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Title: Total Laparoscopic Ureteroneocystostomy for Ureteral Endometriosis: A Single-Center Experience of 160 Consecutive Patients

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1 **Original Article**2 **Total Laparoscopic Ureteroneocystostomy for Ureteral Endometriosis: A Single-Center**
3 **Experience of 160 Consecutive Patients**

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25 **Precis:** Surgical nerve-sparing laparoscopy for deep infiltrating ureteral, parametrial, and bowel
26 endometriosis is viable, safe, and successful when performed by surgeons skilled in pelvic
27 neuroanatomy, laparoscopic nerve-sparing techniques, deep infiltrating endometriosis, and
28 oncologic radical procedures.

29 **ABSTRACT**

30 **Study Objective:** To investigate the efficacy of laparoscopic ureteroneocystostomy in patients with
31 deep infiltrating endometriosis (DIE) with ureteral, parametrial, and bowel involvement.

32 **Design:** Prospective study (Canadian Task Force classification II-2).

33 **Setting:** Tertiary referral center for endometriosis care.

34 **Patients:** One hundred and sixty patients with DIE underwent laparoscopic radical eradication and
35 ureteroneocystostomy between January 2009 and December 2016.

36 **Interventions:** Laparoscopic nerve-sparing radical treatment with ureteroneocystostomy,
37 parametrectomy, and, if necessary, segmental bowel resection.

38 **Measurements and Main Results:** Surgical eradication was radical, and ureteral endometriosis
39 was histologically confirmed in all patients (45.6% intrinsic and 54.4% extrinsic). In 58.7% of
40 patients, ureteroneocystostomy was performed with the psoas hitch technique. Bowel resection
41 was performed in 121 patients (75.6%), and 115 of them had a concomitant ileostomy (71.9%).
42 Unilateral parametrectomy was performed on the left side in 61.9% of patients and on the right side
43 in 30% of patients, respectively, while bilateral parametrectomy was completed in 33 patients
44 (20.6%). Postoperative complications were infrequent: 7 patients underwent reoperation (4.4%), 8
45 patients experienced fever (5%), 4 patients required blood transfusion (2.5%), 3 patients had
46 intestinal fistulas (1.9%), and 24 patients experienced impaired bladder voiding (15%) after 6
47 months. Mean follow-up time was 20.5 months (1–60). The study reported good clinical and
48 surgical results, with a regression of symptoms ($p < .001$) and recurrence of parametrial
49 endometriosis of 1.2% that required opposite side ureteroneocystostomy.

50 **Conclusion:** This is the largest documented series of patients with DIE undergoing laparoscopic
51 radical eradication and ureteroneocystostomy. The collected data show that in patients with
52 ureteral endometriosis, this technique is feasible, effective, safe, and provides good results in
53 terms of relapses and symptom control.

54

55 **Keywords:** Deep infiltrating endometriosis; Laparoscopic nerve-sparing surgery; Parametrial
56 endometriosis; Ureter

57 Introduction

58 It has been estimated that 5% to 15% of women of reproductive age are affected by
59 endometriosis [1]. Deep infiltrating endometriosis (DIE) in the urinary tract is the second most
60 common affected extragenital site, with an incidence of 0.3% to 12% [2–4]. Conversely, ureteral
61 involvement has an incidence of 0.1% to 1%, with a left predisposition in most cases, confined to
62 the distal segment of the ureter at 3 to 4 cm above the vesicoureteric junction [4,5].

63 Ureteral endometriosis usually presents with nonspecific symptoms owing to secondary
64 obstruction, lumbar pain, renal colic, and hydronephrosis [1,3,6]. There is a limited correlation
65 between symptom severity and level of obstruction, as a severe obstruction may be asymptomatic
66 for a long period, leaving a patient at risk of renal failure [7]. Most symptoms presented are related
67 to DIE extended to the rectovaginal septum, the uterosacral (US) ligaments, and bowel [8].

68 Ureteral obstruction in most cases is caused by DIE infiltration through the posterolateral
69 parametrium, spreading from the retrocervical region. Spreading to parametrial ligaments, it
70 generally first involves the posterior parametrium, formed by the US ligaments, rectovaginal
71 ligament, and lateral rectal ligament. This represents the “neural soul” of pelvic viscera being
72 overcrowded by tiny fibers of the orthosympathetic and parasympathetic systems from the inferior
73 hypogastric plexus [9]. In some cases, there is also an anterolateral spread of uterine
74 adenomyosis, with involvement of the anterior and lateral parametria (formed by the junction of
75 cardinal ligament, ventral and dorsal vesicouterine ligament, and paracervix), where the ureter
76 proceeds toward the parametrial tunnel (Fig. 1). Thus, radical surgery for ureteral endometriosis
77 could require partial or complete resection of parametrial ligaments (parametrectomy), with a
78 surgical impact on the visceral efferent neural bundles of the inferior hypogastric plexus, as well as
79 visceral pelvic functions.

80 Ureteral endometriosis can be divided in an extrinsic form, involving only the adventitia and
81 an intrinsic form, with a full-thickness infiltration of tunica muscularis, with an inconstant ratio of 4:1,
82 respectively, evaluated during histopathologic examination [3].

83 Different surgical treatments have been proposed for ureteral endometriosis [3,4,6–8,10–
84 13]. The development of minimally invasive techniques such as ureterolysis, ureteroureterostomy,
85 and ureteroneocystostomy can now be performed [6–8,10–18].

86 The purpose of this study was to investigate the efficacy of laparoscopic
87 ureteroneocystostomy in patients radically treated for DIE and to examine short-, medium-, and
88 long-term postoperative results.

89 **Materials and Methods**

90 This is a prospective study conducted on consecutive patients scheduled for laparoscopic
91 surgery from January 2009 to December 2016 after referral to our center with a diagnosis of DIE
92 and suspicion of ureteral involvement.

93 Among 9600 patients laparoscopically treated for endometriosis during this time, 179
94 patients had documented ureteral involvement.

95 Inclusion criteria for ureteroneocystostomy included ≥ 1 of the following: 1) mild-severe
96 hydronephrosis (≥ 1 cm) with or without radiologic evidence of ureteral stricture; 2) intraoperative
97 detection of the impossibility of performing ureterolysis owing to macroscopic infiltration of
98 endometriosis; 3) ureteral ischemia after extensive ureterolysis. Exclusion criteria were 1) history
99 or presence of bladder cancer or ovarian cancer related to endometriosis; 2) ureteral stricture with
100 complete loss of renal function.

101 Patients were evaluated and treated radically by a multidisciplinary team comprised of
102 gynecologists (MC, MC, RC, SS), urologists (GC and AM), and a general surgeon (GR) with
103 extensive and specific training in laparoscopic endometriosis surgery.

104 Patient characteristics were recorded in a computer database. Endometriosis stage was
105 defined according to the revised American Fertility Society classification of the American Society of
106 Reproductive Medicine (ASRM). Patients expressed the intensity of endometriosis-related pain
107 using the Visual Analogue Scale (VAS) for dysmenorrhea, dysuria, dyspareunia, and dyschezia at
108 baseline, at 1 and 6 months, and then annually after treatment. Hormonal therapy was stopped
109 one month before surgery. This study was approved by the hospital institutional review board.
110 Before the procedure, all patients signed an informed consent.

111 Every patient underwent rectovaginal examination, abdominal and pelvic ultrasound,
112 double-contrast barium enema, or magnetic resonance imaging for suspicion of bowel-related
113 endometriosis. In case of severe hydronephrosis, urologic computed tomography and renal
114 scintigraphy were performed, and patients underwent double-J catheter placement before surgery,

115 or preoperative nephrostomy in case of complete ureteral stenosis. Before surgery, all patients
116 completed bowel preparation with an oral intake of 20 mL Phospho-Lax (Sofar, Trezzano Rosa,
117 Milan, Italy®). Antithrombotic prophylaxis with low-molecular weight heparin was initiated the
118 evening before the operation and prophylactic antibiotic therapy with 2 g of cefazolin was
119 administered before anesthesia induction. Operative time was calculated from umbilical incision to
120 closure of laparoscopic wounds. Blood loss during surgery was estimated by measuring aspirated
121 blood volume, and surgery was completed with a Foley catheter in situ.

122 The laparoscopic procedure started with pneumoperitoneum induction using a Veress
123 needle, followed by the introduction of the 10-mm laparoscope in the umbilical position and three
124 5-mm suprapubic trocars.

125 Parametrial and ureteral endometriosis treatment began with both medial and lateral
126 paravesical spaces, Retzius' retropubic space, and the Bogros space (the caudad and lateral
127 continuation of Retzius' space) being opened starting from the anatomic landmarks (the umbilical
128 artery, uracus, pubic symphysis, pelvic floor muscles) [19] (Fig. 2). This allowed the surgeon to
129 work in healthy tissue and better target the portion of anterior parametrium (vesicouterine ligament)
130 that required resection (together with the distal narrowed ureter) as well as mobilize and precisely
131 incise the bladder achieving a tension-free ureteroneocystostomy.

132 As reported previously, we started to approach the "frozen pelvis" by opening the
133 retroperitoneal avascular spaces (Lazko and Okabayashi pararectal spaces) [20]. The procedure
134 began with 1) adhesiolysis, ovarian mobilization, and 48-hours of temporary ovarian suspension to
135 the abdominal wall using 2/0 polypropylene non-absorbable sutures (to improve access to the
136 posterolateral parametrium and the posterior cul-de-sac); 2) bilateral identification of ureteral
137 courses and resection of the involved US ligaments, close to the rectovaginal nodule, if present; 3)
138 surgical dissection of Waldeyer's presacral space and Heald's retrorectal space, thus allowing the
139 identification and preservation of pelvic sympathetic fibers of the superior hypogastric plexus and
140 hypogastric nerves; 4) dissection of parametrial planes, isolation of the ureteral course (Fig.1),
141 anterolateral parametrectomy, if necessary; 5) posterior parametrectomy, deep uterine vein
142 identification, and preservation of the parasympathetic pelvic splanchnic nerves and inferior
143 hypogastric plexus; 6) rectal resection, if necessary; 7) ureteral resection with anterolateral or

144 posterolateral transected parametrial ligaments, and subsequent ureteroneocystostomy; 8) final
145 colorectal anastomosis with temporary ileostomy.

146 The ureteral procedure typically commenced after placement of a double-J ureteral stent, if
147 not previously positioned. Ureteroneocystostomy was then performed after isolation and resection
148 of the narrowed ureter portion (Fig. 2). The correct surgical strategy was tailored according to
149 length of the proximal residual ureter. If length was adequate, ureteroneocystostomy using the
150 “Lich-Gregoir” technique was typically performed [18,21]; conversely, when the proximal segment
151 had a limited length, a direct reimplantation was completed, with or without psoas-hitch stitches. In
152 extreme cases, with an extremely short residual ureteral length, a cystoplasty was created in
153 addition to the procedures already described to relieve the tension to the anastomosis. No patients
154 required ileal ureter replacement.

155 The bladder was opened transversely and laterally to the bladder dome and attached to the
156 psoas muscle (if needed) using three interrupted Vicryl Rapide (Ethicon, Sommerville, NJ) 2/0
157 sutures, with care to avoid the 2 genitofemoral nerve branches. Then, the ureter was passed
158 through the bladder wall, while maintaining a linear passage during which a submucous path was
159 created usually 3 to 5 times wider than the ureter to avoid post ureteroneocystostomy reflux.
160 Ureterovesical anastomosis was completed using six interrupted sutures in 3/0 Monocryl (Ethicon,
161 Sommerville, NJ), or 3 running sutures in the Lich-Gregoir technique. The bladder incision was
162 then closed longitudinally with double sutures in 2/0 Monocryl (Ethicon, Sommerville, NJ), the first
163 layer including the mucosa and muscular layer, the second comprised the muscular layer and the
164 peritoneum.

165 When ureteroneocystostomy was performed bilaterally, the approach on the Retzius' space
166 was the same as the unilateral procedure. After bladder mobilization, a longitudinal incision of the
167 bladder fundus was made, to create a v-shape cystoplasty allowing bilateral psoas-hitch stitching
168 and subsequent bilateral tension-free ureteroneocystostomy.

169 A drain was left in the Retzius' space or in the Douglas pouch for approximately 2 to 3 days
170 and removed after an intravenous methylene blue test to reveal anastomosis leakage. After 7 to 10
171 days (14–20 days for bilateral procedures), a cystography was typically scheduled to confirm
172 bladder and anastomosis integrity, and the bladder catheter was removed.

173 Clear fluids were allowed the day after surgery, and oral intake began the following day,
174 followed by a gradual diet. Bladder function was then assessed by measurement of residual urine
175 volume (obtained by catheterization or ultrasound) after spontaneous voiding and was considered
176 normal if consistently lower than 100 mL in three consecutive measurements. Before discharge, an
177 ultrasound scan of the urinary tract was performed and removal of the double-J ureteral stent was
178 scheduled after two months (after a negative retrograde pyelography).

179 The grade of vesicoureteral reflux was evaluated in voiding cystourethrography and
180 classified according to the five-grade system of the International Grading System [22].
181 All patients were clinically evaluated at 1 and 6 months and then annually after surgery. Follow-up
182 consisted of pelvic examination, pelvic ultrasound, assessment of renal function, renal tract
183 sonogram, retrograde pyelography, urologic computed tomography and mercaptoacetyltriglycine-3
184 radioisotope renography, if necessary.

185 **Statistical analysis**

186 Statistical analysis was performed with GraphPad Prism version 3.00 for Windows
187 (GraphPad Software, San Diego, CA®). The Wilcoxon matched pairs test was used to compare
188 the gravity of the symptoms at follow-up. The statistical significance was considered to be achieved
189 when $p < .05$.

190 **Results**

191 Among the 179 patients enrolled, 160 were considered eligible for the study. Table 1 shows
192 the preoperative patient characteristics. Eighteen patients did not meet inclusion criteria owing to
193 exclusive laparoscopic nephrectomy and complete loss of renal function, and one patient was
194 excluded following intraoperative finding of ovarian cancer. One hundred patients (62.5%) had
195 previous surgery for endometriosis, and 18 patients (11.2%) had concomitant urologic and
196 endometriosis treatments; only 38 patients (23.7%) experienced urinary symptoms.

197 Mild-severe hydronephrosis was present in 110 patients (68.7%) and a double-J stent was
198 placed before surgery. Seventeen patients (10.6%) underwent ureteroneocystostomy because it
199 was not possible to perform ureterolysis owing to macroscopic infiltration of endometriosis or
200 secondary atony of the fibrosclerotic residual segment after ureterolysis. One hundred and fifty-one
201 patients had unilateral stenosis (39 patients in the right ureter, 112 patients in the left), and 9

202 patients had bilateral stenosis.

203 Table 2 shows the intraoperative findings and procedures. According to ASRM
204 classification, patients suffered from stages I/II to III/IV in 2.5% and 97.5%, respectively. In all
205 patients, endometriosis was histologically confirmed. Histological examination of the ureter
206 resections showed endometriosis inside the muscular ureteral layer in 45.6% of patients (intrinsic
207 endometriosis), adventitial infiltration of the ureter in 54.4% of patients (extrinsic endometriosis).

208 Psoas-hitch was performed in 94 patients (58.7%) because of the need for tension-free
209 anastomosis. Laparoscopic radical excision of the macroscopic localization of endometriosis was
210 performed in all patients. Sixty-five patients (41.4%) underwent Argon beam coagulation of the
211 posterofundal superficial adenomyosis.

212 Bowel resection was performed in 121 patients (75.6%) and 115 of them had a concomitant
213 ileostomy. The most common endometriosis lesions were in the rectosigmoid region (73.1%) and
214 left (anterolateral or posterolateral) parametrium (61.9%). Bilateral parametrectomy was performed
215 in 33 patients (20.6%).

216 Cystography on Day 7 to 10 confirmed the integrity of the anastomosis in 147 cases
217 (91.8%); 12 patients needed to maintain the bladder catheter owing to minimal anastomosis
218 leakage for another 7 to 10 days; after that another cystography showed restoration of normal
219 integrity. A Foley catheter was left for 50 days in one patient and removed after a negative
220 cystography. Positive postoperative bladder capacity (>200 mL) was observed in all patients.

221 Vesicoureteral reflux was detected in 26 patients at the side of ureteroneocystostomy, all
222 classified as stage I [22].

223 The median time to resume voiding function was 3 days (range, 1–18). Median length of
224 hospital stay was 8 days (range, 7–18), and median follow-up time was 20.5 months (range, 1–60).
225 Eleven patients were lost to long-term follow-up. Postoperative complications were classified
226 according to Clavien-Dindo (Table 3) [23]. During the first month, there were 7 reoperations (4.4%),
227 3 for bladder suture leakages (one with an associated pelvic abscess, one with associated
228 hemoperitoneum), one vaginal-cuff dehiscence, one hemoperitoneum, and 2 ileostomy related
229 complications. No patient presented with bowel anastomosis leakage. Anemia caused by blood
230 loss occurred in 6 patients (3.7%), 4 of whom received blood transfusion (2.5%). Eight patients

231 experienced postoperative fever and were successfully treated with antibiotic therapy (5%), while 2
232 patients had transient hematuria (1.2%).

233 In the first postoperative month, 3 patients experienced complications with rectovaginal
234 fistulas (1.9%), 6 urinary tract infections (3.7%); 26 patients experienced impaired bladder voiding
235 evaluated by urodynamic testing (16.2%), with 33% positive postvoiding residual urine volume
236 requiring temporary intermittent self-catheterization.

237 At 6 months follow-up, 11 patients reported urinary tract infections detected by urine culture
238 (6.9%). At the second urodynamic evaluation, 24 patients confirmed bladder dyskinesia (15%),
239 79.2% of them with reduced bladder visceral sensitivity and 70.8% with urethral hypertonia. Two
240 patients revealed minimum stable hydronephrosis and 2 patients an intestinal obstruction with
241 concomitant subocclusion. One patient underwent laparoscopic reoperation for intestinal
242 obstruction from adhesions bridge, the other patient was treated for anastomotic stenosis with
243 endoscopic dilation. At 24 months, endometriosis recurrence rate was 3.1%, with 5 ovarian
244 endometriomas confirmed by transvaginal ultrasound. Two patients with relapsed parametrial
245 endometriosis (1.2%) underwent a second opposite-side laparoscopic ureteroneocystostomy 36 to
246 48 months after the first procedure. Six patients underwent sacral neuromodulation therapy, with
247 substantial improvement of bladder dyskinesia (3.7%). One hundred and nineteen patients
248 underwent postoperative hormone therapy with oral progestin or combined estrogen-progestin
249 (74.4%). An improvement in pain symptoms was noted after surgery ($p < .0001$; Table 4). Sixty-
250 one surgically treated patients expressed interest in future pregnancy (38.8%); 12 pregnancies
251 were spontaneously obtained with 7 vaginal deliveries, 5 Caesarean sections, and a pregnancy
252 rate of 19.7% after DIE excision.

253

254 **Discussion**

255 The optimal surgical approach to ureteral endometriosis has yet to be defined. Different
256 surgical treatments have been proposed, but low prevalence diminishes the possibility for
257 prospective randomized trials to demonstrate optimal treatment, leaving only the most recent
258 retrospective surgical series to help determine appropriate disease management.

259 A review by Cavaco-Gomes et al [24] suggests that ureterolysis should be limited to
260 patients with minimal ureteral involvement and notes reimplantation to be the preferred treatment
261 for ureteral obstruction. Data from more recent series [10–12] indicate that recurrence rates after
262 ureterolysis are not negligible, with reported persistence of ureteral stenosis of 12% and 20% of
263 patients who underwent ureteroureterostomy and ureterolysis, respectively [13]. Recent studies
264 have investigated the technique and feasibility of laparoscopic ureteroneocystostomy in patients
265 with severe ureteral endometriosis [3,6–8,15–18].

266 As it is impossible to differentiate intrinsic and extrinsic ureteral endometriosis
267 preoperatively, the indication for ureteroneocystostomy should be the presence of
268 moderate/severe hydronephrosis owing to posterolateral parametrium involvement that causes
269 ureteral stenosis. When ureteral endometriosis does not cause stenosis and hydronephrosis,
270 ureterolysis with or without ureteral shaving may be considered [24]. Conversely, in case of
271 intrinsic endometriosis it is generally established that ureteral resection is necessary because it
272 seems to evade persistence of disease and renal failure [25].

273 Ureteral layers consist of a mucosal stratum coated by transitional epithelium, a double
274 smooth muscle layer (circular and longitudinal), and an adventitia tunica, where all vascular
275 ureteral supplies merge, arising from the aorta, gonadal artery, and common and internal iliac
276 system; this allows ureteral mobilization during surgeries over a long distance, without endangering
277 blood supply. As shown in Fig. 3, Waldeyer described another layer and called it the ureteral
278 “sheath” that is formed by an encircling fibromuscular layer around the distal ureteral segment
279 entering the bladder, mixing with the detrusor muscle [26,27]. Conversely, if ureterolysis requires
280 ureteral adventitia invasion, compromising its vascularization and altering the Waldeyer sheath, a
281 residual ischemic ureter could result in a subsequent ureteral fistula. Moreover, an involved
282 parametrium can impact external ureteral layers without causing stenosis. In the current
283 experience, parametrectomy with resection of the involved ligaments and ureterolysis is always the
284 best surgical option, including the shaving of the adventitial involved ureteral layer. After that, a
285 final decision regarding ureteroneocystostomy must be considered after a meticulous evaluation of
286 the ureteral course, caliber, peristalsis, and its residual vascularization. In fact, 54.4% of the
287 current patients revealed an extrinsic endometriosis on histopathologic specimens, but

288 ureteroneocystostomy after extensive ureterolysis was found to be necessary. These data show
289 how ureteral stricture cannot be considered alone as the only factor influencing surgical
290 management. The real surgical challenge is to unroof the ureter, removing the surrounding
291 parametrial endometriosis without compromising its vascularization.

292 Ureteroneocystostomy modifies the anatomy of the urinary tract but does not seem to
293 change urodynamic parameters [14]. Postoperative bladder dysfunctions seem unrelated to
294 ureteroneocystostomy itself, but is associated with neuroablative damage during parametrectomy,
295 often overlapping the effects of multiple previous surgeries [9,20]. This clinical aspect was partially
296 confirmed in the current study. In fact, 15% of current patients were found to suffer from bladder
297 dyskinesia, but this was associated with massive parametrial involvement that was recorded in the
298 study, with consequent infiltration of parametrial bladder branches and the need for radical
299 parametrectomy, which was done bilaterally in 33 women (20.6%). Moreover, the percentage of
300 patients requiring urodynamic follow-up has declined since 2013, and this appears to be related to
301 improved control of parametrial surgical anatomy and the nerve-sparing technique introduced and
302 performed by our team [20].

303 To the best of our knowledge, this is the largest series of patients who underwent
304 laparoscopic ureteroneocystostomy for DIE and has the strength of a single-center study with a
305 systematic follow-up. In the current study, the reported recurrence rate was 1.2% with a complete
306 regression of symptoms ($p < .0001$; Table 4). No major complications were reported both
307 postoperatively and at long-term follow-up, and bowel complications (3.1%) were comparable to a
308 previous study [28].

309 More than 95% were classified as stage III/IV according to ASRM classification, with 62.5%
310 having undergone previous surgery for endometriosis.

311 In our experience ureteral endometriosis, both intrinsic or extrinsic, is a direct consequence
312 of a posterolateral and/or anterolateral parametrial involvement. In the majority of patients,
313 endometriosis impacts the parametrial ligaments, spreading from an involved/obliterated anterior
314 and/or posterior cul-de-sac and arising from adenomyosis.

315 When there is a clear indication for surgery, such as with the oncomimetic growth-pattern of
316 endometriosis, radical removal of disease is essential (together with parametrial and bowel
317 surgery) and must be balanced with a fertility- and nerve-sparing approach.

318 **Conclusion**

319 The current manuscript shows that laparoscopic ureteroneocystostomy for ureteral
320 endometriosis is safe, feasible, and effective. The primary goal is to provide minimally invasive
321 techniques, laparoscopic or robotic-assisted, to achieve better surgical outcomes than the open
322 technique.

323 This technique is crucial in distal ureteral obstruction with a risk of subsequent renal failure.
324 On the other hand, when surgery is indicated (after medical treatment failure),
325 ureteroneocystostomy may be considered necessary as well, for wide parametrial involvement and
326 external ureteral infiltration, noting the primary goal to be complete surgical endometriosis excision.

327 In the treatment of DIE with multiple-organ involvement, the standard protocol at our
328 institution is a multidisciplinary team approach (gynecologist, urologist, general surgeon) to achieve
329 optimal treatment preoperatively, intraoperatively, and postoperatively. Surgery should be
330 performed by experienced gynecologic surgeons skilled in pelvic neuroanatomy, laparoscopic
331 nerve-sparing techniques, DIE, and oncologic radical procedures.

332
333

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407

408

409

410 Figure Legends

411 Fig. 1 Different surgical steps for ureterolysis of a left ureter with endometriosis involvement. **(A)**
 412 Overview of a “frozen pelvis”, with the dilated ureter that runs into the posterolateral left pathologic
 413 parametrium attached to the retrocervical and rectovaginal septum infiltrated by endometriosis. **(B)**
 414 Left ureterolysis and development of lateral and medial pararectal spaces (Latzko’s and
 415 Okabayashi’s) and transection of the cardinal ligament. **(C–D)** Left narrowed ureter after
 416 posterolateral parametrectomy with cranial dilation and the required left ureteroneocystostomy. E =
 417 endometriosis nodule; LP = lateral pararectal space; MP = medial pararectal space; OV = ovarian
 418 vessels; R = rectum; U = ureter.

419
 420 Fig. 2 Surgical steps of a left ureteroneocystostomy. **(A)** Dissection and preparation of the
 421 retropubic and lateral retropubic (Retzius’ and Bogros’) spaces with complete bladder mobilization.
 422 **(B)** Proximal left ureteral segment preparation for the ureteroneocystostomy with the double J
 423 ureteral stent. **(C)** Left ureteroneocystostomy according to the Lich-Gregoire technique, beginning
 424 with Monocryl 3/0 (Ethicon, Sommerville, NJ) for the second running suture. **(D)** Final overview of
 425 the left ureteroneocystostomy. B = bladder; BS = Bogros space; IPR = ischiopubic ramus; R =
 426 Retzius space; U = ureter; UA = umbilical artery; UT = uterus.

427
 428 Fig. 3 Ureteral wall layers and intrinsic vascularization. **(A)** Anatomic drawing showing ureteral
 429 layers and the Waldeyer’s sheath enveloping the periadventitial ureteral vascularization. **(B)**
 430 Waldeyer’s fibromuscular sheath enveloping the terminal ureteral inner vascularization (drawn in
 431 white). **(C)** Final view of a de-vascularized ureter after ureterolysis and removal of an extrinsic
 432 endometriotic nodule infiltrating through the Waldeyer’s Sheath (Drawings by Francesca
 433 Ceccarello inspired from Hinman F Jr. Atlas of Urologic Surgery, 2nd Ed. Philadelphia, PA: WB
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435

436 Table 1

437 Patient characteristics

| | |
|---|-------------|
| Patient enrolled, N | 160 |
| Age, years | 36.1 |
| Body mass index, kg/m ² | 22.1 |
| Previous hormonal therapy, n | 73 (45.6%) |
| Previous surgery for endometriosis, n | 100 (62.5%) |
| Previous surgeries per patient, mean number (range) | 1 (1–5) |
| Previous urologic surgery | 18 (11.2%) |
| Dyspareunia, n (%) | 76 (47.5%) |
| VAS score \geq 5, n | 53 |
| VAS score (range) | 3.8 (1–10) |
| Dysuria, n (%) | 38 (23.7%) |
| VAS score \geq 5, n | 21 |
| VAS score (range) | 1.7 (1–10) |
| Dysmenorrhea, n (%) | 127 (79.3%) |
| VAS score \geq 5, n | 102 |
| VAS score (range) | 6.7 (1–10) |
| Dyschezia, n (%) | 76 (47.5%) |
| VAS score \geq 5, n | 52 |
| VAS score (range) | 4 (1–10) |
| Renal colic, n (%) | 11 (6.9%) |
| Recurrent cystitis, n (%) | 2 (1.2%) |
| Preoperative double J stent, n (%) | 114 (71.2%) |

438 Values are reported as mean or (%). VAS = Visual Analogue Scale.

439

440

441

442 Table 2

443 Intraoperative findings and procedures (N = 160)

| | |
|---|-----------------|
| Duration of surgery, minutes (range) | 364.3 (120–600) |
| Duration of ureteroneocystostomy, minutes (range) | 92.3 (30–180) |
| Blood loss, mL (range) | 291.4 (50–1250) |
| Stage of disease, n (%) | |
| I | 0 |
| II | 4 (2.5%) |
| III | 11 (6.9%) |
| IV | 145 (90.6%) |
| Ureteroneocystostomy, n (%) | |
| Right | 39 (24.4%) |
| Left | 112 (70%) |
| Bilateral | 9 (5.6%) |
| Psoas hitch, n (%) | 94 (58.7%) |
| Bilateral | 4 (2.5%) |
| Concomitant urological procedures, n (%) | |
| Nephrectomy | 1 (0.6%) |
| Termino-terminal anastomosis | 1 (0.6%) |
| Concomitant endometriosis sides, n (%) | |
| Vesicouterine pouch | 37 (23.1%) |
| Rectosigmoid | 117 (73.1%) |
| Pouch of Douglas | 58 (36.2%) |
| Right fallopian tube | 13 (8.1%) |
| Left fallopian tube | 10 (6.2%) |
| Right parametrium | 48 (30%) |
| Left parametrium | 99 (61.9%) |
| Bilateral parametrium | 33 (20.6%) |
| Right ovary | 41 (25.6%) |
| Left ovary | 58 (36.2%) |
| Right wide ligament | 75 (46.9%) |
| Left wide ligament | 81 (50.6%) |
| Right uterosacral ligament | 76 (47.4%) |
| Left uterosacral ligament | 93 (58.1%) |
| Rectovaginal septum | 86 (53.7%) |
| Vaginal posterior fornix | 47 (29.4%) |
| Right round ligament | 5 (3.1%) |

| | |
|---|-----------------------|
| Left round ligament | 11 (6.8%) |
| Ileum/Caecum | 12 (7.5%) |
| Appendix | 6 (3.7%) |
| Associated procedures, n (%) | |
| Excision of endometriomas | 96 (60%) |
| Unilateral/bilateral salpingo-oophorectomy | 8 (5%) / 3 (1.9%) |
| Unilateral/bilateral salpingectomy | 20 (12.5%) / 3 (1.9%) |
| Total hysterectomy | 3 (1.9%) |
| Excision of uterosacral ligaments | 126 (78.7%) |
| Excision of rectovaginal nodule | 86 (53.7%) |
| Bowel resection | 121 (75.6%) |
| Bladder resection | 16 (10%) |
| Excision of vaginal posterior fornix nodule | 47 (29.4%) |
| Ileostomy | 115 (71.9%) |

444 Values are reported as mean or (%).

445

446

447 Table 3

448 Complications (Clavien-Dindo grading system for surgical complications)

| | Postoperative | Clavien-Dindo | After 1 month | After ≥6 months |
|--------------------------------|---------------|---------------|---------------|-----------------|
| Reinterventions, n (%) | 7 (4.4%) | IIIb | – | – |
| Blood loss with anemia, n (%) | 6 (3.7%) | I | – | – |
| Blood transfusion, n (%) | 4 (2.5%) | II | – | – |
| Postoperative fever, n (%) | 8 (5%) | II | – | – |
| Hematuria, n (%) | 2 (1.2%) | – | – | – |
| Urinary infection, n (%) | – | – | 6 (3.7%) | 11 (6.9%) |
| Rectovaginal fistula, n (%) | – | – | 3 (1.9%) | – |
| Bladder voiding deficit, n (%) | – | – | 26 (16.2%) | 24 (15%) |

449

450

451 Table 4

452 Symptom improvement after surgery (N = 160)

| | Preoperative symptoms | | Postoperative symptoms | |
|--------------|-----------------------|------|------------------------|------|
| | Mean | SD | Mean | SD |
| Dysmenorrhea | 6.6 | 3.14 | 1.1 | 1.42 |
| Dysuria | 1.7 | 2.57 | 0.8 | 1.42 |
| Dyschezia | 4 | 3.71 | 0.8 | 0.76 |
| Dyspareunia | 3.8 | 3.62 | 0.9 | 1.19 |

453 Values are mean \pm standard deviation (SD) with $p < .0001$ (Wilcoxon test).

454

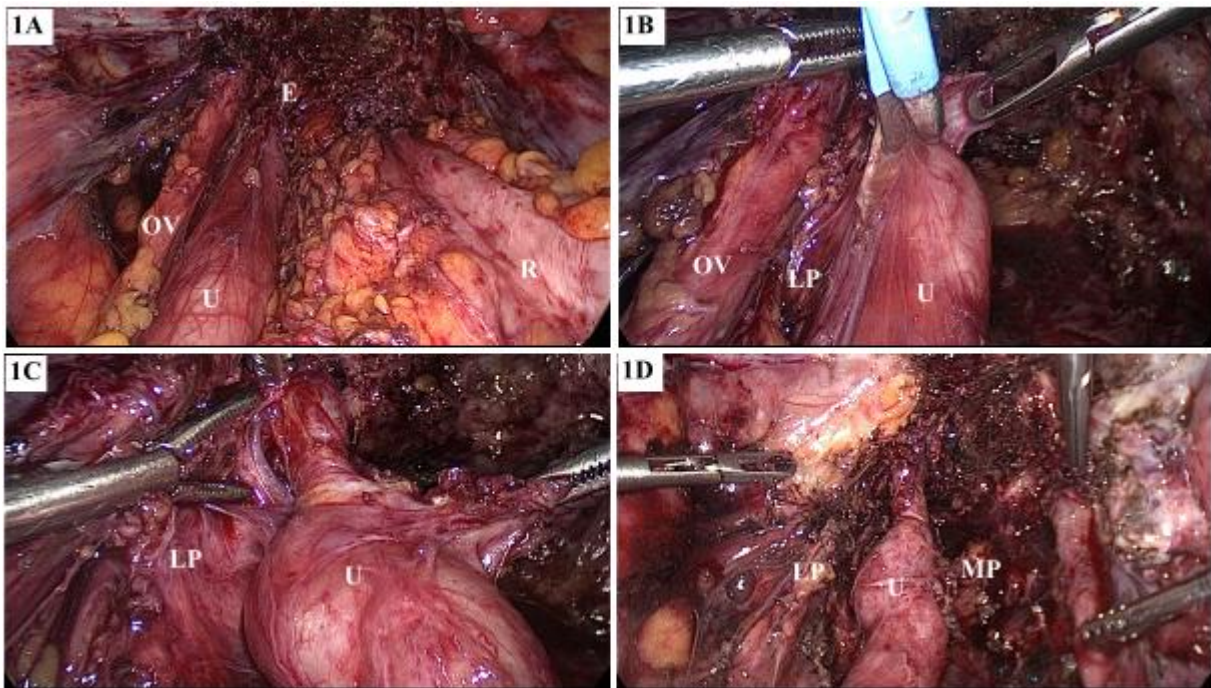
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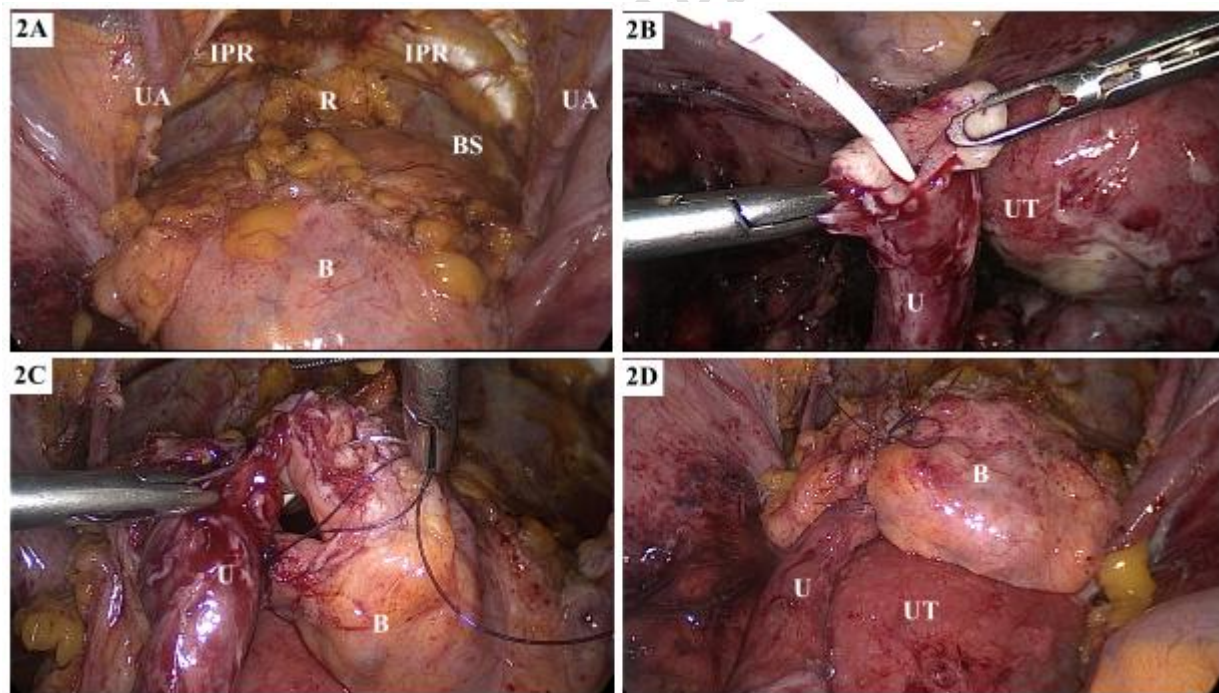
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458 Fig. 1



459

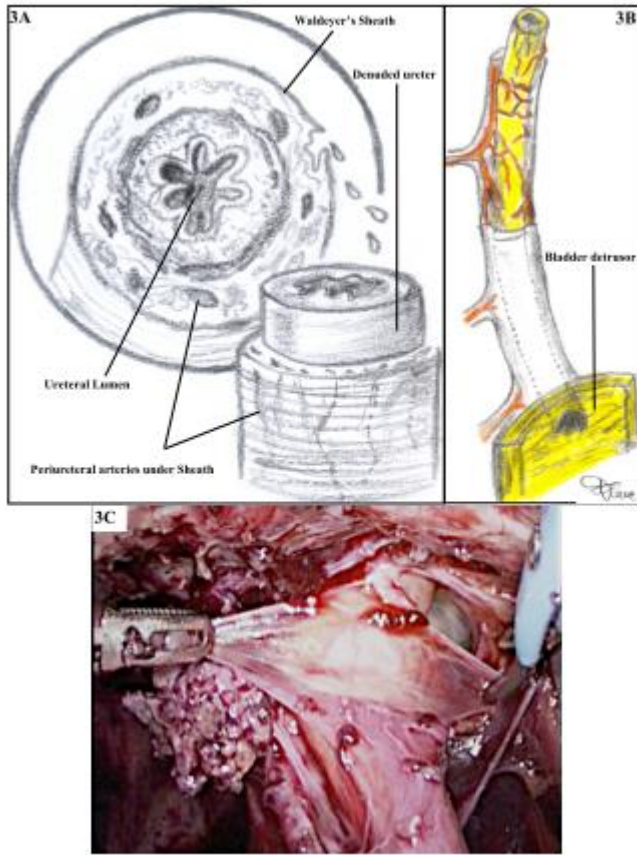
460 Fig. 2



461

462

463 Fig. 3



464