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Systematic Review

Functional Outcomes After Robotic Radical Cystectomy with Intracorporeal Diversion: A Systematic Review

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Abstract.
BACKGROUND: Robotic assisted radical cystectomy (RARC) is considered a safe and feasible technique in patients with bladder cancer who are candidates for curative treatment. Intracorporeal urinary diversions (ICUD) represents one step forward into moving to an utterly minimal invasive procedure with the thought that it may improve patients outcomes and time to recovery after the surgical procedure. Overall, RARC has shown to provide similar oncological outcomes as other procedures. The impact of such approach in continence and sexual function of the patients is an important part of an integral health care of this subset of patients.
OBJECTIVE: To describe the functional outcomes of RARC with ICUD across different manuscript evaluating this field.
METHODS: A systematic literature search related to functional outcomes and diversion technique in RARC with ICUD, was performed on June 2019 using PubMed
RESULTS: Out of 22 manuscripts evaluated we included 11 in our analysis. Although the functional outcomes in the studies we have included in this analysis seem to be adequate and consistent, the evidence is poor when comparing RARC with ICUD versus other approaches
CONCLUSION: We consider that studies with better designs aiming to elucidate the impact of RARC with ICUD in the quality of life of the patients may improve the quality of the outcomes and would help to draw stronger conclusions

Keywords: Urinary bladder neoplasm, urinary incontinence, cystectomy, sexual dysfunction, robotic surgical procedure, urinary diversion

INTRODUCTION

Radical cystectomy (RC) is the standard treatment for patients with muscle invasive bladder cancer (MIBC) [1, 2]. Prior research on outcomes of open radical cystectomy (ORC) showed a significant decline in functional status and health related quality of life (HRQOL) in patients treated with ORC (e.g., sexual barriers due to urinary odor and frequent stoma care in ileal conduit patients and to urinary leakage in neobladder patients). Recently, randomized trials comparing the performance of open radical cystectomy (ORC) and RARC have been done mostly including extracorporeal diversions (ECUD). Parekh et al. reported in a randomized trial comparing ORC and RARC with ECUD that the latter is not inferior

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to the open approach regarding 2 year -progression free survival (PFS) and adverse events [3]. Moreover, a randomized trial comparing oncological outcomes between open and robotic approaches with ECUD showed that there is no significant difference in recurrence, cancer-specific survival (CSS) and overall survival (OS) [4].

The safety of these two interventions has also been evaluated. A randomized three-arm trial comparing 30 and 90- day complications rates among ORC, RARC and laparoscopic radical cystectomy with ECUD showed no significant differences in those outcomes in patients who underwent RARC compared to those who had laparoscopic or ORC [5]. Likewise, a randomized trial that compared outcomes of ORC and RARC with ECUD found no significant difference in 30 and 90 day complication rates, length of stay, pathologic outcomes and 3 – 6 month quality of life related outcomes [6]. attested The findings of that trial on QoL related outcomes were consistent with a study that compared postoperative outcomes including health related quality of life in patients who underwent RARC versus ORC [7].

The literature is scarce when looking at RARC with intracorporeal urinary diversion (ICUD) and few prospective randomized trials are available. A randomized trial that compared perioperative and oncological outcomes between RARC with ICUD versus ORC in patients with up to 4 years of follow up found comparable disease-free survival, CSS and OS rates between the two intervention groups, although, a significant increase in the number of perioperative complications were observed in the ORC group [8]. Ergonomic benefits for surgeons and reduced blood loss were also noted.

Data on functional outcomes of RARC with ICUD is also limited. A systematic review showed that RARC with ICUD is feasible and provides good early, intermediate and long term oncological and functional outcomes, and acceptable complication rates. A benefit was also found in length of stay and blood loss [9]. However, the data in regards to functional outcomes came from only 4 studies that evaluated 97 patients in total. On the other hand, when evaluating the benefits of RARC with ICUD versus laparoscopic or ORC, RARC with ICUD has shown equivalent oncological outcomes along with lower complication rates, in some cases, and similar health related quality of life [9]. Because, patients' functional outcomes following RARC with ICUD can negatively affect their health-related quality of life (HRQOL), synthesizing the evidence may shed some light on short and long-term impact of RARC with ICUD. Thus, the aim of this systematic review of the literature is to evaluate the potential benefit of RARC with ICUD on functional outcomes, specifically urinary continence and sexual function, and their association with the type of urinary diversion.

METHODS

A systematic literature search related to functional outcomes and diversion technique in RARC with ICUD, RARC with ECUD diversion and ORC was performed on June 2019 using PubMed. The keywords robotic assisted radical cystectomy, intracorporeal urinary diversion, extracorporeal urinary diversion and open radical cystectomy were used alone or in combination. The first stage of the selection process consisted of initial screening of titles and abstracts. The second phase consisted of manuscripts reading. Retrospective and prospective comparative observational studies and randomized trials were evaluated. Studies including RARC with ECUD diversion, ORC and laparoscopic radical cystectomies solely were excluded. Studies including patients treated previously with bladder sparing techniques, cystectomy due to benign conditions or case reports were also excluded. Only publications in English were accepted. Functional outcomes and urinary diversion technique were evaluated across the three surgical approaches. This systematic review followed PRISMA guidelines.

Data were extracted independently by two authors. The following variables were extracted. Erectile function, Continence, type of diversion, LUTS.

OUTCOMES MEASURES

Functional outcome for robotic radical cystectomy with intracorporeal urinary diversion technique was the main outcome.

RESULTS

Functional outcomes

Since its introduction by Beecken in 2003 [10], RARC with ICUD has gained traction throughout the world as increasing number of centers are adopting this surgical approach. While various benefits have been shown for this procedure, it has yet to be determined whether there are any functional benefits to this

procedure. Functional outcomes for ileal neobladders include continence and for both ileal conduits and neobladders include sexual function. Sexual outcomes are influenced in part by the level of nerve preservation during the surgery, which also depends on the disease burden determined by preoperative and intraoperative evaluation. While there have been concerns of local recurrence with nerve sparing, several studies have demonstrated the safety of performing a nerve sparing procedure with low rates of recurrence [9, 11], A continued challenge of assessing functional outcomes still exists due to the small number of patients recruited in these studies and the largely retrospective nature of the analyses, which makes it difficult to ascertain differences between the varying techniques.

Continence

A number of factors have been shown to be influential to successful continence after RARC with ICUD including pre-treatment levels of urinary function, age, level of motivation, intact innervation to urethral sphincter, and urethral length [8]. There are factors specific to the newly constructed urinary reservoir, which affect continence such as internal pressure, reservoir capacity and time since surgery, and also patient voiding patterns and habits (e.g., ability to master Valsalva maneuver, number of urine discharge per day).

Continence is often assessed in the literature based on the number of pads used throughout the day and night or the level of wetness of each pad. Most authors define full continence as either no pad use or use of 1 pad per day and then proceed to grade on a spectrum from mild to severe based on additional pads needed. However, the definition of continence is not consistent among the studies. For example, Kulkarni et al. defined daytime continence as no incontinence (0–1 pad/day), mild (1–2 pads/day), moderate (3 pads/day), and severe (>3 pads/day). Nocturnal continence specifically was defined as good (dry with no protection), fair (dry with 1 awakening), or poor (wet, leakage, and incontinence during sleep) [11]. Some reports regarding functional outcomes in patients after RARC with ICUD have been published. Tyritizis et al. found in one of the first RARC with intracorporeal neobladder (ICBN) cohorts that day and nighttime continence rates were between 70–90% at 12 months [12].

One of the challenges of evaluating the impact of of RARC with ICUD has been the small number of patients available for assessment. Prior to the release of Tyritzis et al. study, there were no major centers reporting a patient cohort population adequately sized for review and statistical analysis. Since then, a number of centers have reported over 50 patients in their cohorts. Although the study by Gok et al. was appropriately sized with 98 patients, the study lacked a comparison group to explore differences in functional outcomes following RARC with ICUD outcomes. Follow-up assessment of functional outcomes spanned a minimum of 24-months. However, only 61 patients met the criteria for functional assessment [13]. This subset of patients was sorted into male (57) and female (4) and was further classified into bilateral, unilateral, and none nerve sparing groups [13]. Overall, 60.6% of the cohort was continent (0–1 pad) after 24 months, 22.9% had mild incontinence (1–2 pads), 9.8% had moderate (3 pads), and 6.5% had severe daytime incontinence (>3pads) [13]. In regard to nighttime incontinence, 40.9% had good (dry) nighttime continence, 42.6% had fair (dry + 1 awakening) incontinence, and 16.3% had poor (wet, leakage, urge incontinence) nighttime incontinence. 90.8% of the cohort had bilateral and 4% unilateral nerve preservation [13]. The preferred neo-bladder technique was the Studer pouch. Although, the work by Tyritzis et al. provided a first insight of the RARC with ICUD approach, better studies are needed to assess the potential benefit of such technique over other approaches.

Several other studies also provided data on functional outcomes. Sim et al. reported a cohort that included 28 patients who had undergone RARC with ileal conduit (IC) and 73 a RARC with ICUD neobladder (ICNB). Continence in the ICNB group was defined as no pads per day and was 89.2% for daytime and 67.6% at nighttime. The surgeons employed a nerve sparing technique in 52/57 of the men and 15/16 in the women [14]. Likewise, Schwentner et al. reported a retrospective study encompassing 62 patients, 50 men and 12 women. All women had bilateral nerve sparing while 46/50 men had the same [15]. Continence in this context was defined as <1 pad per day [15]. Functional outcomes were measured at 12 months and the results showed day and night time continence of 88% and 55.1% respectively [15]. These results across studies seem to be consistent and reproducible across high volume centers. However, some of them reported wide range of continence, which might be explained by several factors such as lack of standardization of the evaluation of incontinence across the different

studies and also different time-points at the learning curve of the surgeons participating in each one of the cohorts. Moreover, until this point the studies were more descriptive and lacked comparison groups. In some, the follow up period was too brief to evaluate functional outcomes after the expected recovery post-procedure.

In order to evaluate the impact of the learning curve on the functional outcomes after RARC with ICUD, Porreca et al. aimed to determine whether the use of modular training program instructed by an experienced robotic surgeon could be sufficient to improve outcomes. The first 100 patients were grouped into roughly thirds and assessed for improved outcomes, including continence and sexual function. Continence was defined as either use of 0 or 1 pad. About 50% of patients had either unilateral or bilateral nerve sparing RARC. Overall daytime and nighttime continence was 90.2% and 70.6%, respectively [16]. Though not statistically significant, there was a trend for improvement in continence throughout the different groups of patients. Admittedly while RARC was new to the surgeon, robotic surgery in general was not, which likely played a role in the outcomes. The outcomes did conclude that modular training might be an effective strategy to overcome the learning curve associated with this surgery.

While some studies included did not involve a significant number of patients, they did shed light on a number of factors important in understanding outcomes related to RARC with ICUD. The Studer approach was the most popular neobladder technique used across different cohorts, though in some cases the description of the surgical technique used in some studies were not explained in detail (Table 1). Therefore, comparing novel techniques versus more traditional approaches is challenging. This may also account for the wide range in continence rates within each study and hamper the reproducibility of the technique and results at different centers. Asimakopoulos et al., employed a specific approach of RARC with ICUD while sparing nerves as well as seminal vesicles in men. Similar to the Gok et al. study, there was no control group for comparison. Still, the functional results for this specific subset of patients were excellent with 100% daytime continence at 12-months, with continence being defined as 0 pads used. The nighttime continence rates were also good at 72.5% at 12-months [17]. The authors advocate for the use of nerve sparing even in the setting of older patients with poor sexual function prior to surgery because it would lead to better continence. They used a Y neo-bladder and buttonhole anastomosis technique to attempt to prevent kinking and functional obstruction, which might account for the absence of clean intermittent catheterization in this cohort and the low post void residual urine [17]. On the other hand, Tan et al. reported excellent continence outcomes with the use of the pyramid shaped neobladder. This cohort included 20 patients from a single institution. Results at 3-months follow-up showed 95% of patients achieved daytime continence, whereas only 65% had achieved nighttime continence. Continence defined in this context as 0–1 pads per day [18]. Aiming to introduce technical variations Simone et al. looked at neo-bladder reconstruction by incorporating titanium staples. The concern with using a non-absorbable material in the urinary apparatus relates to the formation of stones. Within this particular cohort, 2/45 patients developed stones. The functional outcomes reported by Simone et al. were similar to that of those reported in literature. The 2-year daytime continence was 73.3% and the nighttime was 55.5%, continence defined as no use of pads [19].

Although the functional outcomes in the studies we have included in this analysis seem to be good and consistent, the evidence is poor when comparing RARC with ICUD versus other approaches because the number and quality of the cohorts is poor, the follow up period is short and most of them do not compare in between approaches. Satkunasivam et al. compared RARC with ICUD to an ORC cohort. In terms of overall pad use within a 24 hr period, no statistically significant difference was found between the 2 groups. However, In the RARC with ICUD cohort 78.3%, 21.7% and 0% used day/night, night only and day only pads, respectively while in the ORC group the rates for day/night, night only and day only pads were 50%, 42.2% and 7.8% respectively. The difference across group was statistically significant. Nonetheless, use of a large pad size was found to be significantly increased after RARC with ICUD than ORC during daytime and night time. It is worth noting that the rate of patients who did not use pads in the RARC with ICUD group was 16.7% and 19% in the ORC. The median follow up time for the robotic cohort was 9.4 months, while the median follow up time for ORC was 62.1 months, which clearly prevents an appropriate analysis [20]. Similarly, Atmaca et al., compared RARC with ICUD versus ORC patients. The successful preservation of neuro-vasculature was higher in the robotic group than the open group (93.7% vs 64.3%, $p = 0.004$) based on the subjective appreciation of the surgeon.

Table 1
Manuscript reporting functional outcomes after Robotic radical cystectomy with intracorporeal urinary diversion

Source	Year	Patients	Number of institutions	Number of Surgeons	NVB sparing	Type of Urinary Diversion	Daytime Continence	Nighttime Continence	Sexual Function
Atmaca et al.	2015	42-OPEN 32-ICUD total: 74	Single	5	93.7%-RARC 64.3%- open		Open- 75% Robotic-84.6%	Open- 58.3% Robot- 46.1%	Open-IIEF 19, 22 + 18.7 Robot 5, 13.6 + 13.6
Gok et al.	2019	98; 92 males, 6 females only 61 for follow-up; 57 males, 4 females			90.8% bilateral 4% unilateral 5.1% none	Studer pouch	60.6%-continent 22.9%- mild 9.8% moderate 6.5% severe	40.9% good 42.6% fair 16.3% poor	R-mild dysfunction- 11.1+/–4.6 IIEF RNone-20.6+/– 7.4
Asimakopoulos et al.	2016-france	40 men RARC + ICUD		1	100%	Y shaped ONB	100%- 12 months (0 pads)	72.5%- 12 months-(0 pads)	IIEF-6 score mean: 21.9 vs 24.4, 3 months and pre-op, respectively. No significant difference
Simone et al.	2016 Italy	45	Single			Partly stapled neobladder	73.2% - 12 months 0 pads	55.5% 12 months 0 pads	
Porreca	2019	100	Single	AP- main with modular training program with PW	 Mono- 33% Bilateral 17%	52%- ONB 32% IC 17% uretero-cutaneostomy	90.2% overall 87.5% G1 88.2%G2 94.4% G3 no significant Difference 12 months no or 1 pad	70.6% overall 75%G1 64.7% G2 72.2%G3 12 months no SS Diff	31% overall 30.3%G1 36.4%G2 26.5%G3 no significant Difference Erection adequate for penetration w/o PDE5I for ONB 3 months
Tyritzis et al.	2013	70	Single	2	8.1% unilateral 58.1% bilateral	Modified Studor	0–1 pad 12 months 88.2%- nerve sparing 88.9% non-nerve sparing 2–4/moderate 5.7%-nerve sparing 6.2% non-nerve sparing 4 total > incontinence 0% 0%	0–1 73.5% 12 months 2–4/ moderate 14.7% nerve sparing 11.8%non-nerve sparing >4 8.8%nerve sparing 11.8%non-nerve sparing	Erection adequate for penetration 81% potent with or without **PDE5** w/o 31.2-nerve sparing 9.5-non-nerve sparing w/ PDE5 50.0 nerve sparing 4.8.% w/ injections 3.1-nerve sparing 9.5-non-nerve sparing

(*Continued*)

Table 1
(*Continued*)

Source	Year	Patients	Number of institutions	Number of Surgeons	NVB sparing	Type of Urinary Diversion	Daytime Continence	Nighttime Continence	Sexual Function
Satkunasivam et al.	2015	28- ONB 79 –open		3		All neo-bladders	Robotic: 0 : 16.7% 1–2 : 62.5% (79.2) 3–4 : 4.1% >5 : 16/7% open: 0 : 19% 1–2 : 64.6% 3–4 : 13.9% >5 : 2.5% **No significant difference		
Tan et al.	2015	20				Pyramid, refluxing ureters	95%		
3 months	65%								
Collins et al.	2014	147 total 118 male 29 female				J shape-reflexing ureters, afferent limb			IIEF-5 >/= 17 is potency Or 50% success when performing intercourse w/wo PDEI
Sim et al.	2015	82- men 19 women 101 total	Multi-center (2)		IC: 0% NB: 52/57-M 15/16- F	IC- 28 ICNB: 73	89.2% 12 months <1 pad/day	67.6% 12 months	Erectile dysfunction Non-nerve sparing: 100% Nerve preservation: 48%
Schwentner et al.	2015	62 total 50 men 12 women	Multi-center (2)	2	Male 46/50 bilateral Female 12/12 bilateral	Studer pouch	88%	55.1%	Spontaneous erections 54%

Table 2
Newcastle Ottawa score

Study	Representa-tiveness of exposed cohort	Selection of the Non-Exposed Cohort from Same Source as Exposed Cohort	Ascertainment of Exposure	Outcome of Interest Was Not Present at Start of Study	Comparability of Cohorts	Assessment of Outcome	Follow-Up Long Enough for Outcome to Occur (Median Duration of Follow-Up $\geq$ 6 Months)	Adequacy of Follow-Up	Quality Score
Atmaca et al	Participants were 74 patients at the Ankar Ataturk Training and Research Hospital in Ankara, Turkey, previously diagnosed with invasive Bladder Cancer. They were not representative of the population and were not randomly selected.	Yes *	RARC vs open RC surgical procedures*	Yes *	Patient age, sex, preoperative BMI, International Index of Erective function, ASA score, and Previous abdominal surgeries were controlled for. Physician expertise and previous experiences were not accounted for.*	Incontinence: Pad use per day (self assessment) Erectile function: International Index of Erectile Function (IIEF)	Yes (9 months)*	Only patients with 9 months follow up were selected.	5*
Gok et al									
Asimakopoulos et al									
Simone et al	Participants were 45 consecutive patients with high grade urothelial carcinoma treated at the same tertiary hospital center in Rome, Italy from 2012 until 2014. They were not randomly selected	N/A. Study compares surgical parameters, functional and oncologic outcomes with those from a " cumulative analysis of 105 papers on oncologic and functional outcomes after RARC"	RARC, extended pelvic lymph node dissection, and intracorporeal-partly stapled neobladder.*	Outcome of interest not stated at beginning of study	Cohorts not comparable (45 patients compared to the literature)	N/A	Yes (2 years) *	Minimum follow up for inclusion in study was 2 years.	2*

(*Continued*)

Table 2
(*Continued*)

Study	Representa-tiveness of exposed cohort	Selection of the Non-Exposed Cohort from Same Source as Exposed Cohort	Ascertainment of Exposure	Outcome of Interest Was Not Present at Start of Study	Comparability of Cohorts	Assessment of Outcome	Follow-Up Long Enough for Outcome to Occur (Median Duration of Follow-Up ≥ 6 Months)	Adequacy of Follow-Up	Quality Score
Porrec a et al.									
Tyritzis et al	Participants were 70 patients who had undergone a RARC with modified Studer ileal neobladder. at the Karolinska Institute in Sweden between December 2003 and November 2012. Their data was selected retrospectively and they were not randomly selected.	N/A. No comparison group reported. Study looks at oncologic, functional, and complication outcomes.	RARC with totally intracorporeal modified Studer ileal neobladder formation. 69 of 70 cases completed by 2 surgeons with significant prior experience in open and robot assisted radical prostatec-tomies.*	Outcome of interest not stated at beginning of study	N/A	Oncologic outcomes: surgical margins assessed, as well as cancer specific mortality and recurrence at 24 months. Complication outcomes: Reported using clavien scores at 30 aand 90 days. Functional outcomes: Patients interviewed by nurse regarding functional outcomes using a customized nonexternally validated questionnaire.	Yes*	All patients with up to 9 year follow ups were included.	2*

Satkunasivam et al	Participants were 28 men who underwent Intracorporeal orthotopic neobladder creation following RARC between 2012 and 2013 compared to previously characterized cohort of 79 men who underwent ORC. These patients were not randomly assigned to individual groups.	Yes*	RARC with iONB creation vs open RC with ONB creation*	Yes*	Covariables: time since surgery (in months), age at time of surgery (in years), ASA score, BMI, presence of diabetes mellitus, previous radiation therapy,and neoadjuvant or adjuvant chemotherapy were accounted for. Cohorts differed in their times of enrollement.*	Study measures mailed in HRQOL questionnaires from patients at least 12 months after surgery.	Yes*	32 iONB men were contacted, 28 were included. Response for ORB cohort was 179/295, of which 79 males with ONB creation were included.*	6*
Tan et al	Participants were 20 patients who underwent a RARC with an intracorporeal neobladder formation using a pyramid detubularised folding pouch configuration between July 2011 and March 2014. These patients were retroactively selected and not randomly assigned.	NA. Study describes surgical technique, and measures functional and oncologic outcomes including renal function. No comparison group is reported.	RARC with iNB and bilateral pelvic lymphadenopa-thy.*	Yes*	N/A	Postoperative upper tract cystogram between 3–6 weeks postop, CT scan of chest, abdomen, and pelvis performed at 6 and 12 months. Continence measured at 6 and 12 months by number of pads required over 24 hr period. *	Yes* Median follow up 21.5 months	Not specified	4*

(*Continued*)

Table 2
(*Continued*)

Study	Representa-tiveness of exposed cohort	Selection of the Non-Exposed Cohort from Same Source as Exposed Cohort	Ascertainment of Exposure	Outcome of Interest Was Not Present at Start of Study	Comparability of Cohorts	Assessment of Outcome	Follow-Up Long Enough for Outcome to Occur (Median Duration of Follow-Up ≥ 6 Months)	Adequacy of Follow-Up	Quality Score
Collins et al	Participants were 80 patients who underwent urinary diversion with an intracorporeal modified Studer neobladder. using Standard Da Vinci (for first 20 patients) and Da Vinci Si (for remaining 60 patients). Patients were retroactively secleted and not randomly assigned.	No: Findings compared to similar studies performed elsewhere.	Urinary diversion with an intracorporeal modified Studer neobladder	Yes*	N/A: no p values reported in comparison of groups.	Outcomes assessed at 3, 6, 12, 18, and 24 months; and thereafter once a year. Functional outcomes: Potency and measured using IIEF score and continence assessed via nurse interview. Oncologic outcomes: overall and cancer specific survival at 36 and 60 months	Yes: mean follow up 31 months	Not specified: retrospective study	
Sim et al	Participants were 101 patients who underwent RARC and intracorporeal urinary diversion at two teriary academic centers between October 2009 and October 2014. The patients were retrospectively selected and weren't randomly assigned	Yes*	RARC followed by either intracorporeal ileal conduit or neobladder formation*	Yes*	N/A: no p values reported in comparison of groups.	Complications: Early (<30 days) and late (>30 days) complication severity measured by Clavien score. Oncologic outcomes: 3 year cancer specific and overall survivals. Functional outcomes: Questionnaire and IIEF score.*	Yes: "Average" follow up 27.5 months*	Not specified: retrospective study	5*

Schwentner et al.	Participants were 62 patients who underwent RARC and orthotopic neobladder formation at two academic centers between October 2009 and October 2014. The patients were retrospectively selected and weren't randomly assigned.	Yes*	RARCs with intracorporeal neobladder formation *	Yes *	N/A: no values reported.	Periooperative variables: operating time, blood loss, hospital stay Complications: Perioperative and postoperative complications measured via Clavien-Dindo system. Functional outcomes: Continence: pad use Sexual function: NA Oncologic outcomes: cancer specific and overall survival rate (time not recorded), as well as mortality	Yes: "average" follow up 37.3 months *	Not specified: retrospective study	4*

The daytime continence with no pad use (84.6% vs 75%, $p > 0.05$) was higher in the robotic group; However, the difference was not statistically significant [11].

Erectile dysfunction

Sexual function remains an important functional outcome after a radical cystectomy. Robotic surgery allows for better preservation of the neurovasculature of the pelvis, which may impact sexual function after surgery. Erectile dysfunction is regularly measured by the IIEF score [21]. IIEF scores range from <7 (severe sexual dysfunction) to >24 (no dysfunction). An additional criterion added to the gradation of sexual function is the need to use PDE5 inhibitors. Others use a more basic definition including spontaneous erections or the ability to achieve successful penetration at least 50% of the time.

Porrecca et al. reported data on sexual health and defined sexual potency as erection adequate for sexual penetration without need for PDE5 inhibitors. Sexual potency was reported as 31% overall within 90 days after surgery [16]. No assessment 12 months after surgery was done, therefore, this functional outcome seems more anecdotal than clinically relevant as it is expected that potency improves gradually during the first postoperative year.

Similarly to reported data for continence, Tyritzis et al. remains an important point of comparison for sexual function. Tyritzis et al. defined potency as the erection adequate for penetration with or without the use of phosphodiesterase type 5 inhibitors at 12 months [12]. All women in their cohort received nerve-sparing surgery, which involves preservation of the autonomic nerves at the anterior vaginal wall at the 10 and 2 o'clock position [12]. 4/6 women remained sexually active postoperatively [12]. Overall, 81.2% of the nerve-spared male patients were potent with or without PDE5 medication at 12 months [12].

Other studies reviewed previously for continence also addressed sexual function. Atmaca et al. provided an additional point of comparison by assessing sexual function pre and postoperatively. Patients were initially grouped into 2 categories based on the type of surgical procedure and preoperative sexual function according to IIEF score. Postoperatively they were further grouped into subcategories of bilateral, unilateral or no neurovascular bundle sparing. Results showed that those with no sexual dysfunction prior to the surgery reported better sexual function or higher IIEF score postoperatively than those that had mild sexual dysfunction [11]. Additionally, those patients with mild sexual dysfunction required more frequent use of PDE5 inhibitors than those that had no dysfunction [11]. Surprisingly, although more of the RARC with ICUD had neuro vascular sparing surgery, this cohort reported a lower mean IIEF 9 months postoperatively than the open group. However, none of these results were statistically significant.

Consistent with those findings, Sim et al. also reported on sexual function using the IIEF5 12 months after surgery [14]. Nerve sparing was attempted for both men and women. Nerve sparing in women involved preservation of the tissues on the lateral aspect of the vagina, which are autonomic nerves. 63.4 % of males and 78.9% of females had a nerve sparing surgery. All the patients who had nerve-sparing technique had ICNB while none of the patient who underwent a ileal conduit had nerve preservation. Surprisingly and consistent with Atmaca et al., the reported erectile function was better in the patient with no nerve preservation (100% vs 48%). However, only descriptive statistics were provided, therefore, no statistical significance was obtained [14].

Gok et al. subdivided a cohort preoperatively into mild sexual dysfunction and no sexual dysfunction using IIEF scores. Among those with mild dysfunction prior to surgery ($n = 8$), 4 needed postoperative use of PDE-5I and had a mean IIEF score of 11.1+/– 4.6 (5–20 range) at follow-up (13). Among those without preoperative sexual dysfunction, 6 required use of PDE5 I, and the mean was 20.6+/– 7.4 (8–25 range). It is important to note that 91.3% of the patients with no ED had bilateral nerve-sparing technique compared to 75% of the patients with mild dysfunction [13].

Some modifications to the technique has been attempted in order to improve sexual function in patients after RARC with ICUD. Asimakopoulos et al. employed a specific technique involving preservation of the seminal vesicles under the assumption that it would preserve the lateral cholinergic fibers that are important for continence and assessed sexual function using IIEF-6 scores pre and postoperatively. Preoperatively the mean IIEF-6 score was 24.4 (21–29), and postoperatively at 3 months it was 21.9. The difference was not found to be statistically significant. Patients were instructed to take Tadalafil for 2 months after surgery and as needed thereafter. Only 9 of the patients did not achieve normal EF [17].

Manuscripts discussing specifically sexual function in women after RARC with intracorporeal diversion could not be find. We found some papers that evaluate this matter marginally. Collins et al. reported a satisfactory sexual function at 12 months ranging from 70–90% in both men and women, which is also consistent with Tyritzis et al., which also reported a satisfactory sexual function at 12 months in 70 to 90% in both genders [12, 22]. Therefore, more and better designed studies are warranted in order to address comprehensively the impact of the surgery in the quality of life of women specifically discussing the sexual domain.

DISCUSSION

The topic of ICUD has gained significant traction since it was first discussed in 2003 [10]. While there have been studies assessing its validity and equality regarding operation time, blood loss and other metrics, few have adequately assessed overall functional outcomes as compared to ECUD or open surgery. Continence and sexual function remain the two most important functional outcomes when studying patients who underwent RARC with ICUD. The first hurdle we found when evaluating continence and sexual function is the lack of consistency of methods to report such outcomes. Different scores and methods were used across studies. Therefore, drawing conclusions from the studies was very challenging. We consider that prospective studies using already validated methods such as IIEF, might improve the quality of the outcomes.

The overall determinants of functional outcomes are based on factors such as the degree of nerve preservation, type of urinary diversion, age, manual dexterity of patients, pre-operative comorbidities, and patient motivation. The vast majority of urinary diversions performed consist of of ileal conduits and neobladders. Because of the lack of contraindications to ileal conduits in patients cleared for RARC, Ileal conduits account for the majority of urinary diversions performed. There are, in contrast, several absolute contraindications to neobladder creation and many more relative ones. However, neobladders remain an attractive option to younger patients and those with a strong desire to preserve their continence.

Regardless of the specific neobladder or urinary diversion technique performed, functional outcomes seem to be significantly better in patients when there is special attention to the preservation of the pelvic neuro-vasculature. In women specifically, Tyritzis et al. have demonstrated that preservation of the pelvic organs can lead to better functional outcomes [12]. Other mechanisms are certainly involved as we showed previously in some cohorts, how patients with reported bilateral nerve preservations did worse compare to patients without nerve preservation technique, which we considered explain the influence of other variables besides nerve sparing [12]

While many of the studies reviewed here did not explicitly state the reason for the adoption of an ICUD versus ECUD, the functional outcomes reported here provide evidence that this technique is a viable option that can provide patients with good functional outcomes with respect to continence and preservation of erectile function. As demonstrated by Porreca et al., training programs can provide surgeons with the tools to be successful in overcoming the learning curve associated with this technique.

In spite of the limitations of this literature review driven by the quality of the studies we found. We consider that RARC with ICUD is a feasible and safe option for patients as it has been previously reported [13]. Moreover, and as part of the main focus of this systematic review we consider that functional outcomes including continence and sexual are equivalent between RARC with ICUD and what has been reported for ORC and RARC with ECUD. Moreover, although the evidence limited to compare the impact of ICNB and ileal conduits in the sexual function of the patients, we did not find any study suggesting a significant difference in the impact of either of the two techniques and the decision of which approach is better in each case should be based on a comprehensive analysis of the multiples factors that may affect the oncological outcomes, presence of contraindications for ICNB and patient motivation. We consider that studies with better designs aiming to elucidate the impact of RARC with ICUD in the quality of life of the patients may improve the quality of the outcomes and would help to draw stronger conclusions

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AUTHOR CONTRIBUTIONS

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ETHICAL CONSIDERATIONS

This paper was IRB exempt. No human or animal research was involved in the elaboration of this manuscript.

CONFLICT OF INTEREST

The authors have no conflicts of interest to report.

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