<u>Minimally Invasive VS Open Radical Cystectomy in Surgical Management of Urinary Bladder Cancer.</u>

Protocol of Thesis

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By

Ayman Abdelhameed Mohamed Elhanafy

(M.B.B.ch, M.Sc)

Under supervision of

Prof. Dr. Hatem Ahmed Aboulkassem
Professor of surgical oncology
National Cancer Institute
Cairo University

Prof. Dr. El Sayed Ashraf Hussein Khalil
Professor of surgical oncology
National Cancer Institute
Cairo University

Prof. Dr. Mahmoud Amr Abdelhakim
Assistant Professor of urology
faculty of medicine
Cairo University

Dr. Waleed Mohamed Mohamed Fadlalla
Lecturer of surgical oncology
National Cancer Institute
Cairo University

National Cancer Institute

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Abbreviations

AAL	Anterior Axillary Line
ASA	American Society of Anesthesiology
ASIS	Anterior Superior Iliac Spine
BMI	Body Mass Index
CI	Confidence Interval
CIA	Common Iliac Artery
CSS	Cancer Specific Survival
DVC	Dorsal Venous Complex
DVT	Deep Vein Thrombosis
EAU	European Association of Urology
EC	Extracorporeal
ECOG	Eastern Co-operative Oncology Group
ECUD	Extracorporeal Urinary Diversion
ERAS	Enhanced Recovery After Surgery
FDA	Food and Drug Administration
Fr	French Size
GI	Gastrointestinal
Hb	Hemoglobin
HbA1c	Hemoglobin A1c
HR	Hazard Ratio
IC	Ileal Conduit
ICG	Indocyanine Green
ICUD	Intracorporeal Urinary Diversion
IIC	Intracorporeal Ileal Conduits
IN	Intracorporeal Neobladder
IRB	Institutional Review Board
LAR	Low Anterior Resection
LE	Level of Evidence
LN	lymph Node
LND	Lymph Node Dissection
LOS	Length of Stay
LRC	Laparoscopic Radical Cystectomy
LRP	Laparoscopic Radical Prostatectomy
MIBC	Muscle Invasive Bladder Cancer
MIN	Minute
MIRC	Minimally Invasive Radical Cystectomy

MIS	Minimally Invasive Surgery
MRI	Magnetic Resonance Imaging
MSKCC	Memorial Sloan Kettering Cancer Center
NA	Not Available
NHS	National Health Service
NMIBC	Non-Muscle Invasive Bladder Cancer
NVB	Neurovascular Bundle
OR	Odds Ratio
ORC	Open Radical Cystectomy
OS	Overall Survival
PE	Pulmonary Embolism
PFS	Progression Free Survival
PLND	Pelvic Lymph Node Dissection
PSM	Positive Surgical Margin
RALP	Robot-Assisted Laparoscopic Prostatectomy
RARC	Robotic-Assisted Radical Cystectomy
RARP	Robotic-Assisted Radical Prostatectomy
RAS	Robot-Assisted Surgery
RC	Radical Cystectomy
RCT	Randomized Controlled Trial
RFS	Recurrence Free Survival
RP	Radical Prostatectomy
RR	Relative Risk
RRC	Robotic Radical Cystectomy
RRP	Retropubic Radical Prostatectomy
SCr	Serum Creatinine
SD	Standard Deviation
SPSS	Statistical Package for Social Sciences
SQ	Study Quality
SSI	Surgical Site Infection
UIA	Uretero-Intestinal Anastomosis
UK	United Kingdom
US	United States
USA	United States of America
UTI	Urinary Tract Infection
VS	Versus
WMD	Weighted Mean Difference

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Abstract

Objective: This feasibility study on bladder cancer patients aimed to compare MIRC versus conventional ORC regarding pathological, operative, and postoperative outcomes.

Methods: This study is a randomized controlled trial, sixty candidates for radical cystectomy were recruited and allocated to two groups thirty patients each, ORC group and MIRC group.

Outcome measures: operative time, EBL, blood transfusion, complications, pT stage, pathological type, retrieved LNs count, the number of positive LNs, time to solids oral intake, hospital LOS and postoperative opioid requirement outcomes between MIRC and ORC.

Results: On comparing the outcomes between the two groups, MIRC showed a significantly higher mean LN yield than ORC (p=0.004), the operative time was significantly longer in the MIRC group (P<0.001). The overall trend toward lower EBL and lower blood transfusion rate in the MIRC group, but this did not reach statistical significance (p=0.119, p=0.207 respectively). We found no statistically significant difference in postoperative high-grade complications between the two groups(p=0.519). time to regular oral diet was significantly shorter for MIRC (p=0.031). hospital LOS was significantly shorter for the MIRC group (p=0.001) and we found a statistically significant difference regarding the lower opioid requirement in the MIRC group (p=0.033).

Conclusions: MIRC improves the lymph node yield, earlier return to regular oral diet with less hospital stay and fewer opioid requirement with comparable complication rates, at the expense of a longer operative time. Our findings demonstrate that the MIRC technique represents a feasible and sound oncological approach, it may be an effective procedure for patients with bladder cancer.

Keywords: bladder cancer, MIRC, RARC, LRC, extracorporeal diversion

Introduction

Introduction

Bladder cancer is a malignant tumor with very high invasiveness and is one of the ten most common cancer types (Smith et al., 2018; Li et al., 2019b). Radical cystectomy (RC) with pelvic lymph node dissection (PLND) is the standard treatment for localized muscle-invasive bladder cancer (MIBC) and non-muscle-invasive bladder cancer (NMIBC) with recurrence or high risk of progression (Witjes et al., 2017).

During the last 20 years, different authors described the benefits of robotic assistance during minimally invasive surgery (MIS) for a variety of surgical techniques in urology, especially in procedures such as robotic-assisted radical prostatectomy (RARP) in terms of decreased morbidity and improved recovery time (Barbash, 2010).

Perioperative outcomes have been extensively described for ORC, with overall and high-grade complication rates reaching 60% and 40% in some series (Shabsigh et al., 2009; Svatek et al., 2010; Novara et al., 2015). Moreover, mortality rates have been reported to reach 3–7% at 90-days after RC (Novara et al., 2009; Svatek et al., 2010). Efforts to minimize perioperative complications have led to the development of minimal invasive cystectomy (Tan et al., 2016b).

Parra et al. described the first laparoscopic cystectomy operation. However, it was not widely adopted due to technical challenges of intracorporeal urinary diversion reconstruction (Parra et al., 1992). With the establishment and widespread utilization of robotic surgery in urology, the RARC has gained traction with the primary aim of lowering the morbidity and mortality related to RC (Soria et al., 2018).

The 2020 updated version of the guidelines on muscle-invasive and metastatic bladder cancer panel defined open radical cystectomy (ORC) as the best surgical approach for MIBC patients (Witjes et al., 2020). Robot-assisted radical cystectomy (RARC) was introduced into clinical practice more than 18yr ago when Tewari et al. pioneered the field and described the technique (Tewari et al., 2003), 4 year after the da Vinci Surgical System was approved by the US Food and Drug Administration(FDA) (Montorsi et al., 2020).

Patient selection for RARC is similar to ORC and there are no absolute contraindications. The Pasadena consensus recommends that surgeons early in their learning curve should avoid operating on morbidly obese patients, those with a history of pelvic radiotherapy and/or patients with large bulky tumor suggesting advanced disease. Patients with previous pelvic surgery such as radical prostatectomy (RP) or low anterior resection (LAR) should be avoided in the learning curve due to the risk of significant adhesions as well as those positive for pelvic lymphadenopathy on cross-sectional imaging (Wilson et al., 2015)

A RARC approach allows access to the deep pelvis and is well adapted for high BMI patients and consistent with this, others have reported that RARC for high BMI cases is not associated with increased postoperative complications (Butt et al., 2008; Butt et al., 2009)

Minimally invasive radical cystectomy (MIRC) techniques include laparoscopic radical cystectomy (LRC) and robot-assisted radical cystectomy (RARC), both of which are associated with lower morbidity than conventional surgery (Cohen et al., 2014). Many studies have compared the advantages and disadvantages of MIRC and ORC.(Fonseka et al., 2015; Shen & Sun, 2016; Tan et al., 2016a; Lauridsen et al., 2017). For example, Tang et al. performed a meta-analysis and found that the RARC seems to be a safer and less invasive treatment than ORC (Tang et al., 2014b).

Aim of the work

Aim of the work

This randomized controlled trial (RCT) aimed to compare MIRC versus conventional ORC regarding the following items:

- pT stage.
- LNs yield
- Positive surgical margin (PSM).
- Operation time.
- EBL.
- Blood transfusion.
- Intraoperative and postoperative complications.
- The time needed to start solid oral intake.
- Hospital length of stay (LOS).
- Postoperative opioid requirement.

Review of literature

Oncological outcomes

Despite significant enthusiasm for LRC in many centers worldwide, there remains a concern over pathologic and long-term oncologic results, particularly in patients with more advanced diseases (Hautmann, 2009).

It has been shown that thorough lymph node dissection (LND) improves survival even in node-negative patients. There is a growing body of evidence suggesting that extended LND template and lymph node (LN) count of more than 20 LNs are associated with the highest benefit (Abol-Enein et al., 2004; Herr et al., 2004). Adequacy of lymphadenectomy has been used as a surrogate for the quality of surgical performance (Hussein et al., 2016).

The therapeutic value of PLND is under ongoing debate, and controversy exists concerning the optimal anatomic extent of PLND (Hautmann et al., 2012). In a recent RCT, the extended PLND failed to show an advantage over standard PLDN regarding recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS). Lymphoceles requiring intervention within 90-days after surgery was higher in the extended PLND group compared with the limited PLND group (8.6% vs 3.4%; p=0.04) (Gschwend et al., 2019).

Herr et al. suggested that complete PLND with large numbers of LNs yield ensured qualified oncologic outcome (Herr et al., 2002). Some authors regarded LNs yield as an index of surgical quality with cystectomy (Buscarini et al., 2007), and surgeons always concentrated on this main part of the operation and paid more attention to the details as their experience accumulates. Removal of LNs in the LRC group was as easy as in the ORC group (Ghazi et al., 2010; Shariat et al., 2013), thus there was no statistical significance in the number of LNs retrieved between LRC and ORC, however, what is interesting was that the LRC group had fewer positive LNs yield which might indicate the patients selected in LRC group were associated with less node metastasis. It is generally believed that qualified RC is indispensable for the treatment of bladder cancer thus oncologic outcomes depend primarily on en bloc dissection of the tumor and peri-vesical soft tissue and a thorough PLND (Challacombe et al., 2011).

Tang et al. reported a meta-analysis that there is a significantly lower PSM rate in LRC than that in the ORC group, which might result from meticulous dissection due to better perspective of anatomical structure, lower pathological stage and decreased blood loss. As for the oncologic recurrence, LRC achieved an identical prognosis to ORC in terms of local recurrence and cancer-free survival, Tang et al. found lower rates of distant metastasis and death in LRC in the original analysis which may be explained with meticulous dissection with lower PSM, and fewer positive LNs might give patients the advantage of acquiring better oncologic prognosis in LRC group. However, this did not reach statistical significance (Tang et al., 2014a).

Oncologic failure in the form of port-site metastasis is another debated issue for LRC. In a previous LRC series study including 171 patients (Huang et al., 2010), only one patient with grade 3 pT3N1M0 TCC developed port-site seeding. no port-site metastasis was found in other studies of LRC (Haber & Gill, 2007; Hemal & Kolla, 2007; Porpiglia et al., 2007; Ha et al., 2010).

Generally, port-site metastasis is a rare event in LRC. Improved techniques, including gentle clamping and entrapping of LNs and specimens into a secured EndoBag before extraction, could minimize the risk. Cathelineau et al. reported that LRC can achieve a low risk of tumor dissemination, they concluded that following the principles of oncologic surgery: do not transgress the tumor boundaries, ensure adequate margins during the resection, immediately close the bladder neck and prostate apex once opened, and avoid any bladder wall perforation, will prevent potential spillage of cancer cells (Cathelineau et al., 2005).

Urothelial cancer is a highly aggressive tumor with elevated seeding abilities as such, manipulation of a tumor-harbouring bladder in a gas-filled cavity as the peritoneum during RARC requires specific surgical abilities and respect of capital surgical oncology principles (Antonelli et al., 2018).

Recently, the New England Journal of Medicine published alarming results comparing open hysterectomy for cervical cancer to minimally invasive approaches, reporting worse oncologic outcomes for the former approaches. This report continues to shed a light on a “dark side” of MIS which has indeed been poorly analyzed in the last years, probably following the worldwide enthusiasm for the emerging techniques. Similarly, in bladder cancer, there have different series in which oncologic failures are described after MIRC (laparoscopic or robotic-assisted) (Ramirez et al., 2018).

Albisinni et al. published results from a large multicentric european cohort, finding unexpected recurrences within two years of surgery even in low volume <pT2N0 patients (Albisinni et al., 2016a). of note, every center included in this multicentric study reported at least one failure, confirming the absence of surgeon-related factors. contemporarily, Nguyen and Scherr detected an increased risk of peritoneal seeding and extra-pelvic LN recurrences after RARC compared to ORC in a cohort from the USA (Nguyen & Scherr, 2016).

Kavaric et al. described the oncologic results of a prospective randomized trial comparing 50 patients undergoing RARC to 50 undergoing ORC: although the absolute rate of peritoneal seeding was not significantly different, unexpected recurrences for low-grade cancer were reported, with high volume abdominal recurrences even in patients who were fully resected of organ-confined disease (Kavaric et al., 2020).

Simone et al. performed a matched-pair analysis comparing RARC to ORC in patients receiving a neobladder as a urinary diversion. RFS at 4 years was not significantly different across the two techniques, calculated 79.3% in the RARC and 73.4% in the ORC (P=0.75). Similarly, CSS (86.4% vs. 85.3%, P=0.75) and OS (82.1% vs. 79.6%, P=0.91) were comparable across the two groups, and on multivariate cox regression, pT and pN were significant predictors of RFS (Simone et al., 2018).

Rai et al. performed a Cochrane database meta-analysis, pooling the results of the five available prospective trials. RARC and ORC presented similar oncologic results, with the meta-analysis yielding a comparable time to recurrence (HR 1.05, 95%CI 0.77-1.43). The authors then explored complication outcomes, confirming a reduction of blood loss and transfusions for RARC, while no significant differences in overall complication rate were detected (Rai et al., 2019).

Given the available results, RARC appears to be an oncological sound approach and a valid alternative to ORC. indeed, the only phase 3 trial available (RAZOR), did confirm the non-inferiority of RARC compared to ORC. Nonetheless, further prospective trials are underway and will pave the way to the affirmation or collapse of RARC. The RAZOR Trial is a prospective multi-center, open-label, randomized, phase 3, non-inferiority trial comparing RARC to ORC, conducted in 15 centers in the USA; 350 patients were randomized with a final per-protocol population of 150 RARC and 152 ORC patients. The primary endpoint of the study was RFS at 2 years: this was calculated 72.3% in the RARC and 71.6% in the ORC arm (P=0.90), thus confirming non-inferiority of RARC in terms of oncologic control of the disease. at the time of data analysis, 28 (19%) of the patients in the RARC and 32 (21%) in the ORC arm had died as a consequence of urothelial cancer (Al Khaldi et al., 2018).

Kavaric et al. analyzed 60 RARC and 58 ORC patients operated in the MSKCC (Memorial Sloan Kettering Cancer Center) within a prospective randomized trial. after a median follow-up of 4.9 years, the authors detected urothelial cancer recurrences in 20 patients in the RARC arm and 25 in the ORC arm, with a non-significant difference in RFS and CSS (P=0.4). although the differences were non-significant, they noted that a trend toward more local and abdominal metastases in the RARC arm was reported (Kavaric et al., 2020).

Nonetheless, these studies remain speculative and are unable to demonstrate a clear causal relationship between RARC and urothelial cancer seeding. of course, respect of surgical oncology principles (en bloc resection, respecting the urinary tract, minimal specimen handling, removal of specimens in bags) remains vital no matter the approach used, and failure to do so will result in inevitable catastrophic cancer recurrences, frequently deadly (Albisinni et al., 2019).

Most studies comparing ORC and MIRC are retrospective and did not report the oncological outcome. Recently, there have been several studies that reported the oncological outcome. however, Hu et al. pooled all relevant RCTs focusing on the comparison between MIS approaches and ORC, and they demonstrated that MIS approaches improved perioperative outcomes and had similar pathological and oncological outcomes compared with ORC as they did not detect a significant difference in terms of PSM (P=0.986), LN yield (P=0.711), OS (P=0.473), CSS (p=0.778), RFS (P=0.880), Progression-free survival (PFS) (P=0.324) between the 2 approaches. They concluded that MIS approaches could serve as a choice in patients with bladder cancer (Hu et al., 2020).

Feng et al. compared oncological outcome between robot-assisted and LRC for bladder cancer at a systematic review and meta-analysis, they found no significant difference concerning PSM, there was a statistically significant LN count (95% CI 1.89–2.87) in the RARC group compared with LRC group, so they conclude that patients with RARC may improve the management of patients with muscle-invasive or high-risk non-muscle invasive bladder cancer (NMIBC) (Feng et al., 2020).

Complications and perioperative outcomes

Although RC is an effective treatment for controlling high-risk bladder cancer, it is associated with higher perioperative morbidity (Shabsigh et al., 2009). MIS techniques have been proposed to kinds of surgical techniques for various diseases in the hope that perioperative complication and recovery could be improved. In terms of RC, two MIS techniques, LRC and RARC, were more widely applied, with the advantage of fewer complications and faster convalescence (Cohen et al., 2014).

The concerns about intraoperative blood loss and subsequent need for transfusion have always been associated with RC. In a recent report, despite various technical modifications to reduce the blood loss during ORC, the estimated median blood loss was 600 mL, with a third of patients required transfusion(Chang et al., 2003).

It was shown that poor performance patients may benefit from a robotic approach. Patients treated with preoperative anemia and poor cardiopulmonary reserved assessed by cardio-pulmonary exercise testing undergoing RARC with intracorporeal urinary diversion was not associated with adverse perioperative outcomes in contrast to open surgery (Chang et al., 2003; Musallam et al., 2011; Prentis et al., 2013; Tan et al., 2017a).

ORC is a highly morbid procedure with significant risks. There is a reported overall complication rate of >60% and a major complication rate of 13-40% (Novara et al., 2009; Shabsigh et al., 2009; Svatek et al., 2010; Aziz et al., 2014). In an attempt to mitigate this, there has been a move towards increased uptake of MIS and enhanced recovery protocols worldwide, with the use of RRC (Robotic radical cystectomy) in the USA increasing from 0.6% in 2004 to 12.8% in 2010 as a proportion of all cystectomies (Leow et al., 2014). In a further study of 12 centers in North America and Europe, this proportion had increased to 54% of all cystectomies in the years 2015–2018 (Zamboni et al., 2019).

In 2014, Tang et al. reported at meta-analysis that Patients undergoing LRC experienced significantly fewer overall complications, indicating that LRC might be safer and more effective than those undergoing ORC. the lower complication rate in LRC is explained with lower EBL, fewer transfusion requirements. Minor complications identified statistically significant differences, but not significant for major complications. A comprehensive and meticulous classification of all complications presented as **(Table 1)** showed that LRC had a lower incidence of infectious disease (wound infection, pulmonary infection, systemic sepsis) and ileus (Tang et al., 2014a).

Table 1: Postoperative complications published in a systematic review and meta-analysis comparing LRC versus ORC in bladder cancer (Tang et al., 2014a) without permission.

Outcome of interest	No. of studies	No. of patients, LRC/ORC	OR (95% CI)	*p*-value	Study heterogeneity				Egger's test (*p* value)
					Chi²	df	I^2	*p*-value	
Overall complications	12	456/434	0.60 [0.44, 0.80]	**<0.001**	11.10	11	1%	0.43	0.50
Major complications	12	456/434	1.04 [0.69, 1.55]	0.86	8.07	11	0%	0.71	0.28
Minor complications	12	456/434	0.45 [0.33, 0.62]	**<0.001**	18.39	11	40%	0.07	0.11
1. Infectious disease	11	406/384	0.31 [0.20, 0.49]	**<0.001**	9.80	10	0%	0.46	0.52
Wound infection	8	323/304	0.24 [0.10, 0.57]	**0.001**	3.36	7	0%	0.85	0.23
Pulmonary infection	7	334/299	0.31 [0.14, 0.69]	**0.004**	0.26	6	0%	1.00	0.10
UTI	9	381/348	0.76 [0.40, 1.44]	0.40	5.05	8	0%	0.88	0.92
GI infection	3	88/81	0.35 [0.08, 1.55]	0.17	2.06	2	3%	0.36	0.50
Systemic sepsis	3	115/105	0.15 [0.03, 0.87]	**0.03**	0.40	2	0%	0.82	0.11
2. Wound Dehiscence	6	182/188	0.64 [0.21, 1.92]	0.43	2.11	5	0%	0.83	**0.02**
3. Neurologic	3	81/76	0.86 [0.24, 3.05]	0.82	2.16	2	7%	0.34	0.06
4. Renal fistula/leak	7	291/269	0.63 [0.31, 1.27]	0.19	3.01	6	0%	0.81	0.92
5. Ureteric obstruction	4	229/189	1.90 [0.79, 4.54]	0.15	4.89	4	18%	0.30	0.48
6. GI fistula/leak	5	246/201	1.17 [0.39, 3.52]	0.78	3.43	4	0%	0.49	0.50
7. Ileus	10	399/376	0.54 [0.31, 0.94]	**0.03**	7.37	9	0%	0.60	0.45
8. Thromboembolic DVT/PE	5	174/164	0.43 [0.14, 1.35]	0.15	1.78	4	0%	0.75	0.17

Abbreviations: CI=Confidence interval; OR=odds ratio; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; UTI=urinary tract infection; GI=gastrointestinal; DVT=deep vein thrombosis; PE=pulmonary embolism.

In 2001, Chang et al. speculated that this might be caused by prolonged abdominal retraction and longer incision during ORC (Chang et al., 2001). Less postoperative pain and the decreased narcotic analgesic requirement resulted in early recovery of bowel function and ambulation. Considering laparoscopic as a new procedure for cystectomy, it is plausible that ORC might be better in operating time but accumulated experience in LRC may improve this index since the learning curve had already shown a gradual reduction in operating time without compromising the surgical outcomes (Zheng et al., 2012).

Guliev et al. focused their work on postoperative complications and quality of life. In 2020, they included 34 studies, exploring results of prospective as well as retrospective studies. although RARC seemed to be associated with a reduction of overall and major complications within the first 30-days after surgery in non-randomized controlled trials (RCT), this difference was insignificant. blood loss and transfusion rates were in favour of RARC compared to ORC in RCTs and non-RCTs (Guliev & Bolokotov, 2020).

In 2019, Albisinni et al. evaluated data from five prospective RCTs included in systematic review and meta-analysis for patients treated with RC **(Table 2)** (Albisinni et al., 2019), they found that the ORC had a shorter operative time (P<0.0001), whereas RARC showed to provide lower estimated blood loss (P=0.005). RARC demonstrated a lower risk of transfusions (P=0.008), as well as shorter LOS (P=0.001). Either RARC and ORC group showed overlapping pathological outcomes in terms of pathological and nodal staging, the number of LN yielded during the procedure, as well as PSM. No statistically significant difference was found in terms of oncological outcome among the two procedure (Albisinni et al., 2019).

Table 2: A systematic review and meta-analysis comparing the outcomes of open with robotic-assisted radical cystectomy (Albisinni et al., 2019).

Reference	Year	Centers	Study design	Study period	ORC	LRC	RARC
Nix JA *et al.* [17]	2009	Single	Randomized controlled trial	2008-2009	20	-	21
Messer JC *et al.* [18]	2012	Single	Randomized controlled trial	2009-2011	20	-	20
Khan MS *et al.* [19]	2015	Single	Randomized controlled trial	2009-2012	20	20	20
Bochner BH *et al.* [20]	2018	Single	Randomized controlled trial	2010-2013	58† 56‡	-	60† 62‡
Parekh DJ *et al.* [21]	2018	Multiple	Randomized controlled trial	2011-2014	152	-	152

Abbreviations: ORC=Open radical cystectomy; LRC=laparoscopic radical cystectomy; RARC=robot-assisted radical cystectomy; LE=level of evidence; SQ=study quality; NA=not available.

The RAZOR Trial is one of the five trials included within the previous meta-analysis, it is the largest randomized multi-centric study, focusing on perioperative data as a secondary objective. The identified advantages of robotic surgery were reduced blood loss (P<0.001) and transfusion need, associated however with a longer operative time (P<0.001). More importantly, it seemed that the hospital stay was shorter when using the robotic approach (P=0.02) even though the absolute difference was only 1 day. again, no difference was shown in terms of complication rate. it must be underlined that urinary diversion in the robotic arm was performed via an extracorporeal (EC) approach, possibly reducing the potential advantage of the robotic approach (Parekh et al., 2018).

A recent systematic review and meta-analysis of RCTs on open vs robotic cystectomies concluded that both procedures have similar rates of major complications and PSM rates, but robotic cystectomy reduced the risk of blood transfusion and minor complications (Rai et al., 2019). These findings were replicated with another recent systematic review, again including only RCTs (Sathianathen et al., 2019).

So, Clement et al. reported at a meta-analysis of 12,640 cases that RRC had a significantly longer operating time, less blood loss and lower transfusion rate. There was no difference in LN yield, rate of PSM, or Clavien–Dindo Grade I–II complications between the two groups. However, the RRC group were less likely to experience Clavien–Dindo Grade III-IV (OR 1.56, 95% CI 1.30–1.89) and overall complications (OR 1.45, 95% CI 1.26–1.68) than the ORC group. The mortality rate was higher in ORC although this did not reach statistical significance (OR 1.52, 95% CI 0.99–2.35) (Clement et al., 2020).

A USA-based population analysis of 1050 hospitals by Yu et al. found that the RRC was associated with reduced mortality as compared to ORC ($p \leq 0.0001$) (Yu et al., 2012), whereas Leow et al. found no significant difference between the two operative techniques in 279 hospitals ($p=0.54$) (Leow et al., 2014).

As the technique of RARC matures, complication rates found to be at least comparable to open surgery (Kauffman et al., 2011; Styn et al., 2012). Wang et al. described no significant difference in complication rates between RARC with extracorporeal urinary diversions (ECUD) and ORC ($p=0.3$) (Wang et al., 2008). Similarly, Nix et al. reported similar results with no significant difference between complication rates of the same two cohorts ($p=0.28$) (Nix et al., 2010). Similarly, in a comparison of readmission rates between patients who received RARC and ORC, several studies have reported no significant difference (Ng et al., 2010; Styn et al., 2012).

In the CORAL RTC (a three-arm study that compares open, laparoscopic, and robotic cystectomy) the 30-days complication rates (Clavien-Dindo system) between the three different techniques were: Seventy per cent for ORC, 55% for RARC and 26% LRC ($p=0.024$). These differences are statistically significant only when ORC was compared to LRC (p<0.01). There was no significant difference in 90-days complication rates between the three arms. No differences were observed between RARC and ORC when Clavien-Dindo grade ≥III was analyzed: twenty per cent of the cases of each group presented at least one event (Witjes et al., 2017).

At present, there have been many studies on the comparison between ORC, LRC and RARC, and it can be concluded that compared to ORC, LRC or RARC can significantly reduce EBL and LOS (Hemal & Kolla, 2007; Raza et al., 2015; Hanna et al., 2018).

Peng et al. noticed that some scholars conducted systematic reviews and meta-analysis of the efficacy of ORC, LRC and RARC, but received a limited number of studies, which did not explain the difference in efficacy between LRC and RARC (Peng et al., 2020).

At present, some scholars have pointed out that RARC has less EBL, lower incidence of complications and faster postoperative gastrointestinal (GI) recovery than LRC (Park et al., 2013; Matsumoto et al., 2019). Other studies have not yielded similar outcomes (Kim et al., 2016; Su et al., 2019). this makes it possible for clinicians to rely more on experience and judgment when choosing a surgical option, but not to be guided by evidence-based medicine, so Peng et al. conducted a meta-analysis (8 studies, on operation time, estimated blood loss, intraoperative blood transfusion, PSM, oral intake time, length of hospital stay, complication and other indicators) and found that there were no statistically significant differences between LRC and RARC, and found that the LRC and the RARC have similar results on the effectiveness and safety of bladder cancer. A subgroup analysis of different Clavien–Dindo grades for postoperative complications showed no significant difference in the postoperative complication grades of LRC and RARC within 30 or 90-days after surgery. Instead of those medical institutions that cannot perform robot-assisted surgery (RAS) but are seeking minimally invasive and faster postoperative recovery, LRC is worth considering (Peng et al., 2020).

In another meta-analysis, Feng et al. compared perioperative outcomes between RARC and LRC for bladder cancer at a systematic review and updated meta-analysis (10 studies, 2 of them were RCTs, four prospective studies and four retrospective studies) including 634 patients (369 in the RARC group and 265 in the LRC group) from six countries and found that there was no significant difference concerning basic demographic variables, the operative time between the 2 groups, There were statistically significant shorter LOS (95% CI −1.24, 0.03), fewer complication rates (the relative risks [RR] were 0.74 and 0.49 for Clavien grade I–II and Clavien grade III–V, respectively) and less death risk (HR 0.26, 95% CI 0.17–0.39) in RARC group compared with LRC group. they concluded that RARC might improve the management of patients with muscle-invasive or high-risk NMIBC (Feng et al., 2020).

Minimally invasive radical cystectomy

A) Laparoscopic radical cystectomy (LRC):

ORC is a complex surgical procedure, with a risk of substantial blood loss, perioperative complications, and mortality (Shabsigh et al., 2009).

LRC is a minimally invasive approach that was initially developed to reduce the complications of open surgery. However, the procedure is associated with an extensive learning curve and thus, it has not been widely adopted in clinical practice. RARC has advantages compared with traditional laparoscopy, including a magnified view and mechanical wrists, which enable more bend and rotation than the human hand (Challacombe et al., 2011).

The procedure represents a reproducible minimally invasive alternative to open surgery, but oncological outcomes have not been compared directly. Potential concerns about robotic cystectomy include the lack of tactile feedback, which is considered to be important for complete resection of locally advanced disease, and possible recurrence of cancer in uncommon locations (e.g., peritoneal carcinomatosis). Concerns have also been raised about the learning curve and cost of robotic surgery (Nguyen et al., 2015).

The first case of laparoscopic cystectomy was reported in 1992 by Parra et al. when they performed a simple cystectomy for a 27-year-old woman with post-traumatic paraplegia complicated with benign pyocystis and retained bladder after urinary diversion (Parra et al., 1992).

The first case of RC with the reconstruction of the ileal conduit (IC) extracorporeally was reported in 1995 by De Badajoz et al. (De Badajoz et al., 1995). Since then, there have been various reports of LRC, but the urinary diversion was performed extracorporeally from the site of removal of the specimen or by a mini-laparotomy incision (Puppo et al., 1995; Hemal & Singh, 2001, 2002).

Puppo et al. also reported five cases of LRC with transvaginal extraction of the specimen (Puppo et al., 1995). Gill et al. first reported two cases of LRC (Gill et al., 2000) and intracorporeal ileal conduit (IIC) formation (Gupta et al., 2002). Turk et al. were the first to report five cases of LRC and intracorporeal continent (recto-sigmoid pouch) urinary diversion and transrectal specimen retrieval (TÜRK et al., 2001). Gill et al. also performed LRC and an orthotopic neobladder in two patients (Gill et al., 2002).

Tang et al. reported at meta-analysis (Sixteen eligible trials evaluating LRC vs ORC were identified including seven prospective and nine retrospective studies) that LRC appears to be a safe, feasible and minimally invasive alternative to ORC with reliable perioperative safety, pathologic & oncologic efficacy, comparable post-operative neobladder function and fewer complications **(Table 3)** (Tang et al., 2014a).

Table 3: Clinicopathological data from a systematic review and meta-analysis comparing LRC versus ORC in bladder cancer (Tang et al., 2014a).

Outcome of interest	No. of studies	No. of patients, LRC/ORC	OR/WMD (95% CI)	*p*-value
Operating time, min	11	280/287	36.91 [16.41, 57.41][†]	**<0.001**
EBL, mL	11	280/287	−410.00 [−632.28, −187.73][†]	**<0.001**
LOS, days	11	280/287	−2.78 [−3.31, −2.25][†]	**<0.001**
Blood transfusion rate	7	203/192	0.25 [0.16, 0.40]	**<0.001**
Time to regular diet, days	10	222/235	−1.63 [−2.16, −1.10][†]	**<0.001**
Narcotic analgesic requirement, mg	6	140/133	−29.55 [−43.70, −15.39][†]	**<0.001**
Positive surgical margins	5	176/168	0.31 [0.13, 0.72]	**0.006**
Positive lymph node	8	245/233	0.54 [0.31, 0.92]	**0.02**
Distant metastasis	3	81/84	0.73 [0.30, 1.77]	0.48
Death	3	65/72	0.82 [0.28, 2.44]	0.72
Overall complications	7	202/199	0.63 [0.41, 0.97]	**0.03**

Abbreviations: CI=Confidence interval; OR=odds ratio; WMD=weighted mean difference; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

B) Robotic-assisted radical cystectomy (RARC):

Traditional laparoscopy has inherent limitations as a result of four degrees of freedom of movement and poor ergonomics which put a lot of physical and mental strain on surgeons performing the surgery. As a result, it has gradually been replaced with robotic surgery which has the unique benefits of superior visualization, a higher degree of freedom of movement, and better ergonomics (Lanfranco et al., 2004; Hussain et al., 2014).

However, the installation and maintenance costs of current robotic surgical systems remain prohibitive and have attracted some criticism, particularly in the "free-for-all" health care systems such as the National Health Service (NHS) in the UK. The benefit of robotic surgery continues to be debated even for procedures such as RP (Yaxley et al., 2016) and partial nephrectomy. but the robotic procedure which has come under the most scrutiny is RC (Xia et al., 2017).

Since the introduction of robotic technology to treat bladder cancer, some authors in the literature performed comparisons between open and robotic radical cystectomies. The RARC has shown to be equivalent to ORC in terms of oncological and functional outcomes (Wilson et al., 2015)

The development of RAS perfectly fits the concept of urology in the field of MIS. In recent years, research reports on urologically assisted robotic surgery have also increased (Mottrie et al., 2018) Robots have been used in the field of urology for more than 20 years. With excellent performance, minimal trauma and rapid postoperative recovery, they have attracted the attention of various medical institutions and clinicians (Navaratnam et al., 2018).

Mani Menon described the development of a technique for performing robotic-assisted radical cystectomy (RARC) in 17 patients from 2002 to 2003 The cases were performed using the original da Vinci Surgical System (Intuitive Surgical). The urinary reconstruction portions of the case were performed extracorporeally with an average total time of 260 minutes for an IC and 308 minutes for an orthotopic neobladder (Menon et al., 2003).

As the technique was popularized, randomized studies showed non-inferiority of RARC to ORC. This finding has culminated in a Cochrane review released in 2019 that included 5 RCTs, including the RAZOR trial, which included 541 patients, 270 ORC and 271 robotic-assisted radical cystectomies (Parekh et al., 2018). The Cochrane review showed a similar time to recurrence, similar major complications (RR, 1.06; 95% CI, 0.76–1.48), for RARC versus ORC as primary outcomes. Secondary outcomes showed a very low certainty of the evidence for comparing minor complications, a high likelihood of decreased blood transfusions (RR, 0.58; 95% CI, 0.43–0.80; 2 trials) with the possibility of a minor decreased LOS in the RARC versus ORC groups (95% CI, –1.22 to –0.12) (Rai et al., 2019).

RARC has come under most scrutiny principally because of the hype created over the perceived benefits of RAS. It may be argued that the surgical community had unrealistic expectations from this technology and anticipated a vast difference in outcomes compared with open surgery (Dotan et al., 2007).

As such, given that the benefits of robotic cystectomy reported to date have been marginal, and coupled with the high cost of robotic surgery, it has been a challenge to justify the introduction of robotic cystectomy in the NHS in the UK. To demonstrate the oncological safety of the technique, PSM and LN yield are considered two critical measures of surgical quality in cystectomy. Large studies have demonstrated that PSMs are important predictors of local recurrence and metastases, and consequently determine CSS (Herr et al., 2004). Higher LN yield has also been shown to be associated with improved CSS (Herr et al., 2002; Koppie et al., 2006; Dhar et al., 2008; Zehnder et al., 2011). Therefore, for MIRC to measure up to ORC in terms of oncological efficacy, it must be able to achieve equivalence in these two pathological measures (Khan et al., 2020).

The US FDA has approved 5 robotic systems to date: AESOP, Endo assist, Neuromate, Zeus, and da Vinci (Cevrioglu et al., 2004); however, the term 'robotic surgery' became synonymous with the da Vinci Surgical System (Intuitive Surgical) soon after that seminal report was published. The system includes 3 components: a surgeon console (the control), patient cart, and vision cart (Mikhail et al., 2020).

The introduction of the da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) has dramatically transformed the landscape of MIS. This surgical platform, whilst maintaining the benefits of standard laparoscopy, provides the surgeon with additional advantages of greater dexterity, a wider range of movement, tremor filtration, three-dimensional vision, and primary surgeon camera control (Honda et al., 2017). These benefits are useful, especially when there is a deep and narrow field and when intracorporeal suturing and fine tissue dissection are required, as is the case for pelvic and retroperitoneal surgery This technology has therefore enabled surgeons to replicate complex open procedures using MIS with a much faster learning curve than standard laparoscopy and the potential to supersede the results of open surgery (Iannetti et al., 2014).

RAS has now become the contemporary 'gold standard' treatment modality for many urological conditions. Perhaps the most established procedure being robot-assisted laparoscopic prostatectomy (RALP) (Iannetti et al., 2014). After first being described by Menon et al, (Menon et al., 2002). RALP has now replaced open retropubic radical prostatectomy (RRP) and laparoscopic radical prostatectomy (LRP) in most modern healthcare systems (Iannetti et al., 2014).

Despite the lack of high-quality RCTs showing a benefit over open RRP (Yaxley et al., 2016), there is an abundance of non-randomized data that have shown clear advantages for intraoperative blood loss, transfusion rates, duration of catheterization, LOS, positive margins, potency, continence, and readmission rates (Ramsay et al., 2012; Tang et al., 2017). since its first report, again by Menon et al., robot-assisted radical cystectomy (RARC) has likewise been adopted by several large institutions (Menon et al., 2003).

A recent systematic review comparing RARC (with mainly ECUD) with open RC showed that RARC benefited from fewer perioperative complications, greater LN yield, lower blood loss, and a shorter LOS (Li et al., 2013). With many units now routinely performing intracorporeal urinary diversion (ICUD), further benefits can be derived by a reduction in incision size, postoperative pain, and bowel-related complications (Ahmed et al., 2014).

A recent study demonstrated that the introduction of RARC and ICUD represented the principal factor leading to the benefits of an RC enhanced-recovery program (Koupparis et al., 2015), and cost-efficiency analyses have shown promising results even when factoring in the purchase, consumable and maintenance expenses (Lee et al., 2011; Mmeje et al., 2013).

The ''learning curve'' is the period when a certain surgical procedure is slower, more difficult, has a greater number of complications and is less effective due to the inexperience of the surgeons. Although there is not a standard definition of the ''learning curve'', it is frequently defined by the minimum number of cases required to reproduce the standard technique. This curve is influenced by certain surgeon-dependent parameters, such as experience in other procedures (open and minimally invasive) as well as a good attitude and self-confidence (Artibani & Novara, 2008).

Buxton's law states that it is always too early for rigorous assessment of a new surgical technique, until, unfortunately, it is suddenly too late. Generally, the clinical community is reluctant to subject new surgical innovation to scientific rigor early on because procedures often have an extensive learning curve, and by the time the technique is widely adopted, it is often too late to do rigorous trials because it would be unethical to deny patients access to cutting-edge care. Thus, a thorough evaluation of new surgical innovations is often avoided before best practice is determined (Buxton, 1987).

Since then, there have been continuous efforts to examine surgical safety, the oncological and functional efficacy, and the cost-effectiveness of RARC compared to the previous standard of care of ORC. Following the initial small, single-center case series (Beecken et al., 2003), a large consortium was formed to prospectively enroll and monitor patients undergoing RARC in tertiary care centers (Raza et al., 2015; Hussein et al., 2019; Hussein et al., 2020).

Subsequently, updated data were published by this multi-institutional collaboration showing that RARC was safe and possibly advantageous in terms of LOS and perioperative transfusions. Along with these retrospective and non-randomized data, five prospective randomized clinical trials (RCTs) (Nix et al., 2010; Bochner et al., 2014; Messer et al., 2014; Parekh et al., 2018; Khan et al., 2020) involving a total of 541 participants compared RARC and ORC in attempts to identify the technique of choice for RC. Individual and pooled results (Rai et al., 2019; Satkunasivam et al., 2019) from these RCTs confirmed that RARC and ORC are similar in terms of oncological control (i e time to recurrence), rates of positive margins, nodal yields, major complications (i e, Clavien-Dindo grades III–V), and quality of life after surgery. An initial concern about aberrant local recurrence patterns and peritoneal carcinomatosis after RARC (Nguyen et al., 2015) has been rebutted and conclusively refuted by these RCT data; equally, this has just not been an issue in the worldwide RARC experience. Besides these similar findings, RARC probably results in lower blood loss and may lead to a shorter hospital stay and a lower rate of minor complications (Clavien grades I and II) compared to ORC (Pourmalek et al., 2015).

Furthermore, preliminary data also suggest that the RARC approach is not negatively affected by neoadjuvant treatments, including both chemotherapy and immunotherapy (Grossman et al., 2003; Powles et al., 2019; Aldhaam et al., 2020; Briganti et al., 2020; Necchi et al., 2020). Here, RARC showed similar rates of perioperative complications and non-inferior surgical safety when compared to the open approach (Vetterlein et al., 2020). Also, the feasibility of RARC was demonstrated in octogenarians and surgically complex patients (Elsayed et al., 2020a; Elsayed et al., 2020b).

Finally, from a surgical standpoint, RARC may reduce the learning curve, allowing faster training of experienced surgeons, who are claimed to be the main trigger for improving surgical safety and surgical outcomes (Ghezzi & Corleta, 2016; Gandaglia et al., 2018). Furthermore, RARC also seems to be favoured from an ergonomic perspective for the urologist and the team members. Taking these points together and given the lack of clear superiority of one approach over the other, it should be concluded that RARC cannot be qualified as the standard of care for the surgical treatment of bladder cancer, but neither can the opposite be the case (Williams et al., 2019; Bruins et al., 2020).

The robotic approach has gained in popularity, with patients increasingly requesting to be treated with RARC given its advantages such as the minimally invasive nature and shorter hospital stay and postoperative recovery. A recent study comparing trends in the use of RARC and ORC across tertiary-care teaching institutions in Europe and North America found that the RARC has become the procedure more commonly performed among contemporary patients, with an increase from 29% in 2006–2008 to 54% in 2015–2018, while ORC decreased from 71% in 2006–2008 to 46% in 2015–2018 ($p<0.001$) (Zamboni et al., 2019).

The pros and cons of a robotic versus an open approach have also been assessed for other urological malignancies. Robot-assisted radical prostatectomy and robot-assisted partial nephrectomy have proved to be non-inferior in terms of surgical safety with similar postoperative rates of complications compared to their open counterparts. Only one RCT comparing open versus robotic radical prostatectomy was published (Yaxley et al., 2016), and a few non-randomized studies compared robotic and open partial nephrectomy (Peyronnet et al., 2016)

Available level 1 A evidence proves that RARC and ORC can both be offered to patients as there are no significant perioperative, postoperative, or long-term functional or oncological outcome differences, similar to the situation for prostate and kidney surgery. The evidence supporting RARC (five RCTs) is indeed much more robust than the evidence available for robotic radical prostatectomy (one RCT) or robotic partial nephrectomy (only retrospective evidence), yet nobody would argue about the contemporary role of robotic surgery in the latter two scenarios. RARC is still not performed in every center and is mainly centralized in tertiary care teaching institutions. This is mainly because RARC is an expensive procedure, primarily owing to the cost of the robot, which therefore is not available everywhere. Also, RC is a complex surgical procedure with high complication rates (Briganti et al., 2020).

In salvage cystectomy cases, the desmoplastic reaction following radiotherapy may make the dissection between the rectum and bladder more challenging, but the robotic approach arguably allows better visualization to promote a more precise dissection compared to open surgery. A potential disadvantage of the robotic approach is the prolonged operation in steep Trendelenburg position which may affect respiratory ventilation function although data from physiological studies suggest that hemodynamic and pulmonary variables are within safe limits and well tolerated by patients (Awad et al., 2009).

Despite the apparent advantage of the robotic approach on several perioperative outcomes such as transfusion requirements, LOS and minor complications, the apparent advantage is less likely to outweigh the fixed costs associated with the robotic platform. Nonetheless, a synergistic effect between these inpatient costs with a concurrent reduction in operating time cannot be ignored. in the future, the fixed cost of the robotic platform will certainly decrease with the new market entrants when the current market monopoly that exists within the robotic industry will disappear (Albisinni et al., 2019).

Recently, RARC has become popular, because RARC has ergonomic advantages compared with LRC. Indeed, MIRC has shifted from LRC to RARC in Japan to some extent. However, all institutions cannot purchase surgical robots because of high costs, and in many parts of the world, laparoscopic surgery still prevails as an alternative to open surgery (Khan et al., 2016; Khan et al., 2020).

Advances in laparoscopic surgery technology do provide a perfect alternative to robotic surgical equipment for some medical institutions. It is true that for RARC, the cost to the patients is high, but if relatively similar results can be achieved, LRC is indeed a good solution. Even though RC has gradually moved from open surgery to minimally invasive, how to control the massive blood loss and related complications caused by UD has always attracted the attention of scholars (Peng et al., 2020).

Urinary diversion

RC remains among the more morbid procedures in urology due to the risk factors for bladder cancer and the resulting patient comorbidities, as well as the extent of surgery with a urinary diversion (Tan et al., 2017b).

Urinary diversion is the cause of the most significant morbidity after RC (Witjes et al., 2017; KOç et al., 2018). in all series, infectious and GI complications are the most frequent (Albisinni et al., 2016b).

Traditionally, urinary diversions were carried out extra-corporeally (ECUD) because of the complexity of the procedure. However, it is associated with a significant rate of complications (Kurpad et al., 2016; Dason & Goh, 2018). ICUD has been suggested to have benefits, such as smaller incision, reduced pain, decreased bowel exposure and early postoperative recovery (Ahmed et al., 2014; Fujimura, 2019; Koie et al., 2019).

The evolution of robotic surgery, with its three-dimensional vision and improved ergonomics using EndoWrist technology, facilitates an easier ICUD owing to improved intracorporeal suturing. Thus, ICUD during RARC is gaining popularity. However, the use of pure laparoscopic ICUD has rarely been reported; this might be primarily attributed to a technical difficulty, particularly in precise intracorporeal suturing (Shao et al., 2015; Li et al., 2019a).

Novara et al. have performed a systematic review and meta-analyses of RARC with ICUD and ECUD. In the subset analysis of ICUD, the overall 30-days complication rate was 67% (range, 42–86%) for IC and 46% (range, 43–62%) for neobladder with high-grade complication rates of 24% (range, 0–54%) and 28% (15–33%), respectively. Mortality rates ranged from 0–3% across ICUD (Novara et al., 2015).

I. Extracorporeal Urinary Diversion (ECUD):

Recent reports provide a step-by-step approach to the different ECUDs that may be performed in the setting of RARC indicate comparable results to open surgery regarding intermediate- and long-term oncological outcomes and the extent of PLND (Pruthi et al., 2010a; Kauffman et al., 2011; Snow-Lisy et al., 2014). However, operative times are one of the main obstacles that hinder widespread acceptance of RARC (Styn et al., 2012). ECUD with RARC provides a method of reconstruction that mirrors that of open surgery regarding operative times. Complication rates and functional outcomes with ECUD also appear at least comparable to the open series (Menon et al., 2004).

Compared to the intracorporeal technique, the key advantage of ECUD is the utilization of open suturing. This results in a shorter learning curve, operative times comparable to open procedures, less time under general anaesthesia for the patient, and ultimately less cost. A prolonged learning curve would be justified if prospective, randomized trials show an obvious advantage to the intracorporeal technique (Chan et al., 2015a). However, retrospectively reviewed data that exist comparing ICUD to ECUD is neither robust nor mature enough to draw definite conclusions and justify the change in surgical technique (Ahmed et al., 2014).

Using a hybrid EC technique that re-docks the robot to perform the neobladder-urethral anastomoses allows efficient and purposeful use of the robot, accessing the deep pelvis and enabling placement of sutures under direct vision. Other advantages of EC diversion include minimizing faecal contamination of the peritoneal cavity and minimizing surgeon fatigue. The main disadvantage of the ECUD is the need for a larger incision. Another potential problem cited with the EC technique is impaired tissue orientation/positional distortion and the need for considerable mobilization of the ureters, both of which may contribute to ischemia and possible ureteral stricture. Other disadvantages include increased evaporative fluid loss and external bowel manipulation, both of which may contribute to ileus (Chan et al., 2015a).

II. Intracorporeal Urinary Diversion (ICUD):

The implementation of a full intracorporeal approach in patients with poor cardio-respiratory status may reduce surgical trauma and cardiorespiratory complications (Lamb et al., 2016).

The full ICUD has been coded and is now performed in expert centers. although performing such an approach requires deep exposure and suturing skills, the robotic platforms greatly help due to the freedom of movement (Cacciamani et al., 2019).

In the majority of available data from a randomized trial comparing ORC and RARC, the urinary diversion was performed via an EC approach. RARC experts advocate that this may account for the absence of a significant difference across the two techniques (ORC vs. RARC), given the loss of advantage of RARC when urinary diversion is performed extracorporeally (Bochner et al., 2015; Cacciamani et al., 2019). To date, this clinical question has no solid scientific answer. However, in a head-to-head comparison at the Cleveland Clinic, Bertolo et al. failed to find a significant difference in complication rate between extra and intracorporeal IC (Bertolo et al., 2019).

Lenfant et al. reported similar complication rates across 108 patients receiving RARC with extra or intracorporeal urinary diversion. it must be underlined that this was a retrospective revision and that patients in the intracorporeal arm had a significantly higher rate of neobladder reconstruction (53% vs. 18%)(Lenfant et al., 2018)

In the international robotic cystectomy consortium (IRCC), the 90-days complication rate was not significantly different between extra and intracorporeal diversion, but a trend favouring intracorporeal was observed (41% vs. 49%, P=0.05) (Johar et al., 2013). Moreover, GI complications were significantly lower in the intracorporeal group ($P \leq 0.001$). A higher blood loss and transfusion rate was reported for ECUD. Prospective randomized trials are underway to compare ORC to RARC with full intracorporeal urinary diversion (Catto et al., 2018).

More recently, the RAZOR trial, a randomized, open-label phase-3 non-inferiority study, demonstrated that RARC was non-inferior to ORC with regards to 2-year progression-free survival (Parekh et al., 2018). Of note, all the patients in these trials had an ECUD. Completely intracorporeal urinary diversion (ICUD) was first described in 2003 (Beecken et al., 2003). Though ICUD was initially performed in only 9% of cases in 2005, the most recent update by the International Robotic Cystectomy Consortium (IRCC) reports an increase to 97% in 2015 among their group (Hussein et al., 2018). While a prospective RCT comparing RARC with ICUD to ORC is enrolling, long-term outcomes following ICUD appear similar to historic open cohorts (Sandberg & Hemal, 2016; Tan et al., 2016c; Catto et al., 2018; Brassetti et al., 2019).

ICUD can reduce postoperative complication rates owing to the potential benefits of a smaller incision, reduced postoperative pain, decreased bowel exposure, reduced risk of fluid imbalance and early postoperative recovery (Ahmed et al., 2014; Fujimura, 2019; Koie et al., 2019). Interestingly, some studies about RARC have shown that ICUD reduces the rate of postoperative complications, whereas other studies have shown no significant difference in terms of complication rates between ICUD and ECUD, or worse complication rates in ICUD (Ahmed et al., 2014), (Hussein et al., 2018; Lenfant et al., 2018; Bertolo et al., 2019; Zhang et al., 2020).

The need for intraoperative or perioperative blood transfusion in patients undergoing RC has been previously identified as an independent risk factor for overall mortality and high-grade complications in the ORC and RARC literature (Morgan et al., 2013; Ahmed et al., 2014; Moschini et al., 2015; Tan et al., 2017b).

ICUD is associated with less blood loss compared to ECUD. Interestingly, the IRCC noted a significantly decreased rate of blood transfusion in the ICUD cohort compared to ECUD (4% vs. 19%), though there was a small but statistically significant increase in the incidence of high-grade complications in the ICUD group (13 vs. 10%, P=0.02). This is likely attributed to high-grade complications occurring more frequently early in the learning curve, as the high-grade complication rate decreased with time in the ICUD cohort but not in the ECUD group. Of note, ICUD was not an independent predictive factor of high-grade complications in their assessment(Hussein et al., 2018).

The theoretical advantage of ICUD is a decreased risk of distal ureteral ischemia and subsequent ureteral leak or stricture given the shorter length of ureter required when compared to ECUD or ORC. The reported benign anastomotic stricture rate in large ORC series is between 3–10% (Shimko et al., 2011; Gillian et al., 2018). Anderson et al. (Anderson et al., 2013) compared ORC to RARC-ECUD and noted a stricture rate of 8.5 vs. 12.6%, respectively (P=0.2). It seems appropriate that the stricture rate would be similar, given that the ureteral length required for the diversion is similar in both arms. In comparison, a review of a series of ICUD with a minimum of 100 patients demonstrates a uretero-intestinal anastomosis (UIA) stricture or leak rate ranging from 2–3.8% (Azzouni et al., 2013; Desai et al., 2014; Tan et al., 2017b).

Schumacher et al. reported 2 UIA strictures (4.4%) successfully managed with balloon dilation in their cohort of 45 patients undergoing ICUD (Schumacher et al., 2011). The use of Indocyanine green (ICG) dye, particularly antegrade via percutaneous nephrostomy tube if in place, can identify ischemic areas of the distal ureter prior to anastomosis due to lack of fluorescence (Pathak & Hemal, 2019).

The intracorporeal urinary diversion after RARC is a major challenge to the surgeon and the assisting team especially due to the limited field of vision and the long operative time during the learning curve (Yohannes et al., 2003; Pruthi et al., 2010b). Therefore, most RARC surgeons perform an EC technique for the urinary diversion using the incision to deliver the cystectomy specimen. Several experienced robotic centers with a high- volume of RARC published their techniques and outcomes of intracorporeal urinary diversion (Jonsson et al., 2011; Goh et al., 2012; Poch et al., 2012; Azzouni et al., 2013; Bishop et al., 2013; Collins et al., 2013; Chan et al., 2015b).

RARC with ICUD is a minimally invasive alternative to conventional ORC. ICUD is technically demanding though the learning curve can be surmounted with consistent exposure to the procedure. Variations in technique exist, though non-continent, continent cutaneous and orthotopic continent diversions have all been reported with acceptable oncologic and functional outcomes. Overall complication rates are similar to ECUD and ORC. Potential advantages of ICUD include decreased rates of intraoperative blood transfusion and distal ureteral ischemia along with faster convalescence. An ongoing prospective, randomized clinical trial comparing RARC with ICUD to ORC will help clarify these benefits (Murthy et al., 2020).

A. Intracorporeal ileal conduit (IIC):

Patient selection is similar to the open technique, inclusion criteria for the robotic-assisted laparoscopic technique itself need to be followed. Bowel preparation before IIC is not necessary (Cerantola et al., 2013).

An IIC is a safe and time-efficient urinary diversion in trained robotic teams with a standardized technique. Experienced teams report an operative time of about 125 min for the intracorporeal conduit (Azzouni et al., 2013). Data show a lower 30-days readmission rate (5% vs. 15%, $p<0.0001$) and a lower 90-days mortality rate (1.6% vs. 4.9%, $P=0.043$) with an intracorporeal technique compared to an EC approach (Ahmed et al., 2014). In a large series of 100 consecutive IIC, 50% of patients had a postoperative infection, there of 9% sepsis. Only 1% needed a transfusion due to anemia, 9% developed hydronephrosis, there of 4% needed a percutaneous nephrostomy. Due to bowel obstruction or fascial dehiscence, 3% needed a surgical exploration (Azzouni et al., 2013).

Compared with robotic ICUD-IC, laparoscopic ICUD-IC is low cost and can be carried out at Roselle Park institution without robot assistance. Furthermore, during the robotic intracorporeal urinary diversion, damage to the bowel and tearing of the mesentery can occur due to a lack of tactile feedback (Elsayed et al., 2020c). In contrast, the surgeon can handle the bowel gently during pure laparoscopy because tactile feedback still exists. Also, bowel reconstruction during laparoscopy is well established in the field of GI surgery. Therefore, except for uretero-enteric anastomosis, laparoscopic ICUD-IC seems not to be technically demanding and has some advantages compared with robotic ICUD-IC (Kanno et al., 2020).

In their report of transition from EC—an IC to IIC (68 vs. 59 patients, respectively), Murthy et al. noted shorter total operative times, blood loss and 30-days overall complication rate in the ICUD cohort (Murthy et al., 2020).

Kanno et al. compared the perioperative and oncological outcomes of LRC with ICUD-IC and ECUD-IC. The operative time in the ICUD-IC group was approximately 1 h longer than that in the ECUD-IC group. The early and late postoperative complication rates were similar in both groups, except for a reduced wound-related complication rate in the ICUD-IC group. The median days to regular oral food intake were 4 and 5 days in the ICUD-IC and ECUD-

IC groups, respectively (P=0.014), there is no significant difference in uretero-enteric stricture and reoperation rates. (Kanno et al., 2020).

B. Intracorporeal Neobladder (IN):

A substantial disadvantage of pure laparoscopy is the reduced range of motion due to a fixed trocar position, which determines the angle of the laparoscopic instrument in the working field (Rassweiler & Teber, 2016). Such a disadvantage in terms of ergonomics is critical during difficult processes, including reconstructing parts. ICUDs are procedures that are technically demanding because of their complexity, and precise suturing is mandatory. Therefore, early reports have shown that ICUD during pure LRC has a longer operative time and higher complication rates than ECUD (Haber et al., 2007).

RARC has been grown steadily during the last years and has replaced LRC in centers where the robot is available. The neobladder can be formed intracorporeally (Balaji et al., 2004; Sala et al., 2006; Hosseini et al., 2011), but operative time may be reduced if this is done extracorporeally through the same incision used to deliver the cystectomy specimen. Most RARC surgeons advocate a combination of robotic-assisted laparoscopy and open surgery, performing the cystectomy and extended PLND with the robot, but due to technical difficulties and longer operative time (Keim & Theodorescu, 2006; Guru et al., 2007; Murphy et al., 2008; Wang et al., 2008). using an EC approach for the construction of the conduit or neobladder (Murphy et al., 2008), However, some centers have developed techniques for RARC with a complete intracorporeal urinary diversion (Sala et al., 2006).

With the introduction of the da Vinci® robotic system (Intuitive Surgical) in urological clinical practice, many robot-assisted surgical procedures have been performed. Compared with the traditional laparoscopic technique, the hand-eye alignment and depth perception provided by the robotic system are advantageous and may eventually be superior to using open procedures, resulting in less surgical morbidity and a shorter learning curve. However, RARC with totally intracorporeal urinary diversion is still considered a technically challenging procedure (Beecken et al., 2003; Keim & Theodorescu, 2006; Sala et al., 2006).

RARC and urinary diversion have been adopted by several institutions worldwide, and today >1500 procedures have been reported to the IRCC. It has been debated whether the intracorporeal technique for urinary reconstruction has many advantages over the EC technique. The intracorporeal technique allows the restoration of small bowel continuity and the construction of the neobladder performed without incision of the abdominal wall. In the female, the specimen may be taken out through an incision in the vaginal wall, and in the male, the specimen is extracted through a small incision at the end of the procedure. It has been argued that the intracorporeal approach should only be used if specimen retrieval may be performed without an additional incision. The intracorporeal reconstruction is less traumatic for the patient, but on the other hand, more technically demanding for the surgeon. Robotics makes an intracorporeal technique a more feasible procedure even though most centers prefer an EC approach for urinary diversion (Guru et al., 2007; Pruthi & Wallen, 2007; Murphy et al., 2008; Wang et al., 2008).

One major advantage of performing the urinary diversion intracorporeally is that performing the running suture of the anastomosis between the urethra and the ileum minimises the risk of urinary leakage. There is also less traction to the anastomosis between the reservoir and the urethra using an intracorporeal approach, as an appropriate ileal segment long enough to reach down to the urethra can be used (Schumacher et al., 2009).

However, the evolution of robotic surgery, with its three-dimensional vision and improved ergonomics with the EndoWrist technology, facilitates ICUD as a result of improved intracorporeal suturing. Thus, ICUD during RARC is gaining popularity. In contrast, the accumulation of ICUD experience during RARC motivated us to carry out ICUD without robot assistance. Indeed, intracorporeal neobladder (IN) requires precise suturing during several steps, such as the formation of the ileal neobladder, urethra-vesical anastomosis and uretero-enteric anastomosis, whereas ICUD-IC only requires precise freehand suturing during uretero-enteric anastomosis. There is a debate on whether to carry out ICUD or ECUD during MIRC (Kurpad et al., 2016; Koie et al., 2019).

Each surgical procedure has its learning curve, and much of the trepidation in the adoption of ICUD is derived from concerns regarding technical proficiency and perioperative morbidity; this is particularly true with intracorporeal orthotopic continent diversion (Desai et al., 2014; Hussein et al., 2018).

Enhanced recovery after surgery [ERAS] protocols

Around one-third of bladder cancers are invasive and require radical treatment. RC with pelvic lymphadenectomy is a complex procedure with frequent morbidity and occasional mortality (Clark et al., 2013; Witjes et al., 2020). The rate of postoperative complications varies with providers, details of follow-up, and reporting criteria (Shabsigh et al., 2009).

Screening patients revealed that a significant number of patients are malnourished. Improving the preoperative nutritional status of patients has been shown to reduce complications and enhance recovery in GI surgery (Barrass et al., 2006; Karl et al., 2009; Gregg et al., 2011).

“Fast track” or ERAS have been incorporated in the preoperative, intra-operative and postoperative management to promote patient recovery and minimize the associated morbidity (Collins et al., 2016).

Following the establishment of the ERAS guidelines, perioperative care for patients undergoing major abdominal surgeries, such as RC, has evolved concerning bowel preparation, preoperative fasting, analgesia, and mobilization (Cerantola et al., 2013).

RC is complex surgery with numerous complications and low mortality risk, and it takes around 3 months for a person to recover from the operation. while ERAS protocols attempt to reduce the morbidity of RC, their implementation has been limited to date (Geltzeiler et al., 2014).

ERAS protocols are heterogeneous, and there is a need for improved reporting of individual components (including the use of audit) to improve understanding of which elements improve outcomes. Since the ERAS Society guidelines for RC (Cerantola et al., 2013), Pang et al. reported RC outcomes using a standard ERAS protocol, with 26 ERAS items using an audit system (Pang et al., 2018).

The RECOVER (20-item) checklist has been developed by the ERAS and ERAS USA Societies to provide a standardized framework that includes 16 elements:

(1) Preadmission patient education regarding the protocol.

(2) Preadmission screening and optimization as indicated for nutritional deficiency, frailty, anemia, HbA1c, tobacco cessation, and ethanol use.

(3) Fasting and carbohydrate loading guidelines.

(4) Pre-emptive analgesia (dose, route, timing).

(5) Anti-emetic prophylaxis (dose, route, timing).

(6) Intraoperative fluid management strategy.

(7) Types, doses, and routes of anesthetics administered.

(8) Patient warming strategy.

(9) Management of postoperative fluids.

(10) Postoperative analgesia and anti-emetic plans.

(11) Plan for opioid minimization.

(12) Drain and line management.

(13) Early mobilization strategy.

(14) Postoperative diet and bowel regimen management.

(15) Criteria for discharge.

(16) Tracking of post-discharge outcomes (Elias et al., 2019).

Omitting mechanical bowel preparation is largely supported by colorectal surgery literature. However, non-digestible vegetables can be seeded into the peritoneum during the reconstruction of the urinary diversion, and vegetables should be avoided for 1 day before RARC (Adding et al., 2015).

Preoperative oral intake of a clear fluid rich in carbohydrates 2–3 h prior to anesthesia reduces thirst, anxiety, catabolism and may promote postoperative muscle strength, and earlier return of bowel function (Gustafsson et al., 2012; Bilku et al., 2014).

Adequate pain control is crucial. Baseline treatment should include regular administration of acetaminophen. Epidural analgesia is very effective but may hinder early mobilization (Collins et al., 2016). Early mobilization has been associated with better cardiac and respiratory functions and psychological well-being, in addition to the prevention of thromboembolic complications (Drolet et al., 2013).

Although gastric decompression may be beneficial in reducing postoperative nausea and vomiting, it has been shown that early removal of the nasogastric tube in the recovery room after extubating is associated with reduced complications (Park et al., 2005). Early institution of an oral diet seems to enhance bowel function and decrease the time to first bowel motion and shorten hospital stay without increasing complications (Gianotti et al., 2011).

Enhanced recovery is becoming the standard of care following RARC. The European Association of Urology (EAU) Robotic Section Scientific Working Group recently published an enhanced recovery consensus for RARC in efforts to guide the standardization of postoperative care (Collins et al., 2016).

A dedicated care pathway can also improve convalescence. Tan et al. evaluated the role of an enhanced recovery after surgery (ERAS) pathway in their transition from ORC, to RARC-ICUD without an ERAS protocol, and subsequently RARC-ICUD with an ERAS protocol (Tan et al., 2018). Despite having a higher American Society of Anaesthesiologists score, the ERAS cohort had a significantly shorter median LOS compared to the RARC non-ERAS group and the ORC group (7 vs. 11 vs. 17 days, respectively). The ERAS group also had significantly lower 90-days readmission rates (Abboudi et al., 2014).

Williams et al. reviewed 22 studies regarding ERAS protocols and RC outcomes involving a total of 4048 patients and found that the application of enhanced recovery in patients undergoing surgery to remove the bladder is associated with fewer surgical complications and a shorter hospital stay. Avoidance of nasogastric tubes and use of local anesthesia after the operation were associated with a shorter LOS (Williams et al., 2020).

Patients and methods

Patients and methods

Study setting:

This study was carried out at the department of surgical Uro-oncology, National Cancer Institute, Cairo University in the period from February 2019 to February 2021.

Study design:

This study is an interventional RCT, Level of evidence: III according to criteria by the center for Evidence-Based Medicine in Oxford, UK (Phillips, 2004).

Patients and methods:

Patients' enrolment in the study is shown in the flow chart **(Figure 1)**

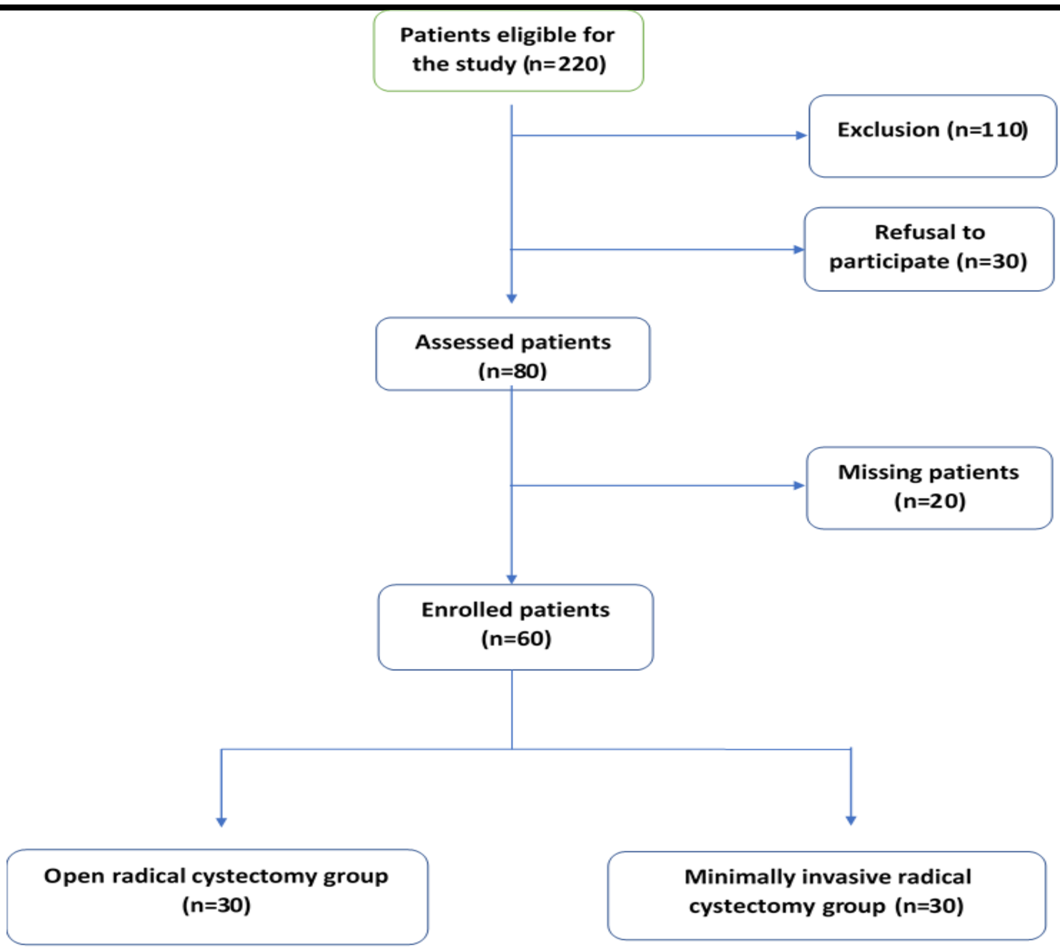

Figure 1: Patients' enrolment flow chart.

Sixty candidates for RC were recruited and allocated to two groups of thirty patients each, ORC group and MIRC group.

Ethical standards:

The study was performed according to the World Medical Association Declaration of Helsinki and the ethical standard of the National Cancer Institute, Cairo University. Institutional Review Board (IRB) full approval was obtained prior to the initiation of the study **(Study ID: S01901-31004)**, Written informed consent was obtained from all individuals before the operation.

Patient selection:

A. ***Inclusion criteria:***

1. Patients aged 30-70 years with bladder cancer.
2. Patients scheduled for RC.
3. Patients were able to comprehend and sign informed consent.
4. Patients fit for surgery (ECOG performance status 0,1) as presented in **(Table 4).**

Table 4: ECOG performance status. (Oken et al., 1982).

GRADE	ECOG performance status.
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair
5	Dead

Abbreviations: ECOG= Eastern Co-operative Oncology Group.

B. ***Exclusion criteria:***

To study a homogenous population, the following exclusion criteria were pre-defined:

1. Patients with medical comorbidities that preclude surgical management or minimally invasive techniques e.g., coagulopathy, morbid chest condition.
2. Patients with low risk or non-muscle invasive bladder cancer.
3. Patients with T4-bladder cancer.
4. Patients with advanced hydronephrosis or renal failure.
5. Patients with urinary bladder cancer invading bladder neck or prostatic urethra.
6. Patients with metastatic bladder cancer.
7. Patients who received preoperative radiation therapy to the pelvis.
8. Patients refusing surgery.
9. Patients refusing randomization.

Data will be collected from:

1. Outpatient medical records.
2. Inpatient Uro-oncology department records.
3. Pathology department records.

Methods:

A. History taking and clinical examination in the outpatient clinic.
B. Investigations:

    1. Laboratory: liver function tests, kidney function tests and coagulation profile.
    2. Radiological: CT abdomen, pelvis with contrast. chest X-ray or CT if clinically indicated. With or without bone scan (according to symptoms of bony pains, elevated alkaline phosphatase).
    3. Cystoscopy and biopsy:

Methodology in details:

Sixty patients who were candidates for RC for treatment of bladder cancer were recruited at the Surgery department, Uro-oncology Unit, National Cancer Institute, Cairo University in the period from February 2019 till February 2021.

The bladder cancer diagnosis was established with cystoscopy and biopsy. Patient workup was completed with CT abdomen and pelvis imaging.

Those patients were randomly allocated using computer-generated randomization to two groups, ORC and MIRC. Informed consent was obtained from each patient after an explanation of the aim and the nature of the procedures.

Full history was taken with a special focus on medical history, surgical history, urinary continence, potency, and special habits of medical importance. General examination was done with a special focus on BMI, previous abdominal surgeries. Abdominal and pelvic examinations were done. Investigations were done which included CBC, coagulation profile, liver, and kidney functions,

Preoperative cystoscopy (KARL STORZ GmbH, Tuttlingen, Germany) was performed by the same surgeon who will perform the RC.

Operative preparation:

The diagnosis was performed by pre-operative cystoscopy and biopsy, and imaging of the pelvis (CT or MRI as indicated) to evaluate tumor extension, regional lymphadenopathy and distant metastasis.

Bowel preparation was administered the night before surgery which consists of one enema taken the afternoon before surgery accompanied by an oral laxative, and one enema the night or the day of surgery.

Antibiotic prophylaxis included a single dose of intravenous broad-spectrum antibiotic delivered prior to the skin incision. Post-operative venous thromboembolism prophylaxis included elastic stockings for one month, and low molecular weight heparin until the patient was ambulant. pneumatic cuff compression devices and elastic stockings were used for intra-operative thrombo-embolism prophylaxis. Examination under anaesthesia was performed, followed by preparing the operative field, draping under sterile conditions.

Anaesthesia:

General anaesthesia using isoflurane, and muscle relaxation. Hypotensive anaesthesia was attempted to limit venous ooze and enhance visualization. Crystalloid restriction to 5 ml/kg/hour was attempted until anastomosis was performed unless contraindicated.

i. Conventional open radical cystectomy (ORC) surgical technique (Control group):

The patient in the ORC group was positioned in the supine position with approximately 10–15-degree inclination, the resection and urinary diversion parts of the procedure were completed with the conventional open surgical approach, A standard lower midline laparotomy was used for either conventional ORC in male patients or anterior pelvic exenteration in females.

Whether the operation was performed through a minimally invasive approach (robotic or laparoscopic) or an open surgical approach, the principles of RC remain the same.

ii. Minimally invasive radical cystectomy (MIRC) surgical technique (study group):

After inducing anesthesia. Patients were positioned supine to secure the patient to the table in Trendelenburg position, use of chest straps was utilized. In case of intracorporeal diversion was planned, steep Trendelenburg will facilitate bowel manipulation. The legs were placed in low lithotomy **(Figure 2)** in well-padded stirrups; the thigh should be close and parallel to the abdomen to minimize distortion of the pelvic floor. Sufficient padding was applied around the shoulder and pressure points, and the arms were tucked in. A urinary catheter was inserted under sterile conditions. A nasogastric tube was inserted which would be removed at the end of the procedure.

A. LRC surgical technique:

LRC equipment list:

1. Laparoscopic tower (KARL STORZ GmbH, Tuttlingen, Germany).
2. Veress needle, suction irrigator 5 mm device and Port closure device for ≥10 mm ports (KARL STORZ GmbH, Tuttlingen, Germany).
3. 3×10/12 mm disposable ports and 2×5 mm assist port. (ENDOPATH XCEL bladeless trocars).
4. Laparoscopic instruments: atraumatic grasper, scissor, suction irrigator, and needle holder.
5. LigaSure blunt tip laparoscopic sealing device.
6. Ligasure Maryland jaw laparoscopic sealing device.
7. LIGACLIP clip applier Ethicon.
8. Echelon flex endopath stapler 60 mm.
9. Sutures: PDS 3-0, PDS 4-0, Vicryl 3-0, STRATAFIX 3-0 and V-lock 3-0 barbed sutures.
10. Endocatch II bag (US Surgical, Norwalk, USA) as specimen retrieval bag system.
11. Appropriate open surgical equipment for completion of urinary diversion.

Figure 2: LRC patient position.

Port positions:

A five-port transperitoneal approach was used; a 10-mm primary umbilical port was inserted, and the entire peritoneal cavity inspected with a 30° laparoscope. The two 5-mm ports for the working instruments were placed 2.5 cm lateral to the rectus muscle and 2 cm below the umbilicus on either side. A 10 mm port was placed in the right iliac fossa 5 cm above the right anterior superior iliac spine (ASIS) in the anterior axillary line (AAL). The fifth port (5 mm) was placed in the left iliac fossa 5 cm above the left ASIS in the AAL **(Figure** 3**3).**

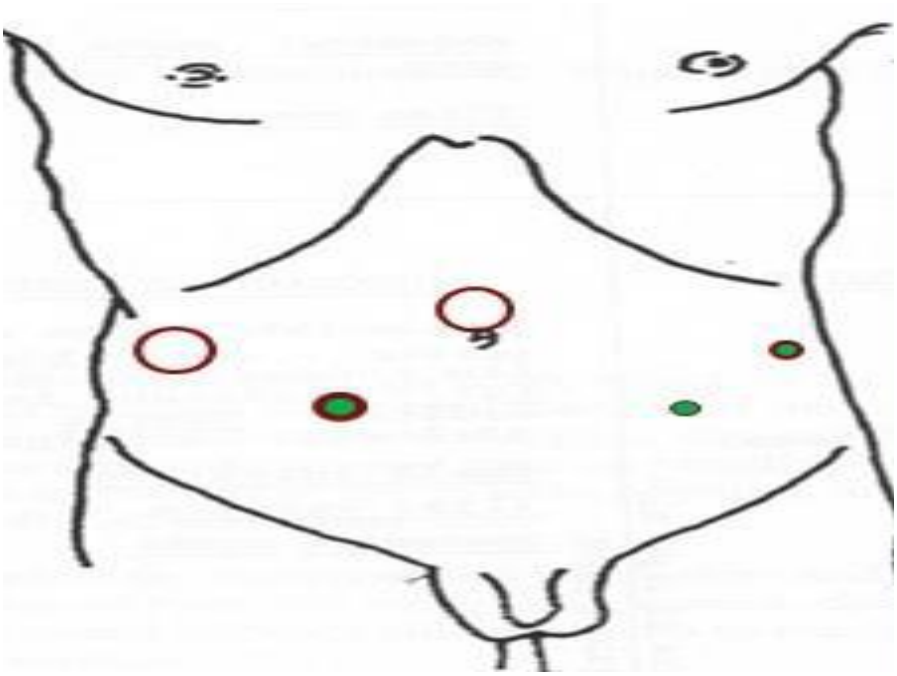

Figure 3: Schematic diagram showing LRC trocar position.

Our approach to male radical cystectomy occurs in steplike fashion as follows:

1. **Ureteral identification and dissection:**

Ureters were identified at the level of the common iliac artery (CIA). using great care to preserve vascular tissue around the ureter as much as possible. the ureter was dissected free for a small distance above the vessels and followed into the deep pelvis to the ureterovesical junction. An identical procedure was completed on the contralateral side; maximization of the length and blood supply on the left side was especially important given the need for tunneling later.

2. **Posterior plane dissection:**

Super forming the posterior dissection initially was essential. We reasoned that the angled lenses, combined with the wristed instrumentation, would allow the development of the rectovesical plane and initial preservation of the neurovascular bundle (NVB) even before the anterior and lateral bladder dissection.

The assistants provide equal counter traction on the transected peritoneal folds and the surgeon dissects all fatty and fibrovascular tissue of the posterior peritoneal fold.

Once the ureters were freed to the ureterovesical junction, the peritoneal incisions were connected, and the retro vesical space developed behind the bladder. Ureters were left intact to assist with orientation. Dissection proceeds behind the bladder and seminal vesicles to the level of the prostate; Denonvillier's fascia was transected, and at the level of the prostate, the prostate was dissected free as far as possible **(Figure 4)**.

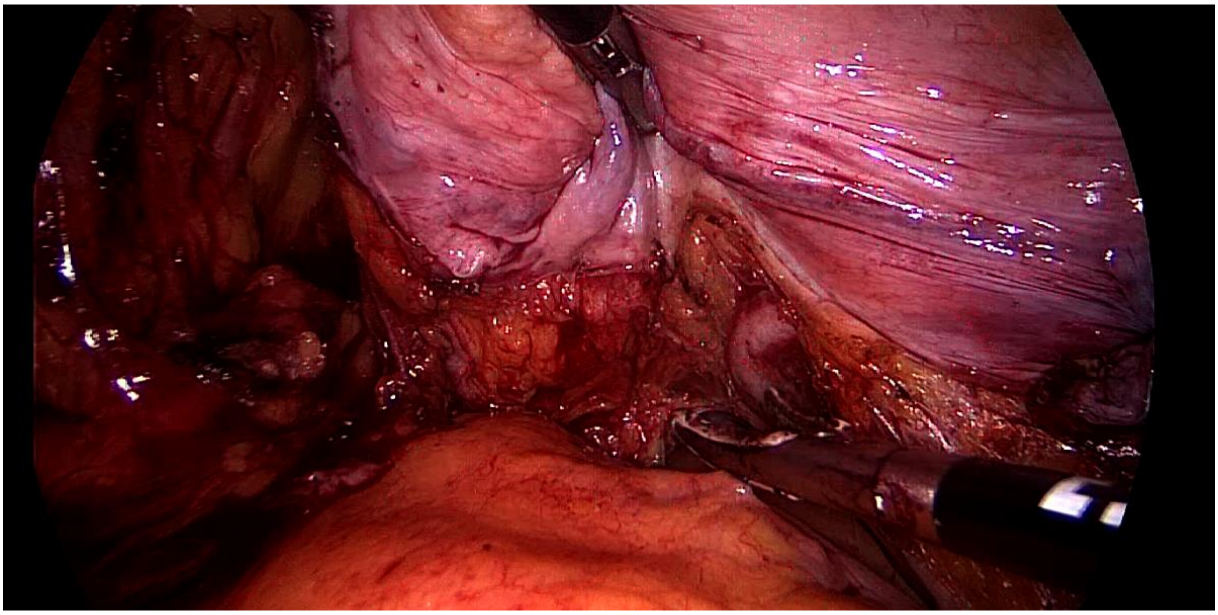

Figure 4: Posterior dissection of the bladder using LigaSure sealing device.

To preserve the nerves, which were located close to the tips of the seminal vesicles, this dissection was immediately next to the walls of the seminal vesicle, between the vesicle and the posterior layer of Denonvillier's fascia (which can be seen with exquisite clarity if the dissection has been in the proper planes). The recto prostatic plane was developed by dividing Denonvillier's fascia.

Vasa deferentia were clipped and cut, and the small arterial branches to the seminal vesicle were carefully controlled with clips **(Figure5)**.

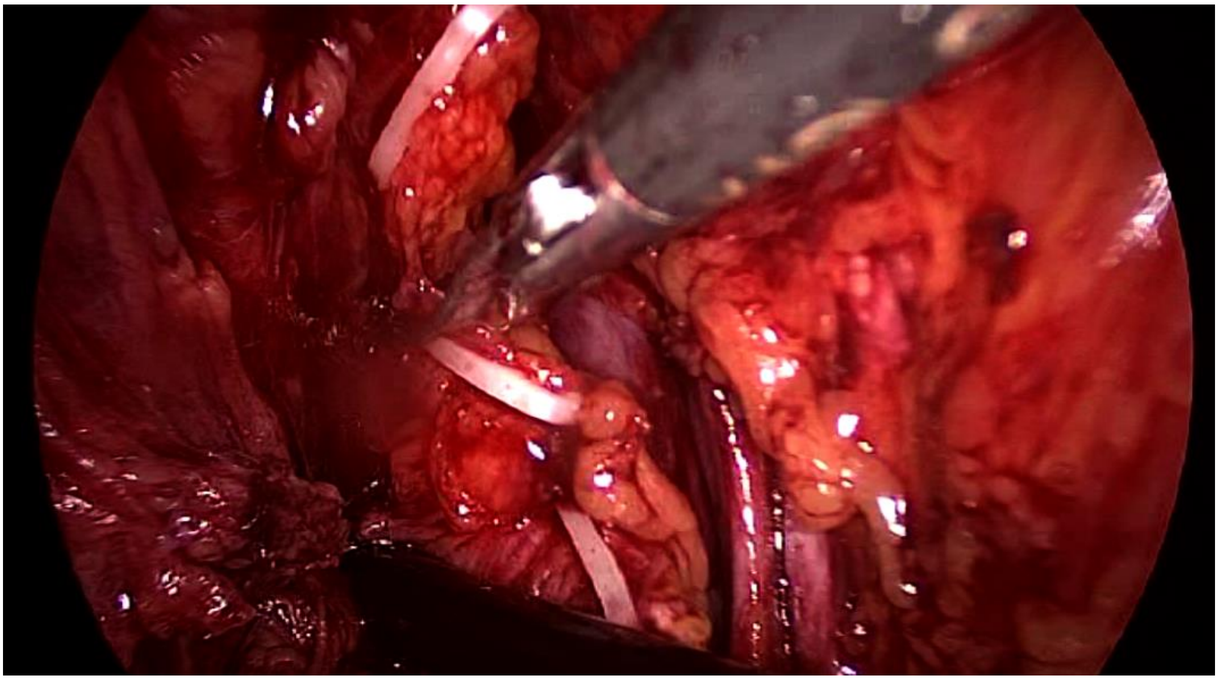

Figure5: Left side inferior vesicle pedicle clipping and division using scissor.

Care was taken to widely establish separation between the rectum and bladder to minimize chances of rectal injury.

3. **<u>Lateral space creation:</u>**

Delineation of the lateral aspects of the bladder and vascular pedicles was performed at this point. The peritoneal incision was performed along the lateral aspect of the medial collateral ligament, with care taken to leave the anterior suspension of the bladder intact. The lateral incisions were connected to the posterior incision to form a “u” and the space lateral to the bladder freed distally to the endopelvic fascia. Next, the medial umbilical ligaments were transected close to their junction with the internal iliac artery.

Once the posterior and lateral spaces have been adequately developed, the ureter was doubly clipped and transected **(Figure 6)** and tucked into the upper abdomen well away from the operative field.

Ligation of the superior vesical artery was contemplated using a sealing device.

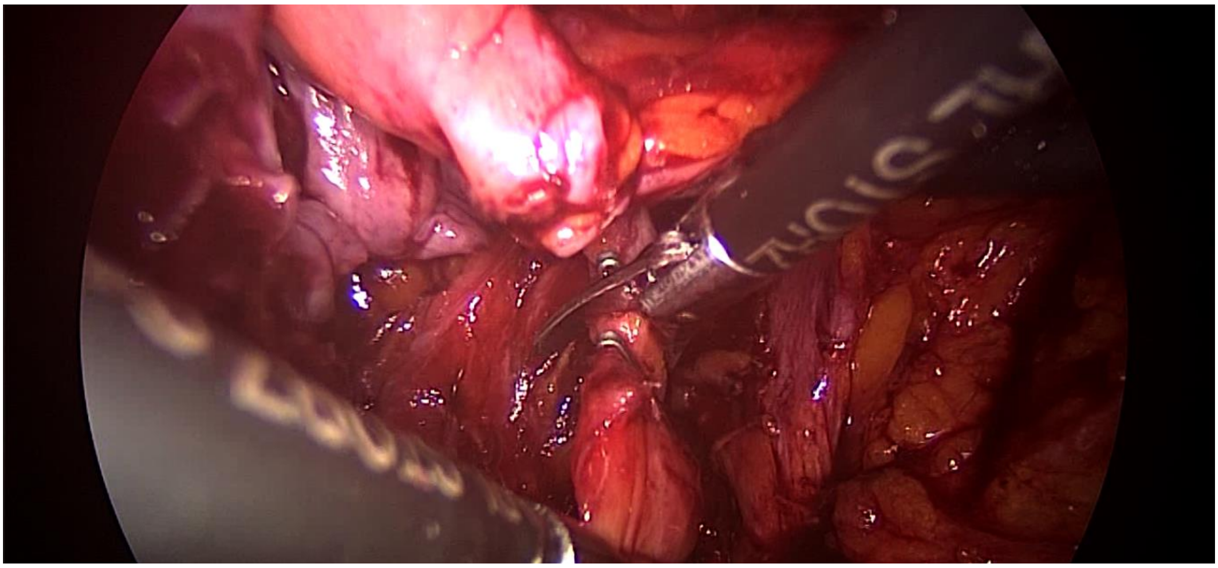

Figure 6: Clipping and transection of the ureter.

4. **<u>Anterior plane dissection:</u>**

Adequate distal division of attachments facilitates mobility and completion of the apical dissection.

Anterior dissection of the bladder from the abdominal wall using a sealing device **(Figure 7)**.

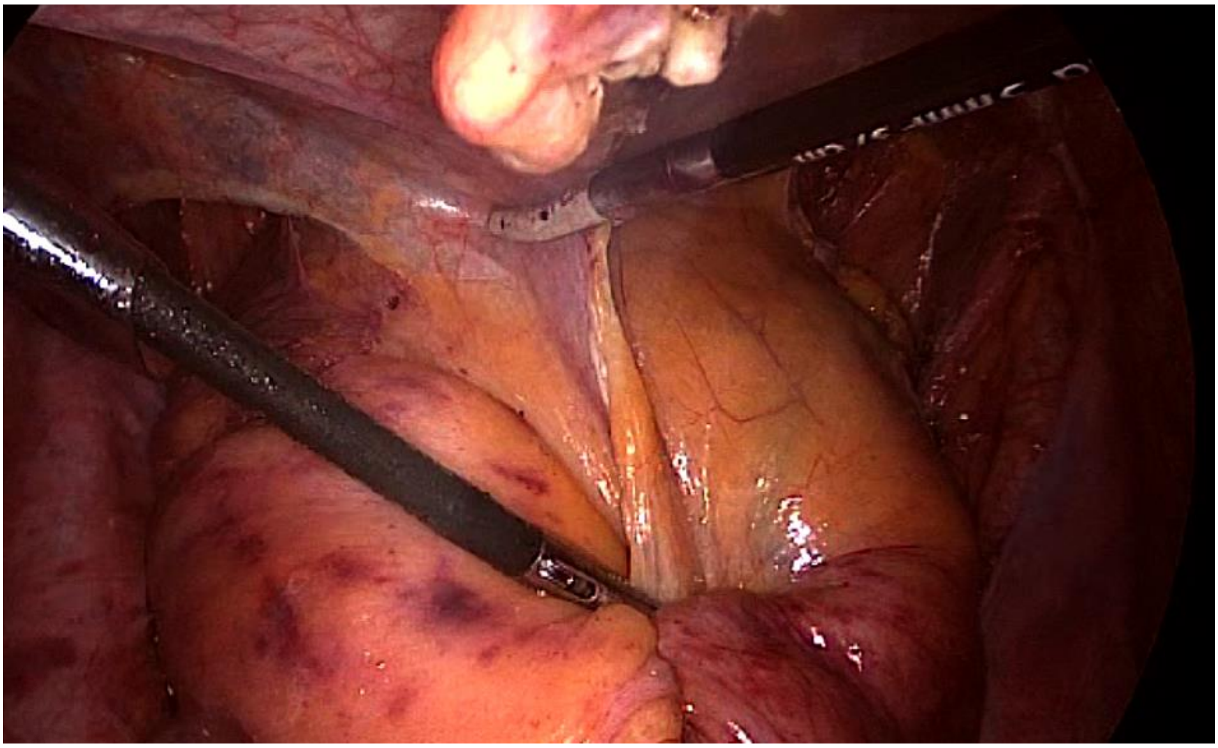

Figure 7: Anterior dissection of the bladder using LigaSure sealing device.

The balance of anterior bladder suspension was released and the anterior space of Retzius dissected till puboprostatic ligaments. Exposure of puboprostatic ligament which was ligated then divided using LigaSure sealing device **(Figure 8).**

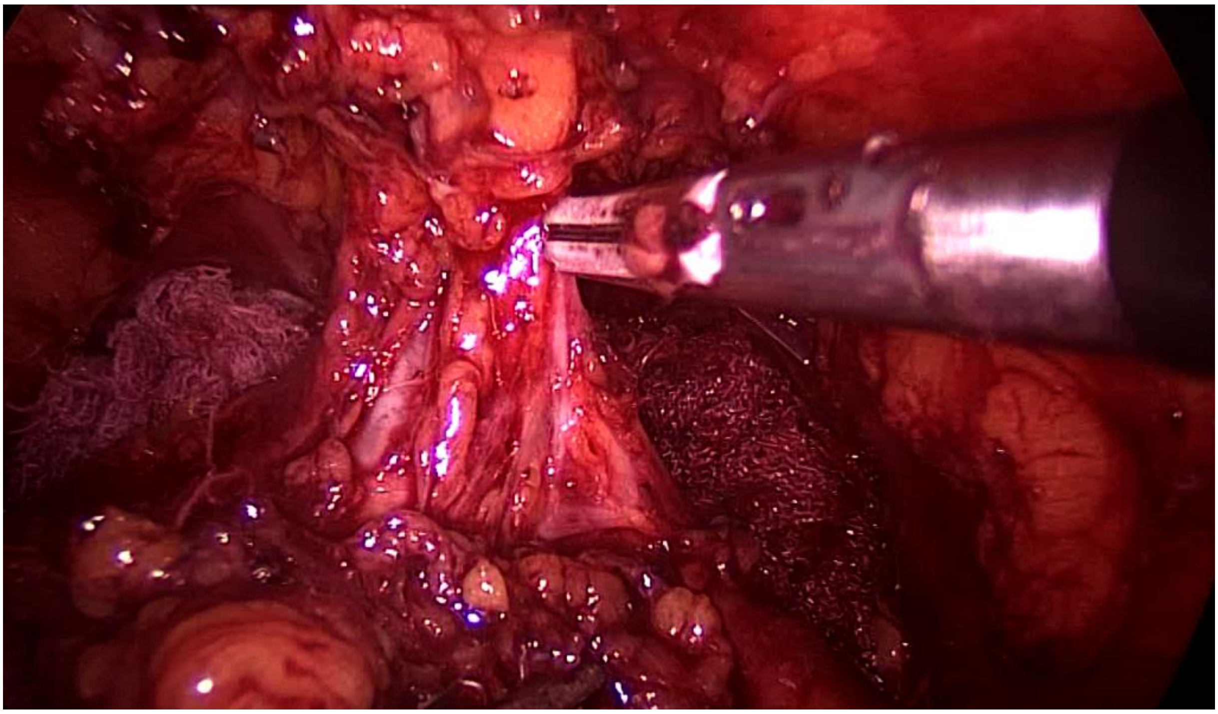

Figure 8: Puboprostatic ligament division using LigaSure sealing device.

The dorsal venous complex (DVC) was controlled with 1–2 securing sutures **(Figure 9)**.

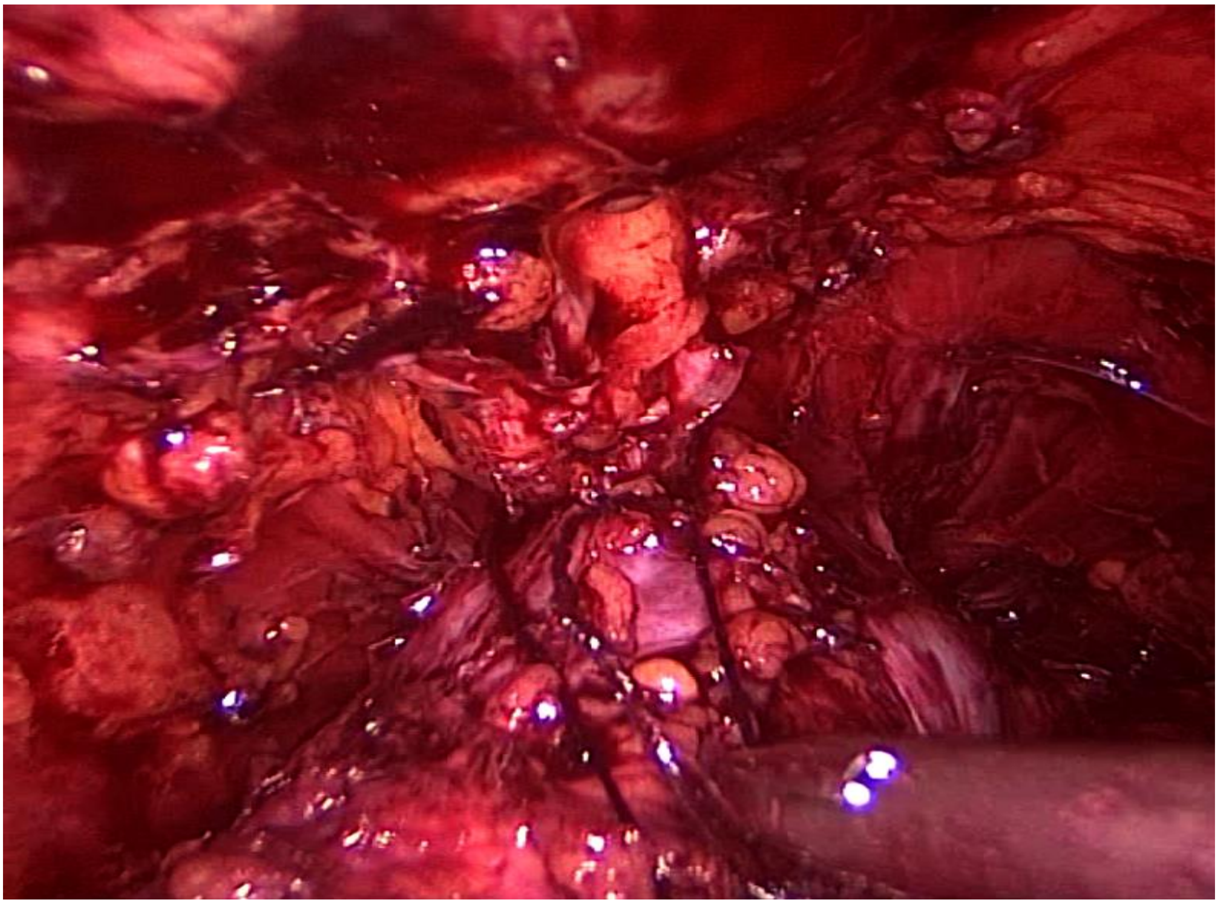

Figure 9: DVC suture ligation.

5. **Urethral transection:**

The urethra was transected **(Figure 10)**. If a neobladder was planned, care was taken to preserve adequate urethral length. The bladder side of the specimen was controlled with a clip to prevent spillage of contents during transection. If IC was planned, the urethra was dissected as far distal as possible.

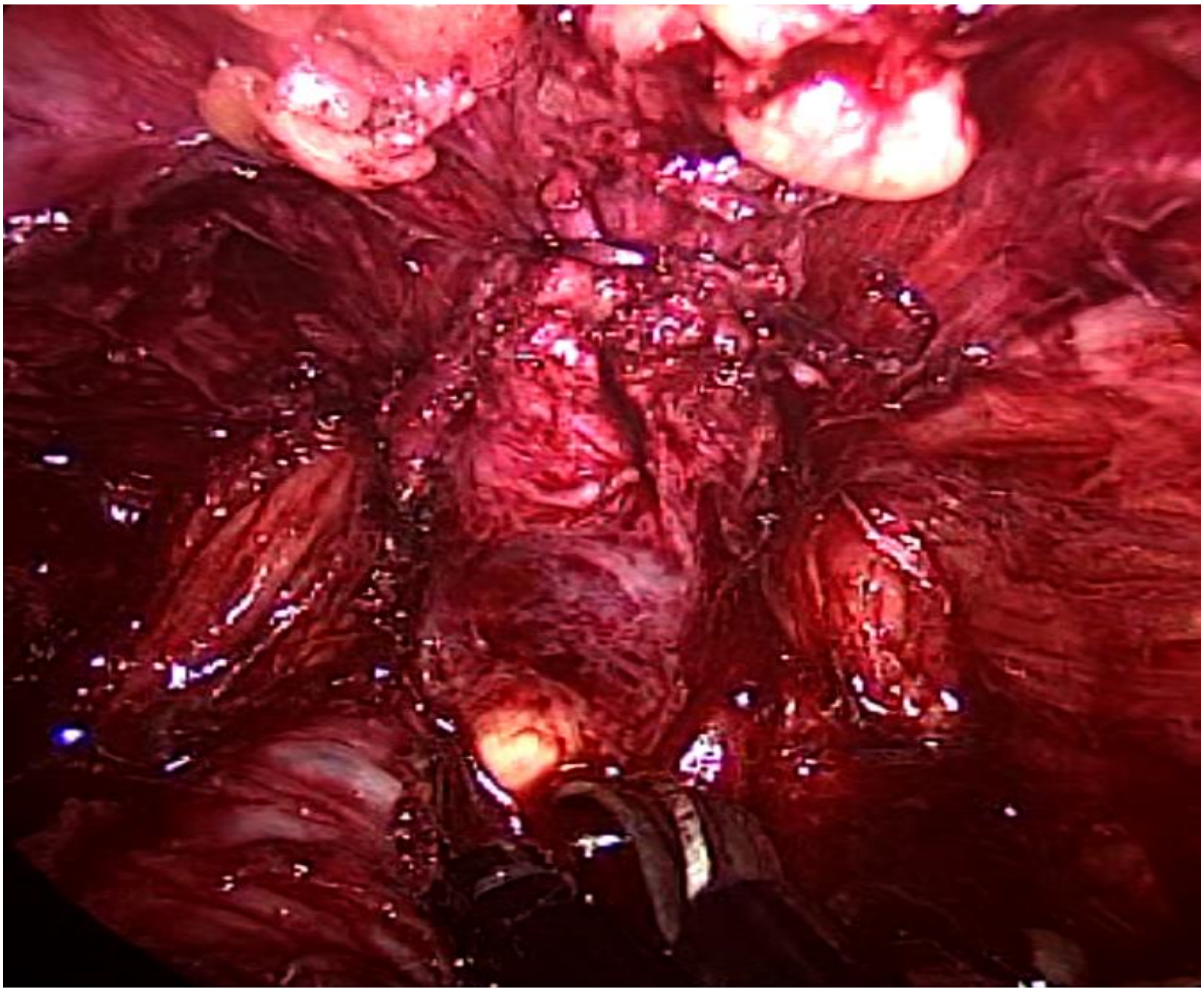

Figure 10: Urethral transection, both cavernosal nerves were preserved.

Manipulation of the urinary catheter helps in traction of the bladder and completion of the resection **(Figure 11).**

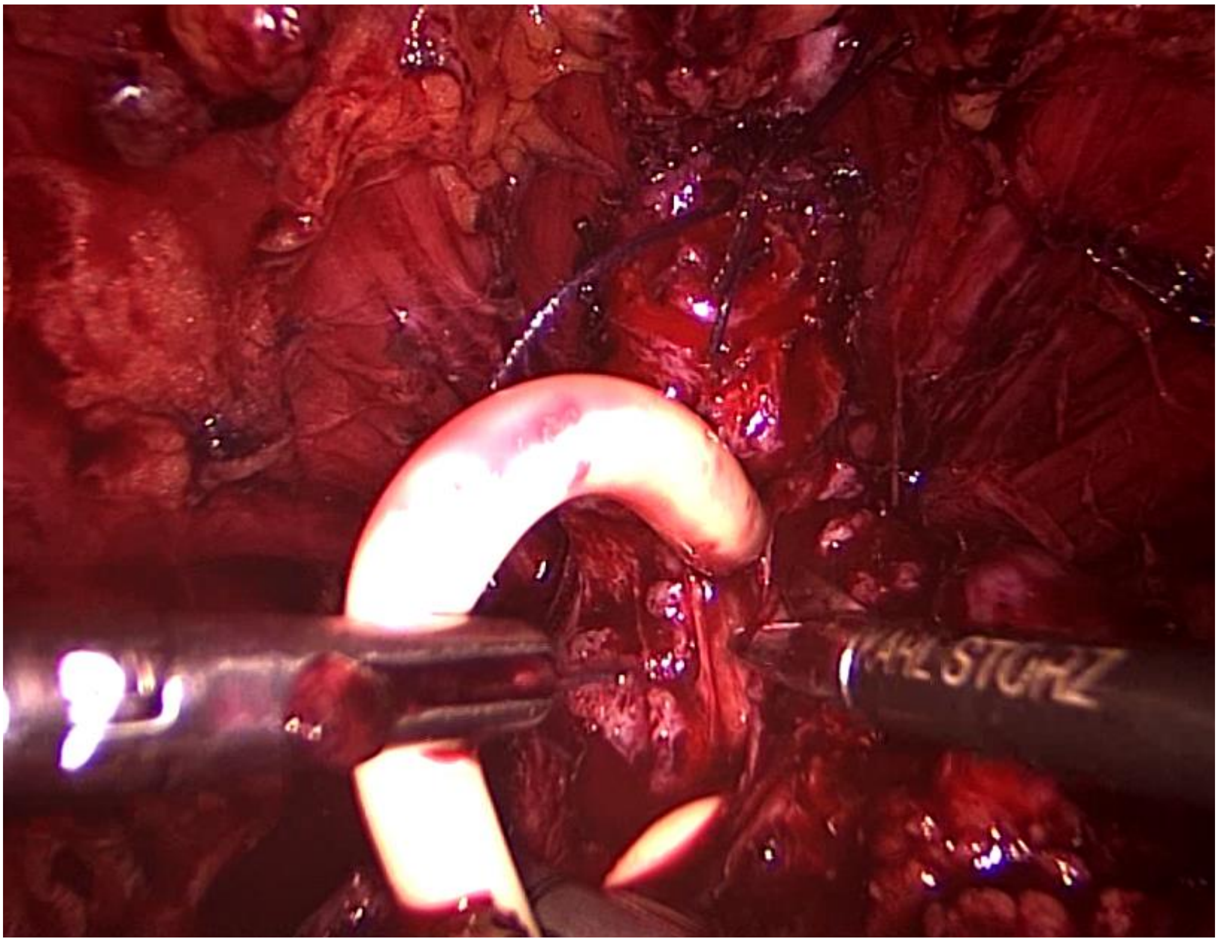

Figure 11: Urinary catheter manipulation using a grasper.

6. **<u>Pelvic Lymph node dissection (PLND):</u>**

After finishing the cystectomy part of the procedure, a bilateral standard PLND was undertaken, which was defined as removal of lymph tissue up to the common iliac bifurcation to include the internal iliac, obturator and external iliac LNs. All nodal tissue was cleared from the genitofemoral nerve laterally to the bladder wall medially, and from the distal CIA superiorly to the lateral circumflex iliac vein and the node of Cloquet inferiorly **(Figure 12).**

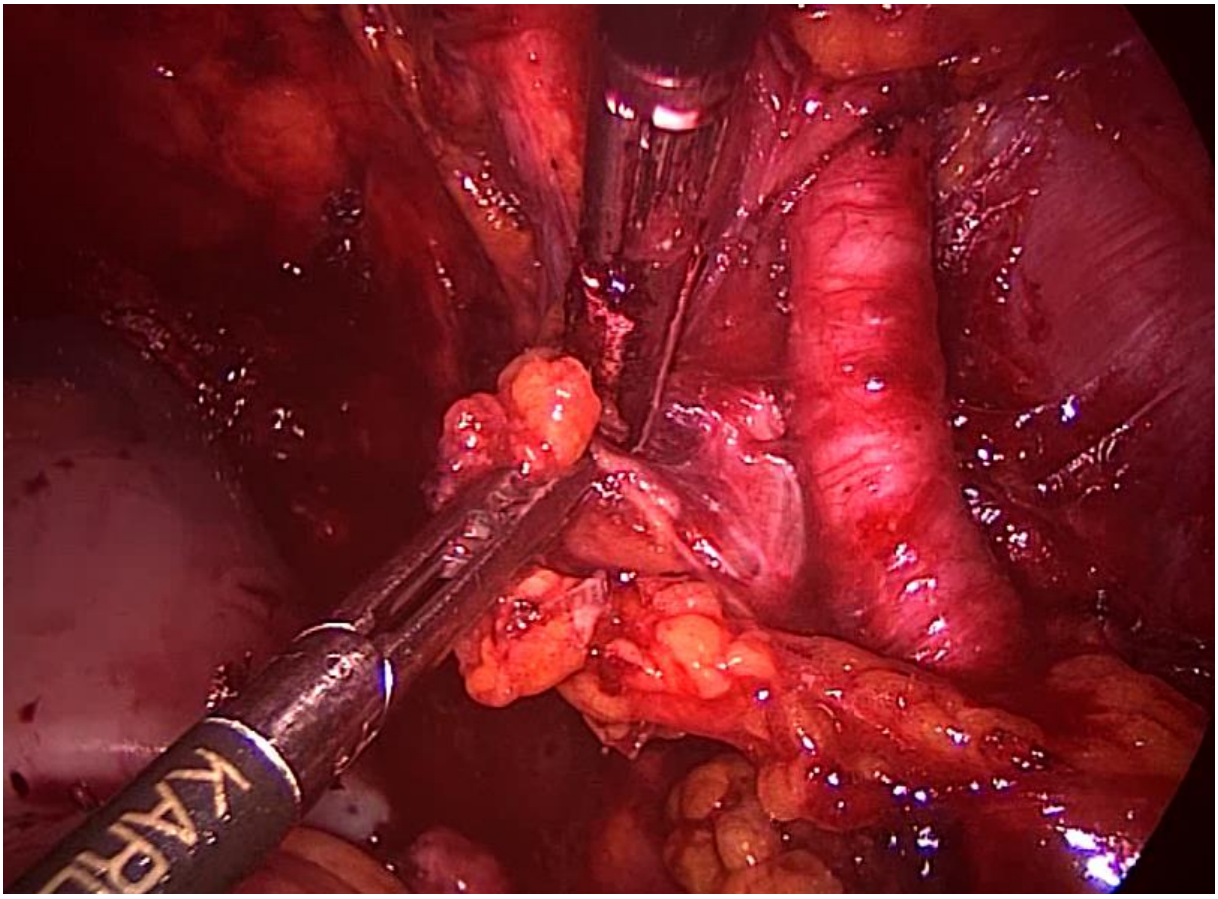

Figure 12: Right side iliac lymphadenectomy using LigaSure sealing device.

The obturator fossa was cleared of nodal tissue, preserving the obturator nerve **(Figure 13)**. The nodal tissue was cleared around the iliac vessels. The nodal tissue seems to form two natural packages, one attached to the bladder wall and one lateral to this. Lymphadenectomy was the most difficult part of the operation because the tissue contains many small blood vessels that must be meticulously coagulated. Otherwise, they retract into the tissues and give rise to hemodynamically insignificant but visually annoying oozing. This impairs visibility and may obscure the detection of precise tissue planes.

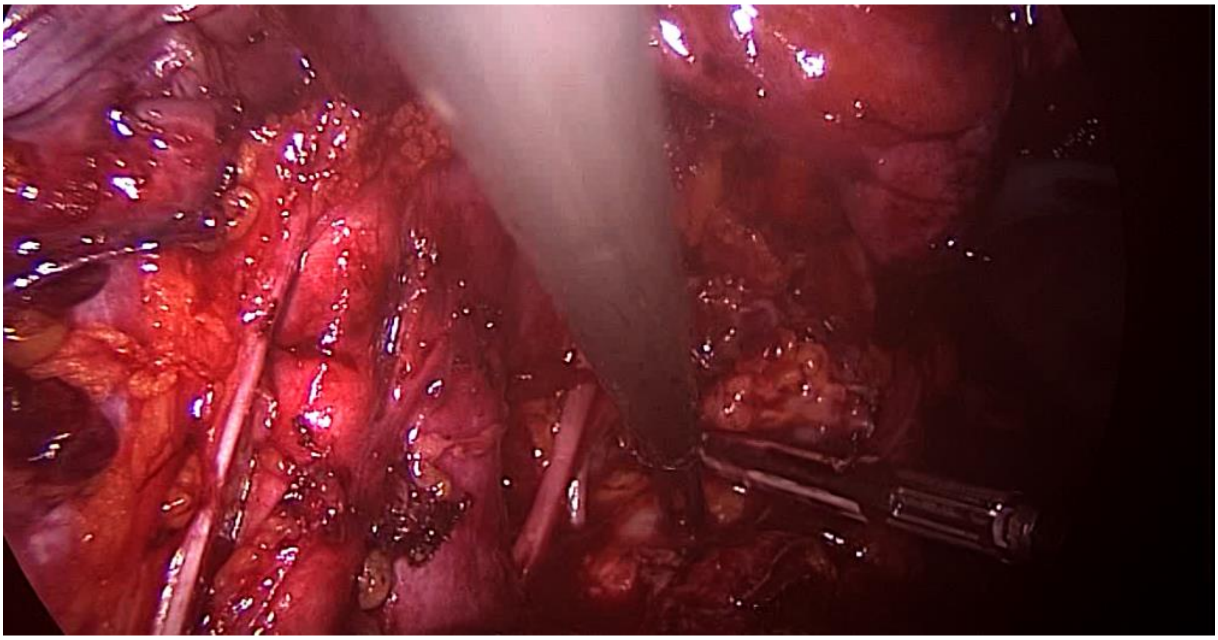

Figure 13: Completion of left side iliac lymphadenectomy till obturator nerve using LigaSure sealing device.

B. RARC surgical technique:

RARC Patient position shown in **(Figure 14).** RARC has the same steps as LRC with some modifications in the surgical technique as the robot helps the surgeon in completing the resection and reconstruction parts of the procedure as the robot was designed to remedy the difficulties of conventional laparoscopy and shorten the learning curve required to master the procedure especially intracorporeal suturing of the neobladder pouch to the urethra.

RARC equipment list:

1. Da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA.).
2. Veress needle, suction irrigator 5 mm device and Port closure device for ≥10 mm ports (KARL STORZ GmbH, Tuttlingen, Germany).
3. 2×10/12 mm disposable port and 5 mm assist port. (ENDOPATH XCEL bladeless trocars).
4. Da Vinci instruments: Monopolar Da Vinci scissors, bipolar fenestrated grasper, and 3×8 mm robotic ports.
5. LIGACLIP clip applier Ethicon.
6. Echelon flex endopath stapler 60 mm.
7. Sutures: PDS 3-0, PDS 4-0, Vicryl 3-0, STRATAFIX 3-0 and V-lock 3-0 barbed sutures.
8. Endocatch II bag (US Surgical, Norwalk, USA) as specimen retrieval bag system.
9. Appropriate open surgical equipment for completion of urinary diversion.

Figure 14: RARC patient position.

Port positions:

The da Vinci optical laparoscope was inserted and a peritoneoscopy performed. The robot was docked between the patient's legs (Central docking)

A five-port transperitoneal approach was used; a 10-mm primary port was inserted, and the entire peritoneal cavity inspected with a 30° laparoscope. The two 8-mm ports for the robotic instruments were placed 2.5 cm lateral to the rectus muscle and 2 cm below the umbilicus on either side. A second 10 mm port was placed in the right iliac fossa 5 cm above the ASIS in the AAL. The fifth port (8 mm) was placed in the left iliac fossa 5 cm above the left ASIS in the AAL for the 3rd arm of the robot used for traction **(Figure 15).**

Figure 15: Docking complete.

Steps of RARC were the same steps as LRC with little modifications as follows:

Most of the dissection was carried out with two instruments, i.e., the da Vinci long-tip forceps and the cautery hook. Alternatively, the bipolar coagulating forceps and the articulate scissors can be used, and we used these two instruments particularly for the nerve-sparing part of the surgery. Two needle holders were used for suturing. The laparoscopic team uses grasping forceps and suction for retraction and exposure.

1. **<u>Ureteral identification and dissection:</u>**

Ureters were identified at the level of the CIA. using great care to preserve vascular tissue around the ureter as much as possible. the ureter was dissected free for a small distance above the vessels and followed into the deep pelvis to the ureterovesical junction **(Figure 16)**. An identical procedure was completed on the contralateral side; maximization of the length and blood supply on the left side was especially important given the need for tunnelling later.

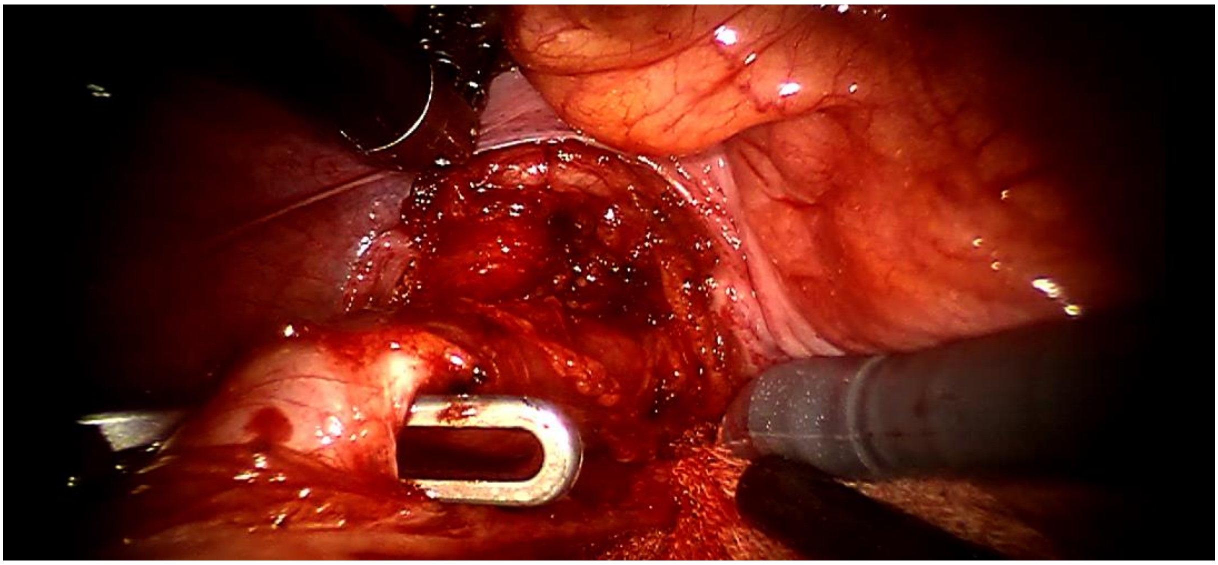

Figure 16: Left side ureteral dissection.

2. **<u>posterior plane dissection:</u>**

The laparoscopic assistants provide equal counter traction on the transected peritoneal folds and the surgeon dissects all fatty and fibrovascular tissue of the posterior peritoneal fold.

3. **Lateral space creation:**

Delineation of the lateral aspects of the bladder and vascular pedicles was performed at this point **(Figure 17)**. The peritoneal incision was performed along the lateral aspect of the medial collateral ligament, with care taken to leave the anterior suspension of the bladder intact. The lateral incisions were connected to the posterior incision to form a “u” and the space lateral to the bladder freed distally to the endopelvic fascia.

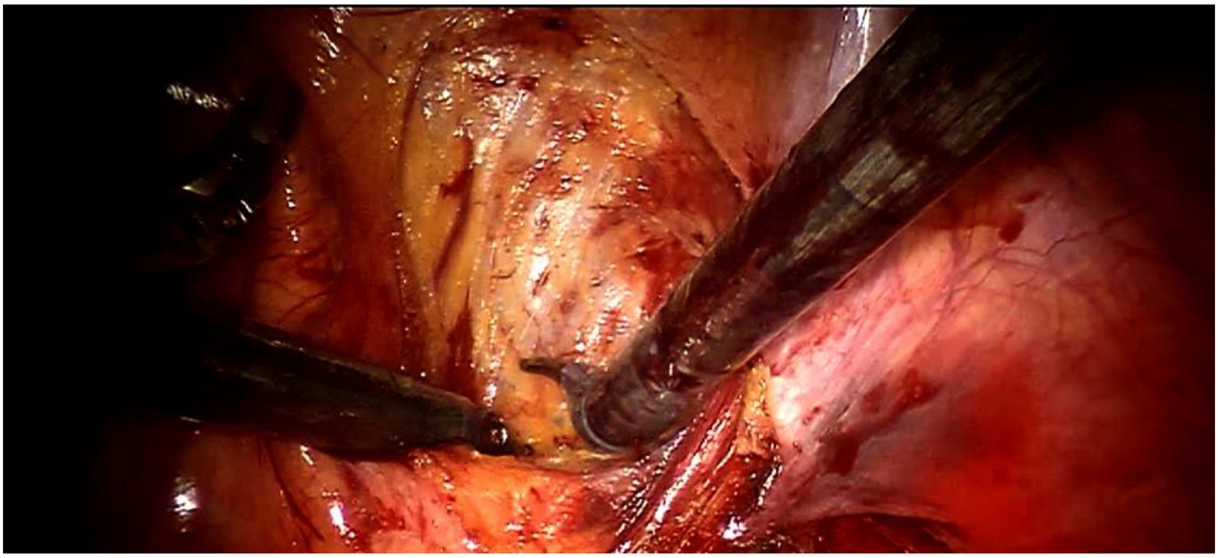

Figure 17: Lateral space creation.

4. **<u>Anterior plane dissection:</u>**

Adequate distal division of attachments facilitates mobility and completion of the apical dissection.

Anterior dissection of the bladder from the abdominal wall **(Figure 18)** using robotic monopolar cautery to reach DVC. The balance of anterior bladder suspension was released and the anterior space of Retzius dissected. In men, the DVC was controlled with 1–2 securing sutures.

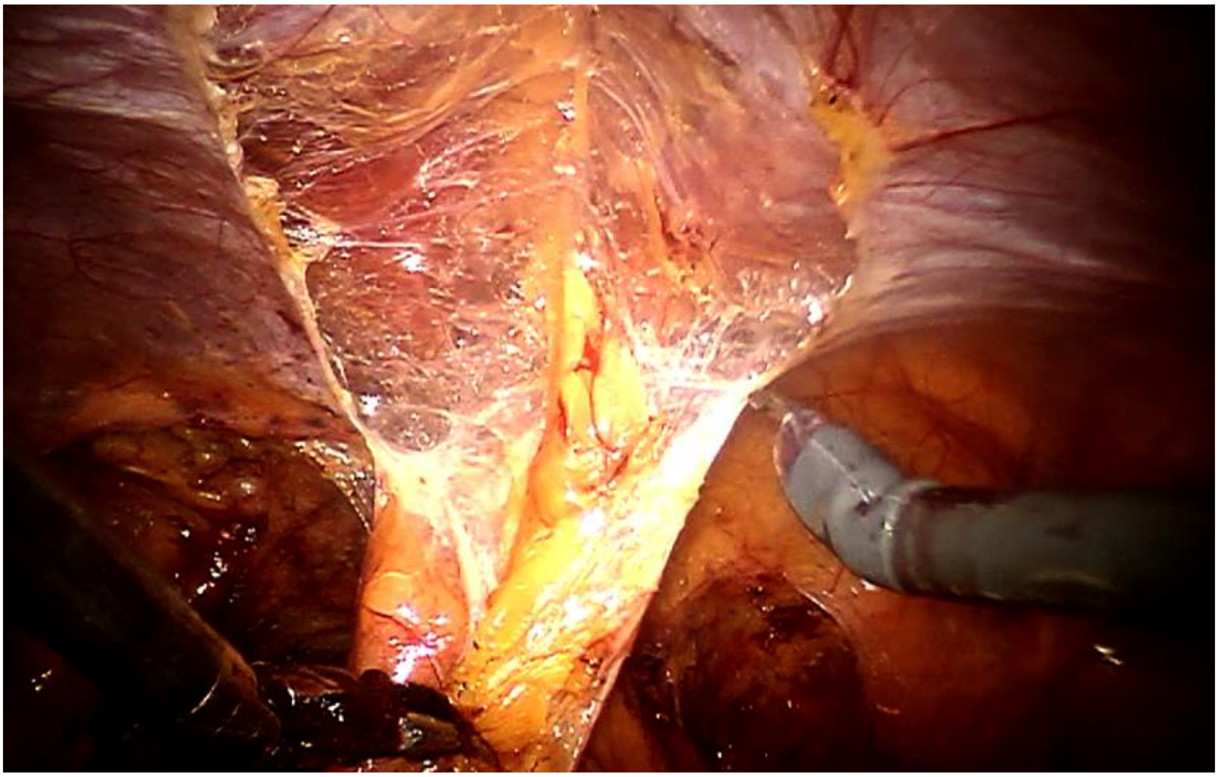

Figure 18: Anterior plane dissection of the bladder using robotic monopolar cautery.

5. **<u>Urethral transection</u>:**

The urethra was dissected free. If a neobladder was planned, care was taken to preserve adequate urethral length. The bladder side of the specimen was controlled with a clip to prevent spillage of contents during transection. If IC was planned, the urethra was dissected as far distal as possible.

The urethra was divided at the apex of the prostate with the help of articulated robotic scissors **(Figure 19)**. An attempt was made to gain the maximum length of the urethra, which would help subsequently in the anastomosis with the neobladder.

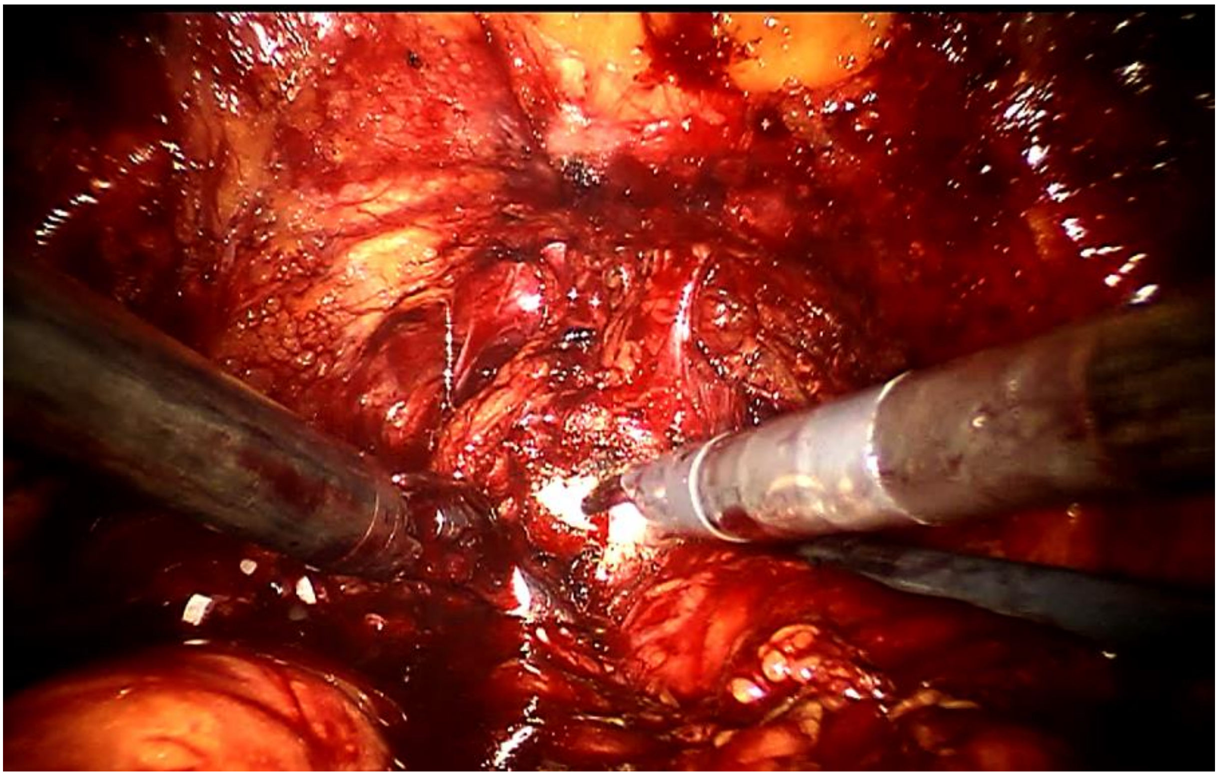

Figure 19: Urethral transection using monopolar robotic cautery.

6. **Pelvic Lymph node dissection (PLND):**

LND was completed with an upper boundary to the level of the ureter crossing the iliac artery. This was carried laterally along the upper edge of the iliac artery adjacent to the genitofemoral nerve, with great care taken to remove all tissue surrounding the great vessels and into the obturator fossa **(Figure 20)**.

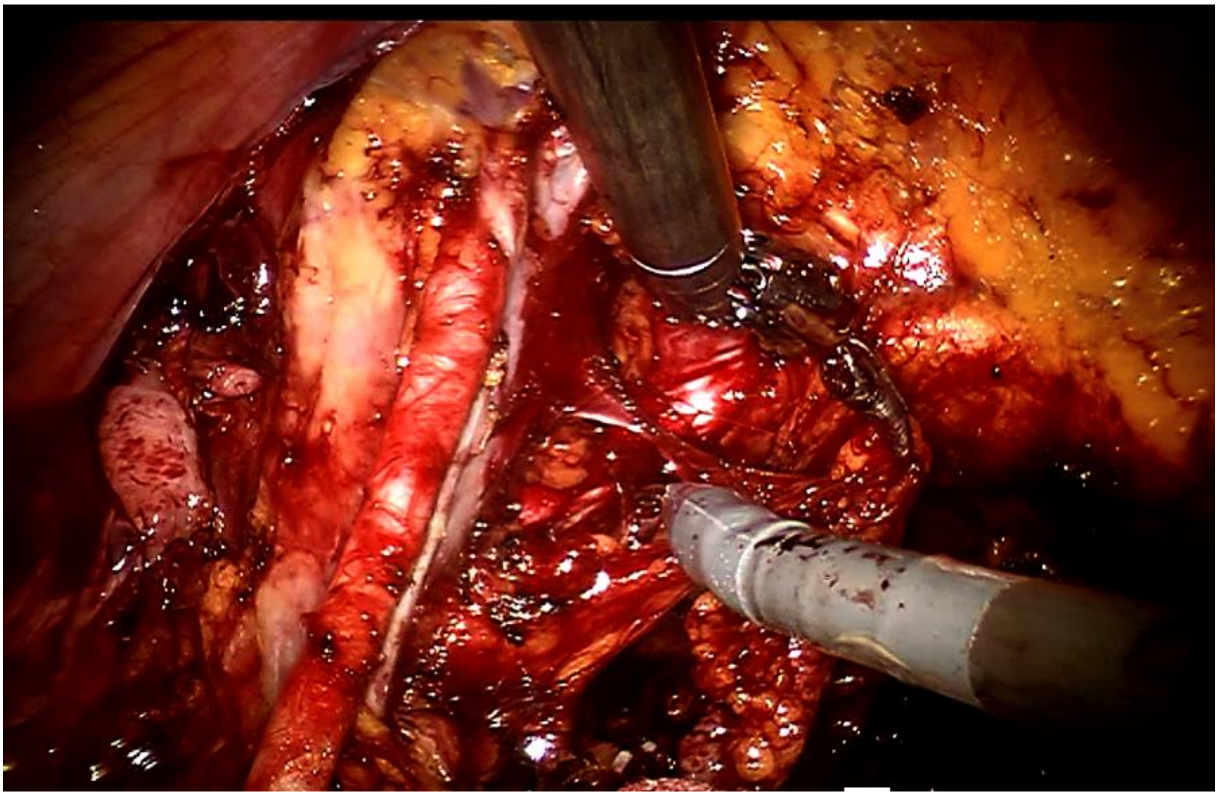

Figure 20: Completion of left side robotic iliac lymphadenectomy down to obturator fossa.

The specimen was entrapped in a laparoscopic Endocatch II bag (US Surgical, Norwalk, USA) and retrieved through a 5–6 cm incision placed midway between the umbilicus and pubic symphysis.

After MIRC, the completion of urinary diversion may be performed via extracorporeal or intracorporeal approaches.

Specimen extraction incision was used for extraction of a segment of ileum which was isolated and reconfigured extracorporeally.

Minimally invasive urinary diversion:

The surgical principles for urinary diversion either extracorporeal or intracorporeal remain the same.

a) Non-continent urinary diversion:

IC as a non-continent urinary diversion was performed either intracorporeally or extracorporeally laparoscopic IIC was performed as follows:

1. Port placement and patient repositioning:

The patient position changed from steep Trendelenburg to a neutral operating room bed position. The assistant had two assistant ports (at least 12 mm) to allow passage of the stapler from the left side of the patient.

2. Bowel segment selection for urinary diversion:

The first step was to identify the ileocecal junction and spare 15–20 cm of the terminal ileum. A 20-cm PDS 3-0 suture was used to aid in the measurement of the appropriate bowel length to be utilized for the IC. Once the segment of the ileum was identified, the proximal and distal ends of the bowel were tagged with a 3-0 PDS suture **(Figure 21).**

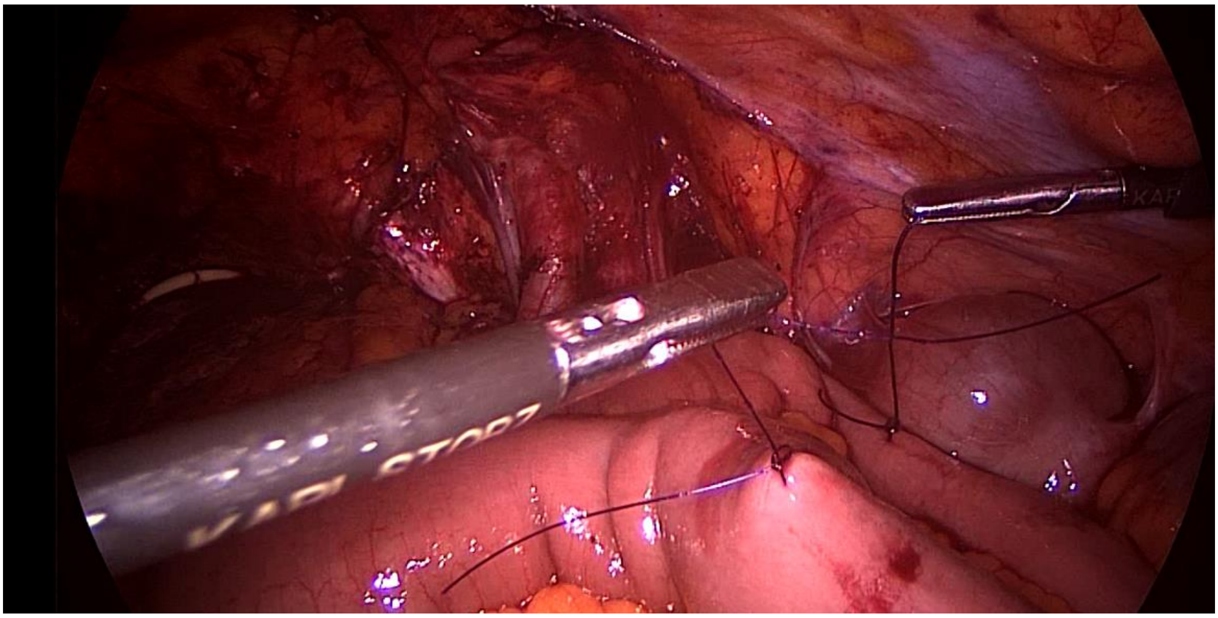

Figure 21: Stay sutures of the proximal and distal ends of the selected bowel planned for ileal conduit (IC) have been placed and tied.

3. Bowel resection and reanastomosis:

The next step was to harvest the ileal segment and restore intestinal continuity. Distal transection of the ileum was performed with a 60-mm laparoscopic stapler. The stapler was introduced through the left lateral 12-mm assistant port while the main surgeon aligns the bowel and mesentery to be divided. The Endo GIA stapler was fired to divide the bowel and mesentery.

The Endo GIA stapler was reintroduced into the 12-mm left lateral port to restore intestinal continuity.

Bowel continuity was reestablished with a standard side-to-side ileoileal anastomosis using a 60-mm laparoscopic tissue stapler load to anastomose the adjacent antimesenteric ileal walls.

To complete the bowel anastomosis, the remaining bowel opening was closed hand sewn with 3-0 vicryl sutures.

4. <u>Uretero-Intestinal Anastomosis (UIA) and Ileal Conduit (IC) stoma:</u>

The distal end of the conduit following the UIA will be fashioned into a stoma at a premarked area for the stoma on the abdominal wall.

Bricker techniques for UIA was employed both ureters were spatulated approximately 2 cm, and an incision was made at the selected site on the IC for the anastomosis. 6 Fr, ureteric stents were ureter to reach the renal pelvis then pushed up into the IC **(Figure 22).**

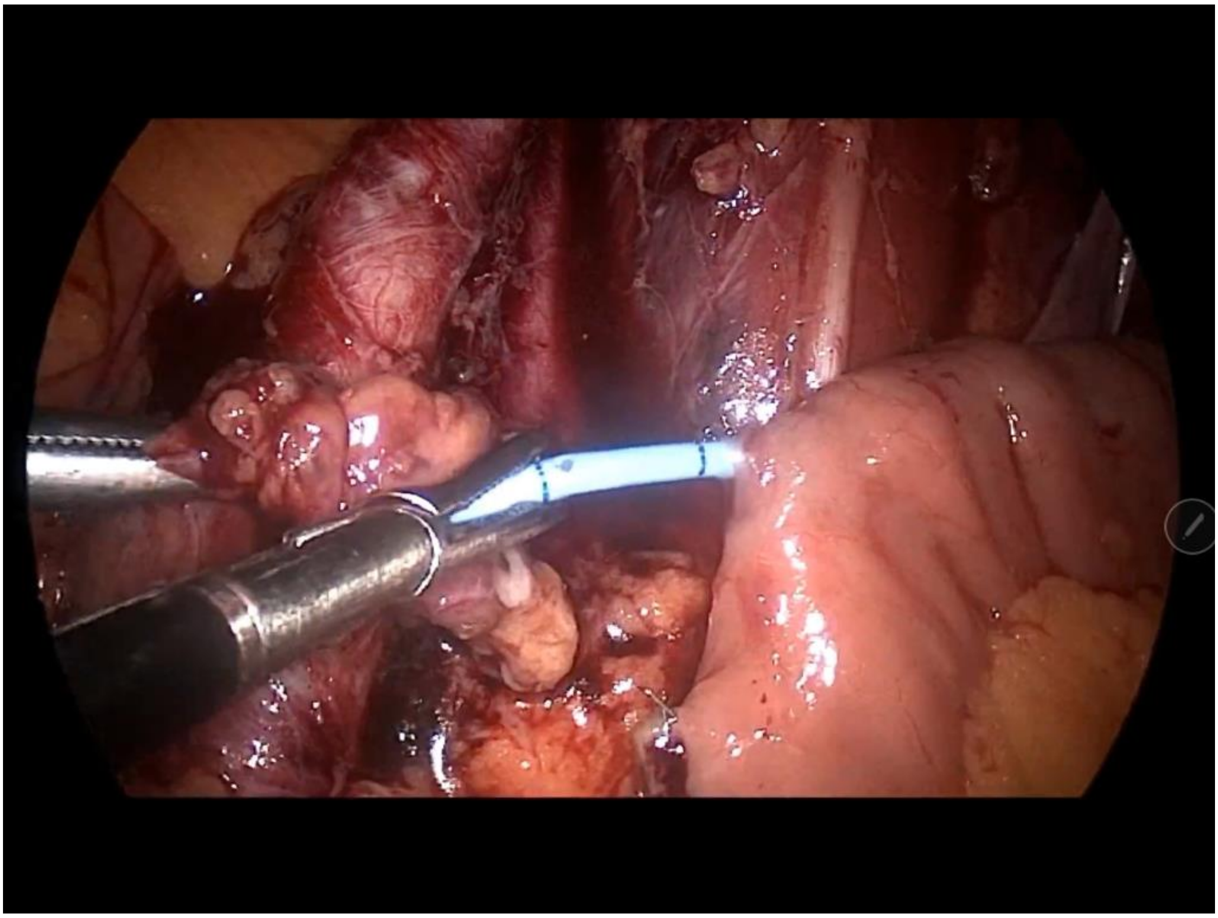

Figure 22: Ureteric stents placement into the ureter and ileal conduit (IC).

Finally, UIA was completed using a continuous 4-0 PDS suture **(Figure 23).**

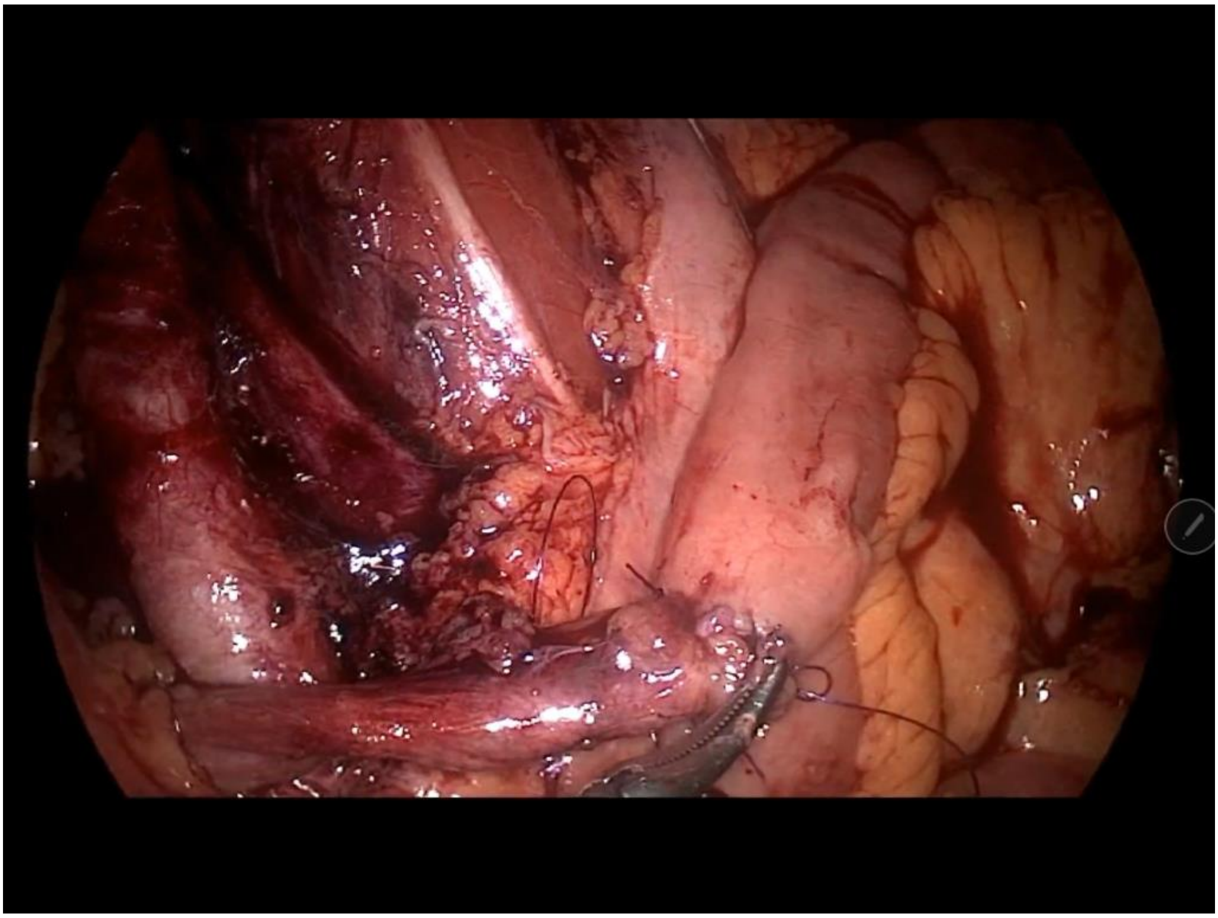

Figure 23: Uretero-intestinal anastomosis (UIA) was completed.

The ostomy side of the conduit was tagged with a 3-0 Vicryl suture and brought out through the closest port site to the ostomy site. to readily locate the conduit at the ostomy site at the abdominal wall.

b) Continent urinary diversion:

Different orthotopic urinary diversion techniques were performed. Y pouch reservoir was performed, the antimesenteric border of the bowel segment was lightly cauterized using the monopolar scissors to distinctly mark the antimesenteric border. Next, the suture identifying the midportion of the bowel segment was grasped, thereby pulling the segment into the deep pelvis **(Figure 24)**, which allows the bowel to be oriented into a Y shape.

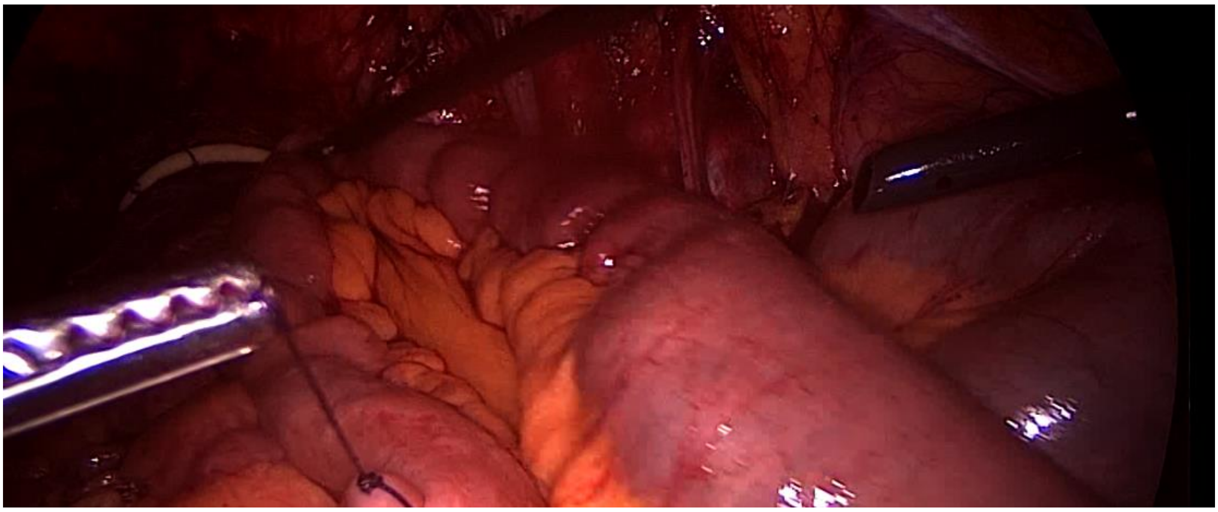

Figure 24: Assessment of neobladder reach to urethra before intestinal division.

The endoscopic stapler was used to divide and staple the proximal end of the ileal segment 10 cm from the ileocecal junction **(Figure 25)**.

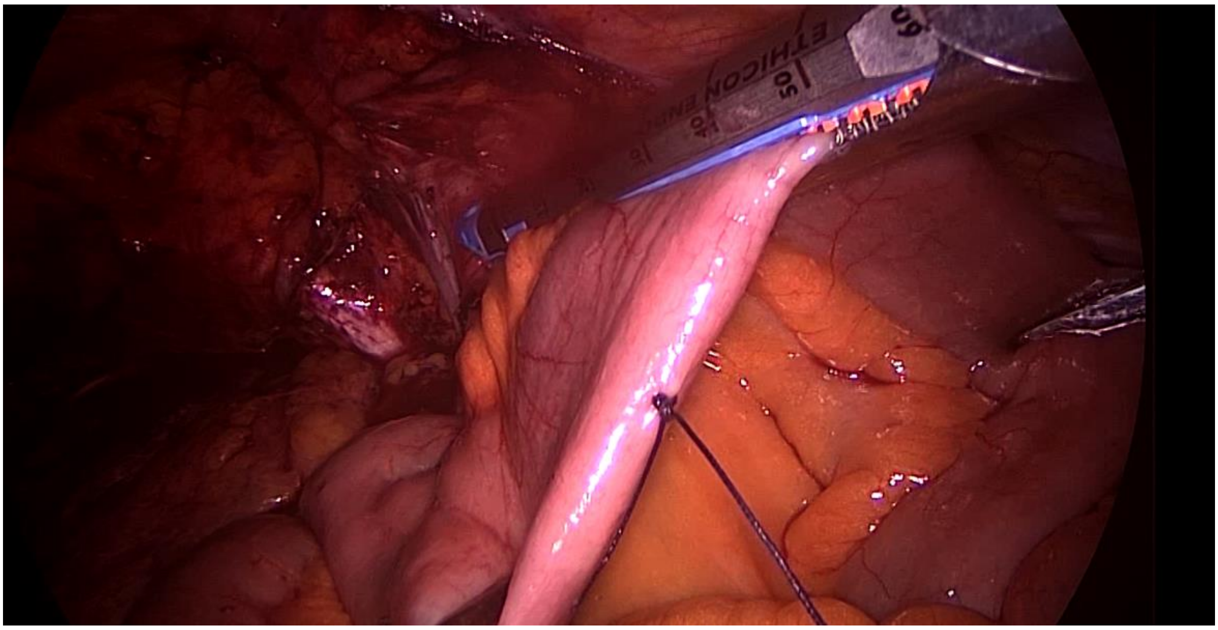

Figure 25: Proximal ileal limb division using an endoscopic linear stapler.

The endoscopic stapler was used to staple and divide the distal end of the ileal segment 50 cm from the ileocecal junction.

Restoration of intestinal continuity with laparoscopic 60 mm stapler as shown in **(Figure 26)**.

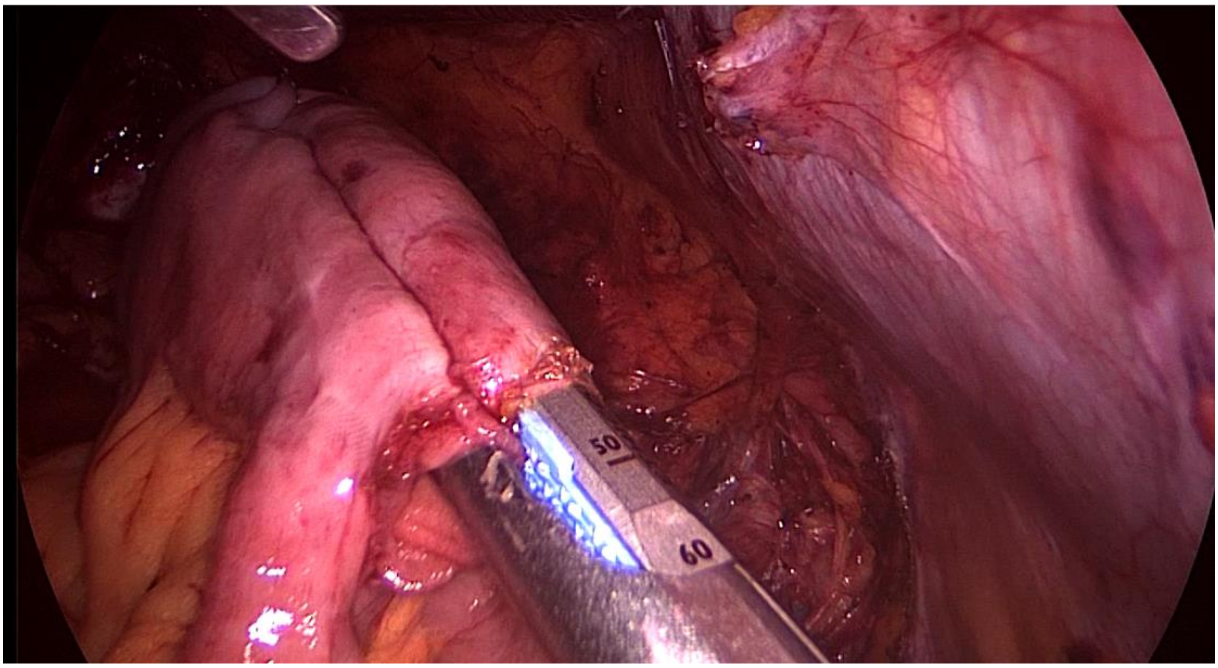

Figure 26: Ileoileal anastomosis using an endoscopic linear stapler.

The endoscopic stapler was advanced so that each jaw of the stapler was placed into the previously opened ends of the proximal and distal bowel segment. the stapler was deployed on the antimesenteric portion of each bowel section, which effectively detubularizes the bowel and forms the reservoir.

Appropriate mobilization of the ileum allows for tension-free neobladder urethral anastomosis.

In the case of robotic intracorporeal urinary diversion, we started with pouch-urethral anastomosis first then ureteral-pouch anastomosis.

The pouch was placed in the pelvis and a Foley catheter passed the urethra into the pouch; the pouch was pulled down to the urethra. The abdominal incision was closed, and the robot re-docked for anastomosis of the neobladder with the urethra. The urethral-neobladder anastomosis was performed robotically with a STRATAFIX spiral knotless tissue control device the suture continues circumferentially; anti-clockwise on the right, and clockwise on the left **(Figure 27).** The anastomosis was stented by a 20 Fr catheter, inflating the balloon with

15 ml of saline. The anastomosis was then tested for integrity by 120 ml of saline solution.

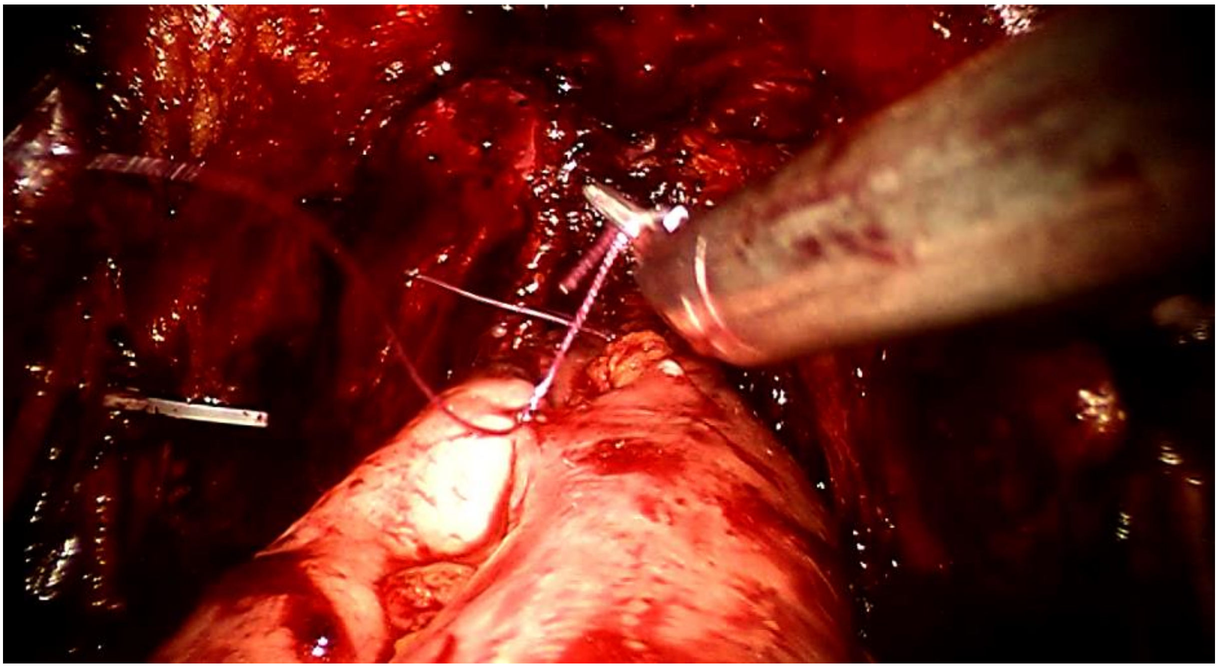

Figure 27: Robotic intracorporeal pouch-urethral anastomosis.

The specimen was placed in an endoscopic retrieval bag. The assistant places the drawstring from the specimen retrieval bag into the abdomen under laparoscopic vision. The console surgeon then grasps the end of the string in the right-hand needle driver and then lines up the camera trocar directly to the string. Then, the camera was placed into the lateral 12 mm assistant trocar. The assistant places a laparoscopic needle driver into the camera trocar site and removes the drawstring from the grasp of the right-hand needle driver. The drawstring was clamped externally for subsequent delivery from the umbilical camera port.

A muscle splitting Pfannenstiel incision was utilized to perform the ECUD if planned. A drain was inserted, trocars were removed under the vision and the robot was undocked **(Figure 28).**

Figure 28: Final appearance after specimen extraction through Pfannenstiel incision.

Patients were discharged once ambulant and tolerating an oral diet, no attempts were made for early discharge. The drain was removed when discharge was less than 50 cc/24 hours. In Continent orthotopic patients, the Urethral catheter was removed at least 14 days post-operatively in the first outpatient clinic visit.

Outcome measures:

A. **Operative outcomes**:

1. Total operative time (min).
2. Docking time (min).
3. Cystectomy operative time (min)
4. Lymphadenectomy operative time(min)
5. Urinary diversion operative time (min)
6. EBL (ml) calculated by measuring the effluent fluid in the suction canister, from which estimates of urine and irrigation fluid have been subtracted, in addition to estimates of gauze swabs if used.
7. blood transfusions need (unit).

B. Post-operative outcomes:

1. Complications:
    i. *Complications classified by systems:*

- Seroma
- Surgical site infection (SSI)
- Urinary tract infection (UTI)
- Ileus
- Urine leak
- Small intestinal injury
- Rectal injury
- Anastomotic bowel leak
- Abdominal wall dehiscence
- Pneumonia
- Pulmonary embolism (PE)

ii. *Complications graded according to the Clavien-Dindo classification system [231].*

2. Time to start solids oral intake (day)
3. Hospital LOS (day)
4. Postoperative opioid analgesia requirement.

C. Pathologic outcome:

1. pT stage.
2. Pathological type
3. Retrieved LNs count.
4. positive LNs number.

Sample size estimation:

Sample size calculation was done using the comparison of operative time between LRC and ORC for bladder cancer patients. As reported in the study published by Lin et al., in 2014, M(mean) ±SD (standard deviation) of operative time in the LRC group was approximately 282 ± 51 min., while in the ORC group it was approximately 235 ± 34 min (Lin et al., 2014)

Accordingly, we calculated that the minimum proper sample size was 26 patients in each arm to be able to reject the null hypothesis with 90% power at $\alpha = 0.05$ level using Student's t-test for independent samples. Sample size calculation was done using StatsDirect statistical software version 2.7.2 (2008) for MS Windows, StatsDirect Ltd., Cheshire, UK.

Statistical analysis:

Data were statistically described in terms of M±SD, median and range, or frequencies (number of cases) and percentages when appropriate. Numerical data were tested for the normal assumption using the Kolmogorov Smirnov test (Shapiro Wilk test). Comparison of numerical variables between the study groups was done using the Student t-test for independent samples. For comparing categorical data, Chi-square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Two-sided p values less than 0.05 was considered statistically significant. All statistical calculations were done using the computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) v22 (2013) for Microsoft Windows.

Ethical issues:

Institutional Review Board (IRB) approval and Consent:

- The IRB Approval was required before the start of the study.
- This study carried no additional risks.
- Informed written consent was taken from each patient before starting this study.
- Benefits from the study were:
  - To compare MIRC versus open technique.
  - To assess the feasibility of RARC and LRC.

Protection of privacy and confidentiality:

- The data of the patients were presented anonymously with the protection of privacy and confidentiality.

Publication policy:

- Any active participant involved in that work will be included in any publications from that work.

Results

Results

A total of sixty patients with MIBC or high-risk NMIBC were randomly assigned to either MIRC or the conventional ORC approaches. Thirty patients in each group who underwent RC were included in the final analysis. Four of the minimally invasive group were operated on with aid of robotic technology **(Figure 29).**

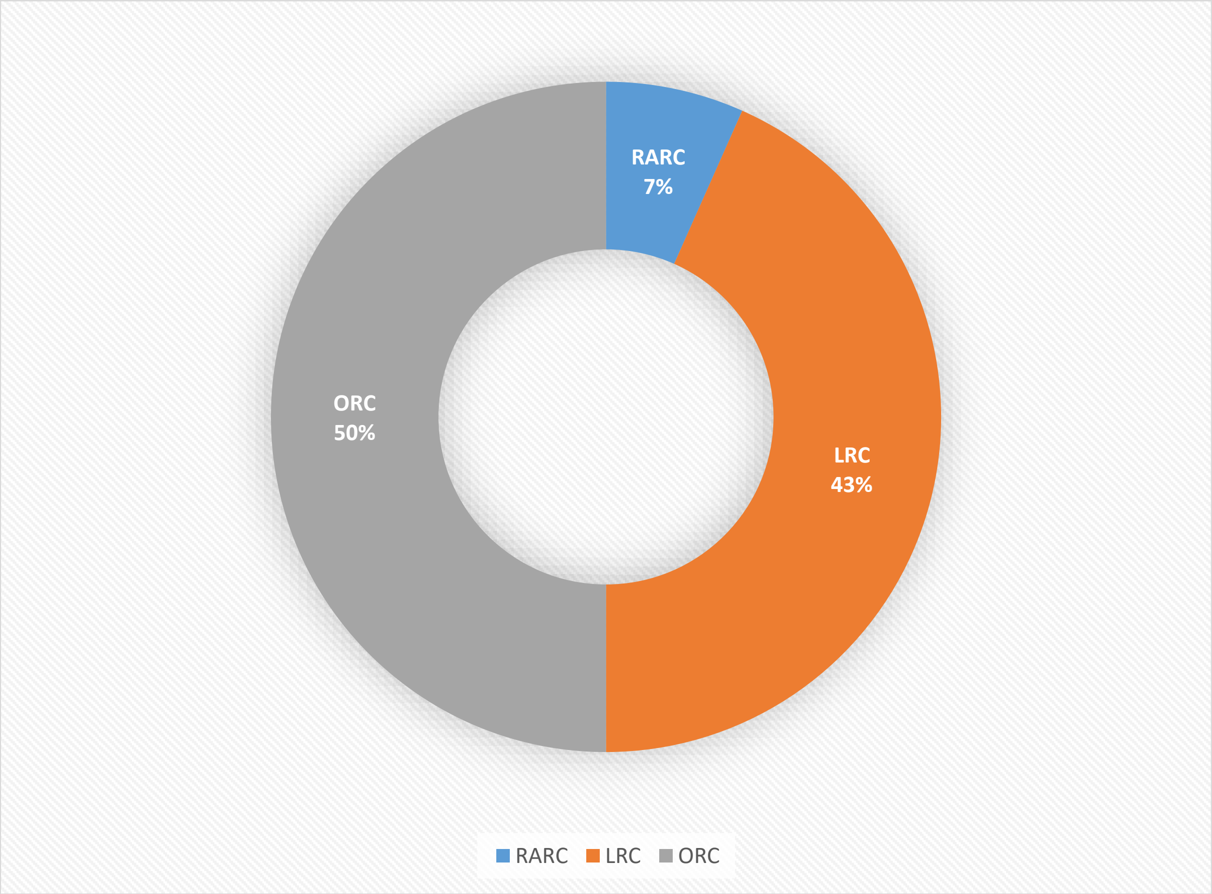

Figure 29: Radical Cystectomy Approaches.

Abbreviations: RARC=robotic assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

The two treatment groups were homogeneous in terms of baseline preoperative characteristics.

Table 5:Comparison of Preoperative characteristics between the MIRC and ORC groups.

		Whole cohort N=60	MIRC N=30	ORC N=30	P value
Age (year)		59.02±7.55	57.20±8.38	60.83±6.24	0.062
Sex	Male	47 (78.3%)	22 (73.3%)	25 (83.3%)	0.532
	Female	13 (21.7%)	8 (26.7%)	5 (16.7)	
ASA	1	22 (36.7%)	12 (40%)	10 (33.3%)	0.838
	2	35 (58.3%)	17 (56.7%)	18 (60%)	
	3	3 (5%)	1 (3.3%)	2 (6.7%)	
Previous abdominal surgery		8 (13.3%)	4 (13.3%)	4 (13.3%)	1.00
Neoadjuvant chemotherapy		22 (36.7%)	14 (46.7%)	8 (26.7%)	0.18

Abbreviation: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy; ASA= American Society of Anesthesiologists' classification
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As shown in **(Table 5)**, We found no statistically significant differences between the two groups in age (p=0.062), sex (p=0.532), ASA(p=0.838), history of previous abdominal surgery(p=1.00), neoadjuvant chemotherapy(p=0.18).

The mean age of the whole cohort was 59 years. The mean age in the MIRC group was 57.2 years vs 60.8 years in the ORC group. percentage of males of the whole cohort was 78.3% (47 patients). percentage of males was 83.3% (25 patients) in the ORC group vs. 73.3% (22 patients) in the MIRC group. Eight patients of the whole cohort had previous abdominal surgery (13.3%): Neoadjuvant chemotherapy was given to twenty-two patients (36.7%) of the whole cohort, and fourteen patients in the MIRC group (46.7%) eight patients (26.7%) in the ORC group.

A
B

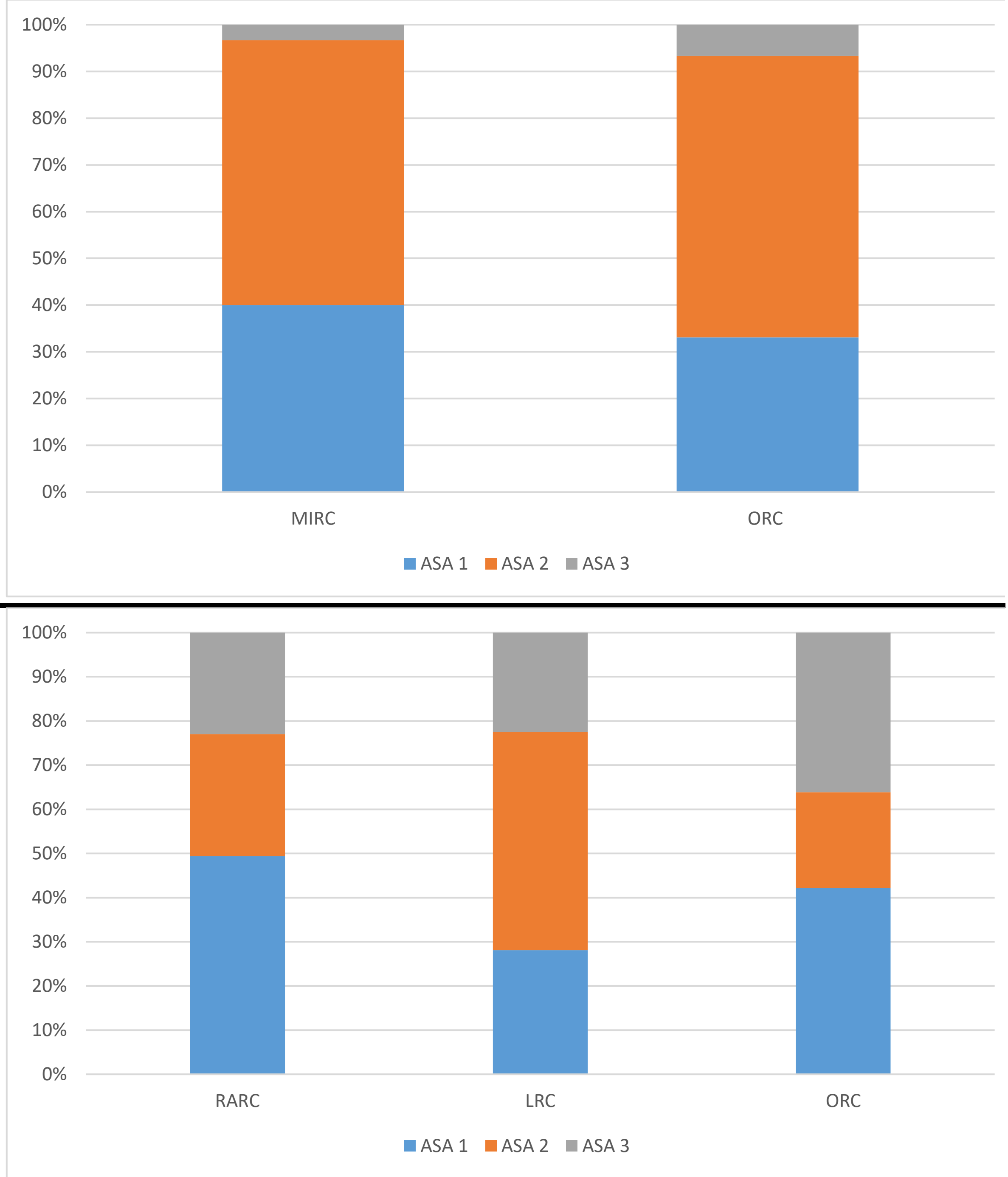

Figure 30: Comparison of ASA score between the MIRC and ORC groups.
A: Comparing MIRC and ORC approach.
B: Comparing RARC, LRC and ORC approach.
Abbreviations: ASA= American Society of Anesthesiologists' classification MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

Table 6: Comparison of perioperative laboratory values between the MIRC and ORC groups.

	Whole cohort N =60	MIRC N =30	ORC N =30	P value
SCr preoperative (mg/dl)	1.12±0.30	1.08±0.25	1.15±0.34	0.323
SCr 1st postoperative day (mg/dl)	1.08±0.19	1.03±0.15	1.14±0.20	0.026*
Hb preoperative (gm/dl)	12.00±1.50	12.01±1.46	11.98±1.57	0.932
Hb 1st postoperative day(gm/dl)	10.62±1.25	10.70±1.24	10.53±1.29	0.611

Abbreviation: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy; Hb=hemoglobin; SCr=serum creatinine.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As presented in **(Table 6)**, Both groups were matched in terms of preoperative parameters, including perioperative Serum Creatinine (SCr) levels, perioperative Hemoglobin (Hb) values.

Table 7: Comparison of clinical stages between the RARC, LRC and ORC groups.

		Whole cohort N=60	RARC N =4	LRC N =26	ORC N=30	P value
cT stage	cT1	10 (16.7%)	1 (25 %)	4 (15.4%)	5 (16.7%)	0.920
	cT2	34 (56.7%)	2 (50 %)	16 (61.5%)	16(53.3%)	
	cT3	16 (26.7%)	1 (25%)	6 (23.1%)	9 (30%)	
cN stage	cN0	49 (81.7%)	3 (75%)	20 (76.9%)	2 (86.7%)	0.488
	cN1-3	11 (18.3%)	1 (25%)	6 (23.1%)	4 (13.3%)	

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As shown in **(Table 7)**, Both groups were matched in terms of cT and cN stages as we found no statistically significant difference in the cT stage between RARC, LRC and ORC groups (p=0.920), also we found no statistically significant difference in the cN stage between RARC, LRC and ORC groups (p=0.488).

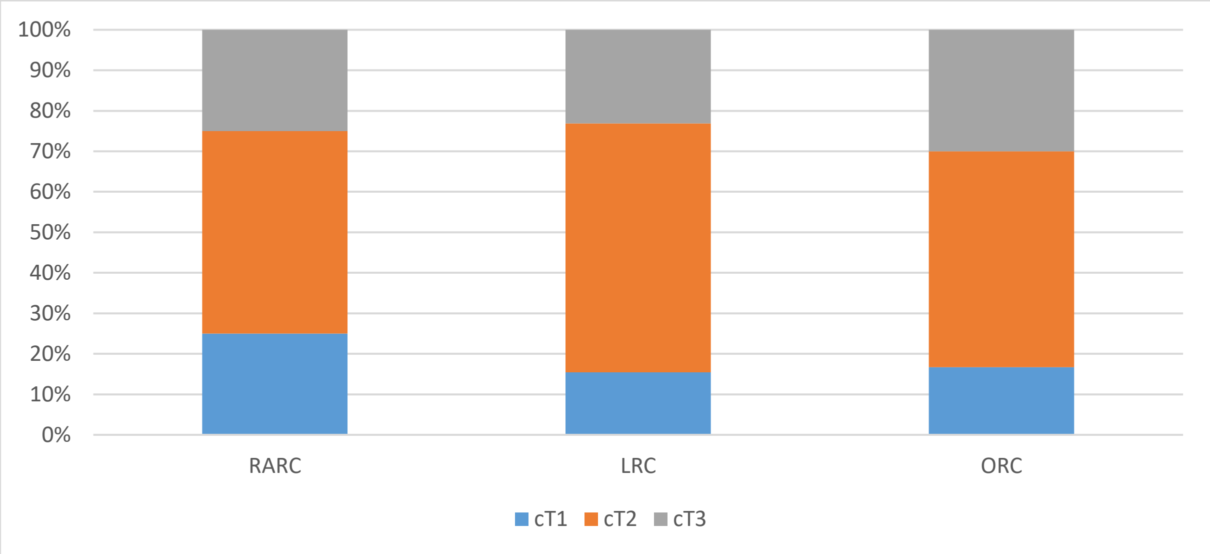

Figure 31: Comparison of different cT stages between the RARC, LRC and ORC groups.

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

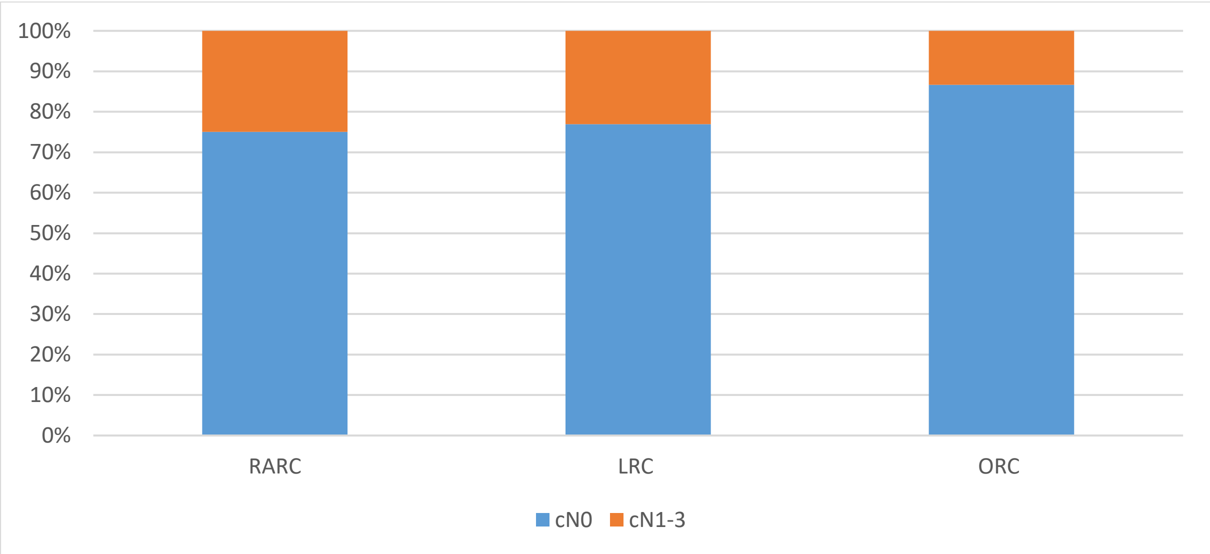

Figure 32: Comparison of different cN stages between the RARC, LRC and ORC groups.

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy

Table 8: Comparison of pathologic outcomes between the RARC, LRC and ORC groups.

		Whole cohort N=60	RARC N =4	LRC N =26	ORC N=30	P value
pT stage	pT0	5 (8.3%)	0	5 (19.2%)	0	0.098
	pT1	3 (5%)	0	1 (3.8%)	2 (6.7%)	
	pT2a	4 (6.7%)	1 (25%)	0	3 (10%)	
	pT2b	6 (10%)	0	2 (7.7%)	4 (13.3%)	
	pT3a	10 (16.7%)	0	7 (26.9%)	3 (10)	
	pT3b	25 (41.7%)	3 (75%)	8 (30.8%)	14 (46.7)	
	pT4a	7 (11.7)	0	3 (11.5%)	4 (13.3%)	
Retrieved LNs		13.82±5.13	18.50±2.08	15.23±4.14	11.97±5.48	0.008*
					RARC vs ORC	0.035*
					LRC vs ORC	0.036*
					RARC vs LRC	0.419
Positive LNs		0.67±1.53	0.50±1.00	0.88±2.07	0.50±0.94	0.634

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; LNs=Lymph nodes
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As presented in **(Table 8)**, According to specimen retrieval analysis, we found a statistically significant difference in favor of the minimally invasive approach regarding the retrieved LNs number., which were 15.67 (LN) in the MIRC group and 11.97 (LN) in the ORC group (p= 0.004)

Also, we found a statistically significant difference in Retrieved LNs number between 18.5 (LN) in the RARC group, 15.23 (LN) in the LRC group and 11.97 (LN) in the ORC group (P=0.008)., We found a statistically significant difference for the RARC group compared to the ORC group (18.5 vs 11.97 LN; p=0.035) also, we found a statistically significant difference for the LRC group compared to the ORC group (15.23 vs 11.97 LN; p=0.036)., but we found no statistically significant difference when comparing the RARC group with the LRC group. (18.5 vs 15.23 LN; p=0.419).

We found no statistically significant difference regarding positive retrieved LNs between MIRC and ORC groups (p=0.402). Even after subgroup analysis of the MIRC group we did not find a statistically significant difference regarding positive retrieved LNs between RARC, LRC and ORC groups (p=0.634).

On the other hand, we found no statistically significant difference in pT stage between RARC, LRC and ORC groups (p=0.098). Additionally, a PSM was detected in only one case which was in the ORC group, no patients from the MIRC group developed positive margins.

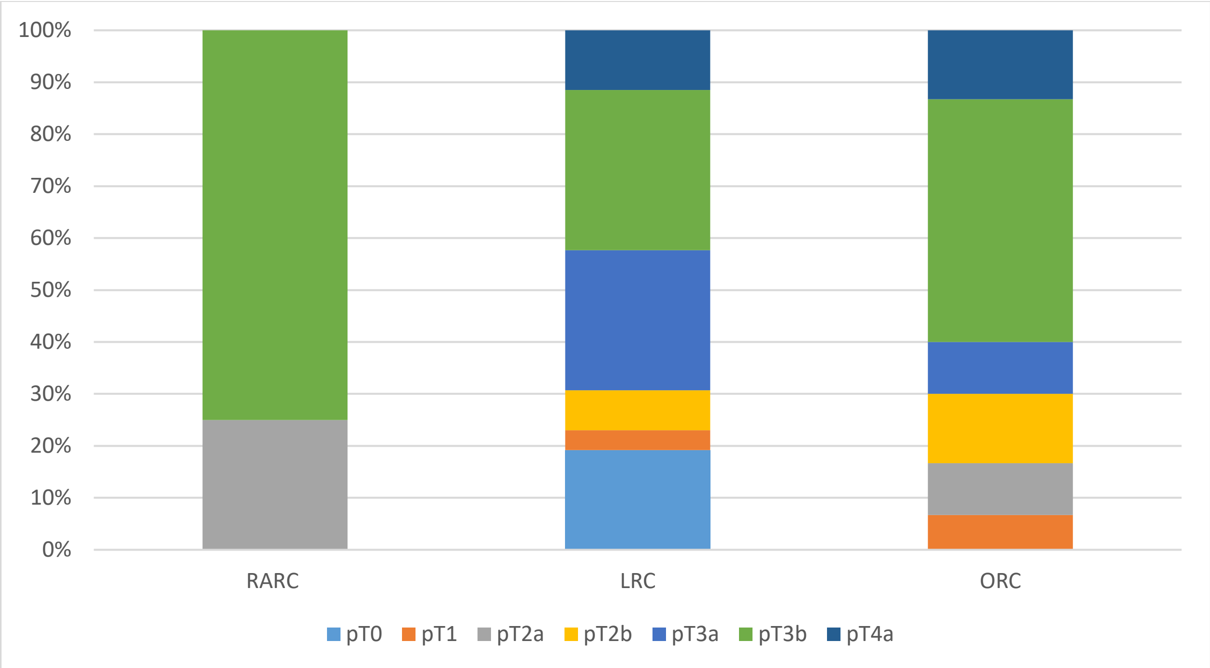

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Figure 33: Comparison of postoperative pathologic outcomes between the RARC, LRC and ORC groups.

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

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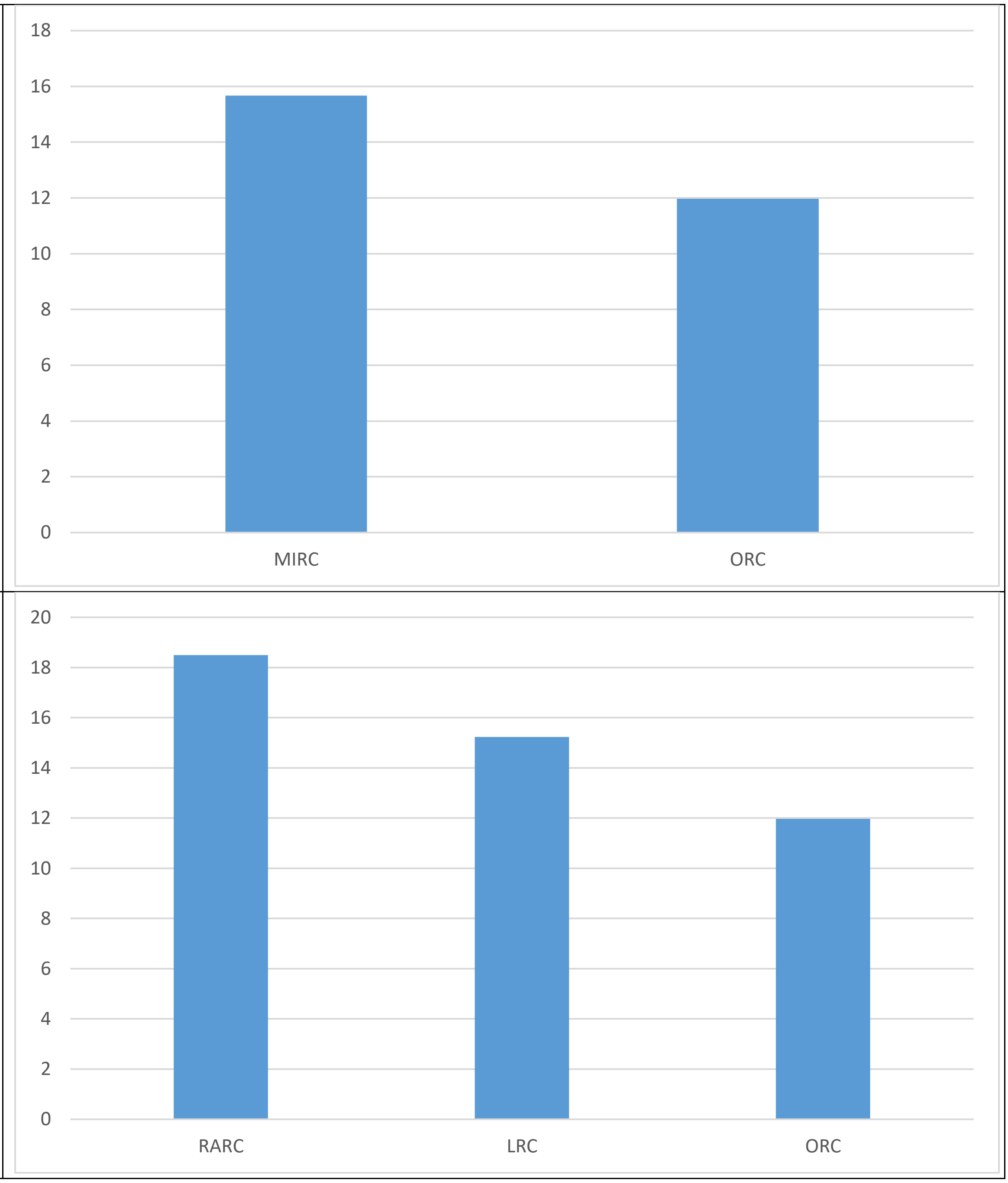

Figure 34: Comparison of the LNs no. retrieved between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; LNs=Lymph nodes.

Table 9: Comparison of different pathological types between the RARC, LRC and ORC groups.

	Whole cohort N=60	RARC N =4	LRC N =26	ORC N=30	P value
Adenocarcinoma	4 (6.7%)	0	1 (3.8%)	3 (10%)	0.393
SCC	15 (25%)	2 (50%)	7 (30%)	6 (20%)	
TCC	41 (68.3%)	2 (50%)	18 (69.2%)	21 (70%)	

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; SCC=squamous cell carcinoma; TCC=transitional cell carcinoma

p-value≤0.05 is considered significant.

Values are given in Means ± SD or n (%).

As presented in **(Table 9)**, on comparing the RARC, LRC and ORC groups, we found no statistically significant difference regarding the final pathological type (p=0.393).

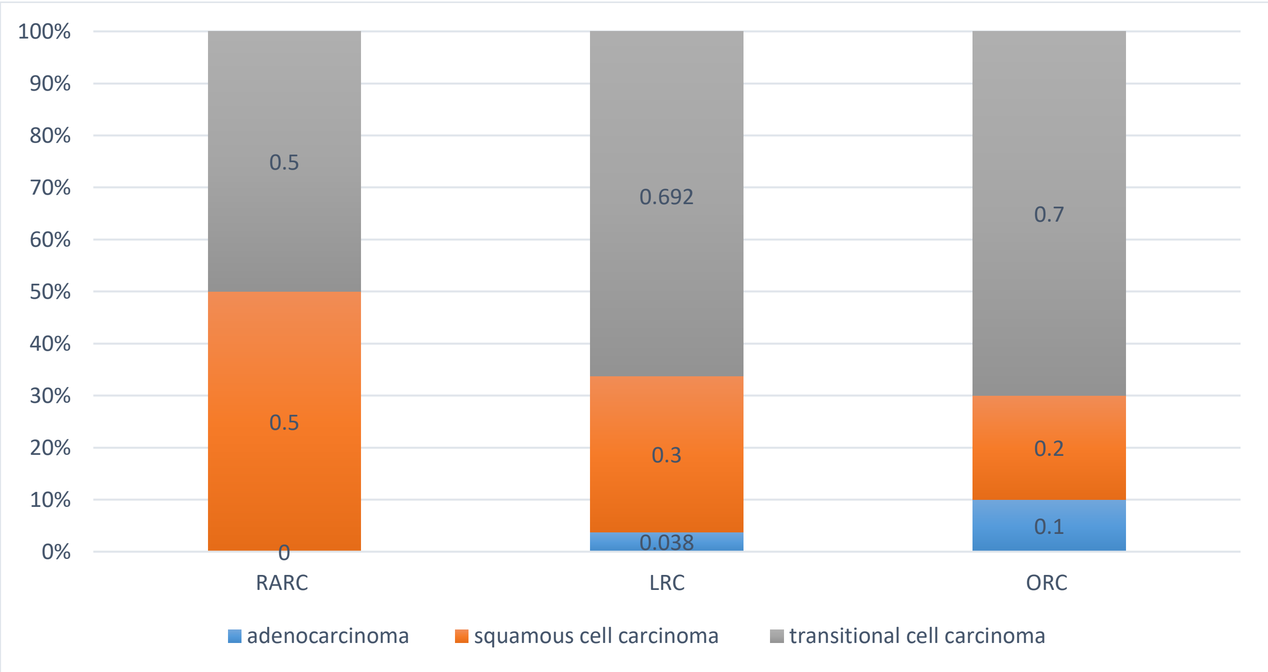

Figure 35: Comparison of different pathological types between the RARC, LRC and ORC.

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

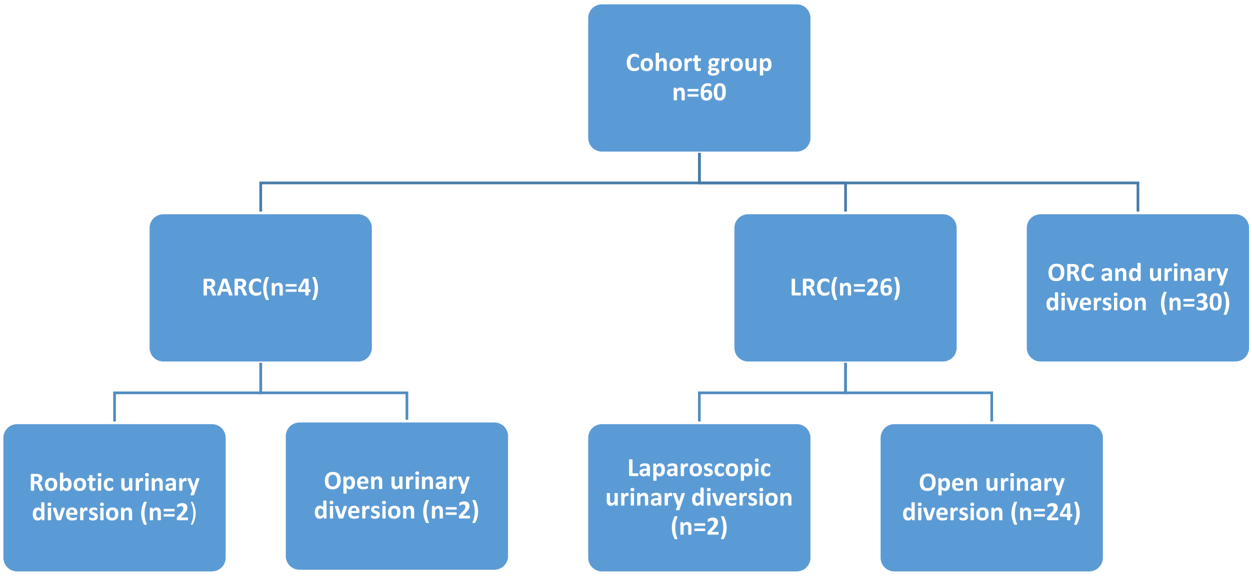

Figure 36: Flow chart of the whole cohort.

All the 30 patients allocated to MIRC received the intended approach. The urinary diversion part of the procedure was operated on intracorporeally in four of them, ECUD was the choice for the remaining twenty-six patients.

Table 10: Comparison of total operative time (min) between the MIRC and ORC groups.

	Whole cohort N=60	MIRC N=30	ORC N=30	P value
operative time (min)	311.7 ±110.45	394.83±94.81	228.57±39.18	<0.001*

Abbreviations: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As shown in **(Table 10)**, the total operative time of the whole cohort was 312min (range: 180–630min). A significant difference in total operative time between the MIRC group and the ORC group (395 vs 229 min; P<0.001).

Table 11: Comparison of total operative time (min) between the RARC, LRC and ORC groups.

	RARC N=4	LRC N=26	ORC N=30	P value
operative time (min)	581.25±53.91	366.15±60.52	228.57±39.18	<0.001*
			ORC vs RARC	<0.001*
			RARC vs LRC	0.263
			ORC vs LRC	<0.001*

Abbreviations: RARC=robotic assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As shown in **(Table 11),** the total operative time was significantly longer in the RARC group compared with the ORC group (581 vs 229 min; P<0.001), the operative time was significantly longer for the LRC group compared with the ORC group (366 vs 229 min; P<0.001), On the other hand, we found no statistically significant difference in the total operative time when comparing the RARC group and LRC group (p=0.263). Docking time was exclusive to the robotic approach, which was 27.5 min (range: 20–35min). which add more time to total operative time when using this approach.

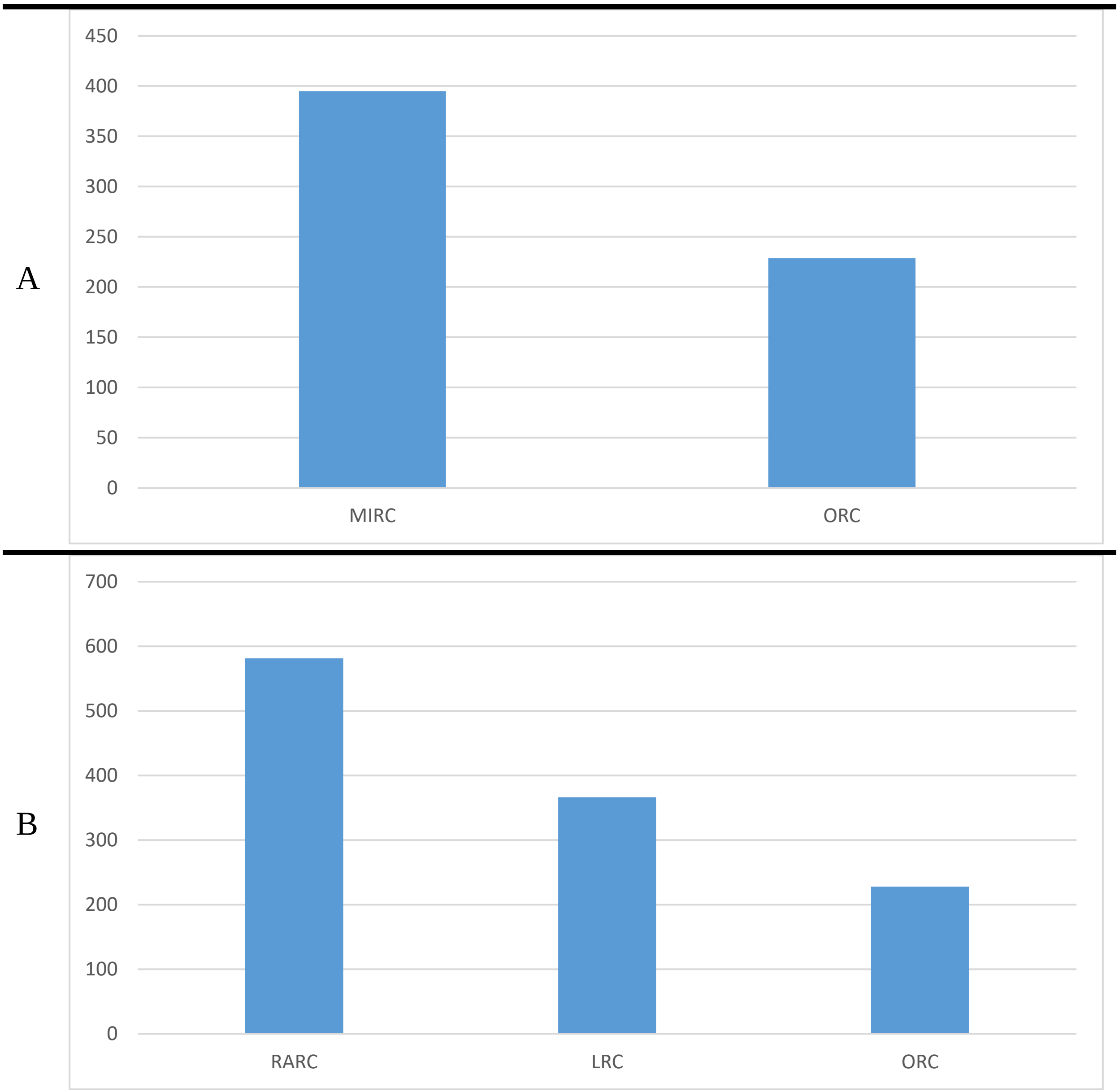

Figure 37: Comparison of total operative time (min) between the MIRC and ORC group.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

Table 12: Comparison of cystectomy and lymphadenectomy operative time (min) between the MIRC and ORC groups.

	Whole cohort N=60	MIRC N=30	ORC N=30	P value
Cystectomy operative time (min)	129.58±76.24	194.67±51.24	64.50±20.94	<0.001*
Lymphadenectomy operative time (min)	61.08 ±15.01	66.50±14.03	55.67±14.19	0.002*

Abbreviations: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As shown in **(Table 12)**, the cystectomy operative time of the whole cohort was 130min (range: 30–330min). cystectomy operative time was significantly longer for the MIRC group compared to the ORC group. (195 vs 65min; P<0.001).

lymphadenectomy operative time of the whole cohort was 61min (range: 40–100min). lymphadenectomy Operative time was significantly longer for the MIRC group compared to the ORC group (66.5 vs 55min; P=0.002)

Table 13: Comparison of cystectomy and lymphadenectomy operative time (min) between the RARC, LRC and ORC groups.

	RARC N=4	LRC N=26	ORC N=30	P value
Cystectomy operative time (min)	282.50±40.31	181.15±37.7	64.50±20.94	<0.001*
			ORC vs RARC	<0.001*
			RARC vs LRC	0.366
			ORC vs LRC	<0.001*
Lymphadenectomy operative time (min)	62.50±17.08	67.12±13.80	55.67±14.19	0.007*
			ORC vs RARC	0.839
			RARC vs LRC	1.00
			ORC vs LRC	0.005*

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%)

As presented in **(table 13)**, cystectomy operative time was significantly longer for the RARC group compared with the ORC group (282.5 vs 64.5 min; P<0.001), cystectomy operative time was significantly longer for the LRC group compared with the ORC group (181 vs 64.5 min; P<0.001). on the other hand, we found no statistically significant difference regarding cystectomy operative time when comparing the RARC group and LRC group (p=0.366).

lymphadenectomy operative time was significantly longer for the LRC group compared with the ORC group (67 vs 56min; P<0.005). on the other hand, we found no statistically significant difference regarding lymphadenectomy operative time when comparing the RARC group and LRC group (p=1.00) or statistically significant difference regarding lymphadenectomy operative time when comparing the RARC group and ORC group (p=0.839).

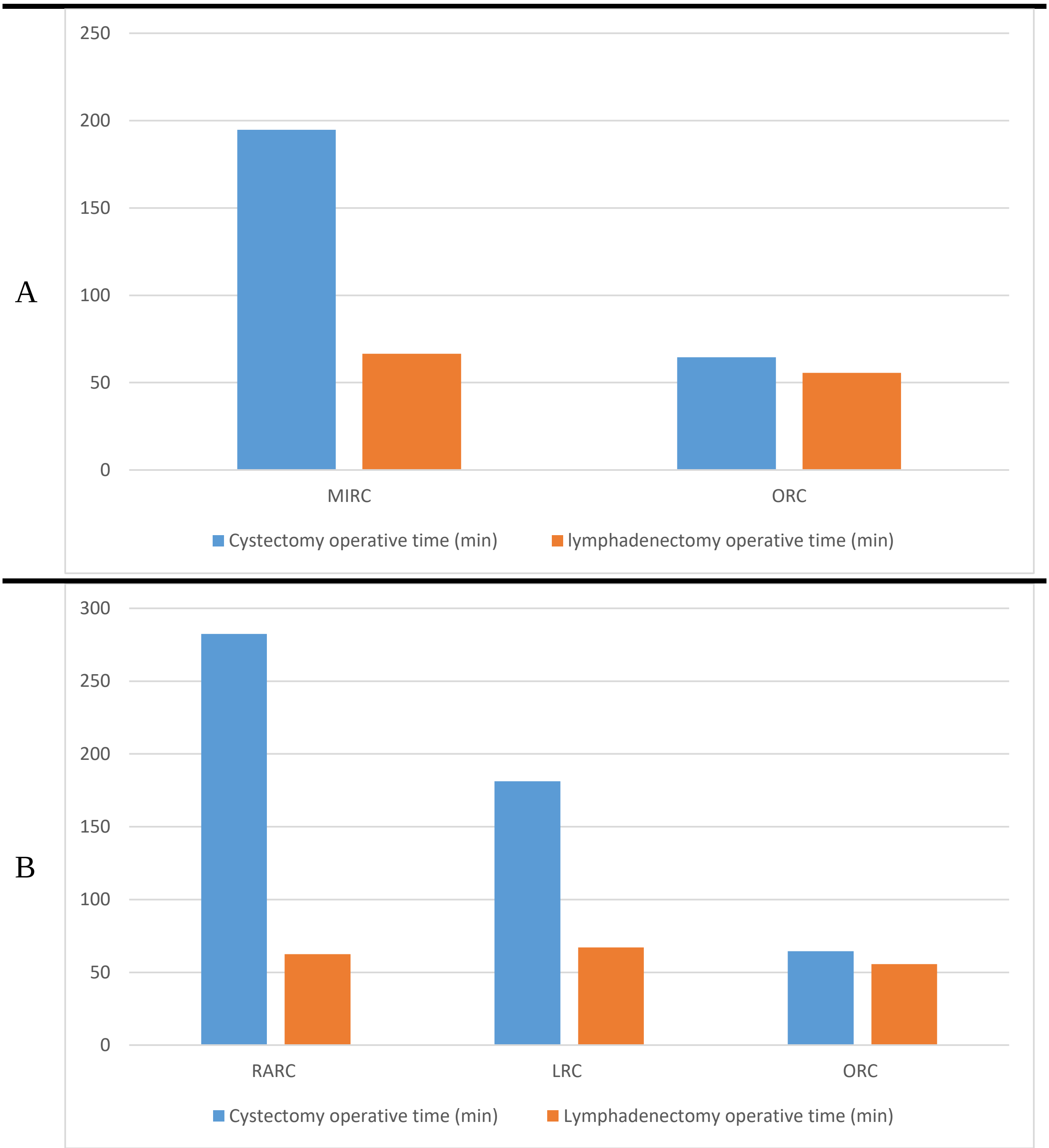

Figure 38: Comparison of cystectomy and lymphadenectomy operative time (min) between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

Table 14: Comparison of urinary diversion approaches between the RARC, LRC and ORC groups.

Urinary diversion Approach	Robotic	2 (3.3%)
	Laparoscopic	2 (3.3%)
	Open	56 (93.3%)

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

As presented in **(Table 14),** The urinary diversion part of the operation was performed with the conventional open surgical approach in fifty-six (93.3%) patients, minimally invasive urinary diversion was performed in four patients, two of them was operated on via robotic-assisted approach, the remaining two patients were operated on via laparoscopic approach.

Table 15: Comparison of urinary diversion types between the RARC, LRC and ORC groups.

		Whole cohort (N=60)	RARC(N=2)	LRC(N=2)	ORC(N=56)
Continent	Studer pouch neobladder	2	2	0	0
	Ileocecal pouch neobladder	1	0	0	1
	Y pouch neobladder	6	0	2	4
Non- continent IC		51	0	0	51

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; IC=Ileal conduit.

As shown in **(Table 15)**, there was no difference regarding the trend of urinary reconstruction in either group, the conventional open non-continent IC urinary diversion was the most utilized urinary diversion approach, which was performed in fifty-one patients. Y pouch continent orthotopic urinary diversion was performed in six patients, four of them was operated on with the conventional open surgical approach, the remaining two were completed laparoscopically, continent orthotopic ileocecal pouch urinary diversion was performed in only one patient which was operated on with the conventional open surgical approach.

Two patients of the RARC group completed the urinary diversion part of the procedure with the conventional open surgical approach, the IC was performed for them, the other two patients were operated on completely robotically with Studer orthotopic neobladder intracorporeal urinary diversion. Two of the twenty-six patients of the LRC group completed the urinary diversion part of the operation intracorporeally in the form of Y pouch orthotopic neobladder, the remaining twenty-four patients completed the reconstruction of the urinary diversion part of the procedure with the conventional open surgical approach, in the form of an IC.

The continent urinary diversion was performed in Nine patients, Y pouch continent orthotopic neobladder was the procedure of choice for Six patient of them, four of them was operated on with the conventional open surgical approach, the remaining two patients were operated on completely laparoscopically with the intracorporeal formation of the pouch and anastomosis to the urethra.

Table 16: Comparison of urinary diversion operative time(min) between the MIRC and ORC groups.

	Whole cohort N=60	MIS approach N=4	Conventional open surgical approach N=56	P-value
Urinary diversion operative time (min)	88.6 ±49.1	222.50±35.0	79.11±33.6	0.001*

Abbreviations: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy; MIS=minimally invasive surgery.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

As shown in **(Table 16)**, the urinary diversion operative time of the whole cohort was 89min (range: 40–260min). The urinary diversion Operative time was significantly longer for the MIS group compared to the conventional Open surgical approach group. (222.5 vs 79min; P=0.001).

Table 17: Comparison of urinary diversion operative time (min) between the Robotic-assisted, Laparoscopic and Conventional open surgical approaches.

	Robotic-assisted approach N=2	Laparoscopic approach N=2	Conventional open surgical approach N=56	P-value
Urinary diversion operative time (min)	195 ±21.21	250 ±14.14	79.11 ±33.60	0.004*

p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

The urinary diversion operative time was significantly longer for the robotic-assisted and laparoscopic urinary diversion group compared with the conventional open surgical approach group (195 vs 250 vs 79min; P=0.004), as presented in **(table 17).**

A

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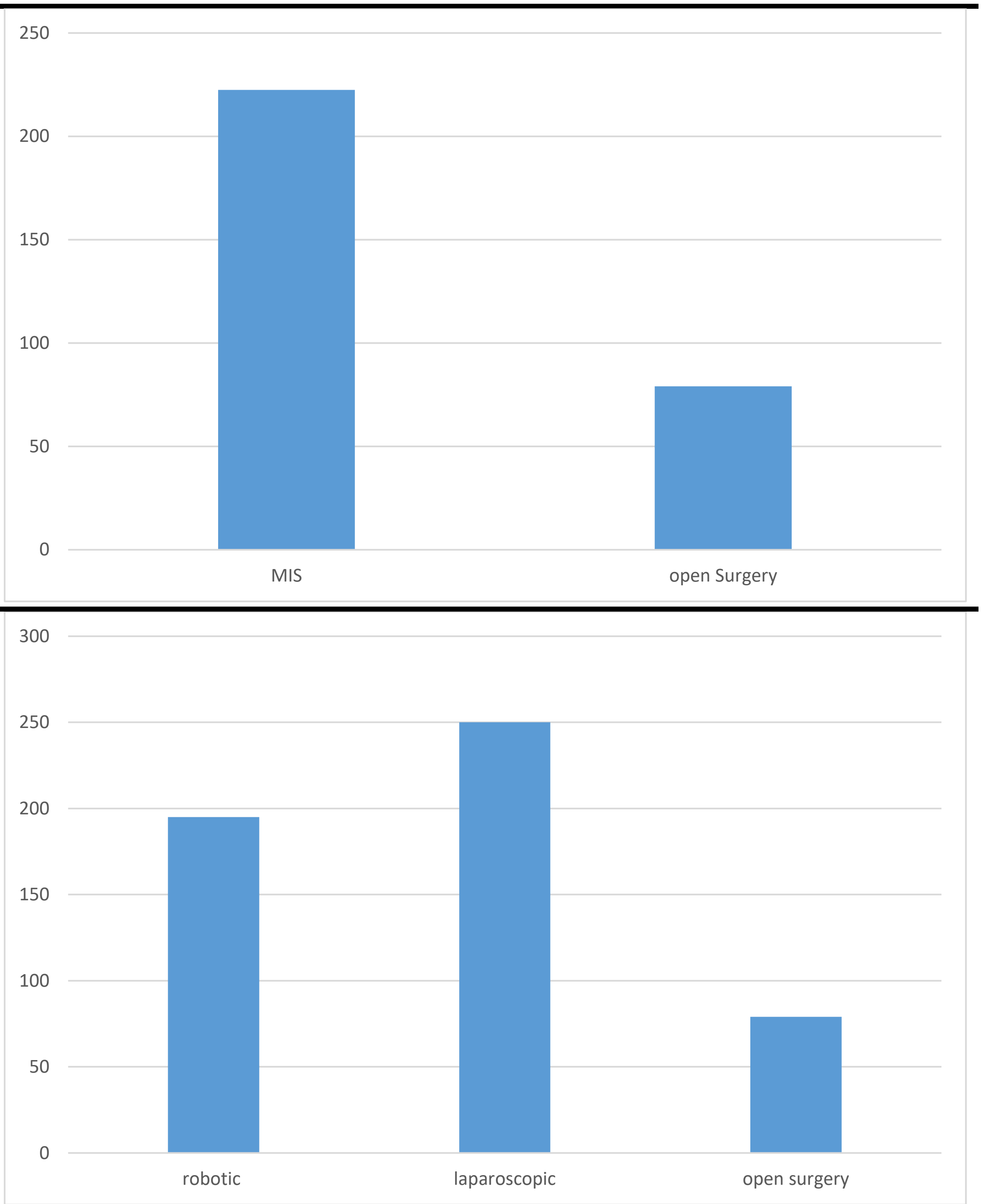


Figure 39: Comparison of urinary diversion operative time (min) between the MIS and open surgery groups.

A: Comparing MIS and open surgery groups.

B: Comparing robotic, laparoscopic and open surgery groups.

Abbreviations: MIS=minimally invasive surgery.

Table 18: Comparison of intra-operative estimated blood loss and required blood transfusion units between the MIRC and ORC groups.

		MIRC N =30	ORC N =30	P value
EBL (ml)		437.33±374.24	602.67±432.44	0.119
Blood transfusion (unit)	0	23 (76.7%)	16 (53.3%)	0.207
	1	3 (10%)	3(10%)	
	2	2 (6.7%)	8(26.7%)	
	3	1 (3.3%)	2(6.7%)	
	4	1 (3.3%)	1 (3.3%)	

Abbreviations: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy; EBL=estimated blood loss.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

We found no statistically significant difference when comparing intraoperative EBL in the MIRC group with the ORC group (p=0.119), the rate of transfusions of more than 1 unit of RBCs was higher in the ORC group (11 cases vs. 4 cases) as shown in **(table 18).**

Table 19: Comparison of intra-operative estimated blood loss and required blood transfusion units between the RARC, LRC and ORC groups.

		RARC N=4	LRC N=26	ORC N=30	P value
EBL (ml)		325.00±170.78	454.62±395.77	602.67±432.44	0.251
Blood transfusion (unit)	0	3 (75%)	20 (76.9%)	16 (53.3%)	0.481
	1	1 (25%)	2 (7.7%)	3 (10%).	
	2	0 (0%)	2 (7.7%)	8 (26.7%)	
	3	0 (0%)	1 (3.8%)	2 (6.7%)	
	4	0 (0%)	1 (3.8%)	1 (3.3%)	

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; EBL=estimated blood loss.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%)

As presented in **(Table 19)**, EBL volume was lower for the RARC group (325.ml) and LRC group (455 ml) compared with the ORC group (603.ml), but this did not reach statistical significance. (p=0.251). Blood transfusion was required in twenty-one patients, four units of packed RBCs were required in two patients, one of them was operated on via the conventional open surgical approach, the other one was operated on via the laparoscopic approach, thirty-nine patients did not receive a blood transfusion, twenty-three of them (58.9%) were operated on via the minimally invasive approach, twenty of them were operated on via the laparoscopic approach. blood transfusion was required in only one patient in the RARC group, for which one unit was given.

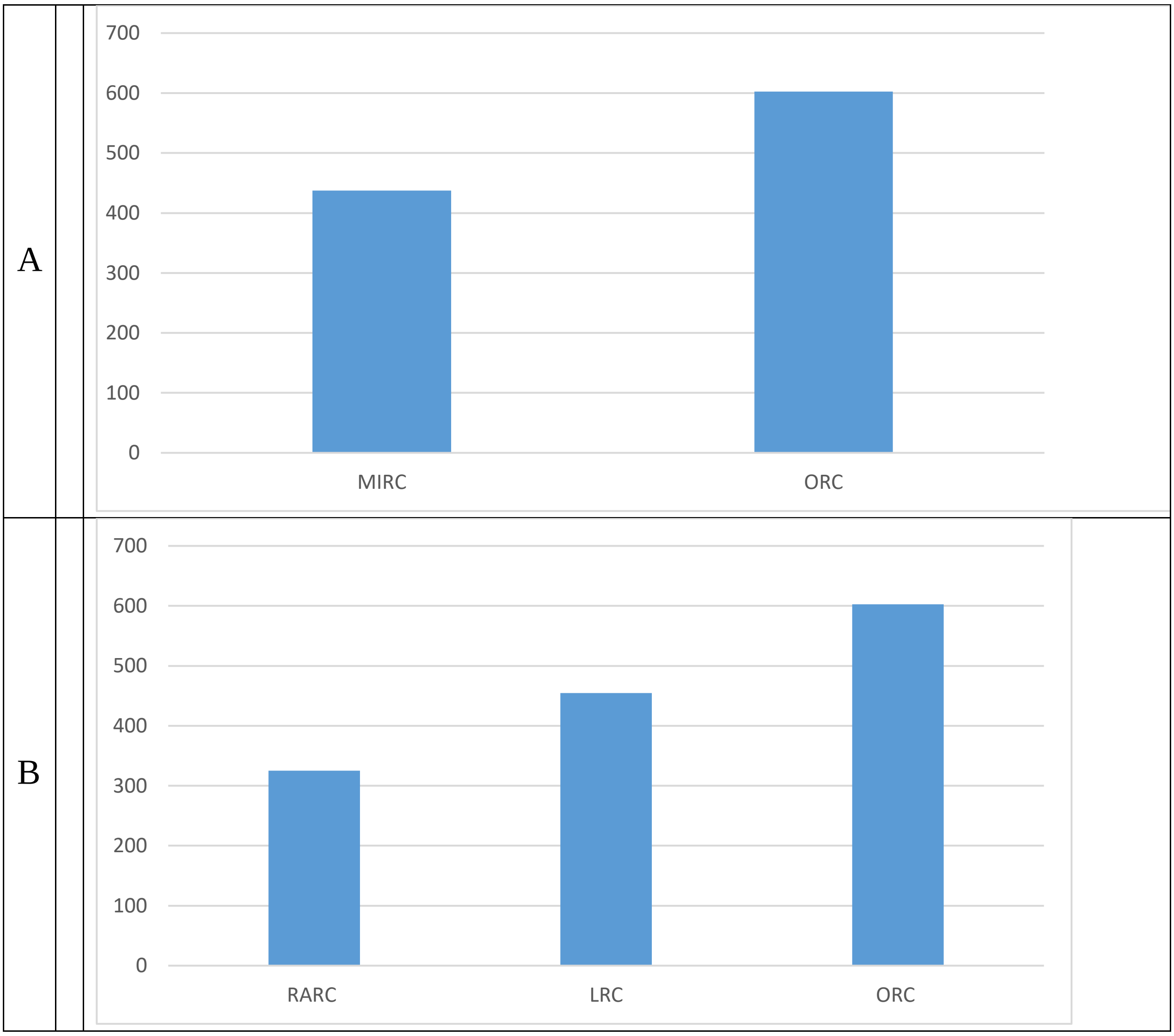


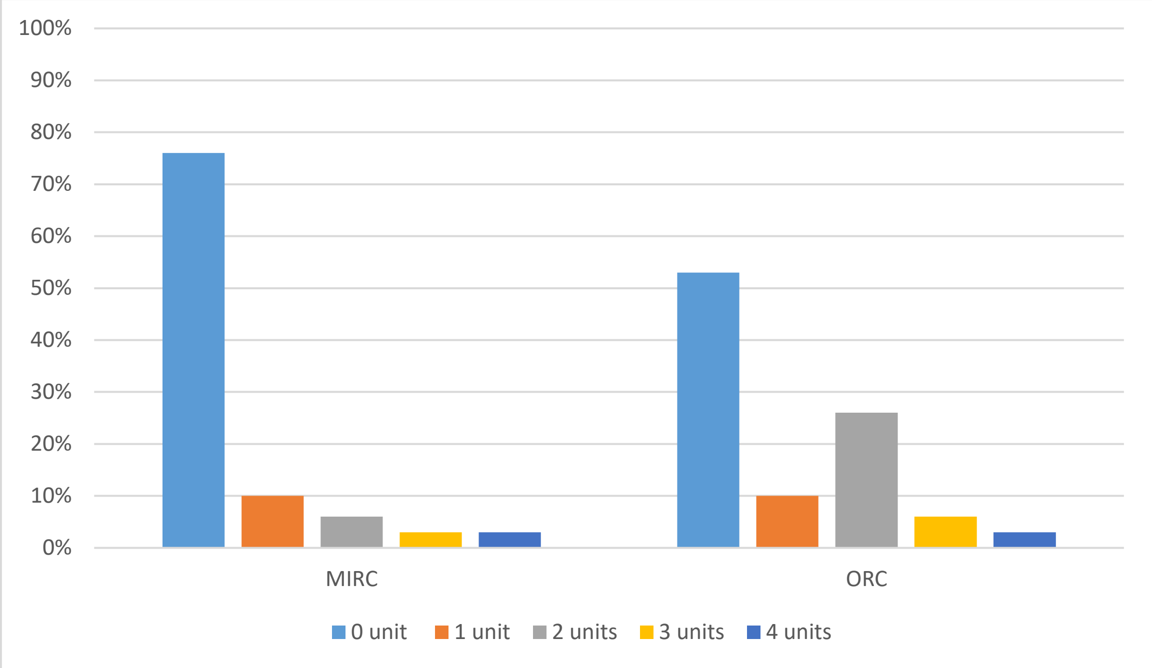
Figure 40: Comparison of intra-operative estimated blood loss (ml) between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

A



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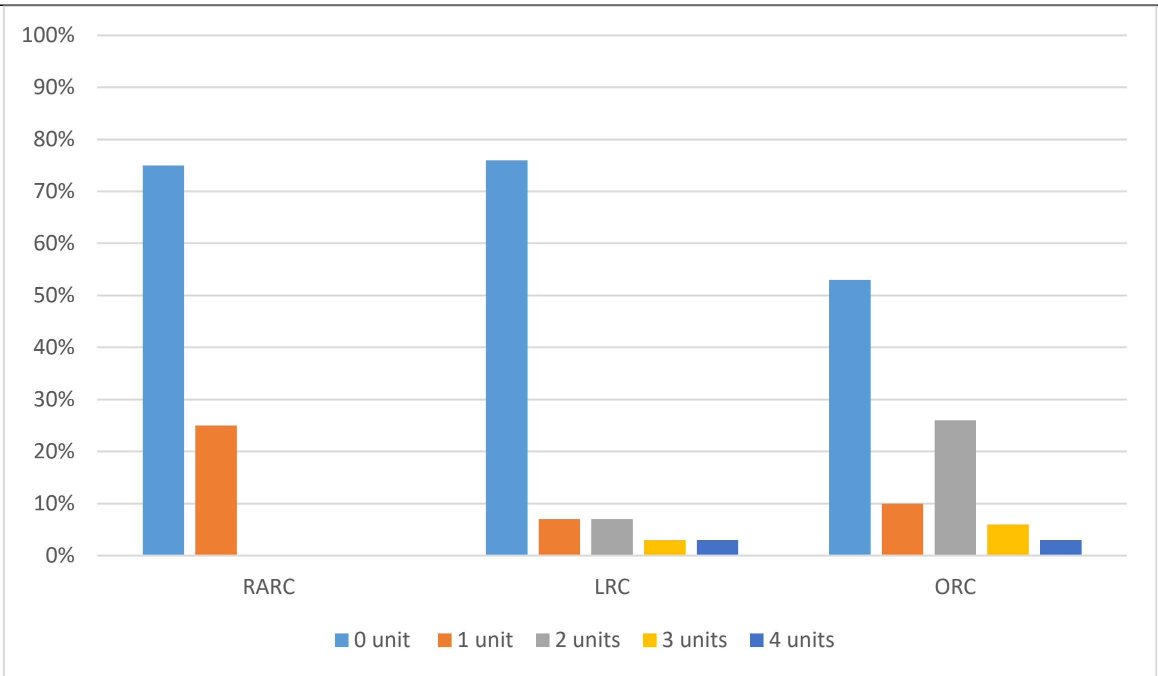

Figure 41: Comparison of required blood transfusion units between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

Table 20: Comparison of complications classified by systems between the RARC, LRC and ORC groups.

	Whole cohort N=60	RARC N=4	LRC N=26	ORC N=30
Seroma	8	1	2	5
SSI	4	1	1	2
UTI	1	0	1	0
Ileus	10	0	2	8
Urine leak	4	1	1	2
Small intestinal injury	1	0	1	0
Rectal injury	1	0	0	1
Anastomotic bowel leak	5	1	2	2
Abdominal wall dehiscence	3	1	0	2
Pneumonia	2	0	0	2
PE	2	1	0	1
Hospital readmission	7	1	1	5
Incisional hernia	3	0	0	3

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; UTI=urinary tract infection; SSI=Surgical site infection; PE=pulmonary embolism.

Postoperative complications are shown in **(Table 20)**, There were intraoperative complications in the form of jejunal loop injury in one patient which was operated on via laparoscopic approach and rectal injury in one patient which was operated on via the conventional open surgical approach.

The most common adverse events were ileus in ten patients, eight of them in the ORC group, the remaining two was operated on via the minimally invasive approach.

Wound seroma formation complicated eight patients, five of them in the ORC group, the remaining three were operated on via the minimally invasive approach. Four patients had surgical site infection, two of them were operated on via the conventional open surgical approach, the remaining two were operated on via the minimally invasive approach.

Urine leakage complicated four patients, two of them were operated on via the conventional open surgical approach, the other two were operated via the minimally invasive approach. Five patients complicated with anastomotic bowel leakage, two of them was operated on via the conventional open surgical approach, two were operated on via the laparoscopic approach and one patient was operated on via the robotic-assisted approach.

Three patients complicated with abdominal wall dehiscence, two of them was operated on via the conventional midline open approach and one patient was operated on via the robotic-assisted approach, for which infra-umbilical midline open incision was done for specimen extraction.

Two patients were complicated with pneumonia, who were operated on via the conventional open surgical approach. Two patients complicated with PE, one of them was operated on via the conventional open surgical approach which was admitted to ICU then complicated with mortality and the other one was operated on via the robotic-assisted approach which was treated with anticoagulants.

The rate of hospital readmission was higher in the ORC group (5 patients) compared to the MIRC group (2 patients), but this did not reach statistical significance (P=0.42).

Table 21: Comparison of complications classified by Clavien-Dindo grading system between the MIRC and ORC groups.

	Whole cohort N=60	MIRC N=30	ORC N=30	P value
Clavien-Dindo grade I-II	47 (78.3%)	25 (83.3%)	22 (73.3%)	0.347
Clavien-Dindo grade III-IV	12(20%)	5 (16.7%)	7 (23.3%)	0.519
Clavien-Dindo grade V	1(1.67%)	0	1(3.33%)	0.313

Abbreviations: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

Postoperative complications graded by the Clavien-Dindo grading system between the MIRC and ORC groups are summarized in **(Table 21)**, On comparing MIRC and ORC groups, we found no statistically significant difference regarding different grades of the complications graded with the Clavien-Dindo grading system. only one grade V complication (mortality) was recorded in the ORC group.

Table 22: Comparison of complications classified by Clavien-Dindo grading system between RARC, LRC and ORC groups.

	RARC N=4	LRC N=26	ORC N=30	P-value
Clavien-Dindo grade I-II	2 (50%)	23 (88.5%)	22 (73.3%)	0.142
Clavien-Dindo grade III-IV	2 (50%)	3 (11.5%)	7(23.3%)	0.164
Clavien-Dindo grade V	0	0	1(3.33%)	0.601

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

Postoperative complications graded by the Clavien-Dindo grading system between the MIRC and ORC groups are summarized in **(Table 22)**, On comparing the RARC group, the LRC group and the ORC groups, we found no statistically significant difference regarding different grades of complications graded with Clavien-Dindo grading system.

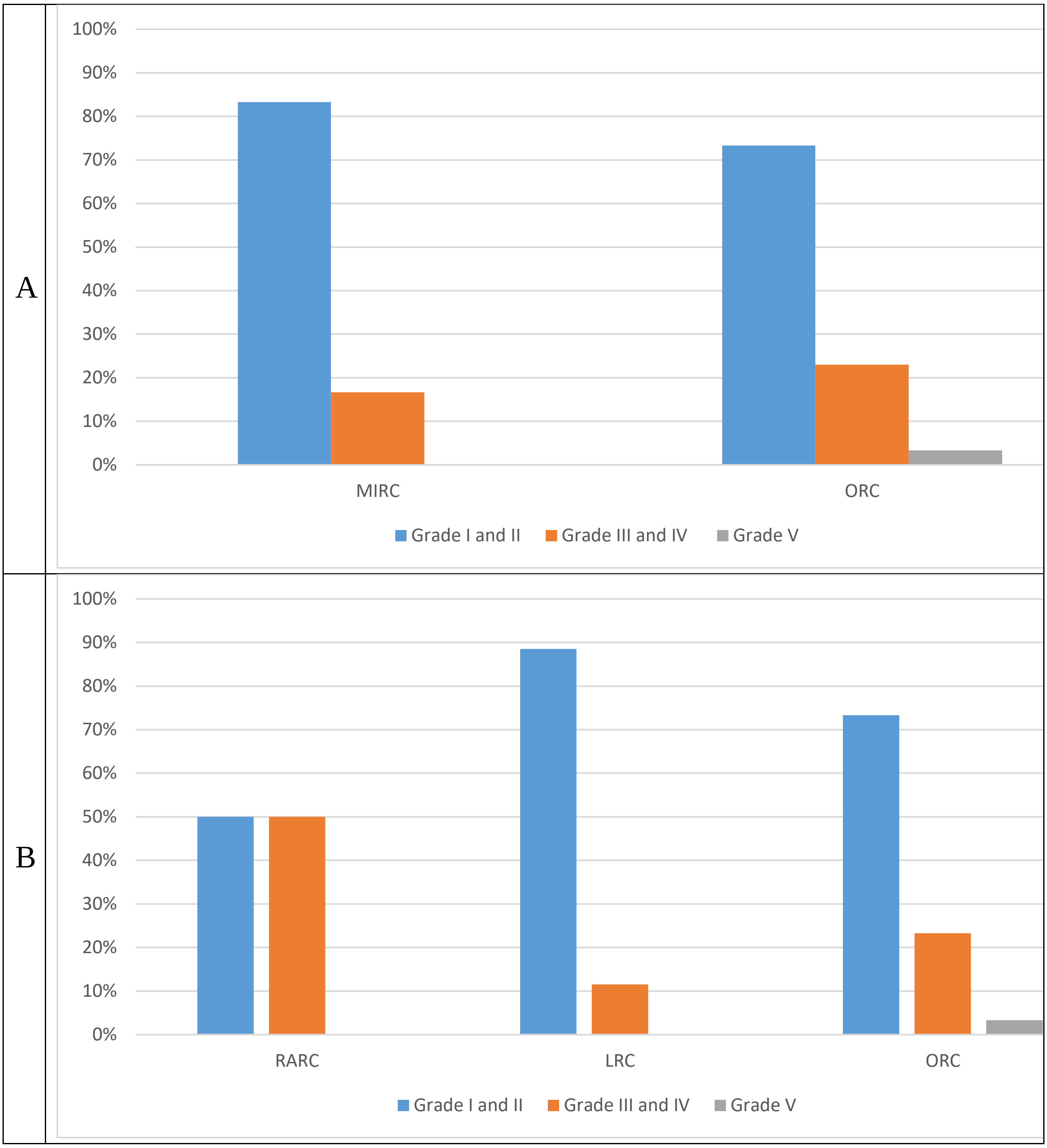

Figure 42: Comparison of complications classified by Clavien-Dindo grading system between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

Table 23: Comparison of postoperative outcomes between the MIRC and ORC groups.

	Whole cohort N=60	MIRC N=30	ORC N=30	P-value
Time to regular oral diet (day)	7.35±4.64	6.07±3.62	8.63±5.22	0.031*
Hospital LOS (day)	11.82±4.83	9.80±4.13	13.83±4.69	0.001*
Postoperative opioid requirement	23 (38.3%)	7 (23.3%)	16 (53.3%)	0.033*

Abbreviations: MIRC=minimally invasive radical cystectomy; ORC=open radical cystectomy; LOS=length of stay.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

Postoperative outcomes between the MIRC and ORC groups are summarized in **(Table 23)**, after the introduction of ERAS protocols to all study group, we found that the time to the regular oral diet of the whole cohort was 7.4 days. time to regular oral diet was significantly shorter for MIRC compared with the ORC group (6 vs 8.6 days; p=0.031).

Additionally, the hospital LOS of the whole cohort was 11.82 day. LOS was significantly shorter for the MIRC group compared ORC group (9.8 vs 13.8 days; p=0.001).

On the other hand, Postoperative opioid analgesia was not required in 37 patients (61.7%) of the whole cohort. On comparing the MIRC group to the ORC group regarding the opioid requirement for postoperative pain control, we found a statistically significant difference regarding the lower opioid requirement in the MIRC group compared ORC group (23.3% vs 53.3%; p=0.033).

Table 24: Comparison of postoperative outcomes between the RARC, LRC and ORC groups.

	RARC N=4	LRC N=26	ORC N=30	P value
Time to regular oral diet (day)	8.75±7.63	5.65±2.62	8.63±5.22	0.044*
			RARC vs ORC	0.406
			LRC vs ORC	0.041*
			RARC vs LRC	0.406
Hospital LOS (day)	13.50±7.77	9.23±3.17	13.83±4.69	0.001*
			RARC vs ORC	0.989
			LRC vs ORC	0.001*
			RARC vs LRC	0.168

Abbreviations: RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy; LOS=length of stay.
p-value≤0.05 is considered significant.
Values are given in Means ± SD or n (%).

Postoperative outcomes between the RARC, LRC and ORC groups are summarized in **(Table 24**), we found that the time to regular oral diet was significantly shorter for the LRC group compared to the ORC group (5.7 vs 8.6 days; p=0.041) but there was no statistically significant difference regarding time to regular oral diet for the RARC group compared to the ORC group (p=0.406), or when comparing the RARC group with the LRC group. (p=0.406)

Additionally, we found that the LOS was significantly shorter for the LRC group compared to the ORC group (9.2 vs 13.8 days; p=0.001) but there was no statistically significant difference regarding LOS for the RARC group compared to the ORC group (p=0.989), or when comparing the RARC group with the LRC group. (p=0.168)

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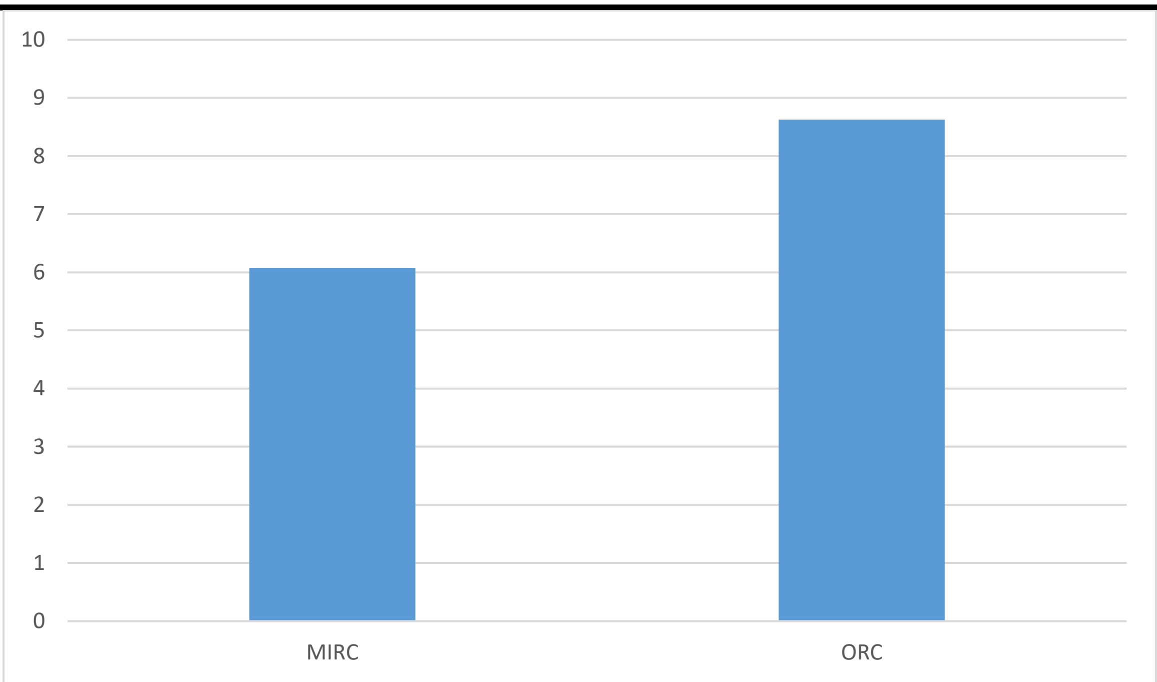

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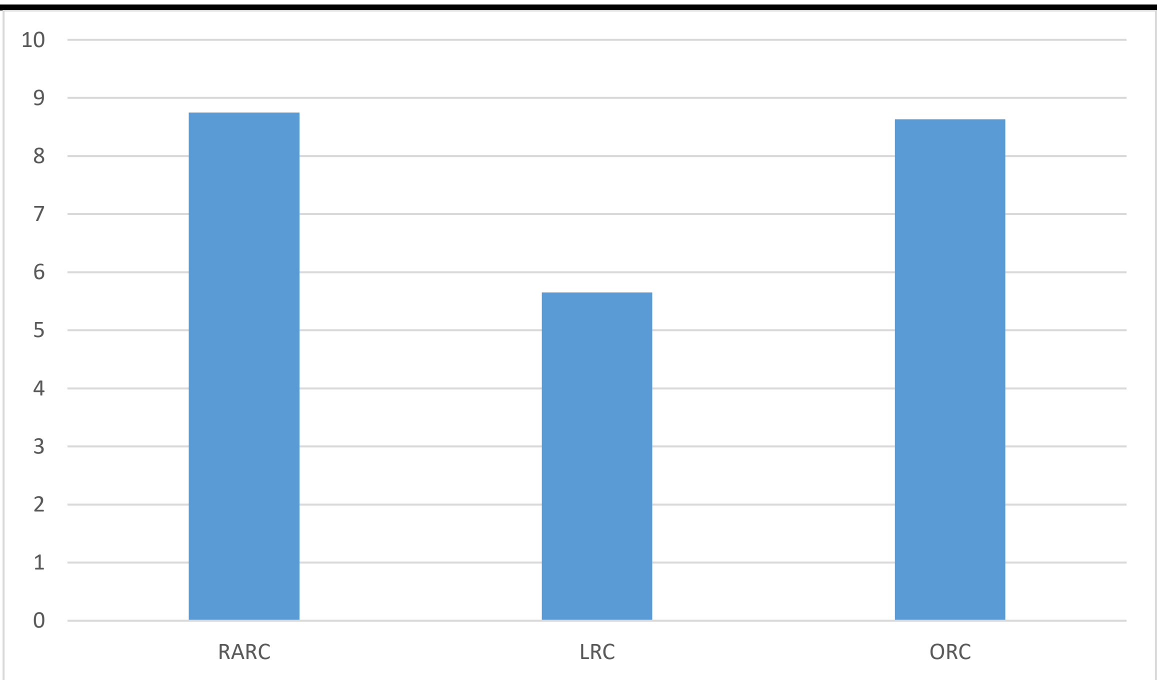


Figure 43: Comparison of time to regular oral diet (day) between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

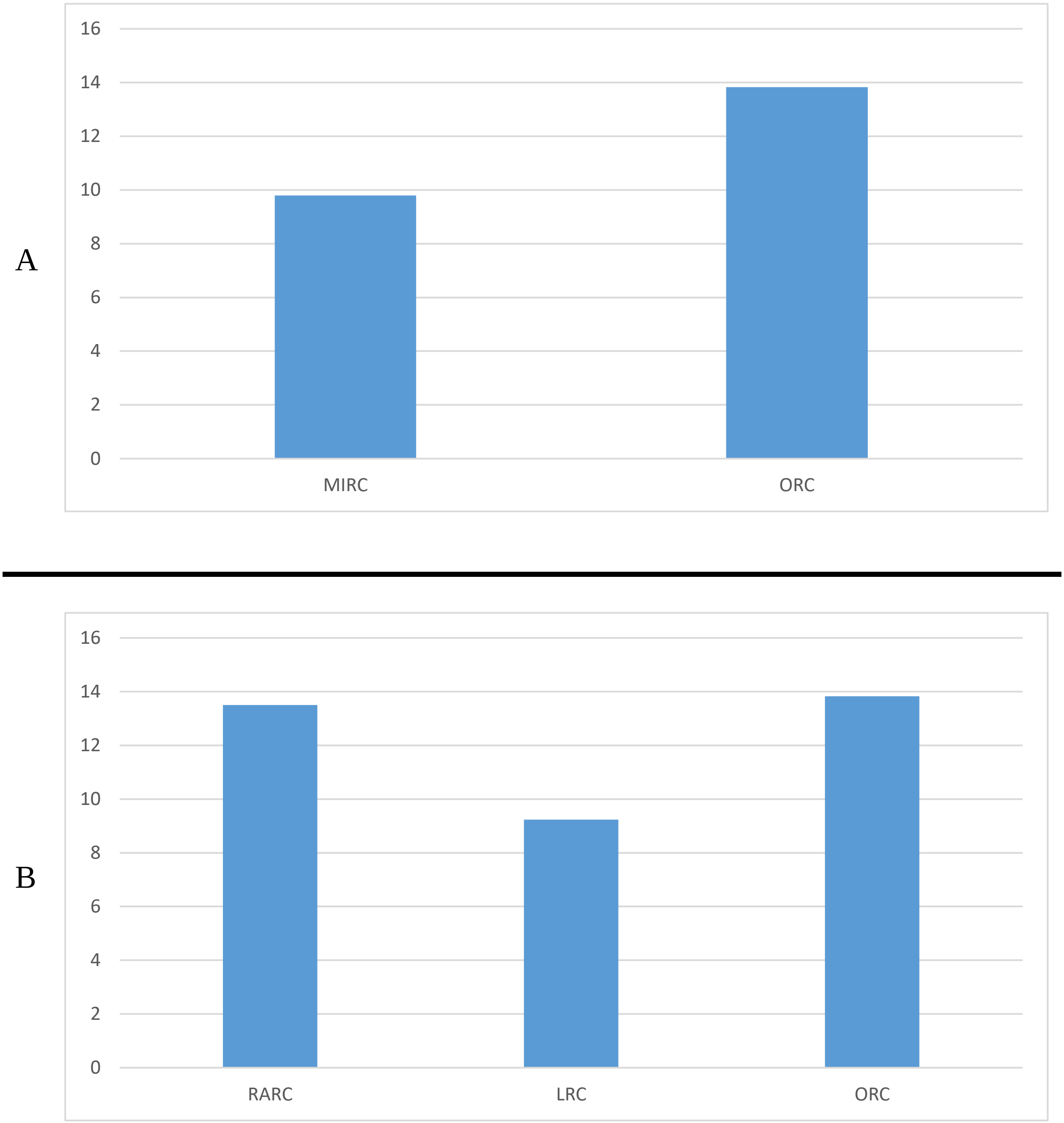


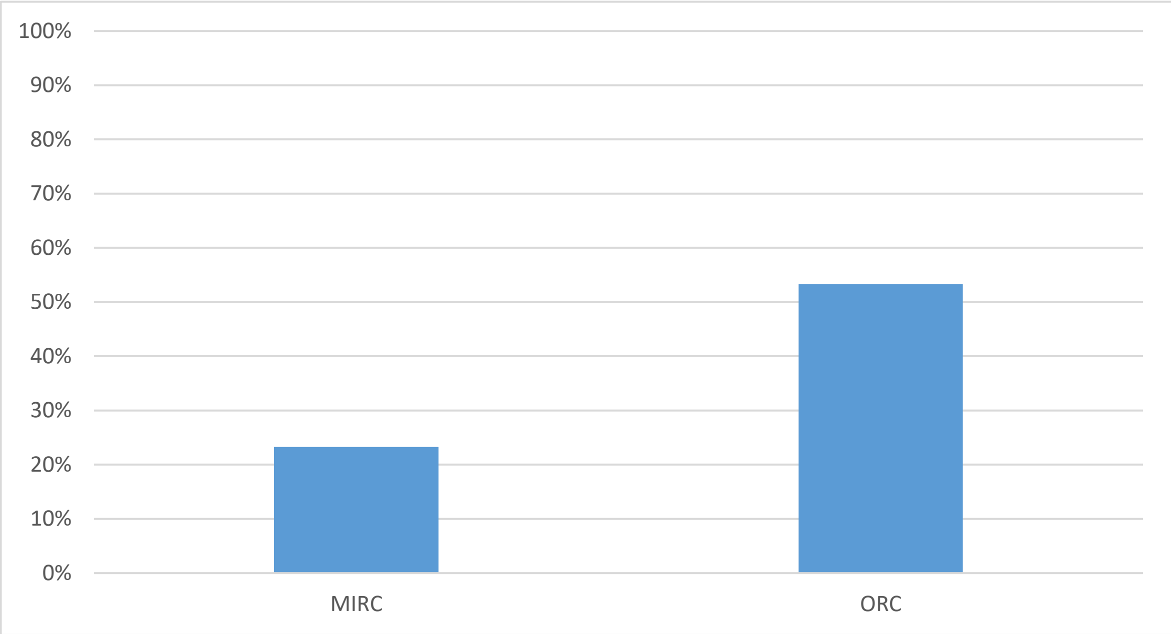
Figure 44: Comparison of hospital LOS (day) between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: LOS=length of stay; MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

A



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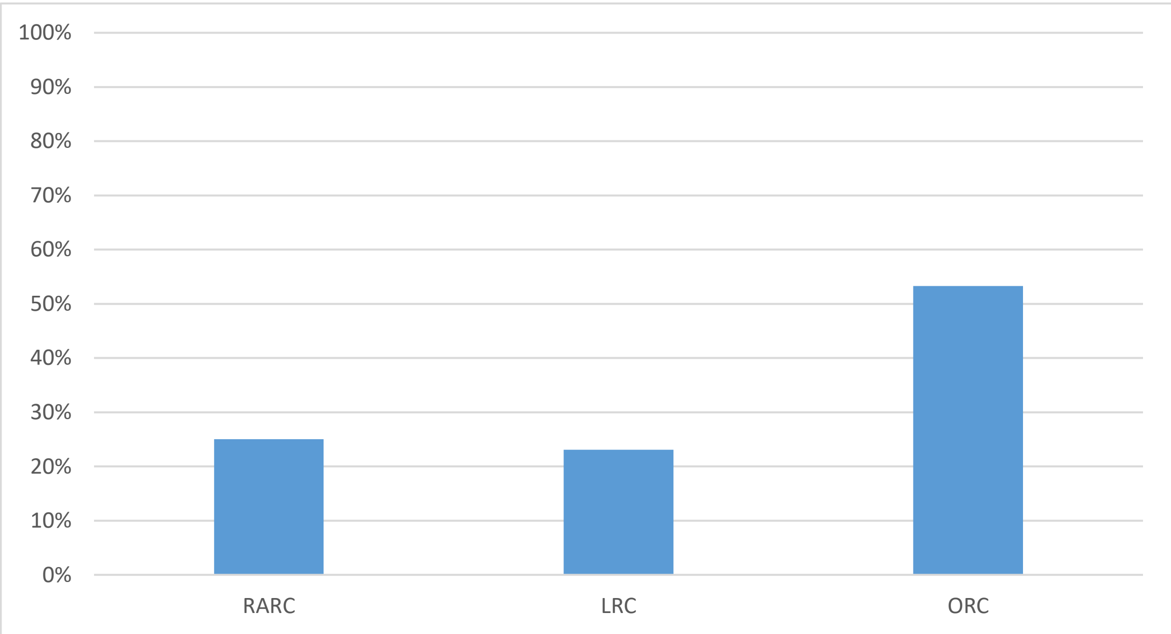

Figure 45: Comparison of postoperative opioid requirement between the MIRC and ORC groups.

A: Comparing MIRC and ORC groups.

B: Comparing RARC, LRC and ORC groups.

Abbreviations: MIRC=minimally invasive radical cystectomy; RARC=robotic-assisted radical cystectomy; LRC=laparoscopic radical cystectomy; ORC=open radical cystectomy.

Discussion

Discussion

In Egypt, bladder cancer is the third most common solid malignancy and the second most common cancer in males after liver cancer, representing a major health problem (Ibrahim et al., 2014). The primary aim of RC for bladder cancer is to remove the primary tumor safely and completely, to perform adequate PLND, to achieve negative margins, and to provide optimal long-term survival (Hemal & Kolla, 2007).

ORC has overall and high-grade complication rates reaching 60% and 40% (Shabsigh et al., 2009; Svatek et al., 2010; Novara et al., 2015). Moreover, mortality rates have been reported to reach 3–7% (Novara et al., 2009; Svatek et al., 2010). Efforts to minimalize perioperative morbidity and mortality have led to the development of MIRC (Tan et al., 2016b).

Significant enthusiasm in research and clinical practice is directed to The introduction of MIRC techniques including LRC and RARC, both of which are associated with lower complications than conventional surgery (Cohen et al., 2014). Various retrospective and prospective studies have compared the advantages and disadvantages of MIRC and ORC (Fonseka et al., 2015; Shen & Sun, 2016; Tan et al., 2016a; Lauridsen et al., 2017).

Our institute has been one of the main hospitals managing bladder cancer in the country since the seventies, however, we have not adopted MIS surgery until recently, and it was primarily reserved for RP, adrenalectomy, and nephrectomy.

The inclusion of LRC was deemed logical at trial initiation because RARC was not yet widely performed in Egypt, and it was believed that LRC could be a valuable tool for institutions lacking the means to set up a robotic program. LRC remains a technically challenging procedure, and it also lacks the ergonomic advantage offered by RARC (Challacombe et al., 2011).

Several reports have shown acceptable perioperative outcomes of MIRC, including laparoscopic and robotic modalities (Fonseka et al., 2015; Novara et al., 2015; Raza et al., 2015). Even during early experiences, the surgical and perioperative findings appeared to be comparable to those of the open modalities (Wang et al., 2008; Gondo et al., 2012).

This feasibility study aims to compare MIRC versus conventional ORC. This study adds to the existing literature regarding pathologic, operative, and postoperative outcomes.

Sixty bladder cancer patients were randomly allocated to two groups thirty patients each, the MIRC group and ORC group. The baseline characteristics of the patients and tumors were well matched. the ORC arm was performed by two expert surgeons, the MIRC arm was performed by the same team throughout the study.

In our study, on comparing the pathologic outcomes, MIRC showed a significantly higher mean LN yield than ORC (15.67 vs 11.97 LN; p=0.004), After subgroup analysis of the MIRC, we found a statistically significant difference for the RARC group compared to the ORC group (18.5 vs 11.97 LN; p=0.035) and, we found a statistically significant difference for the LRC group compared to the ORC group (15.23 vs 11.97 LN; p=0.036), but there was no statistically significant difference when comparing the RARC group with the LRC group (18.5 vs 15.23 LN; p=0.419).

We found no statistically significant differences between MIRC and ORC groups regarding the number of positive LNs (p=0.402), PSM in one patient only which was operated on via the conventional open surgical approach.

Although we did not attempt extended LND in any case, the higher LN yield reported for MIRC in our study may be explained with that the minimally invasive lymphadenectomy part of the procedure was operated on by surgeons who were specifically well trained also on conventional open lymphadenectomy, these results were contradictory to other relevant reports, which reported similar or higher nodal yields in the ORC group, as follows:

CORAL trial by Khan et al., three-arm RCT involving a total of 59 patients, comparing ORC, RARC and LRC demonstrated that mean LN yield was 18.8 in the ORC group, 16.3 in the RARC group, and 15.5 in the LRC group. The differences in LN yield between ORC and LRC were statistically significant (p=0.01). two of 20 ORC patients (10%), three of 20 RARC patients (15%), and one of 19 LRC patients (5%) had PSMs, so There was no significant relationship between surgical arm and PSMs (p= 0.9) (Khan et al., 2016).

Hu et al. pooled a total of eight relevant RCTs involving a total of 805 patients were included focusing on the comparison between MIS approaches and ORC approach and they demonstrated that the MIS group had similar pathological compared with ORC as they did not detect a significant difference in terms of LN yield (P=0.711) and PSM (P=0.986), they also did not detect a significant difference in terms of OS (P=0.473), CSS (P=0.778), RFS (P=0.880), PFS (P=0.324) between MIS group and ORC group .so, they concluded that MIS approaches could serve as a choice in patients with bladder cancer as MIS had similar pathological and oncological outcomes compared with ORC approach (Hu et al., 2020).

Lin et al. compared LRC vs ORC involving a total of 70 patients (Thirty-five patients in each group), they did not find significant differences in the LN yield (14.1±6.3 for LRC and 15.2±5.9 for ORC) (p=0.467) and PSM rate(p=1.0) (Lin et al., 2014).

Tang et al. reported a meta-analysis that included sixteen eligible trials involving a total of 1165 patients, evaluating LRC vs ORC were identified including seven prospective and nine retrospective studies, they found significantly fewer positive LN (p=0.050) and fewer PSMs (p=0.006) in LRC than that in the ORC group, they suggested that LRC appears to be a safe, feasible and minimally invasive alternative to ORC with reliable perioperative safety, pathologic & oncologic efficacy (Tang et al., 2014a).

Regarding the evaluation of oncological efficacy, our results are consistent with the oncology quality criteria in RC established by the Bladder Cancer Collaborative Group in 2004: surgical margins <10% in pT0-2 and <15% in pT3-4 and 10-14 resected LNs in lymphadenectomy (Hayn et al., 2011).

Pathological outcomes including LN yield and PSM rate were considered as an indicator of surgical quality with cystectomy (Buscarini et al., 2007; Huang & Stein, 2007), both of which have implications for oncological outcomes. Several studies also demonstrated that PSM and LN yield were associated with OS and RFS after RC (Boktour et al., 2006; Dotan et al., 2007).

The rate of PSM for the whole cohort is minor, especially considering the Pasadena Consensus Panel recommendation of PSM rates after RC (Yuh et al., 2015). PSM is an independent predictor of metastatic progression in patients undergoing RC, which reportedly increased the risk of metastatic progression at 5 years from 32 to 74% (Dotan et al., 2007). According to Chade et al., 2010, the incidence of PSM ranged from 4 to 5% of the ORC cases, and from 0 to 5% of the LRC cases (Chade et al., 2010).

The perioperative outcomes of this study showed that the operative time was significantly longer in the MIRC group compared to the ORC group (395 vs 229 min; P<0.001). After subgroup analysis of the MIRC, we found that the operative time was significantly longer in the RARC and LRC groups compared to the ORC group (581vs 366 vs 229 min; P<0.001), we found that the operative time was significantly longer for the RARC group compared with the ORC group (581 vs 229 min; P<0.001), operative time was significantly longer for the LRC group compared with the ORC group (366 vs 229 min; P<0.001), we found no statistically significant difference regarding the total operative time when comparing the RARC group and LRC group (p=0.263). The overall trend toward lower estimated blood loss and lower blood transfusion rate in the MIRC group, but this did not reach statistical significance (p=0.119, p=0.207 respectively). Also, the rate of transfusion of more than 1 unit of RBCs was higher in the ORC group compared to the MIRC group (11 cases vs. 4 cases).

These findings were consistent with literature which almost uniformly reports operative times to be longer with minimally invasive approaches as follows:

In 2020, Hu et al. demonstrated that MIS approaches were significantly associated with, longer operative time (P<0.001) and lower estimated blood loss (P<0.001) between MIS approaches and ORC (Hu et al., 2020).

CORAL trial by Khan et al. demonstrated that the mean operative time was significantly longer for RARC (389 min) compared with ORC (293 min) and LRC (301 min) (p<0.001). although EBL mean was lower in the LRC group (460 ml) and RARC group (585 ml) than ORC group (808 ml), it was statistically non-significant (p=0.070) (Khan et al., 2016), which was consistent with our study.

Tang et al. reported that the LRC approach was associated with longer operative time (p<0.001), less blood loss (p<0.001), less need for blood transfusion (p<0.001) than the ORC approach (Tang et al., 2014a).

Subira-Rios et al. retrospectively evaluated the differences between ORC (n = 197). and LRC (n = 196) approaches regarding operative time ($p<0.001$), they observed a lower rate of perioperative blood transfusion ($p<0.0001$) (Subira-Rios et al., 2019).

Matsumoto et al. compared the operative outcomes of patients with bladder cancer according to the three different procedures: RALC(n=10), LRC(n=10), and ORC (n= 16). All patients who underwent RALC and LRC with ECUD found that the EBL was less for RALC than for other procedures (p=0.0004). No blood transfusions were performed for RALC, but ORC required significant blood transfusions (p=0.003). Operative time did not differ among the groups (Matsumoto et al., 2019).

The lack of a statistically significant difference regarding fewer blood transfusions might be attributed to the fact that the cystectomy cases in the ORC group were performed by two highly open experienced surgeons well beyond their learning curves. If the Minimally invasive interface allows surgeons in their early minimally invasive experience to achieve similar or even slightly more favourable blood loss rates and transfusion requirements to experienced open surgeons, this could be considered an advantage for MIS as it adds certain benefits which allow for lower blood loss; the field is magnified which allows pre-emptive control of small potential bleeders especially in areas of restricted exposure, pneumoperitoneal pressure allows for control of small venous oozing, lastly, the surgeon is compelled to operate in a bloodless environment to enhance his visualization.

In our study, on comparing surgical complications of RC after MIRC and ORC, ORC had more complications classified as grade III, IV Clavien-Dindo grading system complications and there was a trend toward reduced complication rates for MIRC, but this did not reach statistical significance (p=0.519), only one grade V complication (mortality) was recorded in ORC group (p=0.313). Despite the longer operative time in MIRC, its complication rate was not higher than ORC.

These findings are consistent with those of previous studies. According to Challacombe et al., major (Clavien grade III-IV), complication rates ranged from 10 to 13% in LRC (Challacombe et al., 2011). Shabsigh et al. analysed complications in 1142 ORC patients and found a major complication rate of 13% (Shabsigh et al., 2009).

These findings are in line with those of previous studies. In the CORAL trial by Khan et al., they found that the 30-days complication rates (classified by the Clavien-Dindo system) varied significantly between the three arms (ORC: 70%; RARC: 55%; LRC: 26%; p=0.024). ORC complication rates were significantly higher than LRC (p<0.01) (Khan et al., 2016).

Hu et al. reported in 2020 that MIS group were significantly associated with fewer 30-days overall complication (P= 0.007) (Hu et al., 2020).

Tang et al. reported in 2014 that the LRC group was associated with significantly fewer overall complications (p<0.001), fewer death rates (p=0.004). when compared with the ORC group (Tang et al., 2014a).

Subira-Rios et al. found a statistically lower rate of global postoperative complications (p<0.0001) and a lower rate of serious complications (Clavien ≥III; p<0.001) in the LRC group. They concluded that the laparoscopic approach is a complication shield for RC. The ORC approach almost triples the risk of complications (Subira-Rios et al., 2019).

Matsumoto et al. compared the perioperative outcomes of the three different procedures: High-grade adverse events were only seen for ORC (Matsumoto et al., 2019).

In our trial, we did not find a high rate of complications specific to the laparoscopic approach, this may be because our mentor surgeon was very experienced in LRC. Also, ileal neobladders were constructed extracorporeally in most cases, which is a safe and effective way to decrease operative time and surgical complexity. Compared with previously published LRC outcomes, grade III and IV complication rates (11.5%) reported in this study were relatively good, which could have resulted from the small numbers in each group, for example, a recent multicenter study reported an LRC complication rate of 54% that is considerably higher than our findings (Albisinni et al., 2015).

Wound complications including SSI, seroma and abdominal wall dehiscence were not statistically significant between both groups. Important potential advantages of transverse incisions are that they are cosmetically more favourable, less liable to evisceration, associated with less pain and pulmonary compromise(Grantcharov & Rosenberg, 2001; Orcutt et al., 2012; Amer et al., 2017), Although this is not a consistent finding in the literature(Greenall et al., 1980; Seiler et al., 2009), in this study the only advantage for the transverse incision was the lower opioid requirement in favour of MIRC(P=0.033).

In our study, the most common adverse events were ileus in ten patients, eight of them in the ORC group, the remaining two was operated on via the minimally invasive approaches. ORC involves packing of the intestine which potentially exposes them to mechanical trauma for the whole duration of the procedure (Sun et al., 2014), this may translate into ileus which is reported in 26% of patients (Nutt et al., 2018)

Lastly, on comparing postoperative outcomes of the MIRC and the ORC, the time to regular oral diet was significantly shorter for MIRC compared with the ORC group (6 vs 8.6 days; p=0.031). After subgroup analysis of the MIRC, we found that the time to regular oral diet was significantly shorter for the LRC group compared to the ORC group (5.7 vs 8.6 days; p=0.041) but there was no statistically significant difference regarding time to regular oral diet for the RARC group compared to the ORC group (p=0.406), or when comparing the RARC group with the LRC group. (p=0.406).

Hospital LOS was significantly shorter for the MIRC group compared ORC group (9.8 vs 13.8 days; p=0.001), after subgroup analysis, we found that the LOS was significantly shorter was for the LRC group compared to the ORC group (9.2 vs 13.8 days; p=0.001) but there was no statistically significant difference regarding LOS for the RARC group compared to the ORC group (p=0.989), or when comparing the RARC group with the LRC group. (p=0.168).

Regarding the opioid requirement for postoperative analgesia, we found a statistically significant difference regarding the lower opioid requirement in the MIRC group compared ORC group (23.3% vs 53.3%; p=0.033).

These findings are consistent with those of previous studies as follows:

CORAL trial by Khan et al. demonstrated that the meantime to regular oral diet was 7.5 days in ORC, 4 days in LRC and 4 days in the RARC group, Time to regular oral diet was significantly longer for ORC compared with RARC (p=0.049) and LRC (p=0.01), but it was statistically non-significant when comparing RARC with LRC (p=0.5), LOS mean was 14.4 day in ORC, 9.7 days in LRC and 11.9 days in RARC group, LOS was significantly longer after ORC compared with LRC only (p=0.005). It was statistically non-significant when comparing ORC with RARC(p=0.3), and RARC with LRC (p=0.4) (Khan et al., 2016).

Hu et al. reported that the MIS group were significantly associated with a shorter time to regular oral diet (P=0.005) and shorter LOS (P= 0.004) when compared to the ORC group (Hu et al., 2020).

Tang et al. reported that the LRC group was associated with shorter time to oral solid diet (p<0.001), shorter length of hospital stay (p<0.001) and less opioid analgesic requirement (p<0.001) when compared with the ORC group (Tang et al., 2014a).

Lin et al. compared LRC vs ORC, they found a significant difference in, shorter time to resumption of oral solid intake (p=0.001) and opioid analgesic requirement (p<0.001) but no significant differences were noted in the length of hospital stay (p= 0.667) (Lin et al., 2014).

Our study reports similar results regarding lower opioid requirement, even though we used a muscle splitting Pfannenstiel incision for specimen delivery and ECUD in most cases, the duration of abdominal wall retraction is much less than in a completely ORC. Studies suggest that the midline laparotomy is more painful than transversely oriented incisions which might be another explanation of the reduced opioid requirements in the LRC group(Brown & Tiernan, 2005).

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Limitations and recommendations

Limitations and Recommendations

Strengths of our study included randomized design and all patients adhered to their follow up schedule with no dropout,

The ORC arm was performed by well-trained surgeons, the MIRC arm was performed by the same team throughout the study with no cases converted to open technique due to attendance of An expert laparoscopic surgeon and a well-trained robotic surgeon as a mentor in all cases, and scrubbed in if required to counter any encountered technical difficulty; also a pilot study was performed prior to our study utilizing the presence of a urologist having a good experience with MIRC, this helped organize the team, adjust the setup, solve early problems and build up confidence. Locally advanced cases were excluded from inclusion criteria, this helped in recruiting suitable candidates before starting our study.

Our study is not devoid of limitations. our study was conducted upon relatively small sample size. and it was a single-institution study. There was a problem with patients' recruitment, as a significant number of patients declined randomization because they preferred the open approach.

There was a disparity in the number of patients who were operated upon with minimally invasive approaches between RRC and LRC, due to the unavailability of the technician of da Vinci® robotic system (Intuitive Surgical) at short notice. So, it was inappropriate to delay the operation for this reason and proceeded with the Laparoscopic approach.

Both the patients and the surgeons could not be blinded because of the surgical nature of the trial.

Each surgical modality was carried out by a different surgeon, which can potentially introduce surgeon bias. We are confident that this bias was minimized to the best of our ability because, MIRC surgeons were well over their learning curves for their respective operative modality, but this point does lend caution to our outcomes.

The intracorporeal urinary diversion was done in only 6.7%. of the whole cohort. Also, so most urinary diversions were performed extracorporeally, which was reflected in complication rates.

We did not collect postoperative pain scores. However, postoperative opiate consumption was significantly different among the procedures. Although pain scores reflect patients' conditions subjectively, we believe opiate consumption reflects pain conditions objectively.

We did not compare patients' post-operative functional outcome in terms of urinary continence and potency after RC between MIRC and ORC.

No cost analysis was performed. Several studies have published comparisons of costs of RARC, LRC and ORC. RARC requires expensive instruments for the procedure, thus leading to an increased cost; however, RARC appears to be more cost-effective when complications rates and long hospital LOS are taken into consideration (Lee et al., 2011).

We recommend a large multicenter randomized controlled study with longer follow-up to provide survival outcome, we do recommend increase utilization of intracorporeal urinary diversion, with special attention to the postoperative quality of life measures and cost analysis for different surgical services.

Conclusion

Conclusion

MIRC versus ORC improves the LN yield, earlier return to regular oral diet with less hospital stay and fewer opioid requirement, at the expense of a longer operative time.

MIRC was associated with comparable postoperative outcomes in the first experience in our center. Benefitting from the assistance of an experienced laparoscopic and robotic surgeon is recommended to shorten the learning curve.

In our center, laparoscopy has been validated as a minimally invasive reference approach in RC, as well as demonstrating reproducibility after a demanding learning curve.

Our findings demonstrate that the MIRC technique represents a feasible procedure for patients with bladder cancer.

Summary

Summary

Bladder cancer is an aggressive malignant tumor and is one of the ten most common cancer types. The primary aim of RC for bladder cancer is to remove the primary tumor safely and completely, to perform adequate PLND, to achieve negative margins, and to provide optimal long-term survival.

Perioperative outcomes have been extensively described for ORC, with overall and high-grade complication rates reaching 60% and 40% in some series. Moreover, mortality rates have been reported to reach 3–7% at 90-days after RC. Efforts to minimize perioperative complications have led to the development of minimal invasive cystectomy.

Several reports have shown acceptable perioperative outcomes of MIRC, including laparoscopic and robotic modalities. Even during early experiences, the surgical and perioperative findings appeared to be comparable to those of the open modalities.

In this study, sixty candidates for RC were recruited and allocated to two groups thirty patients each, ORC group and MIRC group**.** This RCT carried out at the surgical Uro-oncology Department, National Cancer Institute, Cairo University in the period from February 2019 to February 2021. The bladder cancer diagnosis was established with cystoscopy and biopsy, patient workup was completed with CT abdomen and pelvis imaging. Informed consent was obtained from each patient after an explanation of the aim and the nature of the procedures.

On comparing the pathologic outcomes, MIRC showed a significantly higher mean LN yield than ORC (p=0.004), we found a statistically significant difference for the RARC group compared to the ORC group (p=0.035) and, we found a statistically significant difference for the LRC group compared to the ORC group (p=0.036), but we found no statistically significant difference when comparing the RARC group with the LRC group (p=0.419). we found no statistically significant differences between MIRC and ORC groups regarding the number of positive LNs (p=0.402), PSM in one patient only which was operated on via the conventional open surgical approach.

The operative time was significantly longer in the MIRC group compared to the ORC group (P<0.001). we found that the operative time was significantly longer in the RARC and LRC groups compared to the ORC group (P<0.001), we found that the operative time was significantly longer for the RARC group compared with the ORC group (P<0.001), operative time was significantly longer for the LRC group compared with the ORC group (P<0.001), we found no statistically significant difference regarding the total operative time when comparing the RARC group and LRC group (p=0.263). The overall trend toward lower estimated blood loss and lower blood transfusion rate in the MIRC group, but this did not reach statistical significance (p=0.119, p=0.207 respectively).

On comparing surgical complications, ORC had more grade III, IV complications. but this did not reach statistical significance (p=0.519), only one grade V complication (mortality) was recorded in the ORC group (p=0.313).

Time to regular oral diet was significantly shorter for MIRC compared with the ORC group (p=0.031). After subgroup analysis of the MIRC, we found that the time to regular oral diet was significantly shorter for the LRC group compared to the ORC group (p=0.041) but there was no statistically significant difference regarding time to regular oral diet for the RARC group compared to the ORC group (p=0.406), or when comparing the RARC group with the LRC group. (p=0.406).

LOS was significantly shorter for the MIRC group compared to the ORC group (p=0.001), after subgroup analysis, we found that the LOS was significantly shorter was for the LRC group compared to the ORC group (p=0.001) but there was no statistically significant difference regarding LOS for the RARC group compared to the ORC group (p=0.989), or when comparing the RARC group with the LRC group. (p=0.168). we found a statistically significant difference regarding the lower opioid requirement in the MIRC group compared ORC group (p=0.033)

We concluded that MIRC improves the LN yield, earlier return to regular oral diet with less hospital stay and fewer opioid requirement with comparable complication rates, at the expense of a longer operative time. Our findings demonstrate that the MIRC technique represents feasibility for patients with bladder cancer.

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Arabic summary

كان أطول بشكل ملحوظ بالنسبة لمجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي مقارنة بمجموعة الفتح الجراحي. لم يكن هناك فرق يعتد به إحصائيًا فيما يتعلق بإجمالي وقت الجراحة عند مقارنة مجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي ومجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي. الاتجاه العام نحو انخفاض فقدان الدم المقدر وانخفاض معدل نقل الدم في مجموعة الاستئصال طفيف التوغل الجذري للمثانة، ولكن هذا الفرق كان غير معتد به إحصائيًا

عند مقارنة مضاعفات ما بعد الجراحة، كان لدى مجموعة الفتح الجراحي المزيد من مضاعفات الدرجة الثالثة والرابعة. لكنها كانت غير ذات دلالة إحصائية، تم تسجيل مضاعفة واحدة فقط من الدرجة الخامسة (الوفيات) وكانت في مجموعة الفتح الجراحي.

كان الوقت المطلوب لاتباع نظام غذائي منتظم عن طريق الفم أقصر بشكل ملحوظ بالنسبة لـلاستئصال طفيف التوغل الجذري للمثانة مقارنة بمجموعة الفتح الجراحي. بعد تحليل المجموعة الفرعية لـلاستئصال طفيف التوغل الجذري للمثانة، وجدنا أن الوقت المطلوب لاتباع النظام الغذائي الفموي المنتظم كان أقصر بكثير بالنسبة لمجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي مقارنة بمجموعة الفتح الجراحي. ولكن لم يكن هناك فرق يعتد به إحصائيًا فيما يتعلق بالوقت المطلوب لاتباع النظام الغذائي الفموي المنتظم لمجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي مقارنةً بمجموعة الفتح الجراحي، ولم يكن هناك فرق يعتد به عند مقارنة مجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي مع مجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي.

كانت مدة الإقامة في المستشفى أقصر بشكل ملحوظ بالنسبة لمجموعة الاستئصال طفيف التوغل الجذري للمثانة مقارنة بمجموعة الفتح الجراحي، بعد تحليل المجموعة الفرعية، وجدنا أن مدة الإقامة في المستشفى كانت أقصر بشكل ملحوظ بالنسبة لمجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي مقارنة بمجموعة الفتح الجراحي ولكن لم يكن هناك فرق يعتد به إحصائيًا فيما يتعلق بـ مدة الإقامة في المستشفى لمجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي مقارنة بمجموعة الفتح الجراحي، ولم يكن هناك فرق يعتد به عند مقارنة مجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي مع مجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي. وجدنا فرقًا ذا دلالة إحصائية فيما يتعلق بمتطلبات أقل للمواد الأفيونية في مجموعة الاستئصال طفيف التوغل الجذري للمثانة مقارنة بمجموعة الفتح الجراحي.

خلصنا إلى أن الاستئصال طفيف التوغل الجذري للمثانة يحسن إنتاج العقدة الليمفاوية، والعودة المبكرة إلى النظام الغذائي الفموي المعتاد مع إقامة أقل في المستشفى ومتطلبات أقل من المواد الأفيونية مع معدلات مضاعفات مماثلة، على حساب وقت أطول للعملية. توضح النتائج التي توصلنا إليها أن تقنية الاستئصال طفيف التوغل الجذري للمثانة تمثل إجراءً ممكنًا لمرضى سرطان المثانة.

الملخص العربي

يعد سرطان المثانة ورمًا خبيثًا عدوانيًا وهو أحد أكثر عشرة أنواع من السرطانات شيوعًا. الهدف الأساسي من استئصال المثانة الجذري لسرطان المثانة هو إزالة الورم الرئيسي بأمان وبشكل كامل وتفريغ الغدد الليمفاوية للحوض، وتحقيق حواف امان سلبية، وتوفير البقاء الأمثل على المدى الطويل.

تم وصف النتائج المحيطة بالجراحة على نطاق واسع لـجراحه الاستئصال الجذري للمثانة البولية عن طريق الفتح الجراحي التقليدي، مع وصول معدلات المضاعفات الجراحية إلى ٦٠٪ و٤٠٪ في بعض السلاسل. علاوة على ذلك، تم الإبلاغ عن معدلات الوفيات لتصل إلى ٣-٧٪ عند ٩٠ يوم بعد الاستئصال الجذري للمثانة البولية عن طريق الفتح الجراحي التقليدي. أدت الجهود المبذولة لتقليل المضاعفات المحيطة بالجراحة إلى تطوير استئصال المثانة عن طريق التدخل الجراحي طفيف التوغل.

أظهرت العديد من التقارير نتائج مقبولة حول الجراحة طفيفة التوغل لاستئصال المثانة الجذري، بما في ذلك المنظار والروبوت الجراحي. حتى أثناء التجارب المبكرة، بدت النتائج الجراحية وما حولها قابلة للمقارنة مع تلك الخاصة بالطريقة التقليدية للفتح الجراحي.

في هذه الدراسة، تم تجنيد ستين مرشحًا لاستئصال المثانة الجذري وتوزيعهم على مجموعتين، ثلاثين مريضًا لكل مجموعة، مجموعة الفتح الجراحة التقليدي ومجموعة الفتح الجراحي طفيف التوغل. تم إجراء هذه التجارب المعشاة ذات الشواهد في قسم جراحة أورام المسالك بالمعهد القومي للأورام بجامعة القاهرة في الفترة من فبراير ٢٠١٩ إلى فبراير ٢٠٢١. تم تشخيص سرطان المثانة من خلال الخزعة بالمنظار، وتم الانتهاء من فحص المريض مع التصوير المقطعي للبطن والحوض. وتم الحصول على الموافقة المسبقة من كل مريض بعد شرح الهدف وطبيعة الإجراءات.

عند مقارنة النتائج المرضية، أظهر الاستئصال طفيف التوغل الجذري للمثانة متوسط إنتاجية من العقدة الليمفاوية اعلى من الاستئصال عن طريق الفتح الجراحي، وجدنا فرقًا يعتدًا به إحصائيًا لمجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي مقارنة بمجموعة الفتح الجراحي، وكانت هناك دلالة إحصائية على ذلك. كان يوجد فرق لصالح مجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي مقارنة بمجموعة الفتح الجراحي، ولكن لم يكن هناك فرق يعتد به إحصائيًا عند مقارنة مجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي مع مجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي. لم تكن هناك فروق ذات دلالة إحصائية بين مجموعات الاستئصال طفيف التوغل الجذري للمثانة ومجموعة الفتح الجراحي فيما يتعلق بعدد العقد الليمفاوية الإيجابية، الحواف الجراحية الإيجابية وجدت في مريض واحد فقط والتي تم إجراء العملية عليها من خلال الفتح الجراحي التقليدي.

كان وقت الجراحة أطول بشكل ملحوظ في مجموعة الاستئصال طفيف التوغل الجذري للمثانة مقارنة بمجموعة الاستئصال عن طريق الفتح الجراحي. وجدنا أن وقت الجراحة كان أطول بشكل ملحوظ في مجموعات الاستئصال الجذري للمثانة بالروبوت الجراحي ومجموعة الاستئصال الجذري للمثانة بالمنظار الجراحي مقارنة بمجموعة الفتح الجراحي، وجدنا أن وقت الجراحة كان أطول بشكل ملحوظ لمجموعة الاستئصال الجذري للمثانة بالروبوت الجراحي مقارنة بمجموعة الفتح الجراحي، وقت الجراحة

الملخص العربي

دراسه مقارنة التدخل الجراحى طفيف التوغل للاستصال الجذرى للمثانة البولية بالتدخل الجراحى التقليدى فى حالات سرطان المثانة البولية.

توطئة للحصول على درجة الدكتوراة في جراحة الأورام

مقدمة من

أيمن عبد الحميد محمد الحنفي

(ماجستير جراحة الأورام- جامعة القاهرة)

تحت إشراف

أ.د/ حاتم احمد ابو القاسم

استاذ جراحة الأورام

المعهد القومي للأورام

جامعة القاهرة

أ.د/ السيد أشرف حسين خليل

استاذ جراحة الأورام

المعهد القومي للأورام

جامعة القاهرة

أ.د/ محمود عمرو عبد الحكيم

استاذ مساعد جراحة المسالك البولية

كليه الطب

جامعة القاهرة

د/ وليد محمد محمد فضل الله

مدرس جراحة الأورام

المعهد القومي للأورام

جامعة القاهرة

المعهد القومي للأورام

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