade 3	14	5,9
Grade 4	19	8,1
Grade 5	20	8,5
Right VUR Grade		
Grade 1	4	1,7
Grade 2	9	3,8
Grade 3	8	3,4
Grade 4	15	6,4
Grade 5	13	5,5
Left VUR Grade		
Grade 2	1	0,4
Grade 3	1	0,4
Bilateral VUR Grade		
Grade 1	2	0,8
VUR: Vesicoureteral Reflux		

	N	%
VUR		
Grade 2	3	1,3
Grade 3	6	2,5
Grade 4	4	1,7
Grade 5	7	3,0
Total	**236**	**100**
VUR: Vesicoureteral Reflux		

The VCUG test results of the patients included in the study were evaluated (Table 3.3). According to the results obtained; It was determined that 34.7% of the patients had VUR (Vesicoureteral Reflux). It was found that 8.5% of the patients had right VUR, 13.9% had left VUR and 12.7% had bilateral VUR. It was found that 2.5% of the patients had grade 1, 5.1% had grade 2, 5.9% had grade 3, 8.1% had grade 4 and 8.5% had grade 5 VUR. When the right VUR grades were evaluated; it was determined that 1.7% had grade 1, 3.8% had grade 2, 3.4% had grade 3, 6.4% had grade 4 and 5.5% had grade 5 VUR. When the left VUR grades were evaluated; It was found that 0.4% had grade 2 and 0.4% had grade 3. When bilateral VUR grades were evaluated; 0.8% had grade 1, 1.3% had grade 2, 2.5% had grade 3, 1.7% had grade 4 and 3% had grade 5 VUR.

Table 3.4
Distribution of Patients Regarding Anticholinergic and Prophylaxis Reception

	N	%
Anticholinergic		
Yes	169	71,6
No	67	28,4
Prophylaxis		
Yes	181	76,7
No	55	23,3
Total	**236**	**100**

Anticholinergic and prophylaxis intake of the patients were evaluated (Table 3.4). It was determined that 71.6% of the patients received anticholinergic and 76.7% received prophylaxis.

Table 3.5
Distribution of Patients' Follow-up, CIC and Urodynamics

	N	%
Regular Follow-up		
Yes	209	88,6
No	27	11,4
Regular CIC		
Yes	192	81,4
No	44	18,6
CIC Frequency		
3 x 1	6	2,5
4 x 1	34	14,4
5 x 1	10	4,2
6 x 1	88	37,3
8 x 1	2	0,8
Urodynamics		
Yes	180	76,3
No	56	23,7
Total	**236**	**100**
TAK: Clean Intermittent Catheterization		

The distribution of follow-up, CIC and urodynamics applied to the patients was evaluated (Table 3.5). It was determined that 88.6% of the patients were followed regularly and 81.4% received regular CIC. It was determined that 2.5% of the patients received 3x1, 14.4% received 4x1, 4.2% received 5x1, 37.3% received 6x1 and 0.8% received 8x1 CIC. It was determined that 76.2% of the patients received urodynamics.

Table 3.6
Distributions of Patients' Ureteral Diameters, Parenchymal Thicknesses and Bladder Capacities

	N	%
Ureteral Diameter		
Dilation Present	35	14,8
No Dilation	201	85,2
Ureteral Dilation Side		
Right	3	1,3
Left	12	5,1
Bilateral	20	8,5
Parenchymal Thickness		
Normal	200	84,7
Thinned	36	15,3
Bladder Capacity		
Bladder Capacity < Expected Bladder Capacity	117	49,6
Bladder Capacity = Expected Bladder Capacity	11	4,7
Bladder Capacity > Expected Bladder Capacity	48	20,3
Total	**236**	**100**

The patients' ureteral diameters, parenchymal thicknesses and bladder capacities were evaluated (Table 3.6). According to the results obtained; ureteral dilatation was found in 14.8% of the patients, 1.3% had right, 5.1% had left and 8.5% had bilateral ureteral dilatation. It was found that the parenchyma was thinned in 15.3% of the patients and the parenchymal thickness was normal in 84.7%. It was found that the bladder capacity was lower than expected in 49.6% of the patients, the bladder capacity was at the expected bladder capacity (EBC) in 4.7% and the bladder capacity was higher than expected in 20.3%.

Table 3.7
Distributions of Patients' Urological Surgeries

	N	%
Urological Surgery		
Yes	79	33,5
No	157	66,5
Urological Surgeries		
Cystoscopy	53	22,4
Subureteric Injection	20	8,5
Vesicostomy	14	5,9
Bladder Augmentation	11	4,7
Mitrofanoff (MTR)	11	4,7
Ureterostomy	3	1,3
Ureterectomy	3	1,3
Nephrolithotomy	3	1,3
Nephrectomy	2	0,8
Nephrostomy	2	0,8
Other	36	15,3
Total	**236**	**100**

PUV: Posterior Urethral Valve, Pyelolithotomy, Urachal Cyst Excision, Botox Application to the Bladder, Ureteroneocystostomy, Pyeloplasty, Peritoneal Dialysis Catheter Insertion, Urethral Band Ablation, Cystolithotomy, Hypospadias Surgery, Vesicolithotomy, Double J catheter placement in the ureter, Monti and Malone procedure

Information regarding the patients' urological surgeries was evaluated (Table 3.7). It was determined that 33.5% of the patients underwent urological surgery. Among the urological surgeries performed on the patients, cystoscopy came first with a rate of 22.4%, and subureteric injection came second with a rate of 8.5%.

Table 3.8
DMSA (Static Kidney Scintigraphy) Test Results of Patients

	N	%
Renal Scar		
Yes	69	29,2
No	107	45,3
Renal Scar Side		
Right	16	6,8
Left	22	9,3
Bilateral	31	13,1
Total	**176**	**100**

DMSA (Static Renal Scintigraphy) test was performed in 176 patients and the results were evaluated (Table 3.8). Renal scarring was determined in 29.2% of the patients, 6.8% had right renal scarring, 9.3% had left renal scarring and 13.1% had bilateral renal scarring.

Table 3.9
Distribution of Patients Regarding Neurosurgical Pathology and Surgeries

	N	%
Neurosurgical Pathology		
Meningomyelocele	139	58,9
Tethered Cord	42	17,8
Spina Bifida (Patient with more than one NTD pathology)	37	15,7
Syringomyelia	18	7,6
Meningocele	15	6,4
Filum Terminale Lipoma	7	3,0
Caudal Regression	6	2,5
Diastomatomyelia	6	2,5
Lipomeningomyelocele	4	1,7
Encephalocele	3	1,3
Sacrococcygeal Teratoma	2	0,8
Sacral Agenesis	2	0,8
Hydrosyringomyelia	1	0,4
Lumbosacral Sinus	1	0,4
Transverse Myelitis	1	0,4
Corpus Callosum Agenesis	1	0,4
Neurosurgical Surgery		
Yes	188	79,7
No	48	20,3
Neurosurgical Surgeries		
Meningomyelocele Closure	162	68,6
Tethered Cord Release	38	16,1

a: Laminectomy, Duraplasty, Medulla Exploration, Diplomyelia Operation, Encephalocele Closure, Intradural Lipoma Excision, Lipomeningocele Excision, V-P Shunt Insertion Due to Hydrocephalus, Kyphosis Surgery, A.Chiari Type 2 Malf Operation, Lumbosacral Sinus Excision, Filum Terminale Lipoma Excision, Sacrococcygeal Teratoma Excision, Cerebellar Herniation, Dorsal Fibrous Band Excision, Posterior Instrumentation, Fusion, Hemivertebrectomy, Osteotomy, Hemivertebrectomy

	N	%
Neurosurgical Pathology		
Scoliosis Surgery	4	1,7
Other	17	7,2
Shunt		
Yes	104	44,1
No	132	55,9
Total	**236**	**100**

a: Laminectomy, Duraplasty, Medulla Exploration, Diplomyelia Operation, Encephalocele Closure, Intradural Lipoma Excision, Lipomeningocele Excision, V-P Shunt Insertion Due to Hydrocephalus, Kyphosis Surgery, A.Chiari Type 2 Malf Operation, Lumbosacral Sinus Excision, Filum Terminale Lipoma Excision, Sacrococcygeal Teratoma Excision, Cerebellar Herniation, Dorsal Fibrous Band Excision, Posterior Instrumentation, Fusion, Hemivertebrectomy, Osteotomy, Hemivertebrectomy

The characteristics of the patients' neurosurgical pathologies and surgeries were evaluated (Table 3.9). According to the results obtained; among the neurosurgical pathologies found in the patients, meningomyelocele was the first with a rate of 58.9%, tethered cord was the second with a rate of 17.8% and more than one NTD pathology was the third with a rate of 15.7%. It was determined that 79.7% of the patients underwent neurosurgical surgery. It was determined that 68.6% of the patients underwent meningomyelocele closure, 16.1% tethered cord release, 1.7% scoliosis surgery and 7.2% other neurosurgical surgeries were applied. It was determined that 44.1% of the patients had shunts.

Table 3.10
Distribution of Patients' Non-Urinary Pathologies

	N	%
Pathologies Outside the Urinary System		
Cardiac	35	14,8
Costa Anomaly	9	3,8
Scoliosis	8	3,4
Ovarian Cyst	6	2,5
Hip Dysplasia	6	2,5
Hypothyroidism	5	2,1
Cholelithiasis	5	2,1
Pes Equinovarus	4	1,7
Acute Appendicitis	2	0,8
Esophageal Atresia	2	0,8
Cloaca Anomaly	2	0,8
Gastroesophageal Reflux	2	0,8
Pilonidal Sinus	1	0,4
Diaphragmatic Hernia	1	0,4
Pes Planus	1	0,4
Hemangioma	1	0,4
Necrotizing Enterocolitis	1	0,4
Sacral Juvenile Xanthogranuloma	1	0,4
Vaginal Polyp	1	0,4
Peutz Jeghers Syndrome	1	0,4
Colonic Atresia	1	0,4
Annular Pancreas	1	0,4
Hydrocolpos	1	0,4
Hip Dysplasia	1	0,4
Vaginal Atresia	1	0,4

	N	%
Pathologies Outside the Urinary System		
Kyphosis	1	0,4
Lymphangioma	1	0,4
Precocious Puberty	1	0,4
Thrombophilia	1	0,4
Partial Androgen Insensitivity	1	0,4
Hemophilia	1	0,4
Pouch Colon	1	0,4
Meckel Diverticulum	1	0,4
Total	**236**	**100**

The patients' non-urinary system pathologies were evaluated (Table 3.10). According to the results obtained; among the non-urinary system pathologies found in the patients, cardiac pathologies were in the first place with a rate of 14.8%, rib anomaly was in the second place with a rate of 3.8% and scoliosis was in the second place with a rate of 3.4%.

Table 3.11
Distribution of Patients' Gender According to Chronic Renal Failure Status

	Chronic Renal Failure		X^2	p
	Yes	No		
	N (%)	N (%)		
Gender			4,493	**0,034***
Male	10 (32, 3)	108 (52, 7)		
Female	21 (67,7)	97 (47, 3)		
*Pearson Chi-Square Test, *p < 0.05*				

The gender distribution of the patients included in the study was evaluated according to the presence of chronic renal failure (Table 3.11). According to the results obtained; It was determined that 32.3% of the patients with CRF were male and 67.7% were female; 52.7% of the patients without CRF were male and 47.3% were female. A statistically significant difference was found between the patients with CRF and those without in terms of male/female ratios ($X2 = 4.493$; $p < 0.05$). It was determined that the female ratios with CRF were higher than males.

Table 3.12
Urinary System Pathology Rates According to Patients' Chronic Renal Failure Status

	Chronic Renal Failure		X^2	p
	Yes	No		
N (%)	**N (%)**			
Urinary System Pathologies				
Urinary System Stone	7 (22, 6)	29 (14, 1)	1,350	0,169
PUV	0	4 (2,0)	1,137	0,567
Neurogenic Bladder	0	6 (2, 9)	1,713	0,425
Hydrocele	0	1 (0,5)	0,282	0,869
UV Stasis	5 (16, 1)	7 (3, 4)	6,444	**0,021***
Bladder Diverticulum	1 (3, 2)	4 (2,0)	0,187	0,509
Renal Rotation Anomaly	1 (3, 2)	4 (2,0)	0,187	0,509
Inguinal Hernia	0	11 (5, 4)	3,178	0,205
Undescended Testis	1 (3, 2)	5 (2, 4)	0,063	0,575
Penoscrotal Hypospadias	1 (3, 2)	6 (2, 9)	0,008	0,632
Double System	1 (3, 2)	4 (2,0)	0,187	0,509
Crossed Renal Ectopia	1 (3, 2)	2 (1,0)	0,818	0,346
Urachal Cyst	2 (6, 5)	0	8,234	**0,017***
Ureterocele	0	2 (1,0)	0,566	0,754
Unspecified Hypospadias	0	3 (1, 5)	0,851	0,654
Cloaca Anomaly	1 (3, 2)	1 (0,5)	1,589	0,246
Comm Hydrocele	0	1 (0,5)	0,282	0,869
UP Stasis	1 (3, 2)	0	4,088	0,131
Accessory Scrotum	0	1 (0,5)	0,282	0,869
Epispadias	0	1 (0,5)	0,282	0,869
Hemametrotocolpos	0	1 (0,5)	0,282	0,869

*Fisher Exact Test, *p < 0.05, UV: Ureterovesical, PUV: Posterior Urethral Valve, UP: Ureteropelvic Stenosis*

The distribution of urinary system pathologies was evaluated according to the presence of chronic renal failure in the patients (Table 3.12). According to the results obtained; It was determined that 22.6% of the

patients with chronic renal failure had urinary system stones, 16.1% had UV stasis, 3.2% had bladder diverticulum, 3.2% had renal rotation anomaly, 3.2% had undescended testicle, 3.2% had penoscrotal hypospadias, 3.2% had double system, 3.2% had crossed renal ectopia, 6.5% had urachus cyst, 3.2% had cloaca anomaly and 3.2% had UP stasis. In patients without chronic renal failure, 14.1% had urinary system stones, 2% had PUV, 2.9% had neurogenic bladder, 0.5% had hydrocele, 3.4% had UV stasis, 2% had bladder diverticulum, 2% had renal rotation anomaly, 5.4% had inguinal hernia, 2.4% had undescended testis, 2.9% had penoscrotal hypospadias, 2% had double system, 1% had crossed renal ectopia, 1% had ureterocele, 1.5% had unspecified hypospadias, 0.5% had cloaca anomaly, 0.5% had common hydrocele, 0.5% had accessory scrotum, 0.5% had epispadias and 0.5% had hematometrotocolpos.

Table 3.13
Regular Follow-up and Regular CIC Rates According to the Chronic Renal Failure Status of Patients

	Chronic Renal Failure		X^2	p
	Yes	**No**		
	N (%)	**N (%)**		
Regular Follow-up			66,340	**< 0,001****
Yes	14 (45, 2)	195 (95,1)		
No	17 (54, 8)	10 (4, 9)		
Regular TAK			56,717	**< 0,001****
Yes	10 (32, 3)	182 (88,8)		
No	21 (67,7)	23 (11, 2)		
*Pearson Chi-Square Test, **p < 0.001, CAC: Clean Intermittent Catheterization*				

The distribution of regular follow-up and regular CIC application was evaluated according to the presence of chronic renal failure in patients (Table 3.13). According to the results obtained; It was determined that 45.2% of the patients with CRF and 95.1% of the patients without CRF were followed up regularly. A statistically significant difference was found between the patients with CRF and those without CRF in terms of regular follow-up rates (X2 = 66.340; p < 0.001). It was determined that the regular follow-up rates of those with CRF were lower than those without CRF.

It was determined that 32.3% of patients with CRF and 88.8% of patients without CRF received regular CIC. A statistically significant difference was found between patients with CRF and those without CRF in terms of regular CIC application rates (X2 = 56.717; p < 0.001). It was determined that the regular CIC application rates of those with CRF were lower than those without CRF.

Table 3.14
Hydronephrosis Rates of Patients According to Chronic Renal Failure

	Chronic Renal Failure		χ^2	p
	Yes	No		
	N (%)	N (%)		
Hydronephrosis			11,556	**< 0,001****
Yes	34 (41,0)	31 (20, 3)		
No	49 (59,0)	122 (79,7)		
*Pearson Ki – Kare Test, **p < 0,001*				

Hydronephrosis rates were evaluated according to the presence of chronic renal failure in patients (Table 3.14). Hydronephrosis was found in 41% of patients with CRF and 20.3% of patients without CRF. A statistically significant difference was found in terms of hydronephrosis rates between patients with and without CRF (X2 = 11.556; p < 0.001). It was found that hydronephrosis rates were higher in patients with CRF than in those without CRF.

Table 3.15
Urinary System Stone Rates of Patients According to Chronic Renal Failure

	Chronic Renal Failure		χ^2	p
	Yes	**No**		
	N (%)	**N (%)**		
Urinary System Stone			1,603	0,206
Yes	16 (19, 3)	20 (13, 1)		
No	67 (80,7)	133 (86,9)		
*Pearson Ki – Kare Test, **p < 0,001*				

Urinary system stone rates were evaluated according to the presence of chronic renal failure in the patients (Table 3.15). It was determined that 19.3% of the patients with CRF and 13.1% of the patients without CRF had urinary system stones. No statistically significant difference was found between the patients with CRF and those without CRF in terms of urinary system stone rates (p > 0.05).

Table 3.16
Bladder Trabeculation Rates According to Patients with Chronic Renal Failure

	Chronic Renal Failure		χ^2	p
	Yes	**No**		
	N (%)	**N (%)**		
Bladder Trabeculation			0,374	0,541
Yes	49 (59,0)	84 (54, 9)		
No	34 (41,0)	69 (45, 1)		
Pearson Ki – Kare Test				

Bladder trabeculation rates were evaluated according to the presence of chronic renal failure in patients (Table 3.16). Bladder trabeculation was found in 59% of patients with CRF and 54.9% of patients without CRF. No statistically significant difference was found in terms of bladder trabeculation rates between patients with and without CRF ($p > 0.05$).

Table 3.17
Urinary System Infection Rates According to Patients with Chronic Renal Failure

	Chronic Renal Failure		χ^2	p
	Yes	**No**		
	N (%)	**N (%)**		
Urinary System Infection			0,164	0,686
Yes	70 (84,3)	132 (86,3)		
No	13 (15, 7)	21 (13, 7)		
Pearson Ki – Kare Test				

Urinary system infection rates were evaluated according to the presence of chronic renal failure in patients (Table 3.17). It was determined that 84.3% of patients with CKD and 86.3% of patients without CKD had urinary system infection. No statistically significant difference was found in terms of urinary system infection rates between patients with and without CKD ($p > 0.05$).

Table 3.18
VUR (Vesicoureteral Reflux) Rates of Patients According to Chronic Renal Failure

	Chronic Renal Failure		X^2	p
	Yes	No		
	N (%)	N (%)		
VUR			1,208 [a]	0,272
Yes	25 (30, 1)	57 (37, 3)		
No	58 (69,9)	96 (62,7)		
VUR Side			0,997 [a]	0,607
Right VUR	6 (24,0)	14 (24, 6)		
Left VUR	8 (32,0)	24 (42, 1)		
Bilateral VUR	11 (44,0)	19 (3, 3)		
VUR Grade			4,563 [b]	0,323
Grade 1	1 (7, 1)	5 (8, 8)		
Grade 2	0	12 (21, 1)		
Grade 3	4 (28, 6)	10 (17, 5)		
Grade 4	5 (35, 7)	14 (24, 6)		
Grade 5	4 (28, 6)	16 (28, 1)		
Right VUR Grade			4,192 [b]	0,340
Grade 1	1 (11, 1)	3 (7, 5)		
Grade 2	0	9 (22, 5)		
Grade 3	2 (22, 2)	6 (15,0)		
Grade 4	2 (22, 2)	13 (32, 5)		
Grade 5	4 (44, 4)	9 (22, 5)		
Bilateral VUR Grade			7,950 [b]	**0,036***
Grade 1	0	2 (11, 8)		
Grade 2	0	3 (17, 6)		
Grade 3	2 (40,0)	4 (23, 5)		
Grade 4	3 (60,0)	1 (5, 9)		

*a: Pearson Chi-Square Test, b: Fisher Freeman Halton Exact Test, *p < 0.05, VUR: Vesicoureral Reflux*

Grade 5	0	7 (41, 2)
*a: Pearson Chi-Square Test, b: Fisher Freeman Halton Exact Test, *p < 0.05, VUR: Vesicoureral Reflux*		

VUR rates were evaluated according to the presence of chronic renal failure in the patients (Table 3.18). According to the results obtained; VUR was found in 30.1% of the patients with CRF and 37.3% of the patients without CRF. No statistically significant difference was found in terms of VUR rates between the patients with and without CRF (p > 0.05).

Table 3.19
Bladder Capacity Ratios of Patients According to Chronic Renal Failure

	Chronic Renal Failure		X^2	p
	Yes	**No**		
	N (%)	**N (%)**		
Bladder Capacity			0,252	0,882
Bladder Capacity < Expected Bladder Capacity	17 (68,0)	100 (66,2)		
Bladder Capacity = Expected Bladder Capacity	1 (4,0)	10 (6, 6)		
Bladder Capacity > Expected Bladder Capacity	7 (28,0)	41 (27, 2)		
Pearson Chi-Square Test				

Bladder capacities of the patients were evaluated according to the presence of chronic renal failure (Table 3.19). It was determined that 68% of the patients with CRF had lower bladder capacity than expected, 4% had bladder capacity at expected bladder capacity (EBC) and 28% had bladder capacity higher than expected; 66.2% of the patients without CRF had lower bladder capacity than expected, 6.6% had bladder capacity at EBC and 27.2% had bladder capacity higher than expected. No statistically significant difference was found between the patients with and without CRF in terms of bladder capacities (p > 0.05).

Table 3.20
Urological Surgery Rates According to Patients' Chronic Renal Failure

	Chronic Renal Failure		χ^2	p
	Yes	**No**		
N (%)	**N (%)**			
Urological Surgery			4,346 [a]	**0,037***
Yes	35 (42, 2)	44 (28, 8)		
No	48 (57,8)	109 (71,2)		
Urological Surgeries				
Bladder Augmentation	10 (12,0)	1 (0,7)	15,807 [b]	**<0,001****
Mitrofanoff	9 (10, 8)	2 (1, 3)	10,631 [b]	**0,002***
Injection	6 (7, 2)	14 (9, 2)	0,262 [b]	0,405
Vesicostomy	8 (9, 6)	6 (3, 9)	2,987 [b]	0,071
PUV Ablation	0	3 (2,0)	2,621 [b]	0,271
Nephrectomy	2 (2, 4)	0	4,212 [b]	0,123
Ureterostomy	3 (3, 6)	0	6,341 [b]	**0,042***
Penoscrotal Hypospadias	0	2 (1, 3)	1,743 [b]	0,419
Ureterectomy	2 (2, 4)	1 (0,7)	1,245 [b]	0,283
Meatotomy	1 (1, 2)	1 (0,7)	0,186 [b]	0,581
Nephrolithotomy	2 (2, 4)	1 (0,7)	1,245 [b]	0,283
Nephrostomy	2 (2, 4)	0	4,212 [b]	0,123

*a: Pearson Chi-Square Test, b: Fisher Exact Test, *p < 0.05, **p < 0.001, PUV: Posterior Urethral Valve*

The urinary system surgeries performed on the patients included in the study were evaluated according to the presence of chronic renal failure (Table 3.20). According to the results obtained; It was determined that urinary system surgery was performed on 42.2% of the patients with CKD and 28.8% of the patients without CKD. A statistically significant difference was found in terms of the rates of urinary system surgery between the patients with and without CKD ($X2 = 4.346$; $p < 0.05$). It was determined that the rates of urinary system surgery were higher in those with CKD than in those without CKD.

A statistically significant difference was found in terms of bladder augmentation rates between patients with and without chronic renal failure (X2 = 15.807; p < 0.001). It was found that the rates of bladder augmentation were higher in patients with CKD than in those without CKD. A statistically significant difference was found in terms of MTR application rates between patients with and without CKD (X2 = 10.631; p < 0.05). It was determined that the rates of MTR application were higher in patients with CKD than in those without CKD. A statistically significant difference was found in terms of ureterostomy application rates between patients with and without CKD (X2 = 6.341; p < 0.05). It was found that the rates of ureterostomy were higher in patients with CKD than in those without CKD.

Table 3.21
Renal Scar Rates According to Patients with Chronic Renal Failure

	Chronic Renal Failure		X^2	p
	Yes	No		
	N (%)	N (%)		
Renal Scar			13,149	**< 0,001****
Yes	18 (72,0)	51 (33, 8)		
No	7 (28,0)	100 (66,2)		
Renal Scar Side			7,781	**0,020***
Right Skar	3 (16, 7)	13 (25, 5)		
Left Skar	2 (11, 1)	20 (39, 2)		
Bilateral Skar	13 (72,2)	18 (35, 3)		
*Pearson Chi-Square Test, *p < 0.05, **p < 0.001*				

Renal scar rates of the patients included in the study were evaluated according to the presence of chronic renal failure (Table 3.21). According to the results obtained; It was determined that 72% of the patients with CKD and 33.8% of the patients without CKD had renal scars. A statistically significant difference was found between the patients with CKD and those without in terms of renal scar rates (X2 = 13.149; p < 0.001). It was determined that the renal scar rates of those with CKD were higher than those without CKD.

It was determined that 16.7% of the patients with chronic renal failure had right renal scars, 11.1% had left renal scars, and 72.2% had bilateral renal scars; 25.5% of the patients without CKD had right renal scars, 39.2% had left renal scars, and 35.3% had bilateral renal scars. A statistically significant difference was found between patients with and without CKD in terms of the sides of renal scars (X2 = 7.781; p < 0.05).

Table 3.22
Distribution of Patients by Gender According to the Presence of VUR

	VUR		X^2	p
	Yes	No		
	N (%)	N (%)		
Gender			6,055	**0,014***
Male	32 (39,0)	86 (55, 8)		
Female	50 (61,0)	68 (44, 2)		
*Pearson Chi-Square Test, *p < 0.05, VUR: Vesicoureteral Reflux*				

The gender distribution of the patients was evaluated according to the presence of VUR (Table 3.22). According to the results obtained; It was determined that 39% of the patients with VUR were male and 61% were female; 55.8% of the patients without VUR were male and 44.2% were female. A statistically significant difference was found between the patients with and without VUR in terms of male/female ratios (X2 = 6.055; p < 0.05). It was determined that the female ratios with VUR were higher than males.

Table 3.23
Urinary System Surgery Rates According to the Presence of VUR in Patients

	VUR		X^2	p
	Yes	No		
	N (%)	N (%)		
Urinary System Surgery			22,989	**< 0,001****
Yes	44 (53, 7)	35 (22, 7)		
No	38 (46, 3)	119 (77,3)		
*Pearson Chi-Square Test, *p < 0.05, VUR: Vesicoureteral Reflux*				

The rates of urinary system surgery were evaluated according to the presence of VUR in the patients included in the study (Table 3.23). It was determined that 53.7% of the patients with VUR and 22.7% of the patients without VUR underwent urinary system surgery. A statistically significant difference was found between the rates of urinary system surgery between the patients with and without VUR (X2 = 22.989; p < 0.001). It was determined that the rate of urinary system surgery was higher in patients with VUR than in patients without VUR.

Table 3.24
Renal Scar Rates According to the Presence of VUR in Patients

Renal Scar	VUR		X^2	p
	Yes	No		
	N (%)	N (%)		
Those with Chronic Kidney Disease			3,006 [b]	0,102
Yes	12 (85,7)	6 (54, 5)		
No	2 (14, 3)	5 (45, 5)		
Those Without Chronic Kidney Disease			11,973 [a]	**< 0,001****
Yes	29 (50, 9)	22 (23, 4)		
No	28 (49, 1)	72 (76,6)		
Toplam			17,167 [a]	**< 0,001****
Yes	41 (57,7)	28 (26, 7)		
No	30 (42, 3)	77 (73,3)		

*a: Pearson Chi-Square Test, b: Fisher Exact Test, **p < 0.001, VUR: Vesicoureral Reflux*

Renal scar rates were evaluated according to the presence of VUR in the patients included in the study (Table 3.24). According to the results obtained; it was determined that renal scars were present in 85.7% of patients with VUR and 54.5% of those without VUR in patients with chronic renal failure. No statistically significant difference was found in terms of renal scar rates between patients with VUR and those without CKD ($p > 0.05$).

It was found that renal scars were present in 50.9% of patients without CKD and 23.4% of those without VUR. A statistically significant difference was found in terms of renal scar rates between patients with VUR and those without CKD ($X2 = 11.973$; $p < 0.001$). It was determined that renal scar rates were higher in patients without CKD and those with VUR than in those without VUR.

Renal scarring was found in 57.7% of patients with VUR and 26.7% of patients without VUR. A statistically significant difference was found in renal scarring rates between those with and without VUR ($X2 = 17.167$; $p < 0.001$). Renal scarring rates were found to be higher in patients with VUR than in those without VUR.

Table 3.25
Positive/Negative Idiopathic Detrusor Contraction Rates According to Patients' Bladder Capacity

İDC	Bladder Capacity			X^2	p
	BC < EBC	BC = EBC	BC > EBC		
	N (%)	N (%)	N (%)		
Those with Chronic Kidney Disease				1,899 [b]	0,504
Positive	9 (52, 9)	0	2 (28, 6)		
Negative	8 (47, 1)	1 (100)	5 (71,4)		
Those without Chronic Kidney Disease				2,476 [a]	0,290
Positive	81 (81,8)	7 (70,0)	29 (70,7)		
Negative	18 (18, 2)	3 (30,0)	12 (29, 3)		
Total				3,462 [a]	0,177
Yes	90 (77,6)	7 (63,6)	31 (64,6)		
No	26 (22, 4)	4 (36, 4)	17 (35, 4)		

a: Pearson Chi-Square Test, b: Fisher Freeman Halton Exact Test,, IDC: Idiopathic Detrusor Contraction, BC: Bladder Capacity, EBC: Expected Bladder Capacity

The Idiopathic Detrusor Contraction (IDC) rates of the patients included in the study were evaluated according to their bladder capacities (Table 3.25). According to the results obtained; It was determined that 52.9% of those with lower than expected bladder capacity and 28.6% of those with higher than expected bladder capacity in patients with chronic renal failure had positive IDC. No statistically significant difference was found in terms of positive IDC rates according to bladder capacity in patients with CKD ($p > 0.05$).

It was determined that 81.8% of those with lower than expected bladder capacity, 70% of those with BMI and 70.7% of those with higher than expected bladder capacity in patients without CKD had positive IDC. No statistically significant difference was found in terms of positive IDC rates according to bladder capacity in patients without CKD ($p > 0.05$).

It was determined that 77.6% of all patients with bladder capacity lower than expected, 63.6% of those with bladder capacity within BMK and 64.6% of those with bladder capacity higher than expected had positive IDC. No statistically significant difference was found in terms of positive IDC rates according to bladder capacity in patients ($p > 0.05$).

Table 3.26
Renal Scar Rates According to the Presence of Urinary Tract Infection in Patients

	Urinary Tract Infection		X^2	p
	Yes	No		
	N (%)	N (%)		
Renal Scar			8,813	**0,003***
Yes	67 (43, 2)	2 (9, 5)		
No	88 (56,8)	19 (90,5)		
*Pearson Chi-Square Test, *p < 0.05*				

Renal scar rates were evaluated according to the presence of urinary system infection in the patients included in the study (Table 3.26). Renal scars were found in 43.2% of patients with urinary system infection and in 9.5% of patients without urinary system infection. A statistically significant difference was found between patients with and without urinary system infection in terms of renal scar rates (X2 = 8.813; p < 0.05). It was found that renal scar rates in patients with urinary system infection were higher than those without urinary system infection.

Table 3.27
Urinary System Surgery Rates According to Regular CIC Application of Patients

	Regular CIC		X^2	p
	Yes	No		
	N (%)	N (%)		
Urinary System Surgery			8,582	**0,003***
Yes	56 (29, 2)	23 (52, 3)		
No	136 (70,8)	21 (47, 7)		
*Pearson Chi-Square Test, *p < 0.05, CIC: Clean Intermittent Catheterization*				

The rates of urinary system surgery were evaluated according to the regular CIC application of the patients included in the study (Table 3.27). According to the results obtained; It was determined that 29.2% of the patients who underwent regular CIC and 52.3% of the patients who did not undergo regular CIC underwent urinary system surgery. A statistically significant difference was found between the patients who underwent regular CIC and those who did not undergo regular CIC in terms of the rates of urinary system surgery (X2 = 8.582; p < 0.05). It was determined that the rates of urinary system surgery were lower in patients who underwent regular CIC than in those who did not undergo regular CIC.

Table 3.28
Urinary System Surgery Rates According to Regular Patient Follow-up

	Regular Follow-up		X^2	p
	Yes	No		
	N (%)	N (%)		
Urinary System Surgery			4,624	**0,032***
Yes	65 (31, 1)	14 (51, 9)		
No	144 (68,9)	13 (48, 1)		
*Pearson Chi-Square Test, *p < 0.05*				

The rates of urinary system surgery were evaluated according to the regular follow-up of the patients included in the study (Table 3.28). According to the results obtained; It was determined that urinary system surgery was applied to 31.1% of the patients who were followed up regularly and 51.9% of the patients who were not followed up regularly. A statistically significant difference was found in terms of the rates of urinary system surgery between the patients who were followed up regularly and those who were not followed up regularly (X2 = 4.624; p < 0.05). It was determined that the rates of urinary system surgery were lower in the patients who were followed up regularly than in the patients who were not followed up regularly.

REGRESSION ANALYSIS

Table 4.1
Investigation of Factors Affecting End-Stage Renal Failure Using Single Logistic Regression Analysis

Variables	B	SH	Wald	OR	p	%95 Confidence Interval	
						Lower Limit	Upper Limit
Gender (Ref: Male) - Female	0,849	0,409	4,315	2,338	**0,038***	1,049	5,211
Compliance (Ref: Normal)							
Low	0,217	0,470	0,214	1,243	0,644	0,495	3,122
High	-0,234	1,120	0,044	0,792	0,835	0,088	7,106
IDC (Ref: Negative) - Positive	-1,403	0,454	9,563	0,246	**0,002***	0,101	0,598
Hydronephrosis	2,220	0,431	26,503	9,209	**< 0,001****	3,955	21,445
Renal Agnesia	-0,709	1,056	0,450	0,492	0,502	0,062	3,902
Renal Atrophy	0,743	0,510	2,127	2,103	0,145	0,774	5,710
Urinary System Stone	0,571	0,474	1,451	1,770	0,228	0,699	4,482
Bladder Trabeculation	3,391	1,026	10,925	29,709	**0,001***	3,976	221,967
Horseshoe Kidney	0,236	0,661	0,127	1,266	0,722	0,347	4,623
Additional Urinary System Pathologies							
UV Stasis	1,694	0,622	7,425	5,440	**0,006***	1,609	18,393
Bladder Diverticulum	0,516	1,135	0,207	1,675	0,650	0,181	15,494
Renal Rotation Anomaly	0,516	1,135	0,207	1,675	0,650	0,181	15,494
Double System	0,516	1,135	0,207	1,675	0,650	0,181	15,494
Crossed Renal Ectopia	1,219	1,240	0,966	3,383	0,326	0,298	38,465
Cloca Anomaly	1,917	1,428	1,803	6,800	0,179	0,414	111,620
UP Stasis	23,125	40192,969	0,000	1,104E + 10	1,000	0,000	-
Anal Atresia	-0,987	0,756	1,703	0,373	0,192	0,085	1,641

Variables	B	SH	Wald	OR	p	%95 Confidence Interval	
						Lower Limit	Upper Limit
Urinary Infection	19,495	6893,036	0,000	2,93E + 08	0,998	0,000	-
Residual Urine	0,368	0,654	0,316	1,444	0,574	0,401	5,202
VCUG (Ref: No VUR) - VUR Yes	0,961	0,391	6,050	2,615	**0,014***	1,216	5,627
VUR Grade (Ref: Grade 1)							
Grade 2	-19,593	11602,711	0,000	0,000	0,999	0,000	-
Grade 3	0,693	1,245	0,310	2,000	0,578	0,174	22,949
Grade 4	0,580	1,213	0,228	1,786	0,633	0,166	19,246
Grade 5	0,223	1,230	0,033	1,250	0,856	0,112	13,924
Anticolinergic	1,907	0,746	6,528	6,732	**0,011***	1,559	29,069
Prophylaxis	1,154	0,628	3,375	3,172	0,066	0,926	10,869
Regular Follow-up	-3,165	0,485	42,546	0,042	**< 0,001****	0,016	0,109
Regular CIC	-2,810	0,443	40,178	0,060	**< 0,001****	0,025	0,143
CIC Frequency (Ref: 3x1)							
4x1	-0,405	1,218	0,111	0,667	0,739	0,061	7,254
5x1	-19,593	12710,133	0,000	0,000	0,999	0,000	-
6x1	-0,056	1,134	0,002	0,946	0,961	0,103	8,725
8x1	22,812	28420,721	0,000	8,077E + 09	0,999	0,000	-
Parenchymal Thickness (Ref: Normal) - Thin	0,992	0,446	4,941	2,697	**0,026***	1,124	6,468
DMSA Scar	1,782	0,502	12,613	5,941	**< 0,001****	2,222	15,883
Neurosurgical Pathologies							
Meningomyelocele	0,791	0,434	3,323	2,206	0,068	0,942	5,164

Variables	B	SH	Wald	OR	p	%95 Confidence Interval	
						Lower Limit	Upper Limit
Spina Bifida	-1,094	0,754	2,102	0,335	0,147	0,076	1,469
Tethered Cord	-0,429	0,565	0,577	0,651	0,448	0,215	1,971
Meningocele	0,544	0,676	0,647	1,723	0,421	0,458	6,488
Syringomyelia	0,704	0,603	1,361	2,021	0,243	0,620	6,591
Filum Terminale Lipoma	1,683	0,790	4,541	5,384	**0,033***	1,145	25,323
Caudal Regression	0,288	1,113	0,067	1,333	0,796	0,151	11,808
Encephalocele	1,219	1,240	0,966	3,383	0,326	0,298	38,465

In order to determine the factors affecting end-stage renal failure in the patients included in the study, single logistic regression analysis was applied (Table 4.1). According to the results of univariate logistic regression analysis; It was determined that the risk of developing ESRD was 2.338 times higher in women compared to men, 9.209 times higher in those with hydronephrosis compared to those without, 29.709 times higher in those with bladder trabeculation compared to those without, 5.440 times higher in those with UV stasis compared to those without, 2.615 times higher in those with VUR compared to those without, 6.732 times higher in those with anticholinergics compared to those without, 2.697 times higher in those with thinned parenchymal thickness compared to those with normal parenchymal thickness, 5.941 times higher in those with DMSA scars compared to those without, and 5.384 times higher in those with filum terminale lipoma compared to those without. It was determined that the risk of developing ESRD was 0.246 times lower in those with positive IDC compared to those with negative IDC, 0.042 times lower in those with regular follow-up compared to those without regular follow-up, and 0.060 times lower in those with regular CIC compared to those without regular follow-up.

Table 4.2
Investigation of Factors Affecting End-Stage Renal Failure Using Multiple Logistic Regression Analysis

Variables	B	SH	Wald	OR	p	%95 Confidence Interval	
						Lower Limit	Lower Limit
Hydronephrosis	0,211	1,022	0,043	1,235	0,836	0,167	9,164
Bladder Trabeculation	4,098	1,885	4,729	60,219	**0,030***	1,498	2420,138
UV Stasis	-3,508	2,471	2,015	0,030	0,156	0,000	3,801
VCUG (Ref: No VUR) – VUR Present	-0,183	1,002	0,033	0,833	0,855	0,117	5,933
IDC (Ref: Negative) – Positive	-1,783	0,956	3,480	0,168	0,062	0,026	1,095
Regular TAK	-7,900	2,403	10,806	0,0004	**0,001***	0,000	0,041
Parenchymal Thickness (Ref: Normal) – Thin	0,999	0,999	1,001	2,717	0,317	0,383	19,249
DMSA Scar	3,910	1,665	5,516	49,917	**0,019***	1,910	1304,542
Filum Terminale Lipoma	4,826	2,049	5,549	124,730	**0,018***	2,249	6916,607
(Fixed)	-0,897	1,490	0,363	0,408	0,547		
-2 Log Likelihood: 46,164 Cox & Snell R^2: 0,415 Nagelkerke R^2: 0,753				Hosmer and Lemeshow Test: X^2: 1,766 df: 8 p: 0,987			

In order to determine the factors affecting end-stage renal disease, multiple logistic regression analysis was applied including the variables of hydronephrosis, bladder trabeculation, UV stasis, VUR, IDC, regular TAK, parenchymal thickness, DMSA scar and filum terminale lipoma (Table 4.2). As a result of the analysis, it was determined that the developed model had a good fit according to the Hosmer & Lemeshow test (X2 = 1.766; df = 8; p = 0.987). It was found that the variables in the model explained 41.5% of the variance on ESRD according to Cox & Snell and 75.3% according to Nagelkerke. The risk of developing ESRD was increased by 60.219 times in those with bladder trabeculation compared to those without, 49.917 times in those with DMSA scar compared to those without, and 124.730 times in those with filum terminale lipoma compared to those without; It was determined that it reduced the risk of heart disease by 0.0004 times in those who applied regular TAK compared to those who did not apply it regularly.

DİSCUSSİON

Spina bifida is a birth defect in which the spinal cord develops improperly because the neural tube does not close completely by approximately the 28th day of gestation. Management of patients with SB includes lifelong comprehensive neurological, urological, gastroenterological, and musculoskeletal rehabilitation management. SB occurs in 1 to 10 of 1000 live births worldwide. Nongenetic factors associated with SB include environmental exposures, decreased dietary folate intake, hyperthermia, maternal anticonvulsant therapy (valproic acid and carbamazepine), prepregnancy maternal diabetes, and obesity. (1)

Pathologies in critical systems such as the urogenital and musculoskeletal systems also lead to a wide range of comorbidities (2). Mild declines in function or inadequate drainage/decompression of the ventricles can strain an already compromised nervous system and lead to increased problems later on. SB can be acutely life-threatening, and numerous other critical neurologic comorbidities commonly compromise life (3). A neurosurgical perspective is the ground zero for the management of spina bifida and SB treatment (4).

There are several questions that need to be monitored and managed in the neonatal period. Early closure within 72 hours is preferred to prevent significant neurological decline and to minimize the risk of infection or injury in any open defect. Ventriculoperitoneal shunting may be required for hydrocephalus after the defect is closed. Arnold Chiari malformations are common and usually require repair, but this repair carries a significant mortality rate when patients are symptomatic. Long-term management involves a multidisciplinary approach as multiple organs and systems may be affected. Neurogenic bowel and neurogenic bladder are significant problems in patients with SB. Chronic renal failure may develop due to detrusor/sphincter dyssynergia in neurogenic bladders that are not regularly monitored. Urinary ultrasonography is recommended twice a year and clean intermittent catheterization is recommended for long-term management. Patients may also present with neurogenic bowel symptoms due to impaired sensation and poor sphincter control. In these patients, complications related to neurogenic bowel can be prevented by using laxatives and agents that increase bowel motility and by providing mechanical bowel cleansing training (5).

In our study, we emphasized the importance of regular follow-up in terms of early recognition, treatment and early intervention of urinary complications to prevent renal failure, which causes significant comorbidity and mortality due to spina bifida. We investigated the effect of clean intermittent catheterization on treatment and progression to end-stage renal failure.

In our study, 13.1% of 236 patients diagnosed with SB developed CKD, and De Jong et al. In 2008 (6), this rate was reported as 20%, Trudell et al. reported it as 6% in 2014 (7), and Çelakıl et al. reported it as 8.8% in 2021 (8). The results we obtained in our study were found to be similar to the literature.

Vesicoureteral reflux was detected in 34% of our patients diagnosed with SB, and Dönmez et al. In a study conducted in 2023 (9), concomitant vesicoureteral reflux was detected in 24.6% of patients with

SB, and Chang et al. in their study in 2022 (10) showed that the incidence of VUR was higher in patients with SB than in patients without SB, and stated this rate as 3%-41.6%.

Sargent et al. (11) reported in 2000 that the incidence of VUR was 0.4%-1.8% in normal children, while this rate increased to 31.1% in children with urinary tract infection. The prevalence of VUR is higher in patients with SB compared to the normal population. However, accompanying UTI increases this rate even more. In our study, we observed that the incidence of VUR in patients with spina bifida along with accompanying UTI is similar to the literature.

The urinary system in SB patients is negatively affected by bladder detrusor/sphincter dyssynergia and high pressures due to overactive bladder. UTIs accompanying this condition cause the current picture to worsen.

The main aim of treatment in these patients is to ensure urinary continence and prevent kidney scarring, which is one of the criteria of end-stage renal failure, by preventing UTIs.

In the literature, Panicker et al. (12), Chen et al. (13) and Maison et al. (14) support our view in their studies in 2017.

Cameron et al. (15) stated in their study in 2016 that anticholinergic treatment has been the basis of medical treatment in patients with SB for many years. In our study, anticholinergic treatment was started in 71.6% of the patients. In our study, 76.7% of the patients needed prophylactic antibiotics. Filler et al. (16) recommended that appropriate prophylactic antibiotics should be started early within the indication to prevent CKD in their study in 2012. Many studies show that the proactive approach is one of the most effective treatment methods. Our study also supports the literature.

While 90% of SB patients are born with normal renal function, 50% of these patients may develop urinary system complications, which negatively affect their lives if left untreated (16). If urinary system complications are left untreated, they can lead to recurrent urinary system infections, renal scarring, and ultimately chronic kidney disease and end-stage renal failure (17–21). These complications can be significantly reduced with adequate bladder management. The most commonly used treatment modality in bladder management is the proactive approach. Clean intermittent catheterization can increase urinary continence in patients with neurogenic bladder, which improves quality of life. CIC helps prevent nephrological/urological complications that may develop in the future by reducing high intravesical pressure that causes VUR, UTI, and renal dysfunction (22–25).

Elzeini et al. In his study conducted in 2019 (26), he recommended that CIC be performed regularly in all patients with SB after birth to protect renal functions. In another study conducted by Moussa et al. in 2021 (27), anticholinergic treatment and CIC are considered the gold standard for the prevention of urological complications in SB patients.

As an opposing view, Woo et al., in their study in 2014 (28), stated that abnormalities that can be seen in DMSA cannot be prevented with CIC started at an early stage in patients diagnosed with SB. Kaye et al.

(29) showed in their study in 2016 that there was no significant difference in the frequency of UTI in patients with SB who performed CIC compared to those who did not perform CIC. However, they stated that CIC should not be started early in these patients and that more studies should be conducted to determine appropriate indications. In our study, consistent with the literature, CIC was performed regularly in 81.4% of our patients. As a result, the progression to ESRD was significantly reduced in our patients who performed CIC regularly compared to those who did not.

Erturhan et al. (30) stated in their study in 2008 that renal parenchymal thinning was observed in patients with spina bifida, but the percentage was not given. In our study, renal parenchymal thinning was detected in 15.3% of the patients. Renal parenchymal thinning may lead to renal function loss and CRF in the future.

In the literature, renal parenchymal thinning has also been observed in these patients in the future, and we see that our study is consistent with the literature.

According to De Jong et al. (6) in 2008, in order to protect renal function in patients with SB, low bladder pressure should be maintained from birth. The status of pelvic floor activity should be assessed shortly after birth to determine whether a child is at risk for high detrusor pressures. Approximately 50% of children with SBA and 25% of children with SBO have detrusor/sphincter dyssynergia, which poses a serious risk for early upper urinary tract damage due to high bladder pressures and UTI. With CIC, anticholinergic treatment and prophylactic antibiotic therapy initiated in the neonatal period, the need for bladder augmentation in patients with indications decreased from 90% to 5%. In our study, bladder capacity was lower than expected in 49.6% of patients and our study is consistent with the literature.

Sager et al. In their study conducted in 2022 (31), they stated that urological problems may develop in up to 70% of patients in the first years of life and that the main goals of urinary tract infection treatment are to protect and improve renal function. Although there have been discussions until recently about which approach is better for the management of SB, proactive or expectant, the balance seems to be in favor of the proactive approach. Because it is also supported by various studies that the progression to CKD is reduced with a proactive approach. Proactive interventions with CIC and pharmacotherapy have become the cornerstone of early management of SB. With this approach, the need for reconstructive surgery and invasive procedures has been moved to later ages and the need for major surgery in pre-adolescent ages has decreased. Many studies in the literature have stated that surgical procedures are required in selected cases that do not respond sufficiently to proactive treatment. In our study, urological surgery was applied to 33.5% of the patients and is consistent with the literature.

In a study conducted by Shiroyanagi et al. in 2009 (32), renal scars were reported in 25% of patients with SB in imaging studies, and in another study conducted by Woo et al. in 2014 (28), renal scars were detected in 43% of patients in DMSA. In our study, similar to these results, renal scars were detected in 29.2% of patients in DMSA.

The risk of congenital heart diseases may increase in individuals with neural tube defects such as SB. This is because some risk factors, such as folic acid deficiency during pregnancy, can affect both conditions. Therefore, individuals diagnosed with SB should be regularly checked for heart health. When the literature is reviewed, Inagaki et al. In his study conducted in 2005 (33), it was shown that heart diseases can be seen in patients diagnosed with SB, and in our study, various cardiac pathologies were detected in 14.8% of the patients.

In our study, 32.3% of the patients who developed CKD were male and 67.7% were female, and it was seen that the rate of CKD was twice as high in women as in men. In the literature, Ozel et al. in his study conducted in 2007 (34), it was observed that the rate of renal scarring was twice as high in women as in men, and in another study conducted by Ouyang et al. in 2015 (35), it was stated that the frequency of ESRD in the female patient population diagnosed with SB was significantly higher than in women without SB.

In our study, urinary system stones were seen in 15.2% of the patients, and the rate of patients with CKD accompanied by urinary system stones was determined as 22%. Raj et al. (36) showed in their study in 1999 that urinary system stones were detected more in patients with spina bifida compared to the normal population. In addition, Müller et al. (21) stated in their study in 2002 that urinary system stones and urinary system infections may increase the risk of renal function loss and CKD in patients with SB in the future.

In our study, when the regular follow-up and regular CIC application data of patients who developed CRF were examined, it was seen that the follow-up in patients who developed CRF was irregular and CIC application was not applied regularly compared to patients who did not develop CRF. It was seen that 45.2% of the patients who developed CRF came to regular follow-up and 95.1% of the patients who did not develop CRF came to regular follow-up, and it was seen that 32.3% of the patients who developed CRF applied CIC regularly, while 88.8% of the patients who did not develop CRF applied CIC regularly. When the literature was examined, Izumi et al. emphasized in their study in 2023 (37) that awareness should be increased regarding periodic evaluation and dynamic adaptation of interventions for optimum individualized care of patients. In another study conducted by Ahmad et al. in 2007 (38), they advocated the preservation of renal function and maintenance of continence in the face of a growing and changing urinary system with medical and surgical treatment. Again, according to this study, it was emphasized that follow-up should be regular and should be a specialist multidisciplinary approach. They also state that there is no reason why most patients with spina bifida cannot use their own kidneys for the rest of their lives, but this is due to urological treatment and follow-up that is started immediately after birth and continues until adulthood. Elzeini et al. (26) stated in their study in 2019 that CIC should be performed starting from the neonatal period in order to prevent renal scarring, and Kasabian et al. (39) stated in their study in 1992 that CIC should be started at the earliest and used regularly in order to prevent urological complications related to SB. Raimund et al. In their study in 2020 (40), they emphasize that CIC should be performed at the earliest and regularly in order to protect the urinary system. In our study,

it was shown that the progression of ESRD decreased in patients with regular CIC and regular follow-up, which is consistent with the literature.

In our patients with CKD, 41% had accompanying hydronephrosis, and 27% of all patients with SB had hydronephrosis. In the study conducted by Izumi et al. in 2023 (37), hydronephrosis was detected in 7% of patients with SB, and we found that we detected a higher rate of hydronephrosis in our study compared to the literature. In the study conducted by Chu et al. in 2021 (41), they stated that renal dysfunction in SB can usually be detected with glomerular filtration rate (eGFR) or ultrasonography-based hydronephrosis. They also stated that they detected hydronephrosis in 19% of pediatric SB patients in this study. In another study conducted by Ma et al. in 2013 (42), they detected hydronephrosis in 38% of SB patients.

In our study, we found that patients with SB who were diagnosed with CKD needed more urinary system surgery than patients who were not. In the literature, Doğan et al. (43) emphasized in their study in 2024 that a proactive approach to neurogenic bladder management and early preventive surgery should be applied in selected cases where conservative treatment failed to prevent progressive renal failure. The studies in the literature support our study.

While the renal scar rate detected in DMSA was 72% in patients with CKD diagnosed with SB, we found it to be 33.8% in patients without CKD, and we saw that the renal scar rate was significantly increased in patients with CKD. In the literature, Timberlake et al. (44) found abnormal DMSA findings in 31 (23%) of 130 newborn patients diagnosed with SB in their study in 2018. We saw that we had a higher number of patients with renal scars compared to the literature. Filler et al. Another study conducted in 2012 (16) stated that Cystatin C, eGFR and DMSA scans should be used to detect unilateral renal scarring to monitor kidney damage.

In our study, the rate of neurosurgical surgery was determined to be approximately 79%, and in the literature, Tarcan et al. stated in their study in 2006 (45) that urological improvement could be observed in neurosurgical surgery performed at an early stage, but Holzbeierlein et al. In the study they conducted in 2000 (17), they did not observe a significant decrease in urological complications after fetal surgery. Venkataramana et al. in 2011 (46) reported that performing neurosurgical surgery at an early stage positively affects urinary pathologies.

In our study, VUR was detected in 34.7% of our patients, 39% of whom were male and 61% were female. When current literature is examined, for example, Lotfollahzadeh et al. in their study in 2024 (47) stated that VUR is more common in female patients in the normal population. Keskinoğlu et al. In a retrospective study in 2019 (48), VUR was more common in girls, while Chand et al. (49) reported that the probability of VUR in girls was twice as high as in boys in 2003.

In our study, the rate of renal scarring in patients with VUR was 57.5%, while this rate was 85.7% in those with CKD. We observed that urinary system surgery was performed more in patients with VUR than in patients without VUR. Okamura et al. (50) emphasized the necessity of urinary system surgery in

patients with SB and VUR in 1988 to prevent renal function deterioration and renal scarring. Wu et al. In another study conducted in 2017 (51), they stated that urinary system surgery should be considered as an alternative to protect renal functions and prevent renal scarring in urological pathologies that cannot be controlled despite CIC, anticholinergic treatment and prophylactic antibiotics.

Renal scarring was observed in 43.2% of our SB patients with urinary system infection, and in the literature, Forster et al. 2021 (52) emphasized that renal scarring due to UTI should be prevented. In another study by De Jong et al. in 2008 (6), it was stated that aggressive treatment may be required to preserve renal functions in UTIs and even permanent prophylaxis may be required in some patients. In the studies conducted in the literature, the percentage is not specified, but it is stated that recurrent UTIs can cause renal scarring, and our study was found to be compatible with the literature.

Snow-Lisy et al. In their study conducted in 2015 (53), they showed that the rate of urinary system surgery decreased in patients who received regular CIC, anticholinergic, prophylactic antibiotics and regular follow-up. In another study conducted by Kaefer et al. in 1999 (54), they showed that urinary system surgery decreased in patients who received regular proactive treatment. In their study conducted by Wu et al. in 1997 (55), it was also shown that urinary system surgery decreased with early proactive treatment. In our study, it is observed that urinary system surgery decreased in patients who received regular follow-up and regular CIC, which is consistent with the literature.

CONCLUSİON

• Spina Bifida is one of the most common congenital anomalies in the world. It is seen at a rate of 1 to 10 in 1000 births. However, the cause is largely unknown. The genetic component is estimated to be 60-70%. Non-genetic maternal risk factors include low folate intake, anticonvulsant therapy, diabetes mellitus and obesity. It is known that there is a significant decrease in the incidence of spina bifida with appropriate folic acid supplementation during pregnancy.

• Diagnosis can be made with prenatal ultrasonography and maternal amniocentesis.

• With the advances and developments in the field of health, spina bifida can be closed with fetal surgery.

• Urological pathologies are among the most common complications of spina bifida and negatively affect the lives of patients and significantly reduce their quality of life.

• Chronic renal failure is one of the most common causes of morbidity and mortality in patients with spina bifida.

• In our study, we showed that the progression to chronic renal failure decreased in patients diagnosed with spina bifida who underwent regular follow-up and regular clean intermittent catheterization.

• It is predicted that possible nephrourological complications and chronic renal failure can be prevented with clean intermittent catheterization and follow-up starting at the appropriate time from the neonatal

period.

• Complications and pathologies that may lead to chronic renal failure can be prevented with the necessary medical treatment and surgical interventions at the appropriate time, along with regular follow-up examinations and clinical evaluations.

• In patients diagnosed with spina bifida, accompanying orthopedic, gastroenterological, endocrinological, neurological and other pathologies make it difficult to manage the patients. An increase in complications may occur with accompanying pathologies, but with a multidisciplinary approach, complications can be prevented and the quality of life of these patients can be improved.

• We detected a higher frequency of VUR in patients with spina bifida compared to patients in the normal population. We observed that renal scarring, which is one of the criteria for chronic renal failure, was more prevalent in our patients with VUR. This can be prevented with a proactive approach, but surgical treatment should be considered as an alternative in selected cases that do not respond sufficiently to the proactive approach.

• Spina bifida is a disease group in which many complications can be prevented with a multidisciplinary approach, regular follow-up, appropriate treatment protocols, and adequate education for families. We believe that this patient group will make significant contributions to the country's economy, public health, and can be integrated into society as a result of current treatments and approaches.

Abbreviations

EBC : Expected Bladder Capacity

CIC : Clean İntermittent Catheterization

DMSA : Static Renal Scintigraphy

eGFR : Glomerular Filtration Rate

IDC : Idiopathic Detrusor Contraction

UTI : Urinary Tract Infection

CKD : Chronic Kidney Disease

CRF : Chronic Renal Failure

MTR : Mitrofanoff

NTD : Neural Tube Defects

PUV : Posterior Urethral Valve

SB : Spina Bifida

SBA : Spina Bifida Aperta

SBO : Spina Bifida Occulta

ESRD : End-Stage Renal Disease

UP : Ureteropelvic

UV : Ureterovesical

UI : Urinary Incontinence

VCUG : Voiding Cystourethrography

VUR : Vesicoureteral Reflux

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the ethics committee of Başakşehir Çam ve Sakura Şehir Hospital (Approval No: 2023-76) and was conducted in accordance with the principles of the Declaration of Helsinki. All procedures involving human participants were performed in accordance with the ethical standards of the local ethics committee. Due to the retrospective nature of the study, the requirement for written informed consent was waived by the ethics committee.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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Authors' contributions

All authors contributed to the study conception and design, data collection, analysis, and manuscript preparation. All authors read and approved the final manuscript.

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Trial registratio

Not applicable. This study is a retrospective observational study and therefore did not require clinical trial registration.

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