

Original Investigations

Management of Urinary Tract Endometriosis Patients by Gynecologists Topdađı Yılmaz et al. Urinary Tract Endometriosis

Emsal Pınar Topdađı Yılmaz¹, Ömer Erkan Yapça¹, Gülşah Aynaoglu Yıldız²,
Yunus Emre Topdađı³, Fatih Özkaya⁴, Yakup Kumtepe¹

¹Department of Gynecology and Obstetrics, Atatürk University Faculty of Medicine, Erzurum, Turkey

²Clinic of Obstetrics and Gynecology, Nenehatun Hospital, Erzurum, Turkey

³Department of Gynecology and Obstetrics, Sanko University Faculty of Medicine, Gazinatep, Turkey

⁴Department of Urology, Atatürk University Faculty of Medicine, Erzurum, Turkey

Address for Correspondence: Yunus Emre Topdađı

Phone: +90 535 823 46 56 emr-topdagi@hotmail.com **ORCID ID:** orcid.org/0000-0003-0656-0765

DOI: 10.4274/jtgga.galenos.2020.2020.0054

Received: 13 April, 2020 **Accepted:** 13 October, 2020

Abstract

Objective: We aimed to report the postoperative outcomes of urinary tract endometriosis (UTE), which is a form of deep infiltrative endometriosis, and to contribute to the literature by presenting the obtained results.

Material and Methods: In the present study, 70 patients who underwent surgery for endometriosis at our clinic between 2005 and 2019 and had a diagnosis of UTE in the final pathological assessment were examined in detail. Patient information was retrospectively retrieved from the medical records. Data obtained pre-, peri-, and postoperatively were analyzed.

Results: Mean age of the 70 patients included according to the study criteria was 32.73 ± 7.09 years. Ureteral involvement alone was observed in 49% (n = 34) patients, bladder involvement alone was observed in 24% (n = 17) patients, and both bladder and ureteral involvement were observed in 27% (n = 19) patients. Microscopic hematuria was detected in 16% (n = 11) patients (16%), whereas preoperative urinary tract findings, such as recurrent urinary tract infections, were detected in 19% patients (n = 13). Of the patients, 56% (n = 39) were identified with dyspareunia, 56% (n = 39) with dysmenorrhea, and 30% (n = 21) with pelvic pain.

Conclusion: Although postoperative results were typically considered positive, surgical method performed in deep infiltrative endometriosis should aim to preserve fertility, improve quality of life, and reduce the complication rate to a minimum.

Keywords: Urinary tract endometriosis, hematuria, dyspareunia, dysuria

Introduction

Endometriosis is a disease characterized by the localization of functional endometrial tissue outside the uterus, which often affects the genital organs. (1, 2) Although it is most commonly

reported among women in the reproductive age group, its exact prevalence is unknown. However, studies have shown that it is observed in the general population at an average between 5% and 10%. (3) The literature defines three types of endometriosis—superficial endometriosis, deep infiltrative endometriosis (DIE), and ovarian endometrioma. (4) DIE is an aggressive form and is defined as an invasion of the peritoneum deeper than 5 mm. (5) The intestines, urinary tract, uterosacral ligament, and vagina are often affected. The symptoms may become more apparent with increases in the depth of infiltration. (6-8) Although the reported prevalence of urinary tract endometriosis (UTE) is 1%–6%, this includes bladder and ureteral involvement, which is an aggressive form of DIE. (6, 9) It is observed in 14%–20% of all patients with DIE. (10) The bladder and ureter, which are the most frequently involved sites, are affected at ratios of 84% and 10%, respectively. (11-13) In urinary tract endometriosis (UTE), which is difficult to diagnose for clinicians, it is emphasized that endometriosis with bladder involvement should be considered if the patient describes frequent urination, cyclical bladder pain, dysuria, or hematuria. (14) Endometriosis with ureteral involvement is typically asymptomatic and unaccompanied by genitourinary symptoms in 50% of patients. It is observed together with back and pelvic pain. (9, 15, 16) Magnetic resonance imaging (MRI) and ultrasonography exhibit a high specificity for endometriosis with bladder involvement in the diagnosis of UTE in which symptoms are highly nonspecific. However, both techniques are inadequate in identifying lesions <3 cm. (17) Our knowledge in terms of the diagnosis of endometriosis with ureteral involvement is extremely limited. (2)

Laparotomy or laparoscopy can be preferred in the surgical treatment of UTE in cases wherein extremely limited medical approaches are available; however, laparotomy is not preferred due to the inability to completely view lesions as well as lengthy hospitalization and greater blood loss. Nevertheless, despite all these disadvantages, laparoscopy is typically not performed in the treatment of DIE. (2)

In this study, we aimed to present the treatment of patients with DIE characterized by bladder and ureteral involvement and its long-term outcomes. We aimed to contribute to the literature by presenting the effectiveness, safety, and complication rates of the most suitable approach for the patient with UTE characterized by bladder and ureter involvement.

Material and Methods

This was a retrospective study which was performed at the obstetrics and gynecology clinics of a university hospital between 2005 and 2019. All aspects of this research were approved by Ethics Committee of xxxx University of Medical Sciences. All participants had completed informed consent before surgery.

In our study, 70 patients who underwent surgery for endometriosis in our clinic between 2005 and 2019 and had a diagnosis of UTE in the final pathological assessment were examined in detail. The pathological, clinical, and medical records were reviewed, and surgery type, complication rates, preoperative complaints, and duration of hospital stay were examined. Patients with rectovaginal involvement, deep pelvic invasion, and complete or partial obliteration of the pouch of Douglas together with an ovarian endometrioma were considered to have advanced stage (stage 3/4) disease according to the American Fertility Association (AFA) scoring system. (18) Based on their surgery records, patients with bladder and ureteral involvement who underwent ureterolysis, had partial or complete resection of the urethra, had bladder nodule resection, or had partial bladder resection were selected for detailed analysis. From the medical records, it was determined whether the preoperative clinical evaluation of the patients was performed by a multidisciplinary team and whether the operating team was decided by establishing a committee as well as the surgical approach used and the necessity of the imaging method used. All patients had undergone preoperative urinary ultrasonography

(USG), transvaginal USG, and renal function tests. It was found that bilateral double J stent was placed by urologists prior to surgery in patients suspected of having severe ureteral involvement. In cases preoperatively suspected of having a bladder nodule, cystoscopy was performed to determine the localization of the nodule at the beginning of the process and to identify whether the ureteral orifices and trigone in particular were involved. Although it was not possible to obtain the intrinsic and extrinsic distinction of ureteral involvement from medical records, it was observed that this was evaluated in the final pathological assessment of the patient. It was determined that patients with severe ureteral involvement together with symptoms initially underwent ureterolysis, whereas those who developed severe fibrosis and irreversible stenosis underwent resection. In endometriosis with bladder involvement, it was determined that depending on the size of the nodule and infiltration, either the bladder was completely opened or partially resected or the nodule was excised. The medical records revealed that urologists were included in the surgery if deemed necessary by surgeons experienced in endometriosis. Moreover, the excision of bladder nodules and extrinsic ureteral nodules was mainly performed by gynecologists, although in cases with more severe complications, specialist urologists were included in the surgery.

In cases with large ureteral nodules, the nodule was removed via the incision of the ureter and end-to-end anastomosis was performed. It was observed that the bladder was sutured twice (Vicryl 3/0 or Monocryl 3/0) in cases wherein the bladder was completely opened. At the end of the procedure, 200–300 mL of 0.9% NaCl solution diluted with indigo carmine was injected into the bladder for fluid leakage test. It was determined that the bladder catheter remained in place for an average of 10 days, whereas the ureteral catheters remained for 4 to 6 weeks. Prophylactic antibiotics were administered to all patients preoperatively.

Microscopic hematuria was detected in 16% ($n = 11$) patients, whereas preoperative urinary system findings, such as recurrent urinary tract infections, were detected in 19% ($n = 13$) patients. Of the patients, 56% ($n = 39$) were identified with dyspareunia, 56% ($n = 39$) with dysmenorrhea, 16 with cyclical recurrent dysuria, and 30% ($n = 21$) with pelvic pain. There are no significant difference was observed among the groups for Ca-125 levels. Postoperative pain scores using a visual analog scale (VAS score) was significantly lower after the procedure.

Postoperative follow-ups were performed at the Atatürk University multidisciplinary endometriosis center—the tertiary referral center of the region—at the end of the first and sixth months. According to our medical records, patients did not die in the long term and did not apply to our urology or obstetrics&gynecology clinic with the same symptoms. The management of patients who developed complications or who required recurrent surgery was performed by a multidisciplinary team.

Statistical analysis

The analyses were performed using the IBM SPSS 20 statistical analysis software. Data were presented as mean, standard deviation, median, minimum, maximum, percentage, and number. Normal distribution of continuous variables was evaluated using the Shapiro–Wilk W test when the sample size was <50 and using the Kolmogorov–Smirnov test when it was >50 . In the comparison of continuous variables with more than two independent groups, ANOVA test was used in cases where the requirement of normal distribution was met, whereas the Kruskal–Wallis test was used in cases where it was not met. In 2×2 comparisons between categorical variables, the Pearson's chi-square test was used when the expected value was >5 , Yates' chi-square test was used when the expected value was between 3 and 5, and Fisher's exact test was used when the expected value was <3 . In comparisons greater than 2×2 between categorical variables, the Pearson's chi-square test was used when the expected

value was >5 and whereas the Fisher–Freeman–Halton test was used when the expected value was <5 . The level of statistical significance level was considered as $p < 0.05$.

Results

Mean age of the 70 patients included in the study according to the study criteria was calculated as 32.73 ± 7.09 years. Surgical procedure was started laparoscopically in all patients. However, due to technical impossibilities, laparotomy was initiated in 3 patients. Ureteral involvement alone was observed in 76% ($n = 53$) patients, bladder involvement was observed in 51% ($n = 36$) patients, and both bladder and ureteral involvement were observed in 27% ($n = 19$) patients. The medical records revealed that 29 (41%) patients received medical treatment within 6 months prior to the surgery. The patients were observed to use 2 mg of dienogest daily for 6 months as a medical treatment. Moreover, 16 (23%) patients in the study group had undergone previous pelvic surgery (Table 1). During the preoperative period, 12 patients suspected of DIE received double J stents; however, 2 of these patients had ureteral injury despite this and underwent end-to-end anastomosis. Hydronephrosis was preoperatively diagnosed using preoperative imaging in eight patients with ureteral involvement.

Examination of the operative notes of the patients revealed that ureterolysis was performed in 27 (39%) patients, end-to-end anastomosis was performed in 11 (16%) patients, and no kidney loss was observed in any patient. During the follow-up period, four patients developed fistulas within 6 months and three of them had vesicovaginal fistula and one of them had rectovaginal fistula. It was observed that overall five patients in the study group were re-operated in our clinic within a maximum of 6 months postoperatively (Table 2). The operative notes of the patients who developed fistula showed that harmonic scalpel was used during dissection. Because the heat effect generated in the surrounding tissues by the energy can lead to thermal damage in the lateral tissues with the increase in operation time and temperature, it was considered as a factor in the occurrence of the damage. No significant difference was observed among the three study groups in terms of their preoperative symptoms, urogram results, the medical treatment received for endometriosis preoperatively, and previous pelvic surgery (Table 3). When intra- and postoperative complications were examined, ureterolysis was significantly higher in the group with ureteral involvement. Ureterolysis was statistically significantly higher in Both ureteral and bladder nodule group than bladder nodule group ($p = 0.016$; Table 4). The upper limit for the Ca-125 level was considered 35 IU/mL. When the groups were examined with respect to their Ca-125 levels, it was determined as 113 ± 165 IU/mL in the group with ureteral involvement, 117 ± 232 IU/mL in the group with bladder involvement, and 94 ± 56 IU/mL in the group with both ureteral and bladder involvement; however, no significant difference was observed among the groups (Table 5). Further, the medical records of our patients revealed that nine patients applied to the in-vitro fertilization unit of our clinic within 6 months and that seven of them became pregnant.

The patients were questioned in detail especially when they were called for control in terms of preoperative symptoms. Upon comparing the severity of symptoms of the patients at the end of the sixth postoperative month, the medical records revealed that the severity was reduced at least by half in 75% of the patients. Preoperative and postoperative pain scores using a visual analog scale (VAS score) were obtained from medical records. When the postoperative pain scores using a visual analog scale (VAS score) was examined, the mean pain score was 5 before the procedure in the patients with endometriosis and it was 2 when it upon re-examination with VAS scoring in the sixth month after surgical or medical treatment. VAS score was significantly lower after the procedure ($p < 0.0001$). (Table 6)

Discussion

Several studies in the literature have shown that DIE surgery, which has a high probability of complications, requires a multidisciplinary approach both in the pre- and postoperative periods and that it should be performed by an experienced team specialized in the field. Our study demonstrated that it ensures an improvement in the quality of life and a significant reduction in pain complaints. Postoperatively, a significant decline in pain was identified in a significant portion of the 70 patients included in the study, particularly in the follow-up visit after 6 months. With regard to this disease, for which rather different views have been reported in terms of treatment approaches, it is crucial that the surgical approaches employed for preventing recurrence and ensuring patient comfort primarily include the complete excision of nodules. (19) In our study, it was demonstrated that 41% of our patients had previously received medical treatment that was ineffective and that the effective treatment was complete excision of the nodules. Our higher rate of UTE, which is higher compared with that reported in the literature, can be attributable to the fact that our center is the largest endometriosis clinic in its region and that most of the patients were diffuse, advanced, and serious cases at the time of diagnosis.

Endometriosis with bladder involvement, which is observed in approximately 12% of patients with DIE, is characterized by a partial or complete involvement of the detrusor muscle layers. (20, 21) This may be owing to the fact that the detrusor muscle is stronger than ureteral muscles and has a denser vascular network that contributes to the healing process. (22) The incidence of bladder involvement, which is a rare form of DIE, reported in the literature has gradually increased. (19) It is considered that this may have an iatrogenic origin and the increased prevalence of endometriosis with bladder involvement might be particularly due to the increased rate of cesarean surgeries. It has been shown that 50% of endometriosis with bladder involvement occurs in women who have undergone a previous surgery. (23) In our case series, it was observed that 23% of the patients with UTE had undergone previous pelvic surgery.

Studies have shown that the distal ureter is more frequently involved due to its proximity to the posterior compartment of the pelvic organs. (24) Therefore, endometriosis, whose pathophysiology is not completely understood and remains unclear, has been associated with retrograde menstruation (2), and it is thought to be caused by the accumulation of menstrual blood and endometrial cells in the pelvis due to gravity and their presence at that location for a longer time. (25) Based on this theory, it has been shown that rectovaginal involvement is more common than bladder involvement. (26) Although 90% of women have retrograde menstruation, the reason for 10% of them developing endometriosis remains unclear. However, the effect of gravity, more frequent occurrence of endometriosis on the left side, and rarer occurrence of endometriosis with bladder involvement in the retroverted uterus as well as the fact that menstrual blood remains more on the left side due to the sigmoid colon may provide an explanation for this theory remaining the most emphasized one. (2, 20) In the study of Schonman et al., it was observed that half of the patients with endometriosis with bladder involvement had an ovarian endometrioma and almost one-third of them had rectosigmoid lesions. (19) Kovoov et al. reported that 76% of patients with DIE were associated with deep endometriotic lesions in the pelvis, including rectovaginal, parametrial, and uterosacral nodules. (21) Moreover, we found that ureteral involvement was higher than bladder involvement in UTE.

Endometriosis with ureteral involvement is a component of DIE. It is often non-symptomatic and complaints of the patients are nonspecific. Patients typically describe complaints related to lateral pain and cystitis. (22) Reportedly, 30% patients remained asymptomatic and the diagnosis is incidental. (27) At the time of diagnosis, decreased renal function can be observed in approximately one-third (30%) of patients and kidney loss may be present in

25%–43% patients. (28) In the study conducted by Cavaco Gomes et al. on 700 patients with endometriosis with ureteral involvement, they defined no urinary system symptoms. They also determined that 81% of patients described dysmenorrhea, 70% described pelvic pain, and 66% described dyspareunia. (29) Schonman et al. showed in their case series that 40% of their patients had urinary complaints. (19) In our case series, we determined that 39 (56%) patients presented with complaints of dyspareunia, 39 (56%) patients with complaints of dysmenorrhea, and 21 (30%) patients with complaints of pelvic pain. In addition, we determined that 1 (16%) patient had microscopic hematuria and 13 (19%) patients had urinary tract symptoms such as recurrent urinary tract infection. No renal loss was detected in any patient.

In the treatment of endometriosis, whether an aggressive surgical procedure or conservative approach will be preferred may vary depending on the preoperative evaluation of the patient, the experience of the surgeon, and the severity of the symptoms. Preoperative diagnosis is extremely controversial due to variations in the scope of lesions. Ultrasonography (USG) and MRI have high specificity in detecting endometriosis with bladder involvement, but both are insufficient in identifying lesions <3 cm. (17) Nezhat et al. reported that they initially plan cystoscopy simultaneously with USG and laparoscopy prior to surgery when they suspect endometriosis with bladder involvement. (2) Various studies have demonstrated that pelvic MRI achieves a sensitivity of up to 88% and specificity of up to 99% in the diagnosis of endometriosis with bladder involvement and that it has a diagnostic accuracy of approximately 98%. (27) In our study, we determined from the medical records that preoperative imaging methods were used depending on the severity of the disease and that USG and concurrent cystoscopy were performed in patients suspected with severe UTE. We observed that MRI was particularly performed preoperatively in 80% of patients with UTE. The primary goals are to recover the damaged ureter, prevent kidney loss, and reduce patient complaints. Seracchioli et al. successfully performed laparoscopic ureterolysis in 22 of 30 patients with endometriosis with ureteral involvement and treated eight other patients by performing ureteroureterostomy or ureteroneocystostomy. (30) However, despite all these interventions, unpredictable complications, such as fistula, leakage after end-to-end anastomosis, and leakage after reimplantation, can be postoperatively observed. (22) In their study, Rozsnyai et al. reported complications in four patients treated for endometriosis with ureteral involvement and in two patients treated for endometriosis with bladder involvement. These complications were ureteric fistula due to thermal damage caused by harmonic scalpel and pyelonephritis, bladder atony, and vesicovaginal fistula following ureteroneocystostomy. (31) During the postoperative period, we identified recurrent surgery in five (7%) patients, vesicovaginal fistula in three patients, and rectovaginal fistula in one patient within 6 months. Currently, the treatment of endometriosis with bladder involvement remains a controversial subject. Treatment may depend on various factors including the patient age, fertility status, disease prevalence, and symptom severity as well as presence of other pelvic lesions. Medical treatment may be preferred depending on disease severity but the high recurrence rates and symptom recurrence upon treatment discontinuation must be considered. (19) However, considering that endometriosis is a progressive disease, it should be considered that following the surgical excision of endometriotic nodules, hormonal treatment can be administered to prevent recurrence and reduce pain. (32)

In their study, Fedele et al. demonstrated that even if medically induced amenorrhea is achieved, endometriotic nodules regress only by 30%. (33) Smooth muscle fibers and fibrosis constitute 60% of the histopathological component of the nodule that does not respond to hormonal treatment, whereas the remaining tissue is the endometrial epithelium. (34) Price et al. argued for both medical and surgical approaches in treatment, but observed surgical excision to be more effective. (23) In our study, a significant portion of the patients had

previously received hormonal treatment, and the surgical treatment approach had become inevitable thereafter. We believe that laparoscopic approach performed by experienced surgeons is the preferred treatment method for both ureteral and bladder involvement in severe cases of endometriosis, and our study shows that long-term outcomes are extremely satisfactory.

Conclusion

The surgical method used in DIE, whose pathophysiology and treatment methods remain unclear, should aim to preserve fertility, improve the quality of life, and reduce the complication rate to a minimum. We also recommend performing abdominal ultrasound to all DIE patients prior to surgery. It has been demonstrated in our study that the long-term outcomes of this challenging surgical procedure performed by experienced surgeons are extremely satisfactory.

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Table 1. Distribution of endometriotic nodules and patient symptoms		
		N (%)
Ureteral nodule	No	17 (0.24)
	Yes	53 (0.76)
Bladder nodule	No	34 (0.49)
	Yes	36 (0.51)
Both ureteral and bladder nodule		19 (0.27)
Microscopic hematuria	No	59 (0.84)
	Yes	11 (0.16)
Recurrent urinary tract infection	No	57 (0.81)
	Yes	13 (0.19)
Dyspareunia	No	31 (0.44)
	Yes	39 (0.56)
Dysmenorrhea	No	31 (0.44)
	Yes	39 (0.56)
Dysuria	No	54 (0.77)
	Yes	16 (0.23)
Pelvic pain	No	49 (0.7)
	Yes	21 (0.3)
Preoperative medical treatment	No	41 (0.59)
	Yes	29 (0.41)
Previous pelvic surgery	No	54 (0.77)
	Yes	16 (0.23)

		N (%)
Ureterolysis	No	43 (0.61)
	Yes	27 (0.39)
End-to-end anastomosis	No	59 (0.84)
	Yes	11 (0.16)
Ureterocystostomy	No	70 (0)
Fistula (detected within 6 months)	No	66 (0.94)
	Yes	4 (0.06)
Re-operation within a maximum of 6 months	No	65 (0.93)
	Yes	5 (0.07)

		Groups by nodule localization						p
		Ureteral nodule		Bladder nodule		Both ureteral and bladder nodule		
		Count	Column (n %)	Count	Column (n %)	Count	Column (n %)	
Microscopic hematuria	No	26	0.76	16	0.94	17	0.89	0.250
	Yes	8	0.24	1	0.06	2	0.11	
Recurrent urinary tract infection	No	26	0.76	16	0.94	15	0.79	0.321
	Yes	8	0.24	1	0.06	4	0.21	
Dyspareunia	No	18	0.53	4	0.24	9	0.47	0.130
	Yes	16	0.47	13	0.76	10	0.53	
Dysmenorrhea	No	14	0.41	7	0.41	10	0.53	0.692
	Yes	20	0.59	10	0.59	9	0.47	
Dysuria	No	24	0.71	16	0.94	14	0.74	0.155
	Yes	10	0.29	1	0.06	5	0.26	
Pelvic pain	No	21	0.62	13	0.76	15	0.79	0.339
	Yes	13	0.38	4	0.24	4	0.21	
Preoperative medical treatment	No	20	0.59	12	0.71	9	0.47	0.369
	Yes	14	0.41	5	0.29	10	0.53	
Previous pelvic surgery	No	25	0.74	13	0.76	16	0.84	0.707
	Yes	9	0.26	4	0.24	3	0.16	

		Groups according to nodule localization						p
		Ureteral nodule		Bladder nodule		Both ureteral and bladder nodule		
		Count	Column (n, %)	Count	Column (n, %)	Count	Column (n, %)	
Ureterolysis*	No	20	0.59	15	0.88	8	0.42	0.016
	Yes	14	0.41	2	0.12	11	0.58	
End-to-end anastomosis	No	29	0.85	15	0.88	15	0.79	0.761
	Yes	5	0.15	2	0.12	4	0.21	
Urogynecological fistulas	No	33	0.97	16	0.94	17	0.89	0.567
	Yes	1	0.03	1	0.06	2	0.11	
Re-operation within a maximum of 6 months	No	30	0.88	16	0.94	19	1.00	0.296
	Yes	4	0.12	1	0.06	0	0.00	

*Ureterolysis was statistically significantly higher in Both ureteral and bladder nodule group than Bladder nodule group

		CA125		Chi-square	p
		Mean ± SD	Median (min-max)		
Groups according to nodule localization	Ureteral nodule	113±165	78 (7-961)	3.635	0.162
	Bladder nodule	177±232	120 (10-996)		
	Both ureteral and bladder nodule	94±56	78 (19-197)		

Variable	Before treatment (n=70) Median (min-max)	At 6 months after treatment (n=70) Median (min-max)	p
Postoperative pain score (VAS)	5(4-10)	2(3-5)	0.033