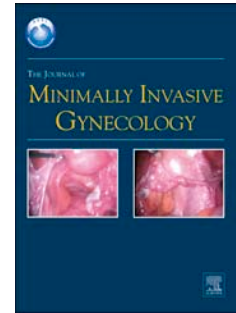


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Surgical Outcomes of Urinary Tract Deep Infiltrating Endometriosis

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1 **Running title: Urinary Tract endometriosis surgical outcomes**

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ACCEPTED MANUSCRIPT

32 **Surgical Outcomes of Urinary Tract Deep Infiltrating Endometriosis**

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62 **Capsule:**

63 Surgical management of urinary tract endometriosis is feasible with good functional outcomes;
64 however, the risk of major complications should not be overlooked.

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93 **Abstract**

94 **Objective:** To report the outcomes of surgical management of urinary tract endometriosis.

95 **Design:** Retrospective study based on prospectively recorded data (NCT02294825).

96 **Design Classification:** II-3

97 **Setting:** University Tertiary referral center.

98 **Patients:** 81 women treated for urinary tract endometriosis from July 2009 to December 2015
99 were included of whom 39 had bladder endometriosis, 31 ureteral endometriosis and 11 both
100 ureteral and bladder endometriosis. Due to bilateral ureteral localizations in 8 women, 50
101 different ureteral procedures were recorded.

102 **Intervention:** Resection of bladder endometriosis nodules, advanced ureterolysis, ureteral
103 resection followed by end-to-end anastomosis or ureteroneocystostomy were performed. Main
104 **Outcome Measures:** Outcomes of the surgical management of urinary tract endometriosis.

105 **Results:** 50 women presented with DIE of the bladder, and underwent either full-thickness
106 excision of the nodule (70%) or excision of the bladder wall without opening of the bladder
107 (30%). Ureterolysis was performed in 78% of ureteral lesions, and 22% ureteral involvements
108 were treated by primary segmental resection. No nephrectomy was required. Intrinsic ureteral
109 endometriosis was histologically revealed in 54.5% of cases. 16% of the patients who had
110 surgery for ureteral nodules had a Clavien-Dindo grade 3 complication and, in those operated for
111 bladder endometriosis 8% had Clavien-Dindo grade 3 complications. Overall delayed
112 postoperative outcomes were favourable as regards urinary symptoms and fertility. Patients were
113 followed up for a minimum of 12 months and up to 7 years postoperatively with no recorded
114 recurrence.

115 **Conclusion:** Surgical outcomes of urinary tract endometriosis are generally satisfactory;
116 however, the risk of postoperative complications should be taken into consideration. Therefore,
117 such procedures should be managed by an experienced multidisciplinary team.

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119 **Keywords:** Deep endometriosis; bladder; ureter; postoperative complications.

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Introduction

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Endometriosis is defined as the presence of endometrial glands and stroma at extra uterine sites. Urinary tract endometriosis is a rare localization of ectopic endometrial implants, and is present in 1-2 % of women with endometriosis. (1)

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The majority of patients with bladder endometriosis are symptomatic and may present with symptoms of bladder irritation which may include urinary frequency, urgency and dysuria. In regards to ureteral endometriosis, symptoms are rare, leading to urinary tract obstruction and silent loss of renal function. (2) In those presenting with signs of urinary tract obstruction, surgery may be considered as a first-line treatment to prevent further organ damage (3).

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In literature only retrospective non comparative studies exist in the management of urinary tract endometriosis. Therefore, this leads to the absence of best practice guidelines especially in the surgical management of ureteral endometriosis. For this reason, surgical techniques may go from 100% ureteral re-implantation (4) to 90% ureterolysis (5).

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In a similar manner, rare complications may occur, and since case reports are nowadays hardly published in the majority of journals, it is only through the collection of case-series that such complications may be discussed. Similar to our series, the prospective collection of data allows a review of complications and outcomes with a minimum loss of follow up.

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Our retrospective study based on data prospectively recorded reports the outcomes of surgical management of urinary deep infiltrating endometriosis managed in our department, the choice of surgical approach, and focuses on specific complications.

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Material and Methods

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We performed a retrospective review of data and included patients managed surgically for urinary tract deeply infiltrating endometriosis in the Department of Obstetrics and Gynecology at Rouen University Hospital in France from July 2009 to December 2015. Patients were prospectively enrolled in the CIRENDO database (*the North-West Inter Regional Female Cohort for Patients with Endometriosis*), a prospective cohort, financed by the G4 Group (The University Hospital of Rouen, Lille, Amiens and Caen, France), and coordinated by one of the

154 authors (H.R.). Data is collected through self-questionnaires obtained pre-operatively and at 1, 3
155 and 5 years postoperatively. Data recording, patient contact and follow-up were carried out by a
156 dedicated clinical research technician.

157 From the database, women selected were those for whom a urologic surgical procedure was
158 carried out. Urinary tract endometriosis is defined as endometriosis involving the bladder or
159 involving/surrounding the ureter leading to ureteral dilatation above, in agreement with the
160 definition of Nezhat et al, who defined "ureteral endometriosis" as being any situation where
161 endometriosis causes compression or distortion of the anatomy of the ureter (6). Surgery was
162 performed in symptomatic patients or in those who presented with signs of urinary tract
163 obstruction. It is our policy to surgically manage all symptomatic women with either bladder or
164 ureteral endometriosis or those presenting with urinary tract obstruction in order to prevent
165 further negative impact on renal function.

166 Surgical reports were then reviewed and only women who underwent either full - or
167 partial-thickness cystectomy, ureteral segmental resection or advanced ureterolysis were
168 included. We defined advanced ureterolysis as being the procedure required when the ureter was
169 completely surrounded by a fibrous endometriosis ring, resulting in either an extrinsic
170 compression or an intrinsic involvement of the ureteral wall responsible for obvious increase of
171 ureteral diameter above the ring. The patients enrolled were only those in whom a deep
172 endometriosis nodule surrounded the ureter leading to a ureteral stenosis and a consequent
173 hydroureter. Some of them presented with associated hydronephrosis as well. In these patients,
174 ureteral endometriosis could be either extrinsic or intrinsic. For all authors in literature,
175 intraoperative differentiation between these two conditions is challenging. Only half of resected
176 specimens may present with intrinsic disease. We always attempt a ureterolysis; once the ureter
177 has been freed, the degree of residual stenosis is then estimated. Resection of the ureter is then
178 carried out in ureters with either severe irreversible stenosis, or because of unintentional injuries
179 during dissection.

180 As for bladder endometriosis, the choice between bladder shaving, which includes nodule
181 resection without opening the bladder, and full-thickness resection depended on the depth of
182 infiltration. We started by detrusor incision around the bladder nodule, then we followed the
183 nodule's macroscopic limits in the depth. In the majority of cases, when the bladder mucosa was
184 obviously involved, a full-thickness bladder resection was performed. Conversely, in cases

185 where the resection appeared complete before opening the bladder, we carried out only a partial
186 thickness bladder resection followed by muscular suture in one layer, to reinforce the bladder
187 wall.

188 Preoperative data and information on surgical procedures were extracted from the
189 CIRENDO database. Information about immediate postoperative outcomes were obtained from
190 the patient's medical records and CIRENDO database. Delayed postoperative outcomes were
191 evaluated using CIRENDO standardized self-questionnaires, with a follow up at 1, 3 and 5 years.
192 Surgical procedures were performed by surgeons experienced in laparoscopic management of
193 DIE, assisted by urological surgeons when needed. Patients underwent pre-operative assessment
194 of deep infiltrating endometriosis through clinical examination and magnetic resonance imaging
195 (MRI). Further assessment including endorectal ultrasound and computed tomography-based
196 virtual colonoscopy were performed in the presence of associated colorectal deep infiltrating
197 endometriosis. Renal scintigraphy was performed to evaluate renal function in cases where
198 imaging shows damaged kidneys. Double-J stents were placed either pre- or intraoperatively.
199 Decisions regarding the type of surgical procedure to be performed depended on pre-operative
200 workup results as well as intra-operative findings. All surgical approaches began with
201 identification of the ureter. Ureterolysis was begun proximal to the diseased area, at a level of
202 healthy tissue. Careful dissection proceeded down to the level of damage. Ureterolysis was
203 considered satisfactory when the fibrous ring surrounding the ureter was completely excised
204 leaving behind a distally free ureter (Fig 1). However, after advanced ureterolysis, any evidence
205 of infiltration of the ureteral muscularis defined the need for a more aggressive surgical
206 intervention. Thus, ureteral resection was performed within the same intervention, with either
207 subsequent end-to-end anastomosis or ureteroneocystostomy. If the distal ureter could be
208 preserved and the length of stenosis does not exceed 1 to 2 cm, ureteral resection and end-to-end
209 anastomosis may be performed over a ureteral stent (Video 1). When ureteral stenosis was
210 adjacent to the vesicoureteral junction or the length of stenosis exceeds 2 to 3 cm, the ureter was
211 resected and reimplanted into the bladder. End-to-end ureteral anastomosis was performed using
212 6 to 8 separate stitches of PDS 4/0. The length of the resected ureteral specimen varied from 10
213 to 15 mm and was sufficient to completely relieve the stenosis. Even though no data exists to
214 recommend a technique over the other, we prefer performing an end-to-end anastomosis
215 whenever it is feasible in order to avoid vesicoureteral reflux following reimplantation into the

216 bladder. When the length of the resected ureter exceeds 20mm, we believe that the ureteral edges
217 are too far to allow a safe end-to-end anastomosis, and thus the risk of leakage would justify a
218 reimplantation into the bladder. A double J stent is left behind for 4 weeks following surgery. A
219 follow up renal ultrasound is performed after three weeks to rule out an eventual hydronephrosis.

220 Deeply infiltrating lesions of the bladder may include partial-thickness infiltrating lesions
221 limited to the bladder muscularis, which can be managed by resection of the nodule without
222 bladder opening (shaving). Full-thickness infiltrating lesions involving total infiltration of the
223 muscularis or mucosa as well result in a full-thickness resection with bladder opening (Fig 2).
224 This can usually be accomplished by laparoscopy alone. In cases where nodules are large, a
225 combined cystoscopy-guided laparoscopic route is preferred with a goal to economize resection
226 while achieving complete removal of the nodule. (7) The bladder is reapproximated in two layers
227 with absorbable running sutures (Vicryl 2/0 or Monocryl 2/0). Seven to 10 days postoperatively,
228 a retrograde cystogram is performed to confirm a water-seal bladder and therefore allows
229 removal of the urinary catheter. When cystogram reveals incomplete healing, the urinary catheter
230 is left in place for another 7 days with a subsequent retrograde cystogram before considering
231 catheter removal. If healing is not achieved within a month, a second surgery can be discussed
232 depending on the size of the bladder defect. However, the surgeon should be aware about the
233 difficulty of this second procedure due to friable bladder tissue. Our various surgical techniques
234 used in the treatment of urinary tract endometriosis are demonstrated in Video 1.

235 Statistical analysis was performed using Stata 9.0 software (Stat Corporation, Lakeway
236 Drive, TX, USA). Qualitative variables were presented as number (%), while continuous
237 variables as mean (SD). The present case-series study was approved by the Institutional Ethics
238 Committee for Non Interventional Research.

239

240 **Results**

241 From July 2009 to December 2015, 81 women treated for urinary tract endometriosis were
242 included, 39 of whom were treated for bladder endometriosis, 31 for ureteral endometriosis and
243 11 for both ureteral and bladder endometriosis, leading to a total of 42 cases of ureteral
244 endometriosis and 50 bladder endometriosis. Due to bilateral ureteral localizations in 8 women,
245 50 different ureteral procedures were recorded. They represented 7% of the 1,140 patients

246 managed for endometriosis in our department and recorded in CIRENDO database. 371 of the
247 patients had deep endometriosis infiltrating the rectum or the sigmoid colon. This results that in
248 our database the ratio “digestive tract endometriosis : urinary tract endometriosis” is 4.6:1. Patient
249 characteristics and pre-operative workup data are presented in Table 1.

250 Table 2 presents the surgical procedures performed in relation to the different
251 localizations of endometriosis. 50 women presented with DIE of the bladder, and underwent
252 either full-thickness excision of the nodule (70%) or excision of the bladder wall up to the
253 submucosal layer without opening of the bladder (30%). Before surgery, 26 patients with ureteral
254 involvement presented with hydronephrosis diagnosed by pre-operative imaging. Ureteral
255 stenosis would first result in dilatation of the ureter located above the stricture; these findings can
256 be revealed intraoperatively by the existence of an obvious increase in ureteral diameter along
257 with a strictured segment at the level of the deep endometriosis nodule. Prolonged stenosis will
258 then lead to hydronephrosis, which was revealed pre-operatively in all our cases by pre-operative
259 imaging. 1 patient showed bilateral involvement leading to a total of 27 hydronephrosis recorded
260 in our series. 4 of them showed grade 3 hydronephrosis with renal atrophy on MRI with an
261 average divided renal function of 25% according to a DMSA (dimercaptosuccinic acid) renal
262 scan. The others presented with grade 2 hydronephrosis without significant loss of renal function.

263 Ureterolysis was performed for 39 (78%) ureteral lesions. Eleven (22%) ureteral
264 involvements were treated by primary segmental resection: 4 (8%) patients underwent immediate
265 end-to-end ureteral anastomosis, and 7 (14%) were managed by ureteral reimplantation into the
266 bladder. No nephrectomy was required. Even in the presence of renal atrophy in almost 15% of
267 cases with ureterohydronephrosis, pre-operative renal scintigraphy showed renal function
268 superior than 10% for all affected women; thus it was decided to preserve those kidneys. Among
269 the 11 ureteral specimens removed, intrinsic ureteral endometriosis was histologically revealed
270 in 6 (54.5%) cases (Fig 3).

271 **Complications**

272 Postoperative complications were classified according to the Clavien-Dindo
273 Classification of Surgical Complications; a classification used to rank a complication in an
274 objective and reproducible manner, and were classified as follows: I, minor complications not
275 requiring medical or surgical intervention; II, complications requiring pharmacological treatment

276 or blood transfusion; III, complications requiring re-intervention; IV, life-threatening
277 complications, and V, death. (Table 3)

278 In 42 women operated for ureteral nodules with overall 50 ureteral interventions, 7 (16%)
279 Clavien-Dindo grade III complications were noted.

280 1. One 28-year old patient managed by right ureterolysis for hydronephrosis by a robotic-
281 assisted laparoscopy had a delayed ureteral fistula on the 7th postoperative day, probably due to
282 thermal diffusion of the bipolar current. She was managed by drainage of the uroperitoneum,
283 placement of a double J stent and direct suture of the ureter, followed 7 days later by a
284 nephrostomy. Urinary tract imaging six months and 2 years after the surgery, was uneventful.

285 2. Two patients who underwent ureteral resection with ureteral reimplantation into the
286 bladder, presented with anastomotic leakage on Day 7 postoperatively, treated by the insertion of
287 both ureteral and bladder catheters for a duration of one month. One of them underwent drainage
288 of a urinoma, due to postoperative fever.

289 3. A 38-year old patient underwent hysterectomy, rectal shaving and segmental ureteral
290 resection with end-to-end anastomosis for severe left hydronephrosis. As the double J stent had
291 been placed 6 months before surgery, an extensive calcified crust developed, leading to intra-
292 operative dispersion of microlithiasis into the renal pyelon, rapid postoperative obliteration of the
293 stent and anastomosis leakage; secondary ureteroneocystostomy was performed 2 weeks later.

294 4. A 27-year old patient managed for hydronephrosis and rectal subocclusion underwent
295 right ureterectomy and end-to-end ureteral anastomosis, full-thickness partial bladder resection,
296 colorectal resection and removal of the right parametrium. Massive hematuria suddenly occurred
297 on postoperative day 10, originating from a uterine artery aneurysm draining into the ureteral
298 anastomosis, which was then successfully treated by uterine artery embolization.

299 5. Two patients required a secondary laparoscopy for drainage of pelvic infected
300 hematoma.

301 Grade II complications occurred in 5 (12%) patients, 4 of whom with transient bladder
302 atony defined as a post voiding bladder volume superior than 100cc, managed initially by regular
303 intermittent self-catheterizations for several weeks. In one patient with history of left
304 ureteroneocystostomy who was managed for deep endometriosis of the right ureter and mid
305 rectum with right ureteroneocystostomy and rectal disc excision, long term bladder dysfunction
306 occurred after surgery with vesicoureteral reflux. The patient was followed up regularly every 6

307 months by a urologist and renal ultrasounds. Antibiotics were administrated in the presence of
308 urinary tract infection. In 50 patients managed for bladder endometriosis, Clavien-Dindo grade
309 III complications were recorded in 4 patients (8%):

310 1. A 28-year patient managed by full-thickness partial cystectomy associated with
311 resection of a vaginal nodule, presented with postoperative vesico-ureteral fistula; she was
312 managed laparoscopically by the suture of the bladder 3 months later.

313 2. Delayed healing of the bladder defect was recorded in 2 patients (4%) managed by full
314 thickness partial cystectomy and colorectal resection each one; second surgery was performed
315 respectively 4 and 6 weeks later to secure the bladder defect, with uneventful outcomes.

316 *Mid and long term outcomes*

317 Delayed postoperative outcomes were favourable with a significant improvement in painful and
318 urinary symptoms (Table 4). In a 26 year old patient managed by ureterolysis, hydronephrosis
319 persisted one month postoperatively. Balloon dilation of the ureter was successful in relieving
320 the persistent ureteral stricture. Renal imaging 6 months and 4 years after surgery showed normal
321 calibre of the urinary system. Among 20 women who intended to become pregnant, 14 (70%)
322 succeeded, among whom 11 (78.6%) did so spontaneously and 3 (21.4%) following assisted
323 reproductive technology (ART). There has been no bladder or ureteral recurrence to date.

324 **Discussion**

325 Our case-series shows that surgical management of DIE of the urinary tract may be
326 successfully performed by a trained multidisciplinary team, including a gynecologist, a urologist
327 and, when the digestive tract is also involved, a digestive surgeon. Specific postoperative
328 complications may occur in as many as 16% of women treated for ureteral endometriosis, while
329 the severity of complications in the management of bladder endometriosis appears more limited.

330 The overall rate of complications in those operated for ureteral endometriosis in our
331 series was 28%; more than 50% of them being of Grade 3 ClavienDindo complication, versus a
332 total of 4% complication rate in those operated for bladder endometriosis, all of which are of
333 Grade 3 Clavien-Dindo complication. This can be explained by the more challenging ureteral
334 surgery when compared to that on the bladder. In addition, it is likely that the ureters are more
335 fragile, due to their thin muscular layer, when compared to that of the detrusor muscle.
336 Moreover, their own vascular supply might play a role in the healing process.

337 Even in the presence of favorable long-term outcomes in the majority of women, with
338 improvement of urinary symptoms and pelvic pain, surgeons should be aware of the complexity
339 of surgical procedures and risk of major postoperative complications including bladder
340 denervation, vesico-vaginal or ureteral fistulae and inadvertent ureteral injury in bladder
341 endometriosis.

342 Our study presents a series of patients with deep endometriosis infiltrating the urinary
343 tract, who were managed in a tertiary referral center and benefited from prospective close follow
344 up at long term. Urinary tract endometriosis represents a relatively rare localization of the
345 disease. In our CIRENDO database from July 2009 to December 2015, we have recorded 454
346 patients managed for deep infiltrating colorectal endometriosis versus only 81 women operated
347 for urinary tract endometriosis, resulting in a ratio of 6:1. This prevalence may explain the lack
348 of randomized trials with therefore no substantial guidelines for the treatment of urinary tract
349 endometriosis. It is in our opinion that the collection of such case-series based on prospective
350 recording of data and their pooling into systematic reviews contributes to improved knowledge
351 in this topic.

352 Although ureteral and bladder endometriosis both occur in the urinary tract, they do not
353 frequently coexist ($11/81=13.6\%$ in our series). In ureteral endometriosis, the distal segment of
354 the ureter is the most frequently involved part due to the proximity to the posterior compartment
355 of the pelvic organs. (1) Moreover, it is more likely to be associated with colorectal lesions for
356 the same reason as opposed to bladder endometriosis. (8) In our study, 85 % of women with
357 ureteral endometriosis had associated deep endometriosis localizations, while in bladder
358 endometriosis only 50% of them presented with other deep endometriosis lesions. Ureteral
359 involvement may be either intrinsic or extrinsic. In the extrinsic type, only ureteral adventitia or
360 surrounding connective tissues are involved, whereas the intrinsic type involvement includes the
361 muscularispropria, lamina propria, or ureteral lumen. (9) On the basis of histologic examination
362 of specimens removed through various previous studies, extrinsic disease appeared being more
363 common than intrinsic disease, thus recommending the use of ureterolysis as frequently as
364 feasible.(9) Among our 50 cases of ureteral endometriosis, only 6 (12%) had intrinsic ureteral
365 involvement.

366 Ureteral endometriosis is a serious localization of disease burden, since a significant
367 proportion of patients with ureteral disease do not have specific urinary symptoms for longtime

368 before the diagnosis; at the same time ureteral involvement can potentially lead to urinary tract
369 obstruction with subsequent hydroureter and hydronephrosis. 30% of patients have reduced
370 kidney function at the time of diagnosis, (10) and may present with silent loss of renal function
371 in up to 25–43%. (11) One-third of patients may present with only nonspecific symptoms
372 consistent with pelvic endometriosis, and only one-third of them will have flank pain or
373 symptoms of ‘cystitis’. (12)

374 The best treatment approach for ureteral endometriosis remains a subject to controversy.
375 Treatment is generally aimed at relieving symptoms and ureteral obstruction and save a damaged
376 kidney. The potential risk of renal function loss is an indication for surgical intervention. Choice
377 between a conservative and a more aggressive surgical approach depends on the pre-operative
378 workup and on whether intra-operatively ureterolysis alone is sufficient to relieve ureteral
379 obstruction. It also strongly depends on the surgeons’ experience and beliefs in relation to a
380 radical or a more conservative approach. Whatever the procedure employed, the risk of major
381 complications exist; some of them are well known, such as ureteral necrosis and fistula following
382 ureterolysis, anastomosis leakage after end-to-end anastomosis or reimplantation, vesicoureteral
383 reflux after reimplantation, while others are rare such as aneurysm of uterine artery or stenosis of
384 the ureter.

385 Our results with laparoscopic ureterolysis are consistent with previous reports that
386 support the efficiency of the conservative laparoscopic strategy. Nezhat *et al.* (13) reported the
387 resolution of ureteral obstruction in a series of 21 patients with severe ureteral endometriosis, 10
388 of which were operated with laparoscopic ureterolysis. Seracchioli *et al.* (14) successfully
389 performed laparoscopic ureterolysis in 22 cases of 30 with ureteral endometriosis, whereas eight
390 patients were treated either with uretero-ureterostomy or with ureteroneocystostomy.

391 Even though 64% of cases showed severe ureteral stenosis leading to
392 hydroureteronephrosis, only 22% ureteral resections were performed. This means that 65% of
393 cases with renal complication could avoid a radical ureteral procedure and that a more
394 conservative ureterolysis could be enough to relieve ureteral obstruction and preserve renal
395 function. Ureterolysis in our daily practice is systematically preferred in patients with risk of
396 bladder atony in an aim to prevent vesicoureteral reflux which may be associated with ureteral
397 reimplantation into the bladder, leading to recurrent urinary infection injuring the kidney. In

398 cases in which ureterolysis appears insufficient or the freed ureter is devascularized and is at
399 significant risk of postoperative necrosis, distal ureterectomy with either end-to-end anastomosis
400 or reimplantation were reported to have good long-term results in regards to renal preservation.
401 (15)

402 Bladder endometriosis nodules may present as the consequence of deep progression of an
403 endometriosis lesion situated on the peritoneum of the anterior cul de sac, or as an extension of
404 an anterior uterine adenomyoma. (16) In this latter case, complete resection of the adenomyoma
405 is unlikely, unless hysterectomy is planned. Bladder endometriosis often mimics recurrent
406 cystitis, but rarely results in severe complications (17) Surgery is the treatment that leads to a
407 more complete cure, long-term relief of symptoms, improvement of quality of life and low
408 recurrence (18-20). Literature demonstrates that resection of bladder endometriosis nodules is
409 usually an unchallenging procedure. Care should be taken when dealing with those extending
410 from a uterine adenomyoma as no dissection plane exists, and the uterine wall should be
411 conserved in those with a desire to conceive.

412 Lesions in bladder endometriosis infiltrate the bladder from the outside towards the
413 mucosa, and therefore cannot always be visualized by bladder endoscopy and cannot be
414 completely excised through the urethra alone by endoscopic procedures such as transurethral
415 resection of the bladder (TURB). Cystoscopy is not mandatory and will infrequently be helpful
416 in the diagnosis of bladder endometriosis. Occasionally, cystoscopy may reveal a bluish tinge to
417 the mucosa, but a negative cystoscopy does not rule out significant invasion of the muscularis.
418 Yet, cystoscopy may be used to assess bladder mucosal infiltration, evaluate the distance of such
419 an infiltration to ureteral openings or in order to simply incise the mucosa surrounding the
420 nodule before laparoscopic removal of the lesion, when endometriosis lesions are large, located
421 on the bladder trigone, or in close contact with the ureteral openings (7). Moreover, ureteral
422 double JJ stents are placed pre-operatively or intra-operatively to avoid direct ureteral injury and
423 reduce the risk of ureteral fistula by thermal diffusion.

424 Surgery of bladder endometriosis may be complicated by incomplete healing of the
425 bladder or suture leakage, mainly due to any inadvertent obstruction of the urinary catheter
426 during the first postoperative week. Therefore, a postoperative cystogram is necessary to detect
427 such a complication before removing the catheter. In our experience, the management of such a

428 complication requires prolonged bladder catheterization rather than secondary surgery, as
429 secondary bladder suturing may be challenging during the month following surgery, due to the
430 high friability of tissue.

431 The type of complications is consistent with that reported in literature even though with a
432 higher rate of complications due mainly to the higher number of concomitant procedures on
433 other organs and previous surgical history. (21-23)

434 Our series confirm previous reports suggesting that the surgery of urinary tract
435 endometriosis may be performed using minimally invasive techniques, with favourable long-
436 term outcomes. Conservative management of ureteral endometriosis may be employed in the
437 majority of patients, as endometriosis may be only extrinsic even in cases with hydronephrosis.
438 In addition, we reveal some less frequent major complications, which surgeons should be aware
439 of, as they require rapid management to avoid unfavourable outcomes.

440
441 **Conflicts of interest:** Horace Roman reports personal fees for participating in a symposium and
442 a master class presenting his experience in the use of PlasmaJet.

443 **Authors' role:** Basma Darwish, Emanuala Stochino-Loi and Horace Roman checked data
444 recording and wrote the first draft of the report. Geoffroy Pasquier, Fabrice Dugardin, Guillaume
445 Defortescu, Basma Darwish and Horace Roman performed surgical procedures. Basma Darwish
446 and Carole Abo revised the manuscript. All authors contributed to the writing of the final
447 manuscript and approved it to be published.

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453 CIRENDO database. The authors are grateful to Nikki Sabourin-Gibbs, Rouen University
454 Hospital, for her help in editing the manuscript.

455

456 **Legends:**

457 Fig 1. Complete ureterolysis before ureteral resection for ureteral endometriosis.
 458 * = intrinsic ureteral endometriosis which has erupted in a fleshy surface lesion
 459 <- = small pool of 'chocolate' fluid released during ureterolysis

460 Fig 2: *Top left:* Magnetic resonance Imaging (MRI) features of bladder endometriosis, by
 461 extension of an anterior uterine adenomyoma, indicated by an arrow. *Top right, bottom left and*
 462 *right:* Laparoscopic view of bladder endometriosis by extension of an anterior uterine
 463 adenomyoma Fig 3: Intrinsic endometriosis ; → Intrinsic endometriosis causing obstruction ;
 464 *Hydroureter.

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530

Table 1 : Patient Characteristics

	Ureteral endometriosis N=42	Bladder endometriosis N=50
Age (yrs; mean +/-SD)	34.8±6.7	30.1±5.1
Parity		
• Nulliparous	28 (66.7)	38 (76)
• Para >1	14 (33.3)	12 (24)
History of painful symptoms		
• Dysmenorrhea (years)	12.4±7.53	6.74±5.84
• Deep dyspareunia (years)	6.78±6.28	4.14±4.01
• Non menstrual pain (days/month)	9.6±9.44	10.28±7.69
Hydronephrosis	27 (64.2) *	5 (10) **
Renal atrophy	4 (9.5)	0 (0)
Divided Renal Function according to renal scintigraphy	25.3 ± 13.8	N/A
Fertility History		
• No infertility	13 (31)	11 (22)
• Primary infertility	20(47.6)	21(42)
• Secondary infertility	1 (2.4)	1 (2)
• Unknown infertility	8 (19)	17 (34)
Ureteral endometriosis		
• Left	17 (40.5)	4 (8)
• Right	17 (40.5)	5(10)
• Bilateral	8 (19)	2 (4)
Bladder endometriosis		
• Supratrigonal	11 (100)	49 (98)
• Trigonal	0	1 (2)
Previous surgery for endometriosis	11 (26.2)	9 (18)
Preoperative workup		
• MR imaging	42 (100)	50 (100)
• EndoRectal Ultrasonography	39 (93)	20 (40)
• Pelvic ultrasonography	13 (31)	17 (34)
• Cystoscopy	1(2.4)	2 (4)
• Renal ultrasonography	17 (40.5)	9 (18)
• Renal Scintigraphy	4 (9.5)	0
• Virtual colonoscopy	26 (61.9)	29 (58)

*3 patients with bilateral hydronephrosis; **1 patient with bilateral hydronephrosis.

Table 2 Surgical Procedures performed in patients with urinary endometriosis (N = 92)

	Ureteral Endometriosis N = 42 (46%)	Bladder Endometriosis N = 50 (54%)
ASFr-Classification		
Stage I	0 (0)	4 (8)
Stage II	2 (4.8)	18 (36)
Stage III	11 (26.2)	8 (16)
Stage IV	29 (69)	20 (40)
Urinary Tract Surgical Procedures *		
Ureterolysis	39 (78)	8 (15.4)
Ureterectomy + end-to-end ureteral anastomosis	4 (8)	2 (3.8)
Ureterectomy + ureteroneocystotomy	7 (14)	3 (5.8)
Nephrectomy	0	0
Partial cystectomy	11 (26.2)	50 (100)
Full thickness	6 (54.5)	35 (70)
Without opening the bladder	5 (45.5)	15 (30)
Digestive Tract Surgical Procedures**		
Rectal shaving	13 (31)	8 (16)
Disc Excision	8 (19)	3 (6)
Colorectal resection + colorectal anastomosis	17 (40.5)	19 (38)
Temporary stoma	9 (21.4)	15 (30)
Small bowel resection	1 (2.4)	7 (14)
Other surgical Procedures		
Excision of vaginal nodules	24 (57.1)	22 (44)
Ovarian endometrioma ablation using plasma energy	17 (40.5)	16 (32)
Ovarian endometrioma cystectomy	1 (2.4)	2 (4)
Total hysterectomy	4 (9.5)	1 (2)
Double J stent	23 (54.8)	26 (52)
Surgical Route		
Laparoscopy	35 (83.3)	45 (90)
Laparotomy	1 (2.4)	1 (2)
Robotic Assistance	6 (14.3)	4 (8)
Intraoperative Complications		
Hemorrhage requiring laparoconversion	1 (2.4)	1 (2)

*Due to bilateral involvement, 50 procedures were performed in the group of women with ureteral endometriosis and 52 in that of women with bladder endometriosis

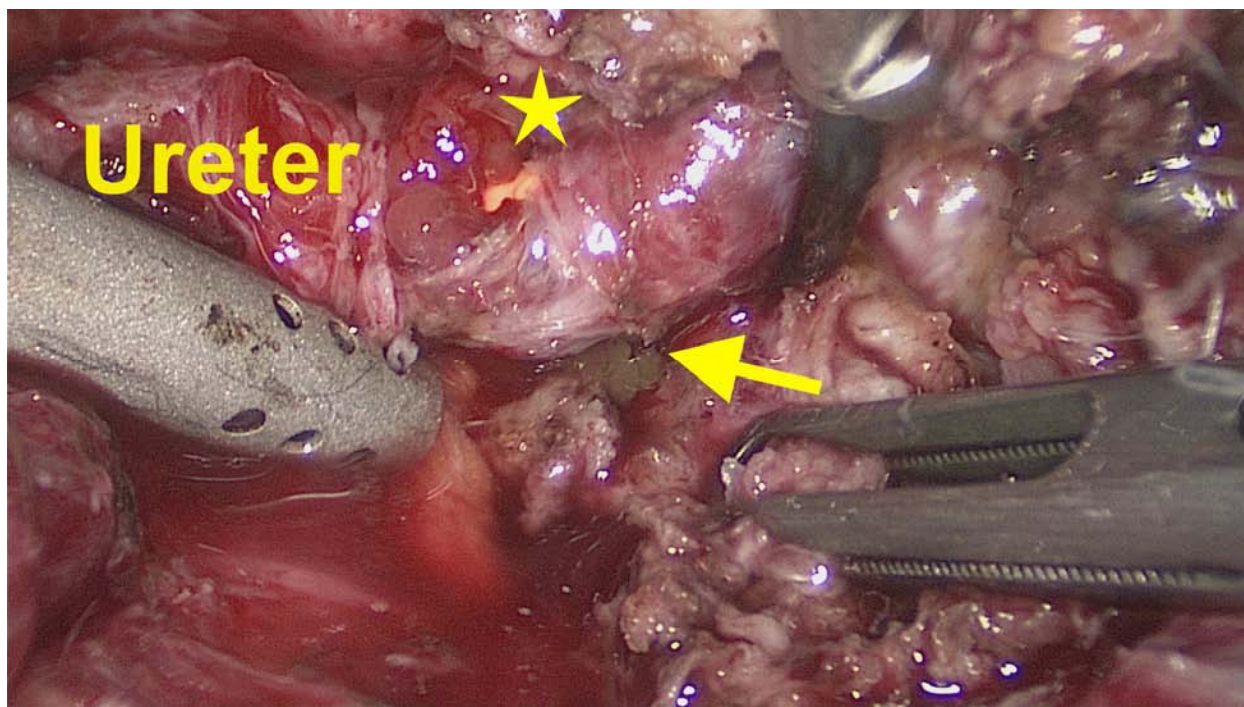
** Several patients underwent more than 1 surgical Procedure

Table 3 Postoperative Complications using Clavien-Dindo Classification

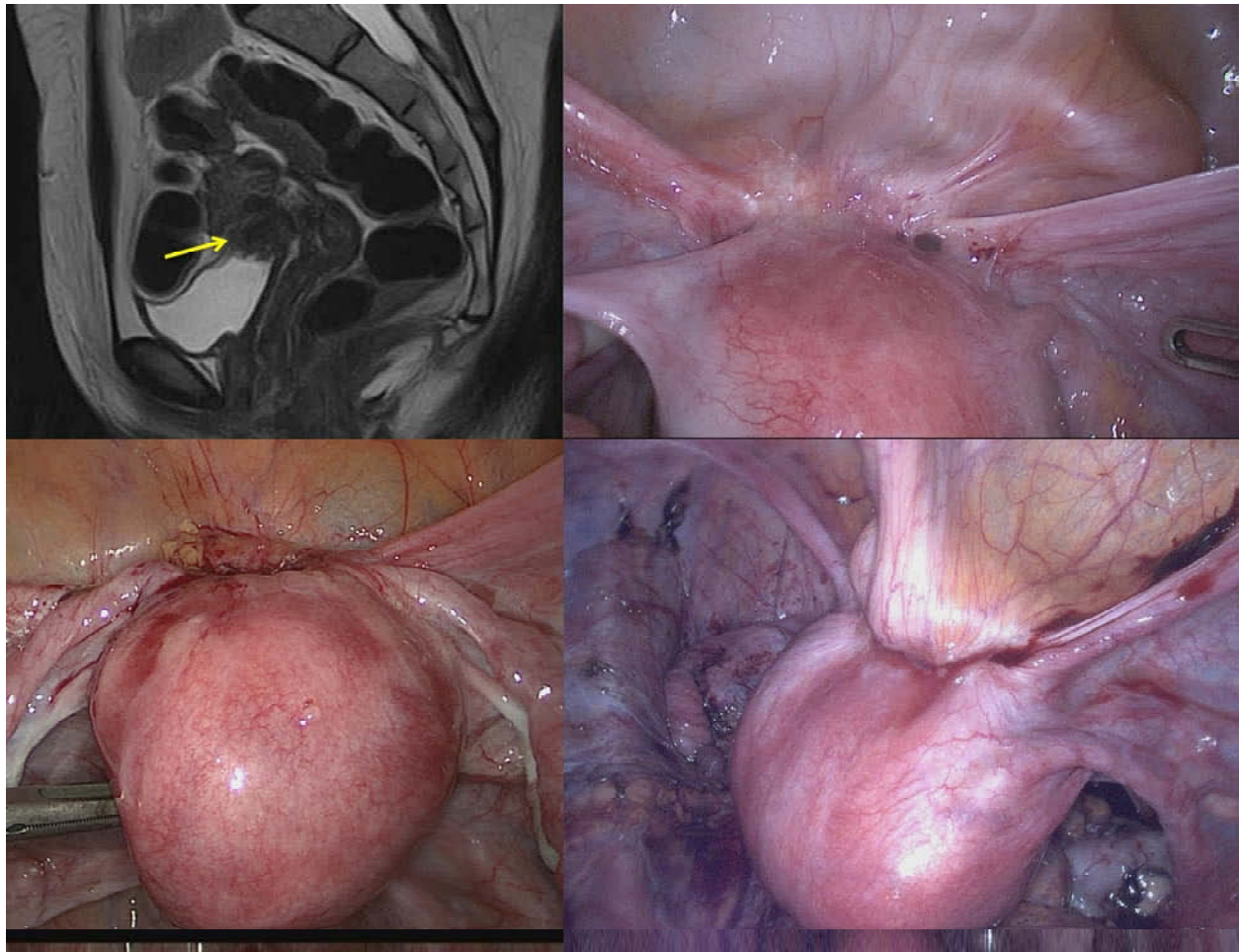
Clavien-Dindo Classification	Ureteral Surgery Complications	N=42 (%)
Grade 2	Long-term bladder dysfunction and vesico-ureteral reflux	1 (2.4)
	Transient bladder atony	4 (9.5)
Grade 3	Ureteral Fistula	1 (2.4)
	Anastomosis leakage	3 (7.1)
	Uterine artery aneurysm	1 (2.4)
	Bladder Surgery Complications	N = 50 (%)
Grade 3	Vesico-ureteral fistula	1 (2)
	Delayed healing of bladder defect	1 (2)

Table 4 Pre and Post Operative Symptoms

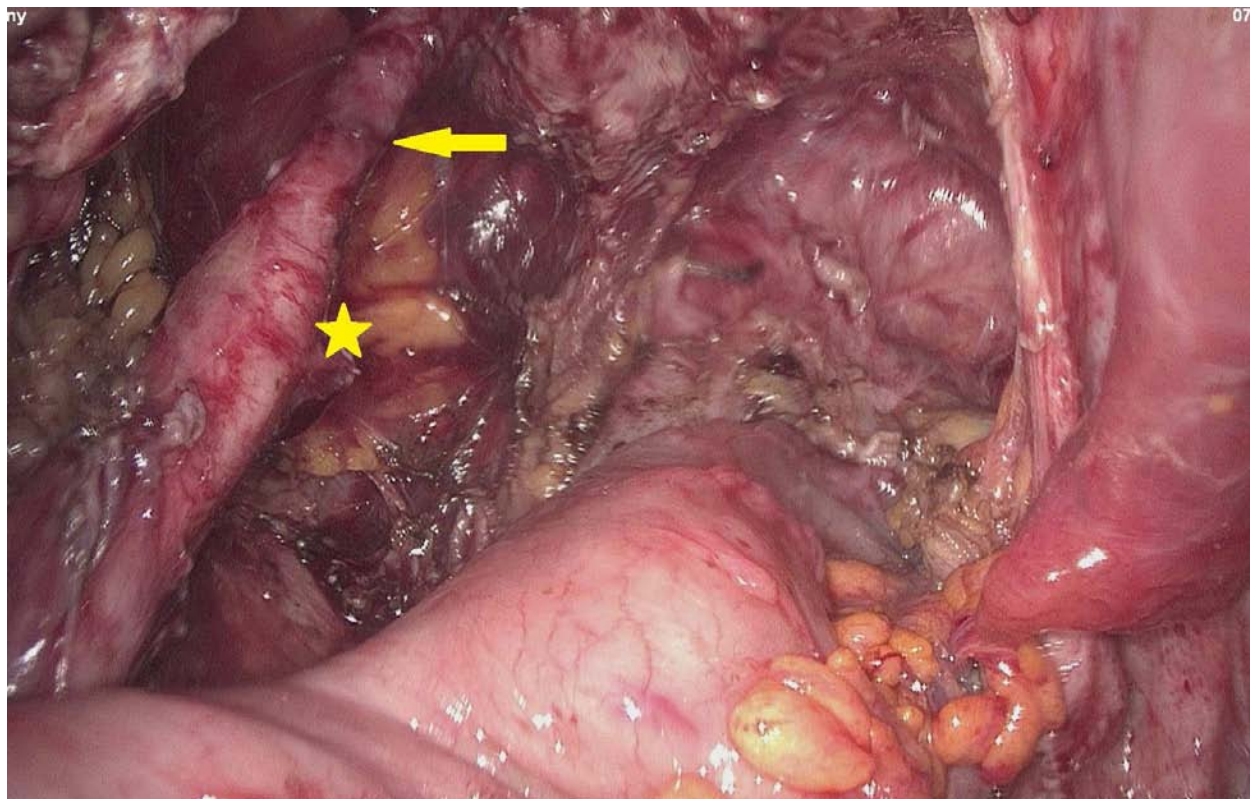
	Preoperative Symptoms Ureteral endometriosis N=42	Preoperative Symptoms Bladder endometriosis N=50	Postoperative Symptoms Ureteral endometriosis N = 42	Postoperative Symptoms Bladder endometriosis N = 50
Urinary Handicap Score				
Urinary Incontinence Score	1.2 ± 0.8	1.5 ± 0.3	1.1 ± 1.3	1.6 ± 1.2
Urinary Urgency Score	1.7 ± 0.9	2.9 ± 1.2	1.3 ± 1.5	2.1 ± 1.7
Pollakiuria Score	2.4 ± 1.3	3.2 ± 1.1	1.6 ± 1.7	1.6 ± 1.8
Dysuria Score	2.3 ± 1.2	3.4 ± 0.7	0.7 ± 1.4	0.9 ± 1.3
Painful Symptoms using 10-point analog evaluation score				
Dysmenorrhea	8.25±1.77	8.6±1.21	1.5 ± 3.3	2.1 ± 2.7
Non menstrual pain	5.34±2.20	6.19±2.55	2.4 ± 3.6	2.3 ± 3
Deep dyspareunia	6.07±2.41	5.98±2.16	2.4 ± 3.8	2.6 ± 3.2



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Precis:

Surgical management of urinary tract endometriosis is feasible with good functional outcomes; however, the risk of major complications should not be overlooked.

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