An In-depth Critical Analysis of Complications following Robotic Assised Radical Cystectomy with Intracorporeal Urinary Diversion

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ABSTRACT

BACKGROUND

Robotic assisted radical cystectomy with intracorporeal urinary diversion (iRARC) is an attractive option to open cystectomy but the benefit in terms of improved outcomes are not established.

OBJECTIVES

To evaluate early postoperative morbidity and mortality of patients undergoing iRARC and conduct a critical analysis of complications using a standardise reporting criteria as stratified according to urinary diversion.

DESIGN, SETTING AND PARTICIPANTS

134 patients underwent iRARC for bladder cancer at a single centre between June 2011 and July 2015.

INTERVENTION

Radical cystectomy with intracorporeal urinary diversion.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS

Patient demographics, pathological data and 90-day perioperative mortality and complications were recorded. Complications were reported according to the Clavien-Dindo (CD) classification and stratified according to urinary diversion type and either surgical or medical complications. Chi square test and t-test were used for categorical and continuous variables respectively. Multivariable logistic regression was performed on variables with significance in univariate analysis.

RESULTS AND LIMITATIONS

The 90-day all complication rate following ileal conduit and continent diversion was 68% and 82.4% while major complications were 21.0% and 20.6% respectively. 90-day mortality was 3% and 2.9% for ileal conduit and continent diversion patients respectively. On multivariate analysis, blood transfusion requirement was independently associated with major (p=0.002) and all 30-day (p=0.002) and 90-day major complications (p=0.012) while male patients were associated with 90-day major complications (p=0.015). Critical analysis identified surgical complications was responsible for 39.4% of all 90-day major complications. The incidence of surgical complications did not decline with increasing number for iRARC cases performed (p=0.742, r=0.31). Limitations of this study include its retrospective nature, limited sample size and limited multivariate analysis due to low number of events.

CONCLUSION

Although complications following iRARC are common, most are low grade. A critical analysis identified surgical complications as a cause of major complications and addressing this issue could have a significant impact in lowering morbidity associated with iRARC.

PATIENT SUMMARY

In this report, we looked at the surgical outcomes in bladder cancer patients treated with minimal invasive robotic surgery. We found that surgical complications account for most major complications and previous surgical experience may be a confounding factor when interpreting results from different center even in a randomised trial setting.

1. INTRODUCTION

Radical cystectomy with lymphadenectomy is the standard of care for patients with muscle invasive bladder cancer (MIBC) and selected high risk non-muscle invasive bladder cancer (NMIBC). Risk factors for bladder cancer include advancing age, tobacco smoking and exposure to industrial carcinogens, resulting in a patient cohort with a high incidence of concurrent cardiovascular and pulmonary disease. In addition to pre-existing co-morbidity, the extent of surgery including urinary diversion places patients undergoing radical cystectomy at significant risk of postoperative complications [1].

Early oncological outcomes have suggested no significant difference between robotic assisted radical cystectomy with intracorporeal urinary diversion (iRARC) and open radical cystectomy (ORC) [2]. An aim of minimal invasive surgery (MIS) is to replicate principles of open surgery with the added advantage of reducing the risk of postoperative complications and allow an early return to normal activity [3]. In the context of radical cystectomy, the MIS has particular relevance as the complication rate for ORC is over 60%, with a significant 90-day mortality rate of 5.1%, having fallen from as high as 10.3% [4-6]. Despite evidence that minimal invasive surgery has benefits over open surgery [7] comparison between the outcomes of open and robotic assisted radical cystectomy (RARC) has not demonstrated major differences. Results from a randomised controlled trial by Bochner et al. which compared ORC with RARC, showed a significantly lower blood loss and longer operating time in the RARC arm, but no difference in Clavien-Dindo (CD) II-IV complications and length of stay (LOS) [8]. The requirement to convert to open extracorporeal urinary diversion may mask potential benefits of the minimal access approach.

In this paper, we evaluate 90-day perioperative morbidity and mortality in 134 iRARC cases stratified according to type of urinary diversion, CD classification, with complications attributed to surgical or medical aetiology.

2. PATIENTS AND METHODS

2.1 Patient population

Data on cases undergoing iRARC are prospectively recorded and maintained using an institutional approved database. iRARC was commenced in June 2011 and between June 2011 and July 2015, 163 radical cystectomies were performed. 134 patients underwent iRARC while 29 patients who underwent planned open radical cystectomy due to previous abdominal surgery or patient / surgeon preference were excluded from analysis. All cases were performed by two surgeons. Since January 2013, 93.4% (113/121) of cystectomy procedures performed have been iRARC which is now the default procedure at our institution with 63 radical cystectomy cases performed in 2015. All patients undergoing iRARC had MIBC or high risk NMIBC. Intracorporeal urinary diversion was either ileal conduit or continent diversion (neobladder or Mitrofanoff). This study was part of a quality assurance programme and registered with our institutional department (Urology2015.2).

2.2 Surgical technique

The technique for iRARC has previously been previously described [9]. Briefly, a standard 6 port transperitoneal approach with the patient in 27°Trendelenburg was used. Pelvic lymph node dissection included external, internal, common iliac and obturator fossa lymph nodes. Specimens were retrieved using an Endocatch bag (Covidien, Dublin, Ireland) which was removed via the vagina if possible in female patients or otherwise via an iliac fossa incision in all others. The left ureter was passed posteriorly to the sigmoid mesocolon. Ileal conduit was constructed by mobilising a 15 cm segment of terminal ilium 15 cm from the ileo-caecal valve using a laparoscopic 60 mm intestinal stapler (Endo-GIA; Covidien Corp., Dublin, Ireland). Continent diversion was constructed using a 50 cm segment of ileum. Uretero-ileal anastomosis for the ileal conduit and continent diversion was performed using either a Bricker or Wallace anastomoses depending on surgeon preference. 6F infant feeding tubes/ Bander stents were used as ureteric stents and externalised.

2.3 Data collected

Patient demographics, clinical and pathological characteristics, perioperative variables, transfusion requirements, hospital length of stay (LOS) and standardised complication data were prospectively recorded. Preoperative cardiopulmonary exercise testing (CPET) variables such as anaerobic threshold (AT), peak oxygen consumption (Peak VO_2) and minute ventilation-carbon dioxide production (VE/VCO_2) were also recorded. All patients were followed up for a minimum of 90 days post-surgery.

2.4 Study outcomes measured

Thirty and 90-day complications were classified according to the modified Memorial Sloan-Kettering Cancer Center (MSKCC) CD system [4]. Minor and major complications were defined as CD I-II and CD III-IV respectively. Complications were divided to: surgical complications which were defined as urinary leak, anastomotic stricture, significant bleeding, or herniation and wound dehiscence; and medical complications were defined as organ dysfunction, sepsis or bowel related not arising from a surgical cause. Ileus was defined as persistent post-operative vomiting requiring a nasogastric tube insertion or inability to tolerate enteral intake for ≥48 hours.

2.5 Statistical methods

Descriptive statistics used to report continuous data which included mean, median, interquartile range (IQR), standard deviation and confidence interval (95% CI). Chi square test and t-test were used for categorical and continuous variables respectively. Pearson's correlation coefficient was used to determine correlation. Multivariable logistic regression were performed on variables with significance in univariate analysis. Statistical significance was set at p value <0.05. Statistical analysis was performed using SPSS v22 (IBM, New York, USA).

3. RESULTS

Patient demographic data for 100 ileal conduit cases and 34 continent diversion cases are detailed in Table 1. There were significantly more patients with ASA score of ≤2 ($p \leq 0.001$) in the continent diversion group compared to the ileal conduit group. Consistent with this was a reduced physical fitness in patients undergoing ileal conduit reflected by a CPET variables (all $p<0.05$) compared to patients undergoing continent diversion. Five ileal conduit patients required open conversion: two patents had extensive locally advanced stage T4 disease, two had significant intraperitoneal adhesions, one of which was converted following identified bowel injury and one case was a salvage procedure.

Histopathological outcomes are listed on Table 1. Ileal conduit cases were of more advanced histopathological stage (≥pT3) compared to continent diversion (26.0% vs 11.7%, p=0.038). Positive nodal disease was five times more common in the ileal conduit group compared to continent diversion (20.0% vs 4.8%; p=0.016).

The overall 30-day complication rate was 52.0% and 61.8% for ileal conduit and continent diversion patients respectively (p=0.323), while the 30-day major complication rate was 16.0% and 14.7% (p=0.858) (Table 2). The 90-day all complication rate was 68.0% and 82.4% for ileal conduit and continent diversion patients (p=0.109) respectively with a major complication rate of 21.0% and 20.6% (p=0.959). Overall post-operative ileus developed in 23.1% (n=31). Patients who developed ileus were significantly more likely to develop a 30-day (35.5% vs 9.7%, p=0.001) and 90-day (38.7% vs 15.5%, 0.005) major complication. There was no significant difference in 30-day and 90-day major complications or ileus between ileal conduit and continent diversion cases.

The overall transfusion rate for iRARC was 21.6%, with no significant difference between ileal conduit or continent diversion cases. After excluding 5 patients who had an open conversion, ileal conduit and continent diversion transfusion rates were 20.0% and 14.7% respectively. There was no difference between estimated blood loss between ileal conduit and continent diversion groups (p=0.967) (Table 2). Overall 90-day mortality was 3.1% (n=4). Three patients (2.2%) in the ileal conduit group died within 90 days including two from cardiac events one patient who died from carcinomatosis due to T4N0 transitional cell carcinoma with perineural and lymphovascular invasion but negative surgical margins. The single continent diversion death (0.75%) was due to disseminated intravascular coagulation (DIC) following post-operative haemorrhage at day 7 post-surgery.

A critical analysis was conducted for all major complications. Collectively, urinary leak, uretero-ileal stricture, wound dehiscence/ abscess, adhesions, incisional hernia and significant bleeding which are complications with a clear surgical etiology represented 39.4% (13/33) of 90-day major complications. This is followed by non-wound infection and stent/ drain migration which represents 30.3% (10/33) and 18.1% (6/33) of 90-day major complications respectively. We did not observe an inverse correlation between the number of surgical complications and number of iRARC cases performed (p=0.742, r=0.31). Medical complications account for 45.5% of 90-day major complications which are mainly attributed to infective causes despite the use of prophylactic antibiotics. Medical complications may be harder to minimise as patient specific factors are responsible. Table 3 describes 90-day major complications according to CD classification while Table 4 describes complications according to type of urinary diversion and stratified according to organ system.

Univariate and multivariable analysis of 30-day complications and 90 day complications are shown in Table 5 and 6 respectively. Requirement for blood transfusion was independently associated with 30-day major complications and 90-day major complications while male patients were associated with 90-day major complications. CPET were associated with either all or major complications.

4. DISCUSSION

This study reports a comprehensive account of post-operative adverse events following iRARC and includes a critical analysis of complications providing insight into the evolving technique of iRARC. The 30-day complication rate of 52.0% (CD≥III: 16%) and 61.8% (CD≥III: 11.8%) and 90-day complication rate of 68% (CD≥III: 21%) and 82.4% (CD≥III: 20.6%) for ileal conduit and continent diversion respectively is consistent with that described by the Pasadena Consensus [10-18]. In their cumulative analysis, the Pasadena Consensus reported a 30-day complication rate of 42%-86% for intracorporeal ileal conduit and 43%-62% for intracorporeal continent diversion while the 90-day complication rate for intracorporeal ileal conduit was 30%-77% and the data for complications of 90-day continent diversion was not reported [19]. The 90-day mortality rate of 3% in the present series is comparable, and within 0-8% summarised by Novara and colleagues [19].

The decision about type of urinary diversion is often complex and requires careful preoperative assessment, counselling and oncological and patient considerations should be taken into account. In this series, patients with continent diversion were on average younger, more likely to be ASA ≤ II and with a higher physiological reserve according to CPET than those with ileal conduit. Nonetheless, there was no difference between 30-day and 90-day complications between ileal conduit and continent diversion.

In the current series, patients who developed ileus were significantly more likely to develop 30-day ($p=0.001$) and 90-day ($p=0.005$) major complications. This indicates that the development of ileus may be an early predictor for the development of significant postoperative complications as reported by Chang et al. [20]. Compared to other series, we report a higher rate of ileus [18, 21] [22]. The development of ileus is multifactorial. In the UK, following a Medicines and Healthcare Products

Regulatory Agency (MHRA) statement restricting the use of non-steroidal anti-inflammatory drugs in cases with cardiovascular risk factors, opiate-based analgesia is favoured and may be a contributing factor to the development of ileus [23]. In addition, the administration of alvimopan, a peripherally acting μ-opioid antagonist, has been shown to significantly reduce the risk of ileus but is not licensed for use in this setting in the UK [24].

A critical analysis of individual complications has highlighted that a significant proportion of morbidity related to iRARC is surgical related. 39.4% of all 90-day major complications have a clear surgical aetiology. We believe these results highlight that efforts to improve cystectomy outcomes focusing on minimising surgical complications may reduce the major complication rates associated with iRARC.

Adopting new technology has an inevitable learning curve and surgical complications would decline with increase surgical experience. Although, a randomised controlled trial to determine the benefit for iRARC compared to ORC will be important, this study highlights that surgeon experience and the learning curve associated with iRARC could introduce a profound bias impacting the result. The incidence of surgical complications did not decline with increasing number for iRARC cases performed (p=0.742, r=0.31). The requirement for a minimum prior surgical caseload should be defined before selecting surgeons and centres contributing to such trials. The Pasadena Consensus has expressed an opinion that only surgeons who have performed >100 RARC cases are considered very experienced [25]. Neither the consensus statement nor our own data has defined the learning curve for iRARC. For robotic prostatectomy, the learning curve has been defined following analysis of large numbers of surgical cases and complications reduce significantly after 150 cases [26] while sexual function and urinary incontinence outcomes continue to improve and plateau after 600 procedures [27]. It is plausible that surgical competency relating to iRARC will be greater than 100 cases and may be similar to robotic prostatectomy.

Similar to other studies, the majority of urinary leaks were managed conservatively with only 25% (2/8) requiring temporary diversion via nephrostomy insertion [21].

While the continent diversion leak rate is lower than that described for extracorporeal urinary diversion [21], the very low rates described by Desai and colleagues [22] indicate that such surgical complications can be further reduced. The uretero-ileal stricture rate of 3.0%, is lower than a recently reported extracorporeal urinary diversion series of 6.2% [21] and comparable to other iRARC series [18, 22]. A lower incidence of uretero-ileal stricture is consistent with the postulate that extracorporeal diversion requires a longer ureteric length, which may promote distal ureteric ischemia resulting in ureteric stricture [28].

Gastrointestinal and infection complications represent 61.2% and 41.0% of all 90-day complications respectively account for most of medical complications. In this series, transfusion requirement was independently associated with 30-day and 90-day major complications. This is consistent with data from 10,100 patients undergoing non-cardiac surgery [29]. A recent report also concluded that that transfusion requirement is associated with reduced survival in non-anaemic patients undergoing radical cystectomy [30]. Requirement for transfusion itself may be a surrogate for surgical performance although we did not see a significant association between transfusion requirement and surgical complications (surgical complication: 31.8% vs medical complication: 19.6%, p=0.205). Male patients were independently associated with 90-day major complications. This finding may be skewed by the three-fold higher number of male patients and that there was a trend towards significance between male patients and 90-day major technical complications.

In contrast to a series of extracorporeal RARC, we did not find that the type of urinary diversion influenced the development of major complications [21]. Moreover, increasing age and poor cardiorespiratory fitness, as indicated by CPET measures was not associated with the occurrence of major complications. These findings lend support to the idea of reducing surgical complications as a means to improve surgical outcomes in patients undergoing iRARC.

We acknowledge there are limitations to this study. Although this study is one of the larger iRARC series, our cohort of 134 patients is small compared to ORC series. Hence, only a limited multivariate analysis was performed. In addition, results might not be generalized to other institutes given that this is a single center study.

5. CONCLUSIONS

Using standardised reporting criteria, complications following iRARC are common, although most are low grade. The incidence of surgical complications is possibly related to the adoption of a new technology and the report highlights that addressing this issue could have a significant impact on morbidity. This study highlights that previous surgical experience may be a confounding factor when interpreting results from different centers even in a randomized trial setting.

6. CONFLICT OF INTEREST

None to disclose

7. ACKNOWLEDGEMENTS

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Table 1: Patient demographics, preoperative and pathological variables stratified according to type of continent diversion.

Variable	Ileal conduit (n=100)	Continent diversion (n=34)	P value
Age, median (IQR)	67.4 (60.4-74.3)	54.5 (48.6-61.6)	≤0.001
Male Female	75 (75.0) 25 (25.0)	28 (82.4) 6 (17.6)	0.380
ASA I II ≥III	 17 (17.0) 61 (61.0) 22 (22.0)	 22 (64.7) 11 (32.4) 1 (2.9)	≤0.001
Preoperative anaemia, men: Hb < 13.0 g/dL, women: Hb < 12.5 g/dL	50 (50.0)	7 (20.6)	0.003
BMI, median (IQR)	27.2 (23.4-31.0)	27.3 (23.0-28.5)	0.893
LOS, median (IQR)	13.0 (8.7-17.0)	12.0 (9.0-17.0)	0.436
AT, median (IQR)	10.0 (8.25-11.0)	11.0 (10.0-12.0)	≤0.029
Peak VO_2, median (IQR)	14.0 (12.0-17.8)	18.0 (15.0-21.0)	≤0.001
VE/ VCO_2, median (IQR)	34.0 (31.0-38.7)	30.9 (28.0-34.0)	≤0.001
NAC	33 (33.0)	13 (38.2)	0.604
TURBT stage pTa pT1 ≥pT2 CIS	 4 (4.0) 23 (23.0) 69 (69.0) 4 (4.0)	 2 (5.9) 14 (41.2) 16 (47.1) 2 (5.9)	0.123
Concurrent CIS	33 (33.0)	13 (38.2)	0.639
BCG failure	22 (22.0)	9 (26.5)	0.638
Salvage cystectomy	10 (10.0)	0 (0)	0.054
Cystectomy stage pT0 cis pTa pT1 pT2 pT3 pT4	 19 (19.0) 2 (2.0) 13 (13.0) 12 (12.0) 28 (28.0) 14 (14.0) 12 (12.0)	 14 (41.2) 3 (8.8) 5 (14.7) 3 (8.8) 5 (14.7) 1 (2.9) 3 (8.8)	0.038
Soft tissue positive margin	10 (10.0)	0 (0)	0.054
Number of lymph nodes	13.6±9.0	17.0±8.9	0.066
Nodal disease	20 (20.0)	1 (4.8)	0.016

Hb: Haemoglobin; ASA: American Society of Anesthesiologist score; BMI: body mass index; LOS: length of stay; AT: anaerobic threshold; Peak VO_2: maximal oxygen consumption; VE/ VCO_2: minute ventilation − carbon dioxide production; TURBT: transurethral resection of bladder tumour; CIS: *carcinoma in situ*; BCG: Bacillus Calmette–Guérin; NAC: neoadjuvant chemotherapy

Normal reference range for CPET variables: AT ≥ 11ml/kg/min; Peak VO_2 ≥ 15ml/kg/min; VE/ $VCO_2 \leq 32$

Table 2: 30 and 90 day complications stratified according to type of continent diversion.

Variable	All patients (n=134)	Ileal conduit (n=100)	Continent diversion (n=34)	P value
Length of stay (days), median (IQR)	10.5 (8.0-15.0)	10.0 (8.0-15.5)	11.0 (8.5-14.0)	0.751
30 day complications (CD grade)				0.722
0	61 (45.5)	48 (48.0)	13 (38.2)	
I	15 (11.3))	9 (9.0)	6 (17.6)	
II	37 (27.6)	27 (27.0)	10 (29.4)	
III	11 (8.2)	8 (8.0)	3 (8.8)	
IV	7 (5.2)	6 (6.0)	1 (2.9)	
V	3 (2.2)	2 (2.0)	1 (2.9)	
30 day CD ≥III	20 (14.9)	16 (16.0)	4 (11.8)	0.549
Ileus	31 (23.1)	21 (21.0)	10 (29.4)	0.315
Urinary leak	8 (6.0)	2 (2.0)	6 (17.6)	0.001
Estimated blood loss (ml), median (IQR)	300 (225-450)	300 (200- 400)	325 (275-500)	0.967
Any blood transfusion (≤ 90 days)	29 (21.6)	24 (24.0)	5 (14.7)	0.256
Blood transfusion (≤ 90 days):				0.633
Intraoperative	15 (11.2)	13 (13.0)	2 (5.9)	
Postoperative	19 (14.2)	15 (15.0)	4 (11.8)	
Number of units transfused, median (IQR)	1 (1.0-4.0)	2 (1.0-4.0)	2 (1.5-4.0)	0.415
90 day uretero-ileal stricture	4 (3.0)	3 (3.1)	1 (3.0)	0.993
90 day complications (CD grade)				0.138
0	38 (28.3)	32 (32.0)	6 (17.6)	
I	21 (15.7)	18 (18.0)	3 (8.8)	
II	47 (35.1)	29 (29.0)	18 (52.9)	
III	16 (11.9)	11 (11.0)	5 (14.7)	
IV	8 (6.0)	7 (7.0)	1 (2.9)	
V	4 (3.0)	3 (3.0)	1 (2.9)	
90 day CD ≥III	28 (20.9)	21 (21.0)	7 (20.6)	0.959

CD: Clavien-Dindo

Table 3: Major 90-day complications according to Clavian-Dindo classification

	Cause & required treatment		Required intervention
III	Urinary leak	2	Nephrostomy
	Uretero-ileal stricture	4	Nephrostomy+/- balloon dilatation +/- JJ stent
	Wound dehiscence	2	Laparotomy
	Wound abscess	2	Incision & drainage of abscess
	Retained drain	1	GA removal of retained drain
	Small bowel obstruction (adhesions/ incision hernia)	2	Laparotomy + adhesiolysis/ hernia repair
	Hydronephrosis due to stent migration	5	Nephrostomy/ radiological repositioning of stent
	Pelvic collection	2	Radiological drainage
	Melena	1	Gastroscopy-normal
IV	Sepsis	8	Intensive care unit admission and inotropes
V	Significant bleeding- return to theatre	1	N/A
	Arrhythmia	1	N/A
	Pulmonary embolism	1	N/A
	Carcinomatosis	1	N/A

Table 4: All 90 day complications stratified according to MSKCC classification

Ileal conduit (n=100)	Continent diversion (n=34)
Haematological Transfusion=26	**Haematological** Transfusion=7 DIC=1
Cardiovascular Arrhythmia=4 MI=1	**Cardiovascular**
Gastrointestinal Ileus/ small bowel obstruction=23 Constipation=8 Clostridium difficile=4 Gastrointestinal bleed/coffee ground vomit=4 Vomiting=6 Diarrhoea=6 Enterocutaneous fistula=3 Malignant ascites=1	**Gastrointestinal** Ileus/ small bowel obstruction=10 Constipation=2 Vomiting=7 Diarrhoea=8
Genitourinary Acute kidney injury=5 Ureteral obstruction (renal calculi)=1 Urinary leak=2 Uretero-ileal stricture=3	**Genitourinary** Acute kidney injury=2 Urinary leak=6 Uretero-ileal stricture=1
Infection Pyrexia of unknown origin=2 Urosepsis=13 Chest sepsis=7 Intra-abdominal collection=9 Abscess=2 Line sepsis=2 Pubis osteomyelitis=1	**Infection** Pyrexia of unknown origin =3 Urosepsis=9 Chest sepsis=1 Intra-abdominal collection=6
Pulmonary	**Pulmonary** Pulmonary oedema=1
Surgical Incision hernia=3 Stoma stenosis=1 Displacement of stent=2 Lymphedema/ seroma=2 Surgical emphysema =1	**Surgical** Retain foreign body=1 Displacement of stent=3
Thromboembolic Pulmonary embolism=1 Iliac vessel thrombosis=1	**Thromboembolic**
Neurological Neuropathy=2 Syncope=3 Confusion/ hallucination=3	**Neurological** Neuropathy=3 Syncope=1
Wound Wound infection=3 Wound dehiscence=2 Stoma bleeding=1 (silver nitrate)	**Wound** Wound infection=2 Wound dehiscence=1

Table 5: Univariate analysis to evaluate 30-day and 90-day complications

Variable	All 30-day complications		30-day major complications		All 90-day compl
Preoperative	OR (95%)	P value	OR (95%)	P value	OR (95%)
Gender: male vs female	1.93 (0.86-4.36)	0.110	3.28 (0.72-14.95)	0.107	1.55 (0.66-3.65)
Age ≤70 vs ≥ 70	1.35 (0.64-2.82)	0.428	0.86 (0.31-2.39)	0.766	0.83 (0.37-1.85)
BMI <25 vs ≥25	1.88 (0.81-4.33)	0.139	1.60 (0.46-5.54)	0.455	0.78 (0.31-1.98)
ASA: I & II vs III	**2.83 (1.04-7.73)**	**0.036**	**3.00 (1.05-8.58)**	**0.034**	1.54 (0.5.3-4.5)
AT	1.00 (0.83-1.20)	0.988	1.07 (0.84-1.37)	0.591	0.96 (0.79-1.17)
Peak VO_2	1.0 (0.92-1.08)	0.923	1.05 (0.95-1.16)	0.325	1.01 (0.92-1.11)
VE/ VCO_2	0.98 (0.91-1.05)	0.539	0.99 (0.90-1.10)	0.908	0.96 (0.89-1.03)
NAC: yes vs no	0.67 (0.33-1.36)	0.264	1.22 (0.46-3.18)	0.692	1.01 (0.46-2.22)
Preoperative anaemia: yes vs no*	0.88 (0.44-1.75)	0.712	0.80 (0.31-2.09)	0.654	1.03 (0.48- 2.19)
Intraoperative					
Transfusion: yes vs no	**4.22 (1.59-11.20)**	**0.002**	**4.50 (1.67-12.08)**	**0.002**	1.68 (0.62-4.52)
Type of diversion: IC vs continent	1.50 (0.67-3.30)	0.323	0.91 (0.31-2.69)	0.858	2.20 (0.83-5.83)
Salvage cystectomy: yes vs no	0.53 (0.14-1.98)	0.339	0.58 (0.07-4.82)	0.608	0.36 (0.10-1.33)
Cystectomy stage: ≤pT2 vs ≥pT3	0.66 (0.33-1.35)	0.255	0.51 (0.17-1.49)	0.211	0.51 (0.23-1.09)

BMI: body mass index; ASA: American Society of Anesthesiologist score; AT: anaerobic threshold; Peak VO_2: maximal oxygen consumption; VE/ VCO_2: minute ventilation − carbon dioxide production; NAC: neoadjuvant chemotherapy; IC: ileal conduit

*men: haemogolbin <13 g/dL, women: haemoglobin <12.5 g/dL,

Table 6: Multivariable analysis of 30-day and 90-day major complications

	OR (95%)	P value
30-day major complications		
ASA: I & II vs III	1.87 (0.59-5.92)	0.287
Transfusion: yes vs no	**3.68 (1.28-10.55)**	**0.016**
90-day major complications		
Gender: male vs female	**6.98 (1.45-33.58)**	**0.015**
Transfusion: yes vs no	**4.33 (1.61-11.67)**	**0.004**