Blood Transfusion Requirement and not Preoperative Anaemia is associated with Perioperative Complications following Intracorporeal Robotic Assisted Radical Cystectomy

Running title: Transfusion associated with cystectomy outcomes

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ABSTRACT

Objectives:

To assess the prevalence of preoperative anaemia and the impact of preoperative anaemia and blood transfusion requirement on 30- and 90-day complications in a cohort of patients undergoing robotic assisted radical cystectomy with intracorporeal urinary diversion (iRARC).

Patients & methods:

IRARC was performed on 166 patients between June 2011-March 2016. Prospective data was collected for patient demographics, clinical and pathological characteristics, perioperative variables, transfusion requirements and hospital length of stay. Thirty- and 90-day complications were classified according to the modified Memorial Sloan-Kettering Cancer Center Clavian-Dindo system.

Results:

Preoperative anaemia was common (43.4%) and greatest in patients receiving neoadjuvant chemotherapy (48.6%) ($p<0.001$). Patients with preoperative anaemia were significantly more likely to have an Ileal conduit ($p=0.033$), higher cystectomy stage (≥pT3) ($p=0.028$) and a lower lymph node yield ($p=0.031$). Preoperative anaemia was not associated with increased perioperative morbidity but was associated with the need for blood transfusion ($p=0.001$).

Blood transfusion was required in 20.4% of patients with intraoperative and postoperative blood transfusion rate was 10.2% and 13.9% respectively. The 30-day all complication rate and 30-day major complication rate was 55.4% and 15.7% respectively while 90-day all complication rate and 90-day major complication rate were 65.7% and 19.3% respectively. Intraoperative blood transfusion was not associated with increased complications but postoperative blood transfusion requirement was independently associated with perioperative morbidity: all 30 day complications ($p=0.003$), all 90-day complications ($p=0.009$) and 90-day major complications ($p=0.004$).

Conclusion:

The presence of preoperative anaemia in patients undergoing iRARC is not associated with increased surgical risk although preoperative anaemic patients were significantly more likely to require blood transfusion. Blood transfusion requirement and specifically postoperative blood transfusion is independently associated with

perioperative morbidity and is an important factor for the optimisation of postoperative outcomes.

INTRODUCTION

Bladder cancer is a disease affecting predominantly elderly patients often with associated co-morbidity such as cardiovascular and respiratory disease secondary to tobacco smoking and exposure to environmental carcinogens. Radical cystectomy with urinary diversion is the gold-standard treatment for muscle invasive and highest risk bladder cancer but carries a risk of significant perioperative complications.

Preoperative anaemia and blood transfusion have been shown to be associated with higher 30-day morbidity and mortality following major non-cardiac surgery.[1-3] While preoperative anaemia in patients undergoing radical cystectomy has been associated with worse oncological outcomes,[4] the relationship between preoperative anaemia and postoperative complications has not been investigated in the setting of radical cystectomy.

Efforts to minimize perioperative complications by means of a minimally invasive approach using a robotic platform have shown limited benefits according to data from randomized controlled trials[5-8] and this has been confirmed in a meta-analysis.[9] However, these trials were either feasibility studies, trials that were closed early prior to planned recruitment or were measuring surrogate endpoints. One advantage of a robotic approach that is consistently reported is the reduction in operative blood loss and blood transfusion requirement. Open radical cystectomy (ORC) has a reported perioperative transfusion rate of 24-83% which is significantly lower than the 0-39% reported for RARC.[10]

In this study, we report the prevalence of preoperative anaemia in patients undergoing radical cystectomy and investigate whether preoperative anaemia is associated with 30 and 90-day morbidity in patients undergoing robotic assisted radical cystectomy with intracorporeal urinary diversion (iRARC). A secondary aim is to explore the interplay between blood transfusion requirement, preoperative anaemia and perioperative morbidity.

PATIENTS AND METHODS

Patient population

Data for patients treated by iRARC were prospectively recorded to an institutional approved database. Patients included in this analysis were treated between June 2011 and March 2016. During this period, 166 patients underwent iRARC and were included in the analysis. Urinary diversion was either ileal conduit or continent diversion (neobladder or Mitrofanoff) and all cases were performed by one of two surgeons. This study was registered with our institutional department and is part of an ongoing quality assurance programme (Urology2015.2).

Surgical technique

Our technique for iRARC has previously been previously described.[11] Briefly, iRARC was performed via a standard 6 port transperitoneal approach in 27° Trendelenburg. Extent of pelvic lymph node dissection included external, internal, common iliac and obturator fossa lymph nodes. An Endocatch bag (Covidien, Dublin, Ireland) was used to retrieve specimens either from the vagina if possible in females or an iliac fossa incision in other cases. Ileal conduit formation was performed using a 15 cm segment of terminal ileum from the ileo-caecal valve which was isolated by a laparoscopic 60 mm intestinal stapler (Endo-GIA; Covidien Corp, Dublin, Ireland). Continent diversion was constructed using a 50 cm segment of terminal ileum. Uretero-ileal anastomosis was constructed using either a Bricker or Wallace anastomosis depending on surgeon preference with 6 Fr infant feeding tubes/ Bander stents which were externalized as ureteric stents.

Data collected

Patient demographics, clinical and pathological characteristics, perioperative variables, blood transfusion requirement, hospital length of stay (LOS) and standardised complication data were prospectively recorded. Preoperative cardiopulmonary exercise testing (CPET) was performed on 115 patients (69.3%) to determine the following results: anaerobic threshold (AT), peak oxygen consumption (Peak VO_2) and minute ventilation-carbon dioxide production (VE/ VCO_2). All patients were followed-up for a minimum of 90 days postsurgery.

Study outcomes measured

Thirty and 90-day complications were classified according to the modified Memorial Sloan-Kettering Cancer Center (MSKCC) Clavien-Dindo (CD) system.[12] CD I-II and CD III-V were defined as minor and major complications respectively. Preoperative

anaemia status was defined as haemogolbin <13 g/dL in men and haemoglobin <12.0 g/dL in women in accordance with WHO criteria.[13] Anaemia severity was classified as mild (men: 11.0-12.9 g/dL, women: 11.0-11.9 g/dL), moderate (men and women: 8.-0-10.9 g/dL) and severe (men and women: <8.0 g/dL).

Medical complications were defined as cardiovascular, neurological, non-infective pulmonary, pre-renal failure, non-surgical related gastrointestinal (GI) complications. Infective complications were defined as the development of pyrexia (38°C) often with an attributable cause such as genitourinary, pulmonary or intra-abdominal collection.

Statistical methods

For continuous data, the following descriptive statistics were used: 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. Multivariable logistic regression was performed on variables with significance in univariate analysis. For the primary analysis all cases were included (n=166); propensity score matching was performed as a subanalysis for 121 cases. Propensity score was derived from a multivariable logistic regression model taking into account the following variables: use of neoadjuvant chemotherapy (NAC), type of urinary diversion, cystectomy stage and lymph node dissection yield. Statistical significance was set at $p \leq 0.05$. Statistical analysis was performed using SPSS v22 (IBM, New York, USA).

RESULTS

Patient demographics, type of urinary diversion, physiological status, prior therapy and histopathological outcomes for 166 cases stratified according to preoperative anaemia status is shown in Table 1 and blood transfusion requirement in Table 2. Overall, 43.4% (72/166) of patients were anaemic preoperatively and 20.5% (34/166) received a blood transfusion. Patients who had NAC ($p<0.001$), ileal conduit reconstruction ($p=0.033$), cystectomy stage ≥pT3 ($p=0.028$) and lower lymph node yield ($p=0.031$) were more likely to be anaemic preoperatively. The results following propensity score matching are shown in Supplementary Table 1 and confirm that preoperative anaemia was not associated with perioperative morbidity. Preoperative blood transfusion was administered in 5.4% (9/166) of patients while intraoperative and postoperative blood transfusion was performed in 10.2% (17/166) and in 13.9% (23/166) of patients respectively. Preoperative anaemic patients were significantly more likely to require intraoperative blood transfusion ($p=0.004$).

The 30-day all complication and 30-day major complication rate was 55.4% and 15.7% respectively while 90-day all complication and 90-day major complication rate was 65.7% and 19.3% respectively. GI and infective adverse events were the two most common complications affecting 43.4% and 33.7% of the patient cohort respectively. There was no relation between GI or infective events and anaemia or transfusion however, postoperative ileus, which developed in 24.1% (40/166) of patients, was associated with blood transfusion requirement ($p=0.031$). The 90-day mortality rate was 2.4%, and deaths were attributed to cardiac arrest in two patients, significant postoperative bleeding resulting in disseminated intravascular coagulation and ischemic bowel in one patient and one patient died from carcinomatosis secondary to a pT4N0 transitional cell carcinoma.

Preoperative anaemia was not associated with 30-day or 90-day morbidity, 90-day readmission rate and median length of stay (Table 3A). No relationship was identified between severity of anaemia and complications when anaemia was further classified as mild or moderate anaemia (only one patient had severe anaemia) (Supplementary Table 2). Additionally, the propensity-score matched cohort confirmed that preoperative anaemia was not associated with perioperative morbidity (Table 3B).

In contrast, blood transfusion requirement was associated with 30-day all ($p=0.002$) and major (0.003) complications as well as 90-day major complications ($p=0.008$) but

not 90-day all complications (Table 4). Median length of stay was significantly longer in patients requiring blood transfusion ($p<0.001$) but no difference was observed for the 90-day readmission rate. Patients who received blood transfusion were more than two fold more likely to develop a 90-day complication and three times more likely to develop a major 90-day complication (Table 4). Of interest, intraoperative blood transfusion was not associated with perioperative morbidity however, postoperative blood transfusion was significantly associated with both 30-day and 90-day all and major complications (Table 5). When analysed according to complication type, postoperative blood transfusion was significantly associated with infection (52.2% vs 30.8%; $p=0.044$) and medical complications (43.5% vs 14.0%; $p=0.001$). Furthermore, postoperative blood transfusion was the only factor associated with 30-day and 90-day all and major complications in a multivariate analysis (Table 6).

DISCUSSION

This is the first study to report the relationship between preoperative anaemia, blood transfusion requirement and perioperative morbidity following radical cystectomy. The prevalence of preoperative anaemia in this contemporary cohort was 43.4% and we report that anaemia alone is not associated with a higher complication rate. In contrast, we show that that requirement for blood transfusion, specifically postoperative blood transfusion, is significantly associated with an increase in complications at 30- and 90-days, as well as longer hospital LOS.

The WHO defines preoperative anaemia as haemogolbin <13 g/dL in men and haemoglobin <12.0 g/dL in women.[13] Anaemia can be further stratified according to severity and this has also not shown any association with perioperative complications. These results were confirmed in a propensity score matched cohort of patients. Our results are in contrast to other reports in which the relationship between preoperative anaemia and complications is established in general, vascular and orthopaedic surgery.[1] In the study by Musallam et al., preoperative anaemia was associated with 30-day morbidity and mortality. This analysis was performed using a large registry dataset and such, data is not available for radical cystectomy hence we cannot discount type II error in our study. In addition, our cohort of patients were treated with a robotic approach with intracorporeal urinary diversion which represents an evolution from conventional ORC.[14] However, to date there is little evidence to support any advantage for iRARC in terms of perioperative outcomes,[8] although early oncological outcomes for iRARC and ORC are comparable.[15] It is interesting to postulate that the relationship between anaemia and perioperative outcomes for iRARC will be different for ORC and well-designed prospective randomised controlled trials will be necessary to understand this.

As reported herein, patients with bladder cancer are often anaemic and as shown by others, anaemia is a poor prognostic indicator for cancer specific survival (CSS).[16] This study did not access CSS but we report that patients treated with NAC are significantly more likely to have preoperative anaemia. The survival benefit for NAC is established and it may be relevant to differentiate between iatrogenic (NAC induced) anaemia and the anaemia attributed to cancer (impaired erythropoietin production or haematuria). However, even when all 37 NAC cases were excluded from analysis, there remained no significant difference between preoperative anaemia and perioperative morbidity.

Although preoperative anaemia itself is not associated with perioperative morbidity, it is associated with blood transfusion requirement. Intraoperative blood transfusion specifically was associated with preoperative anaemia and there was a trend towards significance with postoperative blood transfusion. This is expected given intraoperative blood loss during cystectomy can be significant and patients with a lower preoperative haemoglobin are more likely to require blood transfusion.

The current study supports that unlike preoperative anaemia, blood transfusion requirement is significantly associated with the development of postoperative complications. All blood transfusion and specifically, postoperative blood transfusion requirement, were significantly associated with 90-day medical and infective complications. This confirms a recent report by Sui et al., in which analysis of a radical cystectomy registry dataset showed that blood transfusion requirement was associated with postoperative infection and morbidity.[17] Blood transfusion, particularly transfusion of non-leucocyte depleted blood has an effect on immunomodulation.[18] In patients with bladder cancer undergoing radical cystectomy, and receiving blood transfusion, there is a reduced overall survival (HR: 1.65; 95% CI, 1.08–2.52) and CSS (HR: 1.68; 95% CI, 1.04–2.70).[19] Blood transfusion has been shown to increase the risk of cancer recurrence in other solid organ tumours[20] and is associated with postoperative infection in trauma patients.[21] Immunological studies suggest that it is a reduction in natural killer cells following blood transfusion which can influence the host immune response and may be a factor responsible for the increase in postoperative bacterial infections.[22] Similarly, blood transfusion is reported to be associated with organ dysfunction in intensive care treated patients.[23] In orthopaedic surgery, non-transfusion optimisation of pre-operative haemoglobin has been shown to reduce the requirements for blood transfusion and well as reduce postoperative infection rates.[24] In our study, we found a significant linear association between number of units of blood transfused (1 ,2 or ≥3 units) and both 30- and 90- day all and major complications ($p<0.05$).

We can postulate several hypothesis why postoperative blood transfusion, but not intraoperative blood transfusion is associated with increased morbidity. The number of units transfused intraoperatively is lower than in the postoperative setting and may be a factor for the lack of association observed. Our intraoperative transfusion rate of 10.2% may also be too low to detect any significant difference in perioperative complications. It is not possible to determine if postoperative transfusion is a harbinger of a pending complication or that blood transfusion itself may predispose patients to perioperative morbidity. While a preoperative prognostic factor provides

an opportunity to address the risk factor, we feel that patients requiring postoperative blood transfusion should be investigated and monitored closely due to the high risk of complications.

Randomised controlled trials comparing ORC with robotic cystectomy consistently show a lower operative blood loss favouring robotic cystectomy. Following multivariate analysis, we show blood requirement transfusion is the most significant factor associated with perioperative complications. It is attractive to postulate that a robotic approach which is known to have lower estimated blood loss and requirement for blood transfusion may compensate for the increased perioperative risk attributed to preoperative anaemia.[8] Similarly, other reports have suggested that impaired cardiopulmonary function measured by CPET, is associated with hospital LOS and postoperative morbidity in patients treated with ORC[25] but not in iRARC treated patients.[26]

The results of this study should be interpreted taking into account its limitations. None the less, as a single arm study, it highlights the potential for future comparisons between liberal versus restricted blood transfusion in patients undergoing radical cystectomy. Randomised controlled trials in hip[27] and cardiac surgery[28] have not shown any superiority of liberal blood transfusion over restricted blood transfusion. It remains important that causation between blood transfusion and complications cannot be determined but our results suggest a clear association between blood transfusion requirement and perioperative complications which is independent of preoperative anaemia. It must also be considered that transfusion requirement may be a surrogate for quality of surgery which itself could be the cause of postoperative complications. Indeed, surgical complications have been shown to be responsible for the majority of major complications following iRARC.[29]

CONCLUSION

This study confirms that preoperative anaemia is not associated with increased perioperative complications in patients treated with iRARC. However, requirement for blood transfusion and specifically postoperative blood transfusion is strongly associate with 90-day all and major complications.

CONFLICT OF INTEREST

None to disclose

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Table 1: Patient demographics, preoperative and pathological variables stratified according to preoperative anaemia status.

Variable	All patients (n=166)	Anaemia* (n=72)	No anaemia (n=94)	P value
Sex: Male	125 (75.3)	57 (77.0)	68 (73.9)	0.312
Female	41 (24.7)	15 (36.6)	26 (63.4)	
Age group				0.349
<65 years	83 (50.0)	33 (45.8)	50 (53.2)	
≥65 years	83 (50.0)	29 (54.2)	44 (46.8)	
Type of urinary diversion:				0.020
Ileal conduit	126(75.9)	61 (84.7)	65 (69.1)	
Continent diversion	40 (24.1)	11 (15.3)	29 (30.9)	
ASA:				0.796
I & II	101 (60.8)	43 (59.7)	58 (61.7)	
≥III	65 (39.2)	29 (40.3)	36 (38.3)	
BMI, mean ± SD	27.40±4.73	27.03±4.68	27.66±4.78	0.454
CPET:				
AT, mean ± SD	10.29±2.03	10.19±1.65	10.36±2.25	0.639
Peak VO2, mean ± SD	15.60±4.82	15.04±4.41	15.99±5.07	0.261
VE/ VCO2, mean ± SD	34.06±5.33	34.64±5.80	33.67±4.98	0.304
Neoadjuvant chemotherapy	51 (30.7)	35 (48.6)	16 (17.0)	<0.001
Previous pelvic radiotherapy	14 (8.4)	6 (8.1)	8 (8.7)	0.968
Cystectomy stage				0.028
≤pT2	102 (62.2)	38 (52.8)	64 (69.6)	
≥pT3	62 (37.8)	34 (47.2)	28 (31.1)	
Lymph node yield, mean ± SD	14.54±9.26	12.80±7.68	15.85±10.14	0.031
Transfusion requirement	34 (20.5)	24 (33.3)	10 (10.6)	<0.001
Intraoperative	17 (10.2)	13 (18.1)	4 (4.3)	0.004
Postoperative	23 (13.9)	14 (19.4)	9 (9.6)	0.068
Blood units transfused, mean ± SD	1.03±4.32	1.57±5.66	0.60±2.81	0.152

ASA: American Society of Anesthesiologist score; BMI: body mass index; CPET: cardiopulmonary exercise test; AT: anaerobic threshold; Peak VO_2: maximal oxygen consumption; VE/ VCO_2: minute ventilation − carbon dioxide production

*men: haemogolbin <13 g/dL, women: haemoglobin <12.0 g/dL,
Normal reference range for CPET variables: AT ≥ 11ml/kg/min; Peak VO_2 ≥ 15ml/kg/min; VE/ VCO_2 ≤ 32

Table 2: Patient demographics, preoperative and pathological variables stratified according to blood transfusion requirement.

Variable	All patients (n=166)	Blood transfusion (n=34)	No blood transfusion (n=132)	P value
Male sex	125 (75.3)	23 (67.6)	102 (77.3)	0.246
Age group: <65 years ≥65 years	 83 (50.0) 83 (50.0)	 20 (58.8) 14 (41.2)	 63 (47.7) 69 (52.3)	0.249
Type of urinary diversion: Ileal conduit Neobladder	 126(75.9) 40 (24.1)	 629 (85.3) 5 (14.7)	 97 (73.5) 35 (26.5)	0.151
ASA: I & II ≥III	 101 (60.8) 65 (39.2)	 18 (52.9) 16 (47.1)	 83 (62.9) 49 (37.1)	0.290
BMI, mean± SD	27.40±4.73	28.06±5.71	27.28±4.57	0.512
CPET: AT, mean± SD Peak VO2, mean± SD VE/ VCO2, mean± SD	 10.29±2.03 15.60±4.82 34.06±5.33	 10.00±1.29 14.00±3.54 35.09±6.53	 10.34±2.1 15.88±4.97 33.88±5.10	 0.503 0.108 0.349
Neoadjuvant chemotherapy	51 (30.7)	20 (58.8)	14 (51.2)	0.138
Previous pelvic radiotherapy	14 (8.4)	4 (28.6)	10 (71.4)	0.433
Cystectomy stage: ≤pT2 ≥pT3	 102 (62.2) 62 (37.8)	 18 (52.9) 16 (47.1)	 84 (64.6) 46 (35.4)	0.211
Lymph node yield, mean± SD	14.54±9.26	14.30±8.72	14.60±9.43	0.869

ASA: American Society of Anesthesiologist score; BMI: body mass index; CPET: cardiopulmonary exercise test; AT: anaerobic threshold; Peak VO_2: maximal oxygen consumption; VE/ VCO_2: minute ventilation − carbon dioxide production

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

Table 3: A) Perioperative morbidity of patients stratified according to preoperative anaemia status. B) Propensity score matched perioperative morbidity of patients stratified according to preoperative anaemia status.

A

Variable	All patients (n=166)	Anaemia (n=72)	No anaemia (n=94)	P value
30-day complication rate	92 (55.4)	37 (51.4)	55 (58.5)	0.360
30-day major complication rate	26 (15.7)	10 (13.9)	16 (17.0)	0.582
30-day infective complications	40 (24.1)	19 (26.4)	21 (22.3)	0.546
30-day medical complications	22 (13.3)	9 (12.5)	13 (13.8)	0.802
90-day complication rate	109 (65.7)	46 (63.9)	63 (67.0)	0.674
90-day major complication rate	32 (19.3)	15 (20.8)	17 (18.1)	0.656
90-day infective complications	56 (33.7)	24 (33.3)	32 (34.0)	0.924
90-day medical complications	30 (18.1)	14 (19.4)	16 (17.0)	0.688
90-day readmission rate	35 (21.1)	11 (15.3)	24 (25.5)	0.108
Length of stay, median (IQR)	10.0 (8.0-15.0)	10.0 (8.0-16.0)	10.0 (8.0-14.8)	0.299
90-day mortality	4 (2.4)	1 (1.4)	3 (3.3)	0.453

B

Variable	All patients (n=121)	Anaemia (n=49)	No anaemia (n=72)	P value
30-day complication rate	64 (52.9)	25 (51.0)	39 (54.2)	0.734
30-day major complication rate	14 (11.6)	4 (8.2)	10 (13.9)	0.334
30-day infective complications	28 (23.1)	11 (22.4)	17 (23.6)	0.882
30-day medical complications	14 (11.6)	4 (8.2)	10 (13.9)	0.334
90-day complication rate	77 (63.6)	32 (41.6)	45 (62.5)	0.753
90-day major complication rate	20 (16.5)	9 (18.4)	11 (15.3)	0.653
90-day infective complications	39 (32.3)	15 (30.6)	24 (33.3)	0.753
90-day medical complications	21 (17.4)	8 (16.3)	13 (18.1)	0.805
90-day readmission rate	28 (23.1)	9 (18.4)	19 (26.4)	0.304
Length of stay, median (IQR)	10.0 (8.0-15.0)	11.0 (8.0-16.0)	10.0 (8.0-14.0)	0.330
90-day mortality	2 (1.7)	1 (2.0)	1 (1.4)	0.782

*men: haemogolbin <13 g/dL, women: haemoglobin <12.0 g/dL

Table 4: Perioperative morbidity of patients stratified according to blood transfusion requirement.

Variable	All patients (n=166)	Blood transfusion (n=34)	No blood transfusion (n=132)	P value
30-day complication rate	92 (55.4)	27 (79.4)	65 (49.2)	0.002
30-day major complication rate	26 (15.7)	11 (32.4)	15 (11.4)	0.003
30-day infective complications	40 (24.1)	12 (35.3)	28 (21.2)	0.087
30-day medical complications	22 (13.3)	9 (26.5)	13 (59.1)	0.011
90-day complication rate	109 (65.7)	27 (79.4)	82 (62.1)	0.058
90-day major complication rate	32 (19.3)	12 (35.3)	20 (15.2)	0.008
90-day infective complications	56 (33.7)	15 (44.1)	41 (31.1)	0.151
90-day medical complications	30 (18.1)	12 (35.3)	18 (13.6)	0.003
90-day readmission rate	35 (21.1)	8 (23.5)	27 (20.5)	0.695
Length of stay, median (IQR)	10.0 (8.0-15.0)	14.0 (8.3-25.0)	10.0 (8.0-14.0)	<0.001
90-day mortality	4 (2.4)	1 (2.9)	3 (2.3)	0.821

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

Variable	All 30-day complications		30-day major complications		All 90-day complications		90-day major complications	
Preoperative	OR (95%)	P value	OR (95%)	P value	OR (95%)	P value	OR (95%)	P value
Gender: male vs female	1.38 (0.68-2.80)	0.371	2.86 (0.81-10.06)	0.090	1.31 (0.63-2.72)	0.466	3.83 (1.10-13.31)	0.025
Age <65 vs ≥ 65 yrs	1.05 (0.57-1.94)	0.876	0.47 (0.20-1.13)	0.088	0.69 (0.36-1.31)	0.253	0.53 (0.24-1.18)	0.115
BMI <25 vs ≥25	1.54 (0.74-3.21)	0.244	1.06 (0.37-3.00)	0.920	0.60 (0.27-1.32)	0.199	0.89 (0.34-2.29)	0.804
ASA: I & II vs ≥III	1.90 (1.00-3.60)	0.048	1.42 (0.61-3.31)	0.410	1.02 (0.53-1.97)	0.950	1.28 (0.59-2.80)	0.533
AT	0.95 (0.80-1.12)	0.553	1.00 (0.79-1.26)	0.990	0.93 (0.78-1.10)	0.375	1.02 (0.83-1.26)	0.850
Peak VO_2	1.01 (0.94-1.08)	0.824	1.05 (0.96-1.14)	0.320	1.03 (0.95-1.11)	0.507	1.06 (0.97-1.15)	0.192
VE/ VCO_2	0.98 (0.92-1.05)	0.582	0.99 (0.90-1.08)	0.765	0.96 (0.90-1.03)	0.213	0.98 (0.90-1.06)	0.591
NAC: yes vs no	0.64 (0.33-1.24)	0.181	1.83 (0.78-4.33)	0.163	1.07 (0.53-2.14)	0.856	1.73 (0.78-3.84)	0.177
Preoperative anaemia: yes vs no*	0.75 (0.40-1.39)	0.360	0.79 (0.33-1.85)	0.582	0.87 (0.46-1.66)	0.674	1.19 (0.55-2.59)	0.656
Intraoperative								
Transfusion: yes vs no	5.11 (1.99-13.16)	<0.001	3.73 (1.52-9.15)	0.003	2.35 (0.95-5.80)	0.058	3.06 (1.31-7.14)	0.008
Intraoperative transfusion	2.13 (0.71-6.34)	0.168	1.78 (0.53-5.95)	0.346	1.29 (0.43-3.85)	0.652	1.33 (0.40-4.39)	0.639
Postoperative transfusion	23.6 (3.1-179.77)	<0.001	4.77 (1.79-12.68)	0.001	6.56 (1.48-29.01)	0.005	4.23 (1.65-10.85)	0.002
Type of diversion: IC vs continent	1.51 (0.73-3.14)	0.263	1.20 (0.46-3.09)	0.714	3.10 (1.27-7.56)	0.010	1.30 (0.55-3.10)	0.553
Previous pelvic radiotherapy: yes vs	0.81 (0.27-2.42)	0.705	1.53 (0.40-5.91)	0.535	0.36 (0.12-1.09)	0.060	0.68 (0.144-3.19)	0.621
Cystectomy stage: ≤pT2 vs ≥pT3	0.81 (0.43-1.53)	0.512	0.69 (0.28-1.70)	0.420	0.62 (0.32- 1.20)	0.151	1.16 (0.53-2.55)	0.714

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 <12.0 g/dL

Table 6: Multivariate analysis to evaluate perioperative morbidity.

	OR (95%)	P value
All 30-day complications		
ASA: I & II vs ≥III	1.49 (0.77-2.88)	0.233
Postoperative transfusion: yes vs no	9.46 (2.13-42.00)	0.003
90-day all complications		
Type of diversion: IC vs continent	3.43 (1.40-8.44)	0.007
Postoperative transfusion: yes vs no	7.39 (1.65-33.1)	0.009
90-day major complications		
Gender: male vs female	0.45 (0.17-1.23)	0.121
Postoperative transfusion: yes vs no	4.2 (1.62-10.97)	0.004