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## Surgery in Motion

## **Robot-assisted Radical Cystectomy with Orthotopic Neobladder Reconstruction: Techniques and Functional Outcomes in Males**

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Article info	Abstract	
<i>Article history:</i> Accepted April 3, 2023	<b>Background:</b> Little is known regarding functional outcomes after robot-assisted radical cystectomy (RARC) and intracorporeal neobladder (ICNB) reconstruction.	
Associate Editor	RARC and ICNB reconstruction and investigate predictors of these outcomes.	
Alexandre Mottrie	<b>Design, setting, and participants:</b> We used data from a multi-institutional database of patients who underwent RARC and ICNB reconstruction for bladder cancer.	
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*Keywords:* Bladder cancer Functional outcomes Robotic surgery

Measurements: The outcomes measured were UC and EF at 12 mo.

**Results and limitations:** A total of 732 male patients were identified with a median age at diagnosis of 64 yr (interquartile range 58–70). The ICNB reconstruction technique was Studer/Wiklund in 74%, S pouch in 1.5%, Gaston in 19%, vescica ileale Padovana in 1.5%, and Hautmann in 4% of cases. The 12-mo UC rate was 86% for daytime and 66% for nighttime continence, including patients who reported the use of a safety pad (20% and 32%, respectively). The 12-mo EF rate was 55%, including men who reported potency with the aid of phosphodiesterase type 5 inhibitors (24%). After adjusting for potential confounders, neobladder type was not associated with UC. Unilateral nerve-sparing (odds ratio [OR] 3.85, 95% confidence interval [CI] 1.88–7.85; p < 0.001) and bilateral nerve-sparing (OR 6.25, 95% CI 3.55–11.0; p < 0.001), were positively associated with EF, whereas age (OR 0.93, 95% CI 0.91–0.95; p < 0.001) and an American Society of Anesthesiologists score of 3 (OR 0.46, 95% CI 0.25–0.89; p < 0.02) were inversely associated with EF.

**Conclusions:** RARC and ICNB reconstruction are generally associated with good functional outcomes in terms of UC. EF is highly affected by the degree of nerve preservation, age, and comorbidities.

**Patient summary:** We investigated functional outcomes after robot-assisted removal of the bladder in terms of urinary continence and erectile function. We found that, in general, patients have relatively good functional outcomes at 12 months after surgery.

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#### 1. Introduction

Bladder cancer (BC) is the seventh most common cancer diagnosed in males, with an age-standardized incidence of 20 new cases per 100 000 every year in Europe [1]. BC has a high mortality rate and it has been shown that up to 85% of patients with muscle-invasive BC (MIBC) would succumb to the disease within 5 yr of diagnosis if left untreated [2]. The European Association of Urology (EAU) guidelines recommend radical cystoprostatectomy (RC) with or without perioperative chemotherapy in patients with MIBC and selected cases of high risk non-muscle-invasive BC [1]. Although RC represents a potentially curative approach, it is hampered by high rates of perioperative morbidity [3,4]; it also has a profound impact on postoperative sexual function and urinary continence (UC) in cases of orthotopic neobladder reconstruction [5].

After the first description of robot-assisted RC (RARC) in 2003 [6], there has been a steady increase in the use of RARC in an effort to reduce perioperative complications and improve functional outcomes. RARC combines the benefits of a minimally invasive approach with the improved vision and precision of a robotic surgical platform [7]. With the increase in cumulative surgical experience, we have witnessed several refinements in the surgical technique, moving from extracorporeal to a complete intracorporeal technique for urinary diversion [8].

The recent publication of the first multicenter randomized control trial comparing RARC with intracorporeal reconstruction to open RC showed a moderate but statistically significant increase in the number of days alive and out of the hospital within 90 d of surgery, providing level 1 evidence in support of RARC with intracorporeal urinary diversion over open RC [9].

While techniques aimed at improving functional outcomes after RARC have been described [10,11], there is a paucity of data on postoperative UC and erectile function (EF) in patients who have undergone RARC and neobladder reconstruction, and such data are usually derived from relatively small single-center series. With that in mind, we conducted a multicenter study in an effort to evaluate EF and UC in male patients undergoing RARC with neobladder reconstruction.

#### 2. Patients and methods

#### 2.1. Patient population

For the present study, data were collected from high-volume robotic surgical centers across Europe. For the scope of the study, we included only male patients who underwent RARC with neobladder reconstruction and had at least 12 mo of follow-up. The project was sponsored by the Scientific Working Group of the Robotic Urology Section of the EAU.

#### 2.2. Surgical technique

Patients were treated with neoadjuvant chemotherapy (NAC) or directly underwent radical cystoprostastectomy and bilateral pelvic lymph node dissection. NAC was administered according to the EAU guidelines. Patients underwent surgery without NAC in cases of cisplatinineligibility, if they refused NAC, or at the physician's discretion.

The robotic surgical approach consisted of a multiport technique with four robotic arms and laparoscopic assistance via two assistant ports, generally one 5-mm port and one 12-mm or 15-mm port. If laparoscopic assistance was provided from the left-hand side of the patient, an additional 12-mm or 15-mm trocar was placed on the patient's right-hand side where the fourth arm was inserted, as this was used to insert and use the laparoscopic stapler. If assistance was provided from the lefthand side, the fourth arm was placed on the right-hand side of the patient and only a 12-mm or 15-mm trocar was used for laparoscopic assistance. The patient was placed supine in the Trendelenburg position. De-docking and reduction of the Trendelenburg angle after the extirpative phase of the procedure were performed at the physician's discretion.

The cystoprostatectomy sensu stricto followed the conventional steps. In brief, the ureters were isolated. The seminal vesicle and the posterior plane of the prostate were freed. The lateral aspects of the bladder were dissected free and the pedicles were sectioned. The prostate was dissected in toto and the urethra was spared. In general, the neurovascular bundles were preserved completely in the absence of clinical suspicion of prostate cancer in patients with good preoperative EF.

For the reconstructive phase of the procedure, an ileal segment of approximately 40–50 cm in length was typically identified and isolated. The segment was then detubularized on its antimesenteric side and the reconstruction was initiated. This phase followed the steps of the surgeon's preferred technique. Examples of surgical techniques for neobladder reconstruction are provided in the video that accompanies the article.

The main difference among the techniques used in the different hospitals was anastomosis of the left ureter. If a modified Studer or Wiklund technique was adopted, the left ureter was going to cross the patient's midline via an incision in the mesosigmoid. In this case, the left and right ureters were anastomosed together to the afferent limb (chimney) of the orthotopic reservoir (Fig. 1A). For the other techniques, anastomosis of the left ureter to the neobladder was realized on the left-hand side of the neobladder without a need for the ureter to cross the midline (Fig. 1B). Ureteral-ileal anastomosis was realized via continuous or interrupted stitches, according to the surgeon's preference. Ureteral stents were placed before the ureteral anastomosis and generally left in situ for approximately 15 d after surgery. The neobladder catheter is generally removed at 14–21 d after surgery.

#### 2.3. Functional outcomes

#### 2.3.1. Urinary continence

UC was recorded separately for daytime and nighttime. Continence was defined as complete dryness along with no need for pads or condom

devices. The use of pads or condom devices during the day or night was recorded. In addition, patients were asked about the need for clean intermittent catheterization (CIC) if they were not able to spontaneously empty their orthotopic reservoir. Continence rates were assessed at 12 mo after surgery

#### 2.3.2. Erectile function

EF results are reported for patients who underwent nerve-sparing surgery and for whom data were available. Patients were asked about their EF, their need for medication, and, if so, what class of medication. Potency was defined as the ability to achieve and maintain a penile erection sufficient for sexual intercourse. Data on EF at 12 mo are reported.

#### 2.4. Statistical analyses

Descriptive statistical analyses were performed, with the median (interquartile range [IQR]) reported for continuous variables and the frequency (proportion) for categorical variables. In an effort to identify factors associated with functional outcomes, we used multivariable logistic regression to predict UC and EF at 12 mo. Logistic regression was chosen over a time-dependent analysis as the outcomes were assessed at a prespecified time point. The analyses were adjusted for age, American Society of Anesthesiologists (ASA) score, body mass index, and proxies for a more extensive dissection, such as pT stage and number of lymph nodes removed.

#### 3. Results

#### 3.1. Patient population

Overall, 732 male patients with complete data were considered for the study. Detailed characteristics of the patient population are provided in Table 1. The median age at diagnosis was 64 yr (IQR 58–70) and median BMI was 26 kg/m<sup>2</sup> (IQR 24–29). The median total operative time was 368 min (IQR 300–450). Overall, RARC was performed in 344 cases (48%) of high-risk or treatment-refractory non-muscle-



Fig. 1 – Anastomosis of the left ureter after its passage below the mesosigmoid (A). The left and right ureters are anastomosed together and then to the afferent limb (chimney) of the orthotopic reservoir. This step represents the main difference between the Studer/Wiklund technique and the other ones. For the other techniques, anastomosis of the left ureter to the neobladder is realized on the left-hand side of the neobladder without a need for the ureter to cross the midline (B).

Table 1 – Descriptive characteristics of the patient population (n = 732)

Parameter	Result		
Median age at diagnosis, yr (IQR)	64 (58-70)		
ASA score, n (%)			
1	115 (16)		
2	434 (59)		
3	183 (25)		
Median BMI, kg/m <sup>2</sup> (IQR)	26 (24-29)		
Pathologic T stage, $n$ (%)			
pT0	253 (35)		
PTa/pT1/carcinoma in situ	209 (29)		
pT2	110 (15)		
pT3	107 (15)		
pT4	53 (6)		
PLND template, $n$ (%)			
Limited	38 (5)		
Standard	212 (29)		
Extended	461 (63)		
Superextended	21 (3)		
NVB, n (%)			
None	252 (34)		
Unilateral	84 (12)		
Bilateral	396 (54)		
Lymph node status, n (%)			
Negative	620 (85)		
Positive	112 (15)		
Concomitant prostate cancer, n (%)			
Absent	475 (65)		
Present	257 (35)		
Soft tissue margins, n (%)			
Negative	713 (97)		
Positive	19 (3)		
Prostate margins, n (%)			
Negative	711 (97)		
Positive	21 (3)		
Median total operative time, min (IQR)	368 (300-450)		
ASA = American Society of Anesthesiologists; BMI = body mass index;			
IQR = interquartile range; NVB = neurovascular bundle; PLND = pelvic			
lymph node dissection.			

invasive BC. NAC was administered to 295 individuals (40%). A total of 462 patients (64%) had pT0 or pTa/1/carcinoma in situ (CIS) disease on final pathology, of whom 130 had MIBC and had been downstaged after administration of NAC. Positive lymph nodes were observed in ten patients (4%) with pT0 and 24 (12%) with pTa/1/CIS disease.

The neobladder reconstruction technique was the Studer/Wiklund in 534 patients (74%), the S pouch in 11 (1.5%), the Gaston in 137 (19%), the vescica ileale Padovana in 12 (2%), and the Hautmann in 29 (4%).

#### 3.2. Functional outcomes

#### 3.2.1. Urinary continence

Data on UC are reported in Table 2. A total of 487 men (66%) were completely continent during the day without a need for pads or condom devices. A total of 145 (20%) reported wearing a safety pad or use of one pad during the day. If the two groups are considered together, UC during the day was reported by 86% of the patients. Thirty-four patients (5%) reported the use of two pads per day. A minority of the patients were incontinent: 27 (3.7%) reported use of three or more pads per day and five (0.7%) used a condom device to collect any leakage. Finally, 34 men (4.6%) had hypercontinence and an inability to properly void their orthotopic reservoir and reported performing CIC when

Table 2 – Daytime and nighttime urinary continence outcomes at 12 mo after surgery

Outcome	Patients, n (%)
Daytime continence	
No need for pads	487 (66)
Security pad or one pad	145 (20)
2 daily pads	34 (5)
$\geq$ 3 daily pads	27 (3.7)
Uridom	5 (0.7)
Hypercontinent	34 (4.6)
Nighttime continence	
No need for pads	246 (34)
Security pad or one pad	237 (32)
2 pads	95 (13)
$\geq$ 3 pads	46 (6)
Uridom	78 (11)
Hypercontinent	30 (4)

feeling the stimulus of abdominal distension or at specific time intervals. The daytime continence rates across the different neobladder types were: 68%, for the Studer/Wiklund, 91% for the S pouch, 62% for the Gaston, 58% for the vescica ileale Padovana, and 52% for the Hautmann technique.

Regarding nighttime continence, a total of 246 patients (34%) were completely continent, and 237 men (32%) reported wearing a safety pad or using one pad overnight. If the two groups are considered together, nighttime UC was reported by 66% of the patients. Ninety-five men (13%) reported the use of two pads during the night. Forty-six (6%) reported the use of three or more pads and 78 (11%) used a condom device to collect any leakage. Finally, 30 individuals (4%) complained of hypercontinence and woke up at regular intervals during the night to perform CIC. The complete nighttime continence rates across the different neobladder types were 32% for the Studer/ Wiklund, 18% for the S pouch, 43% for the Gaston, 33% for the vescica ileale Padovana, and 24% for the Hautmann technique.

We used multivariable analysis to evaluate predictors of the use of one or more pads per day, after exclusion of the patients who had hypercontinence (n = 34; Supplementary Table 1). No significant predictor of 12-mo daytime continence emerged, including neurovascular bundle preservation, either unilaterally or bilaterally (both  $p \ge 0.7$ ). Notably, neobladder type was not associated with continence at 12 mo (all  $p \ge 0.08$ ).

#### 3.2.2. Erectile function

Data on EF are reported after exclusion of patients who did not undergo nerve-sparing surgery (n = 133, 18%) and those for whom potency data were not available (n = 86, 12%; Table 3). Overall, 158 patients (31%) reported full potency without a need for any medication; 125 men (24%) were potent with the use of an oral phosphodiesterase type 5 inhibitor (PDE5i). If the two groups are considered together, EF was achieved by 55% of the patients. A total of 25 men (5%) reported EF with the use of intracavernosal injections; 124 patients (24%) were not potent at 12 mo after surgery and 81 (16%) were not sexually active.

After adjusting for potential confounders, predictors of EF (as either full EF or with the use of oral PDE5i) were unilateral nerve-sparing (odds ratio [OR] 3.85, 95% confidence

#### Table 3 – Erectile function outcomes at 12 mo after surgery <sup>a</sup>

Erectile function	Patients, n (%)			
Potency with no need for medication	158 (31)			
Potency with PDE5i	125 (24)			
Potency with intercavernosal injections	25 (5)			
Impotent	124 (24)			
Not sexually active	81 (16)			
PDE5i = phosphodiesterase type 5 inhibitor.				
<sup>a</sup> Data are reported after exclusion of patients who did not undergo				
nerve-sparing surgery ( $n = 133, 18\%$ ) and those for whom potency				
data were not available ( $n = 86, 12\%$ ).				

Table 4 – Multivariable analysis predicting erectile function at 12 mo after surgery

Covariate	OR (95% CI)	p value		
Age at diagnosis	0.93 (0.91-0.95)	<0.001		
ASA score				
1	Reference			
2	0.84 (0.49-1.43)	0.5		
3	0.46 (0.25-0.89)	0.02		
BMI	0.98 (0.94-1.03)	0.5		
NVB preservation				
None	Reference			
Unilateral	3.85 (1.88-7.85)	< 0.001		
Bilateral	6.25 (3.55-11.0)	< 0.001		
Number of LNs removed	1.01 (0.99-1.03)	0.2		
Pathologic T stage				
pT0	Reference			
pTa/pT1/CIS	0.64 (0.40-1.03)	0.06		
pT2	0.63 (0.35-1.12)	0.1		
pT3-4	2.12 (0.93-4.81)	0.07		
ASA = American Society of Anesthesiologists; CI = confidence interval; CIS = carcinoma in situ; LNs = lymph nodes; NVB = neurovascular bundle; OR = odds ratio				

interval [CI] 1.88–7.85; p < 0.001) and bilateral nervesparing (OR 6.25, 95% CI 3.55–11.0; p < 0.001), which were positively associated with EF; whereas age (OR 0.93, 95% CI 0.91–0.95; p < 0.001) and an ASA score of 3 (OR 0.46, 95% CI 0.25–0.89; p < 0.02) were inversely associated with EF (Table 4).

#### 4. Discussion

We report on the largest multi-institutional series of patients who underwent RARC with orthotopic neobladder reconstruction. Our data demonstrate that the functional outcomes following neobladder reconstruction are generally good, especially regarding UC.

Neobladder reconstruction is generally more technically demanding than reconstruction of an incontinent diversion and a steep learning curve is involved [12,13]. In the case of neobladder reconstruction, patients have to be counseled about potential postoperative surgical complications and long-term complications related to interposition of a bowel segment in the urinary tract [14–17]. Such complications include electrolyte and/or acid base imbalance, cholelithiasis, nephrolithiasis, and neobladder calculi due to impaired reabsorption of bile acids and oxalate reabsorption, vitamin B12 deficiency, infections, and potential reabsorption of certain medications [15]. While these potential postoperative issues have been thoroughly described in prior articles,

our study, focusing on functional outcomes, provides important data for patient counseling regarding expected rates of postoperative UC and EF. Notably, the technique for neobladder reconstruction was not associated with postoperative UC. However, this analysis was limited by the fact that the vast majority of neobladders in our study were reconstructed using the Studer/Wiklund technique.

The lack of uniform definitions of UC and EF following neobladder reconstruction [18] must be acknowledged. In addition, the rate of UC changes over time because of many factors, one of which is that a neobladder usually requires 6-8 mo to reach its final volume [19]. For this reason, we chose to report functional outcomes at 12 mo after surgery. While some series report continence as complete dryness with no need for pads or condom devices, the majority of published studies define continence as no use of pads (or condom devices) or the use of one pad or safety pad per day. Similarly, regarding EF, patients are generally regarded as potent if they either have spontaneous erections or they use oral PDE5i. With that in mind, we reported our results in a detailed manner, highlighting UC rates according to different continence definitions to facilitate a meaningful comparison across studies with different UC definitions [18].

In a recent review of functional outcomes after RARC and neobladder reconstruction, the postoperative UC rate among male patients ranged between 17% and 100% during the day and between 51% and 75% during the night [18,20]. Most of the studies defined continence as use of zero to one pads. In our multi-institutional series, the daytime and nighttime continence rates were 86% and 66%, respectively, which are in line with literature reports. For example, our results are similar to those reported by Hautmann et al [21] for ileal neobladder reconstruction during open RC in a study spanning 11 yr, in which daytime continence was achieved by 83.7% of patients and nighttime continence by 66.3% within 5 yr of surgery.

In some cases, patients might require CIC. This could be because of strictures between the neobladder and the urethra or to overdistension of the neobladder, which ultimately impairs the possibility to void without a significant postvoid residual volume. The rate of CIC reported ranges between 0% and 33% [18,22]. In our series, the rate of CIC was 4.6% at 12 mo, which is in line with, if not lower than, results reported in the literature.

Data on EF after RARC are sparse. As briefly mentioned, the definitions of potency and the time points for assessment during follow-up vary across different studies [18]. At 12 mo, the post-RARC potency rate ranges between 40% and 86%, depending on the age of the cohort, preoperative sexual status, nerve-sparing status, and postoperative medication use [18,23,24]. One study reported a potency rate of 5% at 6 mo after surgery, which was attributed to the relatively short follow-up and lack of PDE5i use [23]. The largest study on potency after RARC (100 patients) was conducted by Porreca et al [24], who found a potency rate of 31%, with potency defined as adequate erection for intercourse without PDE5i use. In our series, the overall potency rate at 12 mo was 55% (31% without the need for PDE5i and 24% with PDE5i use). Our results are consistent with literature reports, but are limited by the fact that this

outcome was not assessed in all patients included in the current series.

Limitations to the current study include the retrospective design and the fact that patients underwent surgery performed by experienced surgeons at tertiary referral centers. Our study also lacks a comparison of functional outcomes between open RC and RARC with extracorporeal neobladder reconstruction. While our results are indeed important for patient counseling, the aforementioned rates of UC and EF might not be generalizable to surgeons who are at an earlier point of their learning curve. Another limitation, common to all studies in this regard, is the lack of uniform definitions of UC and EF. In an effort to overcome this issue, we reported both outcomes according to prior definitions of each as either more "strict" or more "liberal", together with the overall results, facilitating a meaningful and fair comparison with prior series. Finally, we acknowledge the fact that outcomes were not assessed using validated questionnaires, but this limitation is common to the majority of the studies in this setting.

#### 5. Conclusions

In this multi-institutional study based on the largest database of patients who underwent RARC and intracorporeal neobladder reconstruction, we found that at 12 mo the overall UC rate was 86% for daytime and 66% for nighttime continence, including patients who reported the use of a safety pad (20% and 32%, respectively). Regarding EF, the 12-mo overall rate was 55%, including men who reported potency with the aid of PDE5i use (24%).

**Author contributions**: Abolfazl Hosseini had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hosseini, Wiklund, Martini. Acquisition of data: All authors. Analysis and interpretation of data: All authors. Drafting of the manuscript: Martini, Falagario. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Martini. Obtaining funding: None. Administrative, technical, or material support: None. Supervision: Hosseini, Wiklund.

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#### **Peer Review Summary**

Peer Review Summary and Supplementary data. The Surgery in Motion video accompanying this article can be found in the online version at https://doi.org/10.1016/j.eururo.2023.04.009 and via www.europeanurology.com.

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