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Robot-assisted versus open radical cystectomy: A cohort study on perioperative outcomes accounting for stage selection bias and surgical experience

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Abstract

Background: Most comparisons of robot-assisted (RARC) versus open radical cystectomy (ORC) for urothelial carcinoma do not factor the inherent stage selection bias or surgical experience.

Methods: We compared the perioperative outcomes of 229 RARC and 335 ORC at a single tertiary referral centre with propensity score matching and multiple regression models, when controlling for tumour and patient characteristics, surgeon's experience and type of urinary diversion.

Results: RARC had less major complications (19.8% vs. 34.1%) and ICU admissions (6.6% vs. 19.8%), with lower blood loss (400 vs. 500 ml) and transfusion rates. The operating time was longer (336 vs. 286 min), but decreased with surgeon's experience. RARC had less positive surgical margins (3% vs. 8.4%) and a higher lymph node count (14 vs. 11).

Conclusions: In this large single centre series comparing RARC with ORC controlling for stage selection bias and surgical experience, RARC proved significantly better outcomes, especially with intracorporeal urinary diversion.

KEYWORDS
bladder cancer, cystectomy, robot-assisted surgery, urologic neoplasms, urologic surgical procedures

1 | INTRODUCTION

Since the first robot-assisted radical cystectomy (RARC) in 2003, RARC has been increasingly performed and is now considered a standard surgical approach besides open radical cystectomy (ORC) for the treatment of muscle-invasive bladder cancer.[1–3] However, the gold standard for radical cystectomy is still a matter of controversial debate, and RARC has not fully replaced the open approach, even in experienced centres.[3,4]

Like other interventions, the outcomes of RARC are influenced by a learning curve. According to the International Robotic Cystectomy Consortium (IRCC), acceptable results can be achieved after 30 cases for all urinary diversions, whereas an ongoing decrease of complications has recently been illustrated even after 60 intracorporeal urinary

diversions (ICUD).[5,6] However, RARC is no everyday intervention, which explains why the learning curve is long.[7]

Another factor contributing to the deferred transition from the open to the robotic approach were reports on atypical metastases after RARC, which peaked in 2016.[8–10] The reasons for this phenomenon have not yet been fully understood, but meta-analyses recently indicated that the risk for atypical metastases is low after RARC and decreases with growing surgical expertise.[11–14]

These aspects have led to a significant stage selection bias in most analyses comparing RARC and ORC. Not only in our centre, locally advanced tumours (≥cT3, cN+) have been preferably treated with ORC in recent years. Currently, only five randomised controlled trials (RCTs) have compared both surgical approaches and could not demonstrate a significant superiority of RARC in terms of oncologic or perioperative outcomes.[13,15–18] In contrast, retrospective studies, including meta-analyses, found a lower blood loss and less complications or shorter hospital stays for RARC.[19,20]

For this reason, we performed a longitudinal single centre comparison of more than 550 RARC and ORC to analyse the perioperative outcomes in one of the largest monocentric cohorts so far. For the first time, we aimed to control not only for differences in patient and tumour characteristics, but also for surgeon experience and the type of urinary diversion. The impact of the surgical approach, patient- and tumour-specific factors on outcomes, including complications and intensive care unit (ICU) admissions were compared.

2 | MATERIALS AND METHODS

In a retrospective cohort study, all consecutive ORC and RARC in adults performed for urothelial carcinoma at a tertiary referral centre between 2007 and 2019 were analysed, starting with the initiation of a robotic program for RARC. Data acquisition was performed by reviewing the individual medical records. The robotic surgeons were consultants and experienced in all other urologic robotic interventions, including at least 50–100 radical prostatectomies, (partial) nephrectomies or pyeloplasties.[21,22] They performed RARC as previously described.[23] Neobladders were performed in the 'W'-shaped technique by Hautmann, irrespective of the surgical approach.[24] After radical cystectomy (RC), all patients were admitted to an intermediate care unit by default, and only in the case of severe complications were they admitted to the ICU.

The patient's age, gender, body mass index (BMI) and Charlson Comorbidity Index (CCI) served as patient-related factors. The type of urinary diversion, blood loss, total operating time (including the docking process for RARC), conversions and intraoperative complications were obtained. The intraoperative complications were graded according to the European Association of Urology intraoperative adverse incident classification (EAUiaiC).[25] The experience of a surgeon was defined as the current number of radical cystectomies he or she performed. A robotic surgeon was considered as 'experienced' if he or she had conducted more than 30 RARC, as proposed by the IRCC, and the same threshold was applied for all ORC accordingly.[5] The pathologic results were reviewed, including positive surgical margins (PSMs) and the total lymph node yield. ICU admissions and complications according to Clavien Dindo within 30 days after surgery (major complications defined as ≥grade 3) served as primary outcomes. As secondary outcomes, the operating time, blood loss, number of blood transfusions, rate of PSMs, total lymph node count and length of stay were analysed.

First, an overall comparison was performed between ORC and RARC. In a separate subgroup analysis, all robotic extracorporeal urinary diversions (ECUD) were compared with ICUD. To assess the impact of the urinary diversion on perioperative outcomes, all patients with either ileal conduits or neobladders were compared between ORC, RARC with ICUD and RARC with ECUD in two separate subgroup analyses, too. Next, a propensity score matching was conducted for the surgeon's experience (binary: experienced vs. not experienced), type of urinary diversion (ileal conduit, neobladder vs. other), pT- (≤T1, T2, T3 vs. T4) and pN-stage (N0/Nx, N1 vs. N2) as categorical variables and patient age and CCI as continuous variables (Figure 1). The tolerance rate was set to 0.05 and the matched pairs were compared again between ORC and RARC. To compare the impact of the surgical approach, type of urinary diversion, surgeon's experience, patient age (per 10 years), gender, BMI, CCI (over vs. under median), tumour stage (≤pT2 vs. >pT2) and lymph node metastases (pN+ vs. pN0/X) on outcomes, univariate and multiple linear and logistic regression analyses were conducted in the overall cohort. Independent variables were only included in the multiple regression analysis if the respective effect was significant in the univariate analysis. For multiple regression analyses, forward selection was applied.

Categorical variables were reported as frequencies and proportions, continuous data as the median and range. Fisher's exact, Mann–Whitney U, Kruskal Wallis, McNemar and Wilcoxon rank-sum tests were applied. The statistical analyses were performed with SPSS version 25 (IBM, Armonk, USA). All tests were two-sided, p-values < 0.05 were considered significant. In the event of missing data, cases were excluded. This study was approved by the responsible ethical review board (Bu 181/11, 141/14); all patients provided written informed consent. This analysis has been conducted in adherence with the Helsinki Declaration and the STROBE guidelines (checklist in Supplement).

3 | RESULTS

3.1 | Overall comparison

In total, 564 radical cystectomies (229 RARC and 335 ORC) were included from 2007 to 2019. The median annual caseload did not significantly differ between the groups (20 RARC/year vs. 29 ORC/year) and increased from 10 in 2007 to 31 in 2013 for RARC (Figure 2). All RARC were conducted by five surgeons with a median experience of 28 interventions (range 2–92). All of them performed ORC, which was also conducted by 13 other surgeons.

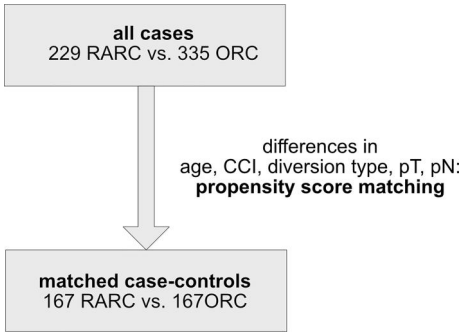

FIGURE 1 As the open and robotic cohorts differed in age, CCI, diversion type, pT- and pN-stage, a propensity score matching was conducted to improve the comparability of 167 matched case-controls

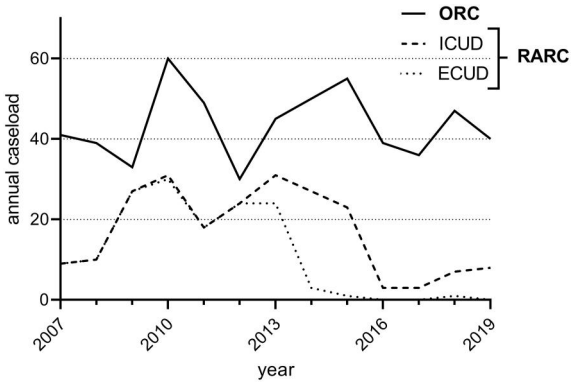

FIGURE 2 Annual caseload of open (bold line) and robot-assisted radical cystectomies (RARC), divided into intra- (dashed line, ICUD) and extracorporeal urinary diversions (dotted line, ECUD), between 2007 and 2019

Patients in the RARC group were younger (68 vs. 73 years) and had a lower CCI (3 vs. 5.5, both $p < 0.001$, Table 1). They had lower pT-stages (pT4 9.2% vs. 17.3%) and less lymph node metastases (pN+ 17.8% vs. 34.9%, both $p < 0.01$). In total, 74 (32.3%) RARC were followed by ICUD, which were predominantly performed after 2013 (Figure 2). Ileal conduits were the most common urinary diversion in both groups (RARC 70.7%, ORC 86.3%, Table 1).

Concerning the primary outcomes, RARC had less overall and major complications (major 21% vs. 32.8%, $p = 0.002$, Table 2) as well as intraoperative complications (13.1% vs. 19.4%, $p = 0.041$). Eight (3.5%) RARC had to be converted, in two cases due to significant obesity and the impossibility to inflate the abdomen and in two other cases because of the suspicion of peritoneal carcinosis. In one case, a bleeding from the periurethral plexus could not be controlled robotically and one lesion in the ileum had to be sutured in an open fashion at the beginning of the learning curve. One patient with significant abdominal adhesions required open division, while the rest of the procedure was performed with robotic assistance. One patient had a pelvic kidney with significant anatomical variations. While grade 3 intraoperative complications only occurred after ORC (2.7% vs. 0%, $p = 0.012$), there was one grade 5 complication during RARC (intraoperative death due to cardiac arrest in the absence of major bleeding, Table S1). ICU admissions were almost three times more frequent after ORC (7.4% vs. 20.3%, $p < 0.001$). As for the secondary outcomes, blood loss (400 vs. 600 ml) and transfusion rates were lower for RARC and the length of stay was shorter (16 vs. 17 days, for all $p < 0.001$). The PSM rate was lower for RARC (2.2% vs. 10.4%) and the total lymph node yield higher (15 vs. 12, both $p < 0.001$). In contrast, the operating time was shorter for ORC (377 vs. 270 min, $p < 0.001$).

3.2 | Subgroup analyses

When comparing only robotic ICUD with ECUD, patients in the ICUD group were significantly older (69 vs. 66 years) and had a higher CCI (4 vs. 3, both $p < 0.05$, Table S2). The robotic surgeons performing ICUD were more experienced than for ECUD (median experience for ICUD: 52.5 RARC vs. ECUD: 20 RARC, $p < 0.001$). There were no significant differences regarding the perioperative outcomes, except for blood loss which was significantly lower for ICUD (300 vs. 400 ml, $p = 0.01$).

When analysing patients with ileal conduits, only 289 patients treated with ORC were significantly older (74 vs. 70 years) and had a higher CCI than 110 patients treated with ECUD (5 vs. 3, for both $p < 0.001$, Table 3). There were no differences compared to 52 patients with ICUD. Patients in both robotic groups had tumours with lower pT and pN stages compared to ORC (for all, $p < 0.05$). A total of 78.8% robotic intracorporeal ileal conduits were performed by experienced surgeons, in contrast to 30.9% extracorporeal and 50.2% open ileal conduits (for both $p < 0.001$). Both approaches for robotic ileal conduits had better perioperative outcomes compared to ORC with lower postoperative complications, ICU admissions, lower blood loss, transfusion rates, PSMs and a shorter length of stay (for all $p < 0.01$). However, intracorporeal robotic ileal conduits had better perioperative outcomes than extracorporeal robotic ileal conduits with a shorter operating time (332.5 vs. 356.5 min, $p = 0.035$), less blood loss (200 vs. 400 ml, $p < 0.001$) and a higher lymph node count (16.5 vs. 14, $p = 0.018$, Table 3).

Twenty-one patients received robotic intracorporeal neobladders, 44 robotic extracorporeal neobladders and 32 open neobladders after ORC (Table S3). Patients in the ICUD group were older compared to ECUD (61 vs. 54 years, $p = 0.004$). A total of 100% of robotic intracorporeal neobladders were performed by experienced surgeons, in contrast to 77.3% robotic extracorporeal and 46.9% open neobladders after ORC (for both $p < 0.001$). None of the perioperative outcomes significantly differed, except for the operating time, which was significantly longer with ICUD and ECUD compared to ORC (429 vs. 441.5 vs. 312 min respectively, $p < 0.001$).

3.3 | Propensity score matched analysis

After propensity score matching, 167 matched pairs of ORC and RARC did no longer differ concerning patient or tumour characteristics, diversion types and surgeon's experience (Table 4). All

TABLE 1 Patient and tumour characteristics, urinary diversions and surgeon's experience within the study cohort consisting of 564 RARC and ORC

	RARC (n = 229)	ORC (n = 335)	p-value
Patient characteristics			
Age (yr)	68 (27; 88)	73 (30; 101)	<0.001
Gender male	191 (83.4%)	260 (77.6%)	0.091
BMI (kg/m^2)	26.4 (16.3; 41.7)	27.1 (18.3; 49.6)	0.360
CCI	3 (0; 11)	5.5 (0; 15)	<0.001
Urinary diversion			
Intracorporeal diversion	74 (32.3%)	n.a.	
Diversion type			<0.001
Ileal conduit	162 (70.7%)	289 (86.3%)	<0.001
Neobladder	65 (28.4%)	32 (9.6%)	<0.001
Other	2 (0.8%)	14 (4.2%)	0.02
Tumour characteristics			
pT			<0.001
≤pT1	77 (33.6%)	60 (17.9%)	<0.001
pT2	67 (29.3%)	88 (26.3%)	0.435
pT3	64 (27.9%)	129 (38.5%)	0.009
pT4	21 (9.2%)	58 (17.3%)	0.006
pN			<0.001
N1	23 (10%)	44 (13.1%)	0.265
N2+	18 (7.8%)	72 (21.8%)	<0.001
Surgeon			
Experienced surgeon	107 (46.7%)	169 (50.4%)	0.392

Note: Absolute numbers are given as median (range), proportions as absolute and relative frequencies.

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; n.a., not applicable; ORC, open radical cystectomy; RARC, robot-assisted radical cystectomy.

differences in primary and secondary outcomes remained significant between the groups, except for the intraoperative complication rate, which was still lower for RARC, but no longer statistically significant (RARC 10.8% vs. 18.6%, $p = 0.067$).

3.4 | Multiple regression analysis

The surgical approach was the only factor which had a significant impact on all primary outcomes in the multiple regression analysis (Table 5). The robotic approach had a lower risk for intraoperative complications (OR 0.41, 95% confidence interval (CI) 0.28–0.59), postoperative minor (OR 0.52, 95%CI 0.34; 0.79) and major complications (OR 0.38, 95%CI 0.23; 0.61) and ICU admissions (OR 0.32, 95%CI 0.15; 0.55, all $p < 0.01$, Table 5). Older patients had a higher OR for minor complications (OR 1.25 per 10 years, 95%CI 1.03; 1.53, $p = 0.028$) in the multiple analysis.

All of the secondary outcomes were impacted by the surgical approach too (Table S4). The blood loss was lower for RARC (B-value -315.6 ml, 95%CI -179; -453, $p < 0.001$). Correspondingly, RARC had a lower OR for blood transfusions (OR 0.23, 95%CI 0.15; 0.35, $p < 0.001$). The OR for blood transfusions was also impacted by the type of urinary diversion and was lower for neobladders (OR 0.52, 95%CI 0.27; 0.99), increased with patient age (per 10 years: OR 1.33, 95%CI 1.08; 1.64) and was higher for women (OR 1.61, 95%CI 1.08; 2.55, all $p < 0.05$). The operating time was influenced by five different factors in the multiple analysis and was longer for RARC, neobladders and patients with an increasing BMI, but was shorter for experienced surgeons and older patients. PSMs were less likely after RARC (OR 0.27, 95%CI 0.1; 0.71), but more common with experienced surgeons (OR 3.06, 95%CI 1.48; 6.34, both $p < 0.01$) and advanced tumours (OR 14.4, 95%CI 4.3; 47.7, $p < 0.001$). The lymph node count was higher for RARC (B-value 3, 95%CI 1.4; 4.5), but lower with increasing patient age (per 10 years -1.1, 95%CI -1.8; -0.4, both $p < 0.01$). The length of stay was shorter for RARC (B-value -4.3, 95% CI -1.7; -6.9), longer for neobladders and other urinary diversions, and increased with BMI (B-value 0.56, 95%CI 0.3; 0.81, both $p = 0.001$).

TABLE 2 Primary and secondary outcomes in overall cohort

	RARC (n = 229)	ORC (n = 335)	p-value
Primary outcome			
Intraoperative complications	30 (13.1%)	65 (19.4%)	0.043
Grade 1 (EAUiaiC)	12 (5.2%)	25 (7.5%)	0.295
Grade 2	17 (7.4%)	31 (9.3%)	0.444
Grade 3	-	9 (2.7%)	0.012
Grade 4	-	-	1.000
Grade 5	1 (0.4%)	-	0.226
Postoperative complications	135 (59%)	261 (77.9%)	<0.001
Minor (Clavien Dindo 1, 2)	87 (38%)	150 (44.8%)	0.094
Major (Clavien Dindo ≥3)	48 (21%)	110 (32.8%)	0.002
ICU admission rate	17 (7.4%)	68 (20.3%)	<0.001
Secondary outcome			
Operating time (min)	377 (198; 774)	270 (70; 874)	<0.001
Blood loss (ml)	400 (20; 2500)	600 (50; 6500)	<0.001
Transfusion rate	48 (21%)	200 (59.7%)	<0.001
Lymph node count	15 (0; 35)	12 (0; 52)	<0.001
PSM	5 (2.2%)	35 (10.4%)	<0.001
Length of stay (d)	16 (8; 96)	17 (7; 185)	<0.001

Note: Absolute numbers are given as median (range), proportions as absolute and relative frequencies.

Abbreviations: EAUiaiC, European Association of Urology intraoperative adverse incident classification; ICU, intensive care unit; n.a., not applicable; ORC, open radical cystectomy; PSM, positive surgical margin; RARC, robot-assisted radical cystectomy.

4 | DISCUSSION

Within this study, 564 consecutive radical cystectomies (229 RARC and 335 ORC) performed for urothelial carcinoma at one tertiary referral centre from 2007 to 2019 were included. During this period, the proportion of RARC increased from 24.4% in 2007 to 80% in 2012, but was then limited to less than 10 per year. This decrease was caused by reports on early recurrences and atypical metastases after RARC, which might have affected the oncological outcome. Therefore, we narrowed our indication and performed RARC only in patients with organ-confined disease from 2016.[8,9] Recently, the risk for atypical metastases has proven to be low in several studies, including the 5- and 10-years oncological outcomes of the IRCC which also comprised many of our RARC.[12,26] Of great importance, the oncological outcomes are comparable to ORC irrespective of the urinary diversion, including orthotopic intracorporeal neobladders.[3,11,12,18,27] For this reason, we have broadened our indication for RARC again. However, even two robotic systems cannot cover the high demand for robotic surgery, wherefore we cannot offer RARC to all patients. Overall, we found RARC to have a lower morbidity with less complications and ICU admissions, regardless of the type of urinary diversion and surgical experience. Moreover, RARC was superior in terms of all other secondary outcomes, including PSMs or lymph node count, except for the operating time, which was longer.

As primary outcome, the complication rates of our series are comparable with those of others.[28] In total, the major (RARC 21% vs. 32.8%) and overall (RARC 59% vs. 77.9%) postoperative complication rates clearly favoured RARC. To date, five RCTs have prospectively compared RARC and ORC and two had complication rates as the primary outcome.[29,30] In contrast to our results, both RCTs did not find significant differences between the two surgical approaches, just like the recent Cochrane meta-analysis which summarised all five RCTs.[31] However, the CORAL trial only compared 20 ORC with 20 RARC and 20 laparoscopic RCs (LRC) with extracorporeal urinary diversions. The power calculation estimated a 10%–15% complication rate for RARC with a true result of 55%, wherefore the authors state that the sample size had been too small to derive definite conclusions.[30] Bochner et al. compared 60 RARC with 58 ORC in the intent-to-treat analysis, but neither included intracorporeal urinary diversions. In contrast to the RCTs, the large meta-analysis of Novara et al. described lower overall and major complications after RARC, which is in line with our findings.[20] This could result from the inclusion of intracorporeal diversions, which can have a lower risk for complications than ECUD according to the IRCC.[32] Some authors even state that RARC with an extracorporeal diversion does not have

TABLE 3 Subgroup analysis of patients with ileal conduits only

	RARC (n = 162)		p-value		p-value	
	Intracorporeal (n = 52)	Extracorporeal (n = 110)	Intracorporeal versus extracorporeal	ORC (n = 289)	Intracorporeal versus open	Extracorporeal versus open
Patient characteristics						
Age (yr)	71 (48; 87)	70 (27; 88)	0.182	74 (36; 90)	0.244	<0.001
Gender male	42 (80.8%)	90 (81.8%)	0.873	226 (78.2%)	0.678	0.426
BMI (kg/m^2)	26.5 (16.3; 41.7)	27.0 (17.3; 40.1)	0.788	27.3 (18.4; 49.6)	0.905	0.546
CCI	4 (2; 11)	3 (2; 10)	<0.001	5 (0; 15)	0.255	<0.001
Tumour characteristics						
pT			0.722		0.010	0.018
≤pT1	16 (30.8%)	31 (28.2%)	0.560	47 (16.3%)	0.007	0.011
pT2	18 (34.6%)	32 (29.1%)	0.477	77 (26.6%)	0.238	0.624
pT3	15 (28.8%)	36 (32.7%)	0.620	113 (39.1%)	0.160	0.240
pT4	3 (5.8%)	11 (10.0%)	0.371	52 (18.0%)	0.027	0.050
pN			0.263		0.005	0.019
N1	5 (9.6%)	10 (9.1%)	0.914	37 (12.8%)	0.520	0.304
N2+	2 (3.8%)	13 (11.8%)	0.102	65 (22.5%)	0.002	0.016
Surgeon						
Experienced surgeon	41 (78.8%)	34 (30.9%)	<0.001	145 (50.2%)	<0.001	<0.001
Primary outcome						
Intraoperative complications	7 (13.5%)	15 (13.6%)	0.976	57 (19.7%)	0.287	0.158
Postoperative complications	27 (51.9%)	66 (60%)	0.332	227 (78.5%)	<0.001	<0.001
Minor (Clavien Dindo 1, 2)	20 (38.5%)	46 (41.8%)	0.685	132 (45.7%)	0.335	0.489
Major (Clavien Dindo ≥3)	7 (13.5%)	20 (18.2%)	0.452	95 (32.9%)	0.005	0.004
ICU admission rate	5 (9.6%)	6 (5.5%)	0.326	60 (20.8%)	0.060	<0.001
Secondary outcome						
Operating time (min)	332.5 (198; 523)	356.5 (203; 618)	0.035	267 (125; 874)	<0.001	<0.001
Blood loss (ml)	200 (50; 1000)	400 (20; 2000)	<0.001	600 (50; 6500)	<0.001	<0.001
Transfusion rate	7 (13.5%)	30 (27.3%)	0.051	180 (62.3%)	<0.001	<0.001
Lymph node count	16.5 (0; 35)	14 (0; 29)	0.018	12 (0; 52)	0.002	0.073
PSM	1 (1.9%)	3 (2.75%)	0.759	31 (10.7%)	0.045	0.011
Length of stay (d)	14.5 (8; 68)	14.5 (8; 46)	0.655	16 (7; 99)	<0.001	<0.001

Note: The results are compared between robotic intracorporeal and extracorporeal conduits, but also between intracorporeal versus open and extracorporeal versus open ileal conduits. The corresponding p-values are given and absolute numbers as median (range), proportions as absolute and relative frequencies.

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; ICU, intensive care unit; n.a., not applicable; ORC, open radical cystectomy; PSM, positive surgical margin.

TABLE 4 Comparison of propensity score matched groups regarding primary and secondary outcomes

	RARC (n = 167)	ORC (n = 167)	p-value
Patient characteristics			
Age (yr)	70 (27; 88)	71 (36; 90)	0.582
Gender male	138 (82.76%)	137 (82%)	1.0
BMI (kg/m^2)	26.2 (16.3; 41.7)	27.5 (18.3; 49.6)	0.218
CCI	3 (2; 11)	4 (0; 12)	0.436
Urinary diversion			
Intracorporeal diversion	45 (26.9%)	n.a.	-
Diversion type			0.580
Ileal conduit	132 (79%)	139 (83.2%)	0.360
Neobladder	23 (20.4%)	24 (14.4%)	0.175
Other	1 (0.6%)	4 (2.4%)	0.375
Tumour characteristics			
pT			0.642
≤pT1	46 (27.5%)	43 (25.7%)	0.680
pT2	51 (30.5%)	52 (31.1%)	0.903
pT3	52 (31.1%)	49 (29.3%)	0.714
pT4	18 (10.8%)	23 (13.8%)	0.423
pN			0.938
N1	19 (11.4%)	16 (9.6%)	0.710
N2+	18 (10.8%)	20 (12%)	0.850
Surgeon			
Experienced surgeon	66 (39.5%)	77 (46.1%)	0.267
Primary outcome			
Intraoperative complications	18 (10.8%)	31 (18.6%)	0.067
Postoperative complications	98 (58.7%)	129 (77.2%)	0.001
Minor (Clavien Dindo 1, 2)	65 (38.9%)	72 (43.1%)	0.525
Major (Clavien Dindo ≥3)	33 (19.8%)	57 (34.1%)	0.006
ICU admission rate	11 (6.6%)	33 (19.8%)	0.001
Secondary outcome			
Operating time (min)	336 (198; 618)	286 (125; 874)	<0.001
Blood loss (ml)	400 (20; 2500)	500 (150; 6500)	0.007
Transfusion rate	36 (21.6%)	101 (60.5%)	<0.001
Lymph node count	14 (0; 35)	11 (0; 52)	<0.001
PSM	5 (3%)	14 (8.4%)	<0.001
Length of stay (d)	15 (8; 96)	17 (7; 185)	0.002

Note: Absolute numbers are given as median (range), proportions as absolute and relative frequencies.

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; ICU, intensive care unit; n.a., not applicable; ORC, open radical cystectomy; PSM, positive surgical margin; RARC, robot-assisted radical cystectomy.

any benefit over ORC at all.[33] We are therefore very pleased that our longitudinal analysis not only included 155 (67.7%) RARC as ECUD, but also 74 (32.3%) as ICUD. The first ICUD was conducted in 2014 and continued to be maintained afterwards. In comparison with ECUD, the complication rates were not statistically different, but had a tendency to be lower for ICUD. However, when including patients

TABLE 5 Multiple regression analysis to assess the impact of the surgical approach, urinary diversion and surgeon's experience on primary outcomes, accounting for patient (age, gender, BMI, CCI) and tumour characteristics (pT, pN stage)

	Intraoperative complications		Minor complications		Major complications		ICU admissions	
Variable	**OR (95%CI)**	***p*-value**	**OR (95%CI)**	***p*-value**	**OR (95%CI)**	***p*-value**	**OR (95%CI)**	***p*-value**
Robotic approach (ref.: open)	0.41 (0.28; 0.59)	<0.001	0.52 (0.34; 0.79)	0.002	0.38 (0.23; 0.61)	<0.001	0.32 (0.18; 0.55)	<0.001
Diversion (ref: conduit)								
Neobladder	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-
Experienced surgeon (ref: inexperienced)	-	-	-	-	-	-	-	-
Age (per 10 years)	-	-	1.25 (1.03; 1.53)	0.028	-	0.789	-	0.169
Female gender (ref: male)	-	-	-	-	-	-	-	-
BMI	-	-	1.05 (1.0; 1.1)	0.039	1.11 (1.06; 1.16)	<0.001	-	-
CCI	-	-	-	-	-	-	-	-
Locally advanced tumour (ref.: ≤ pT2)	-	-	-	0.167	-	0.787	-	-
pN+ (ref.: pN0)	-	-	-	-	-	-	-	-

Note: The odds ratio (OR) with 95% confidence intervals (95%CI) is only given for significant associations.

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; ECUD, extracorporeal urinary diversion; ICUD, intracorporeal urinary diversion; ref, reference.

with ileal conduits only, RARC proved not only better perioperative outcomes than ORC, but robotic intracorporeal ileal conduits also rendered better perioperative outcomes possible than for robotic extracorporeal ileal conduits. They had a shorter operating time, less blood loss and higher lymph node count, supporting the results of Tan et al.[33] In contrast, ICUD did not prove better results than ECUD or ORC in our subgroup analysis with neobladders only, which can be explained with lower case numbers. We perform intracorporeal neobladders in the 'W'-shaped Hautmann technique, but also other methods, such as the intracorporeal Padua neobladder, can provide favourable long-term results.[34,35]

Consequently, our results highlight a lower morbidity after RARC, especially with intracorporeal diversion, but also underline the importance of prospective trials comparing ORC and RARC with ICUD. Fortunately, the iROC trial has recently been initiated and is currently ongoing (NCT03049410).[36] As another primary outcome, we compared the ICU admission rates. Reports on ICU admissions are highly variable, ranging between 1.3% and 38% for RARC and 7% and 46% after ORC. Our ICU admissions were three times more common in the ORC group (RARC 7.4% vs. ORC 20.3%), further confirming a lower morbidity after RARC.[37,38]

These results were reached in a patient cohort resembling other published series.[39] However, patients treated with ORC had a median CCI of 5.5 and were not only more comorbid compared to the RARC group, but also to most other published cohorts. Recently, two database analyses including more than 20 000 patients only graded 12.1% patients CCI ≥ 2 and 1.7% patients CCI ≥ 3.[40,41] As a consequence, the proportion of patients with neobladders after ORC was relatively low in our cohort (9.6%). In contrast, 28.4% of patients received robotic neobladders, which is a comparably high proportion of continent urinary diversions, especially for a robotic cohort. Patients treated with ORC had higher pT stages (55.8% vs. 37.1% ≥ pT3) and more lymph node metastases (pN+ 34.9% vs. 17.8%). Again, these tumour stages are higher than in most other single centre series.[28,37,42] Only a very few patients received neoadjuvant chemotherapy prior to surgery, as our department aims to avoid it due to the current lack of predictive biomarkers. Consequently, mainly the ORC cohort comprised many cases at high risk for complications.

Moreover, we assumed that the surgical results were impacted by 1) a selection bias, as more advanced tumours were primarily treated with ORC, and 2) a learning curve for RARC, as all robotic cystectomies from the very first one conducted in our department were included. For this reason, we performed a propensity score matching, accounting for the differences between ORC and RARC cohorts (age, CCI, pT- and pN-stage), as well as the urinary diversion type and surgical experience as potential confounders. The IRCC has described significant improvements in perioperative outcomes after 30 RARC.[5] We applied this threshold to our analysis and considered a surgeon to be experienced after his or her 30th RARC and 30th ORC.

Remarkably, the differences concerning complications and ICU admissions remained significant in the propensity score matched analysis comparing 167 RARC with 167 ORC. Thus, one can deduce that neither tumour-specific aspects nor the surgeon's experience, but the surgical approach had a major impact on complications and ICU admissions, which was confirmed in the multiple regression analysis. In a similar analysis, Brassetti et al. also found the surgical approach to be associated with ICU admissions or reoperations.[37] Nevertheless, complications were also impacted by patient-specific factors in our

multiple regression analysis. A higher BMI increased the risk for minor and major complications, which has also been postulated by other authors.[43] Moreover, the patient age increased the risk for minor complications. An increasing age has been identified as a predictor for complications after RC elsewhere.[44] No further factors had an impact on complications and ICU admissions in the regression analyses, which underlines the importance of the surgical approach.

Concerning the secondary outcomes, RARC had less blood loss and transfusions, less PSMs, a higher lymph node yield and a shorter length of stay, but a longer operating time not only in the overall, but also the propensity score matched cohort. Correspondingly, all of these outcomes were impacted by the surgical approach in the multiple regression analysis. The PSM rates were not only influenced by the surgical approach, but also by the experience of the surgeon and the tumour stage. Faraj et al. illustrated a significant increase in PSMs with higher pT-stages, but in contrast Dell'Oglio could not find an association between surgical experience and PSMs.[6,28] According to our results, experienced surgeons had a *higher* OR of 3.06 for PSMs in the multiple regression analysis, which is clearly counterintuitive. This association can be related to an interaction of surgical experience with tumour stage, as experienced surgeons operated on more advanced tumours with higher pT stages, and the tumour stage itself had a much higher OR of 14.4 for PSMs. However, PSMs were rare, especially in the RARC cohort. The total lymph node count was not impacted by the surgeon's experience, but higher for RARC. This finding confirms the results of other analyses, including the prospective RCT of Nix et al. comparing 21 RARC with 20 ORC.[17] The median length of stay was shorter after RARC, but still much longer than in most other works ranging from seven to nine days.[20] This can be explained by differences in health care systems, as the German reimbursement system covers a longer hospital stay.[45] Earlier discharge after RARC is possible from a surgical point of view, as we have also begun discharging patients earlier in recent years (first 100 RARC: 17 days, rest: 15 days); however, it has not been a crucial parameter for us.[23] Finally, the operating time was not only impacted by the surgical approach, but also the diversion type, patient age, BMI, and of high importance, the surgeon's experience. The impact of the learning curve on perioperative and especially functional outcomes of RARC has also been demonstrated elsewhere.[46,47] In this context, the current EAU guidelines highlight the experience of the surgeon as a key factor for the surgical outcomes of RARC.[3] However, the diversity of associations in our multiple regression analysis also underlines the complexity of associations when comparing ORC with RARC.

This study is not devoid of limitations. Due to its retrospective nature, cohorts were not balanced in terms of surgeon's experience, patient and tumour characteristics. For this reason, we performed a propensity score matching and multiple regression analyses and aimed to control for the most important group differences and potential confounders. Nonetheless, statistics cannot replace prospective, randomised controlled trials. Furthermore, not all surgeons conducted both RARC and ORC and no mid- or long-term follow-up was included to compare the oncological outcomes, which is currently ongoing.

5 | CONCLUSIONS

RARC has not replaced ORC, mainly because of doubts about its oncological safety and a long-lasting learning curve. This has led to a selection bias in most studies, which has potentially rendered it hard to prove a superiority of the robot. In this large single-centre cohort, we performed a propensity score matching and multiple regression analyses to control for differences in surgeon's experience, patient, tumour characteristics and type of urinary diversion between RARC and ORC. Regardless, RARC had lower complication rates and blood loss, less ICU admissions and transfusions, but longer operation times. Thus, RARC appears to be superior to ORC.

AUTHOR CONTRIBUTIONS

Conception: Philip Zeuschner and Matthias Saar. *Performance of work*: Philip Zeuschner, Rebecca Mohr, Sara van Heemskerk and Matthias Saar. *Interpretation or analysis of data*: Philip Zeuschner and Matthias Saar. *Writing the article*: Philip Zeuschner, Matthias Saar and all other authors. All authors had access to the data.

DATA AVAILABILITY STATEMENT

The fully anonymised data that support the findings of this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

There are no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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