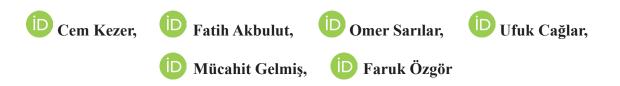# Factors Affecting Evisceration Following Open Radical Cystectomy

Açık Radikal Sistektomi Sonrası Eviserasyona Etki Eden Faktörler

iD Cem Kezer,   iD Fatih Akbulut,   iD Omer Sarılar,   iD Ufuk Cağlar,

iD Mücahit Gelmiş,   iD Faruk Özgör

Department of Urology, Haseki Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Introduction: To clarify predictive factors for evisceration after open radical cystectomy (ORC).

Methods: Charts for patients who underwent ORC between 2017 and 2021 were reviewed retrospectively. Patient demographic characteristics and operative outcomes were recorded. Patients who underwent ORC were divided into two groups as patients who developed evisceration (Group 1) and patients who did not develop evisceration (Group 2). The groups were compared according to patient preoperative characteristics, intraoperative parameters and postoperative outcomes.

Results: Total, 164 patients met study inclusion criteria, and 24 patients with evisceration and 140 patients without evisceration were enrolled into Group 1 and Group 2, respectively. In contrast, the presence of diabetes mellitus was significantly higher in eviscerated patients (25.0% and 5.7% p= 0.002), and eviscerated patients had significantly higher BMI (28.8 kg/m2 and 24.9 kg/m2, p= 0.001). Also, non-eviscerated patients had significantly higher preoperative albumin level (p= 0.001). Moreover, the operation time was significantly longer in patients with evisceration (332.5 min and 268.3 min, p= 0.001) and lymph node positivity was significantly higher in patients with evisceration (50.0% and 26.4%, p= 0.020). Multivariate regression analysis revealed that higher BMI, lower preoperative albumin level, and longer operation time were significantly associated with evisceration after ORC. Also, the presence of diabetes mellitus increased the risk of evisceration seven-fold following ORC.

Conclusion: Present study showed for the first time that higher BMI, lower preoperative albumin level, longer operation time and presence of diabetes mellitus were predictive factors for evisceration following ORC.

ÖZET

Amaç: Açık radikal sistektomiden (ORC) sonra eviserasyon için prediktif faktörleri netleştirmek.

Gereç ve Yöntem: 2017-2021 yılları arasında ORC uygulanan hastaların çizelgeleri geriye dönük olarak incelendi. Hastaların demografik özellikleri ve ameliyat sonuçları kaydedildi. ORC uygulanan hastalar eviserasyon gelişen hastalar (Grup 1) ve eviserasyon gelişmeyen hastalar (Grup 2) olarak iki gruba ayrıldı. Gruplar hasta preoperatif özellikleri, intraoperatif parametreler ve postoperatif sonuçlara göre karşılaştırıldı.

Bulgular: Toplam 164 hasta çalışmaya dahil edilme kriterlerini karşıladı ve eviserasyonlu 24 hasta ve eviserasyonsuz 140 hasta sırasıyla Grup 1 ve Grup 2'ye alındı. Buna karşılık, eviserasyon olan hastalarda diabetes mellitus varlığı anlamlı olarak daha yüksekti (%25.0 ve %5.7 p= 0.002) ve yine bu hastalarda VKİ anlamlı olarak daha yüksekti (28.8 kg/m2 ve 24.9 kg/m2, p= 0.001). Ayrıca evisere olmayan hastalarda preoperatif albümin düzeyi anlamlı olarak daha yüksekti (p= 0.001). Ayrıca eviserasyonlu hastalarda ameliyat süresi anlamlı olarak daha uzundu (332.5 dk ve 268.3 dk, p= 0.001) ve eviserasyonlu hastalarda lenf nodu pozitifliği anlamlı olarak daha yüksekti (%50.0 ve %26.4, p= 0.020). Çok değişkenli regresyon analizi, daha yüksek BMI, daha düşük preoperatif albümin seviyesi ve daha uzun operasyon süresinin ORC sonrası eviserasyon ile anlamlı şekilde ilişkili olduğunu ortaya koydu. Ayrıca, diabetes mellitus varlığı, ORC'yi takiben eviserasyon riskini yedi kat arttırdı.

Sonuç: Bu çalışma ilk kez daha yüksek BMI, daha düşük preoperatif albümin seviyesi, daha uzun operasyon süresi ve diabetes mellitus varlığının ORC sonrası eviserasyon için prediktif faktörler olduğunu göstermiştir.

INTRODUCTION

Radical cystectomy (RC), including pelvic lymph-node dissection, is accepted as a standard surgical method for patients with non-metastatic muscle invasive bladder cancer and patients with non-muscle invasive bladder cancer which cannot be treated with endoscopic methods (1). Although RC can be performed as laparoscopic and robot-assisted surgery, open radical cystectomy (ORC) is widely performed due to the extended learning curve for laparoscopic RC, the high cost of robotic surgery and the difficulty of accessing the robotic system. Despite the improvements in preoperative assessment methods

and surgical techniques, ORC remains one of the most complex surgeries in urology practice (2). Previous studies showed that ORC involves some potential complications including acute renal failure, haemorrhage, lymphocele, wound infection and evisceration (3).

Evisceration following ORC is associated with prolonged hospital stay, additional healthcare costs, and requirements for additional surgical procedures. Also, the evisceration rate following ORC was reported to have a wide range in the literature due to the heterogeneous nature of bladder cancer characteristics, different patient demographic properties and different surgical techniques. Shiavina and colleagues investigated the short-term complications following ORC, and found evisceration in 15 (3.7%) of 404 patients (4). In another study by Cantiello and colleagues, they analysed the complications after ORC, and evisceration was found in 12.9% of the whole study population (5). However, these studies did not mention predictive factors for evisceration after ORC.

Although previous reports stated that evisceration was a serious complication following ORC, no study has investigated the risk factors for evisceration after ORC. In the present study, we aimed to clarify predictive factors for evisceration after ORC.

MATERIAL AND METHOD

Charts for patients who underwent ORC including pelvic lymph-node dissection between January 2017 and February 2021 were reviewed retrospectively. The study was planned in accordance with the Helsinki Declaration Principles and all patients signed informed consent before surgery. The study was approved by Ethical Board (Meeting Decision No. 2020/172). Presence of non-metastatic muscle invasive bladder cancer or non-muscle invasive bladder cancer which could not be treated with endoscopic methods were accepted as indications for ORC. The urinary diversion type (ileal loop, orthotopic neobladder, or ureterocutaneostomy) was chosen according to the joint decision of the patient and the doctor. Patients who underwent laparoscopic RC, patients with missing data, patients who underwent salvage RC, and patients who underwent urethrectomy during ORC were excluded from the study. Also, other exclusion criteria were; being younger than 18 years old, presence of muscle and soft tissue disease, history of open abdominal surgery, and history of radical prostatectomy in men and history of hysterectomy and/or oophorectomy in women.

Patient demographic characteristics including, sex, age (years), presence of comorbidities, American Society of Anesthesiology (ASA) score, body mass index (BMI), and preoperative haemoglobin level (g/dL), creatinine level (g/dL) and albumin level (g/dL) were recorded. Also, transfusion requirements, operation time of procedure (minutes), type of diversion, final pathology of cystectomy, and positivity of lymph nodes were noted.

All patients were evaluated with complete blood count, serum biochemistry profile, coagulation profile, electrocardiography, contrast enhanced abdominal and chest computer tomography before surgery. Bowel preparation was done only one day before surgery and elastic compressive stockings were used on the day of surgery. Additionally, use of low molecular-weight heparin

was started on day of ORC and continued for at least 4 weeks after operation. All procedures were performed under general anaesthesia and antibiotic prophylaxis was administered with a combination of intravenous metronidazole and third-generation cephalosporin. ORC with extended pelvic lymphadenectomy was performed in accordance with the International Consultation on Bladder Cancer recommendations. In men, ORC included the removal of the bladder, seminal vesicles, prostate, and distal ureters, and in women the operation included the "en-bloc" removal of the adnexa, bladder, anterior and posterior vaginal wall, and urethra (except in cases of orthotopic neobladder). Extended lymph node dissection included obturator fossa, internal iliac, presacral, and external iliac nodes. The nasogastric tube was removed on the first day of the operation and the patients began to be fed orally. All ureterocutaneous or ureterointestinal anastomoses were stented for at least two weeks.

Patients who underwent ORC were divided into two groups as patients who developed evisceration (Group 1) and patients who did not develop evisceration (Group 2). The groups were compared according to patient preoperative characteristics, intraoperative parameters and postoperative outcomes. Moreover, multivariate regression analysis was used to clarify predictive factors for evisceration following ORC.

Statistical Analysis

Statistical analysis was done with the Statistical Package for the Social Sciences version 25 (SPSS IBM Corp., Armonk, NY, USA). Normality of the distribution of variables was evaluated by Shapiro-Wilk test and Q-Q plots. The Student-t test was chosen for comparison of normally distributed variables, and non-normally distributed values were evaluated with Mann Whitney u test. Quantitative data are expressed as mean ± standard deviation values. Categorical variables were classified and analysed using the χ^2 test or Fisher's exact test. Binary logistic regression analysis was used to evaluate risk factors for the occurrence of evisceration. The data were analysed at 95% confidence level and p values of less than 0.05 were accepted as statistically significant.

RESULTS

At the end of the evaluation, 164 patients met study inclusion criteria, and 24 patients with evisceration and 140 patients without evisceration were enrolled into Group 1 and Group 2, respectively. The mean age of the study population was 63.8 years old and 89.6% of patients were male. The mean BMI was 25.5 kg/m2 and the mean pre-operative albumin level was 3.7 g/dL. The mean operation time was 277.7 minutes and transfusion was required in 74 (45.1%) patients. Ileal loop was the most preferred urinary diversion type with 130 (79.3%) cases, and lymph node positivity was detected in 49 (29.9%) patients. Preoperative, operative and postoperative parameters of the entire study population are summarized in Table 1.

Comparison of eviscerated and non-eviscerated patients revealed that sex, age, presence of hypertension, coronary artery disease and, chronic obstructive pulmonary disease, preoperative haemoglobin level, haemoglobin decrease, and preoperative albumin level were similar between the groups (p= 0.724, p= 0.860, p= 0.625, p= 0.485,

Table 1: Demographic data and postoperative results of all patients

	n:164
Sex	
Female	17 (10.4%)
Male	147 (89.6%)
Age (Years)*	63.8±8.4
Presence of Diabetes Mellitus	14 (8.5%)
Presence of Hypertension	62 (37.8%)
Presence of Coronary Artery Disease	58 (35.4%)
Presence of Chronic Obstructive Pulmonary Disease	16 (9.8%)
ASA Score*	1.7±0.7
Body Mass Index*	25.5±5.0
Pre-operative Hemoglobin (g/dl)*	12.8±2.1
Hemoglobin Decrease (g/dl)*	2.4±1.4
Pre-operative Creatine (g/dl)*	1.1±1.2
Pre-operative Albumin (g/dl)*	3.7±0.6
Operation Time (minute)*	277.7±72.7
Diversion type	
İleal loop	130 (79.3%)
Orthotopic neobladder	27 (16.5%)
Ureterocutaneostomy	7 (4.2%)
Post-operative intensive care unit	26.8±19.6
Pathology of Cystectomy	
pT0-pT1-pT2	104 (63.4%)
pT3-pT4	60 (36.6%)
Lymph node positivity	49 (29.9%)
Transfusion requirement	74 (45.1%)

*mean ± standard deviation, ASA: American society of anesthesiologists

p=0.708, p= 0.721, p= 0.767 and p= 0.593, respectively). In addition, pathology of cystectomy and diversion type were comparable (p= 0.720 and p= 0.745). In contrast, the presence of diabetes mellitus was significantly higher in eviscerated patients (25.0% and 5.7% p= 0.002), and eviscerated patients had significantly higher BMI (28.8 kg/m2 and 24.9 kg/m2, p= 0.001). Also, non-eviscerated patients had significantly higher preoperative albumin level (p= 0.001). Moreover, the operation time was significantly longer in patients with evisceration (332.5 min and 268.3 min, p= 0.001) and lymph node positivity was significantly higher in patients with evisceration (50.0% and 26.4%, p= 0.020).

Multivariate regression analysis revealed that higher BMI, lower preoperative albumin level, and longer operation time were significantly associated with evisceration after ORC. Also, the presence of diabetes mellitus increased the risk of evisceration seven-fold following ORC. Conversely, the present study showed that lymph node positivity did not have a significant effect on evisceration.

DISCUSSION

Radical cystectomy with pelvic lymph node dissection is a well-known and complex surgical procedure with serious potential complications. Although many studies reported complication types and complication rates following ORC, most of these studies did not focus on clarifying possible risk factors for complication development (3, 4, 5). We believe that identifying predictive factors for complications is an important step to prevent and manage complications. Thus, in the present study, we aimed to clarify risk factors for evisceration following ORC. Our study revealed that higher BMI, lower preoperative albumin level, longer operation time and presence of diabetes mellitus were predictive factors for evisceration after ORC.

The relationship between diabetes mellitus and tissue healing is a hot topic in medicine. Greenhalgh stated that coexistence of atherosclerosis and neuropathy in diabetes mellitus patients is a reason for poor tissue healing (6). Mahey and colleagues investigated the predictive factors for abdominal evisceration in 50 patients, and the authors claimed that presence of diabetes mellitus was a risk factor for abdominal evisceration (7). In parallel, we found diabetes mellitus was a predictive factor for evisceration following ORC. However, we did not evaluate fasting glucose levels in the present study, which could be examined in further studies.

Obesity results in increased abdominal pressure which could reduce abdominal wall blood flow and tissue healing. Pavlidis and colleagues compared 178 patients with and without evisceration in 1:1 ratio, and found that obesity was significantly common in patients with evisceration (8). In another study, Spiliotis et al. analysed the demographic characteristics of patients with abdominal wound dehiscence, and the authors stated that one of third patients with abdominal dehiscence had BMI ≥35 kg/m2 (9). In the present study, evisceration was significantly common after ORC in obese patients. Also, we believe that effect of waist circumference on evisceration following ORC may be the subject of another study.

Albumin is a serum protein with several important functions including maintaining osmotic pressure of the blood, and transporting hormones, drugs, and other substances such as calcium throughout the organs. Previous reports which investigated the importance of albumin level and tissue healing had controversial results. Riou and colleagues found that serum albumin level was 2.3 g/dL and 3.6 g/dL in patients with and without wound dehiscence, and stated that lower serum albumin level was a predictive factor for wound dehiscence (10). On the other hand, Kenig et al. claimed that serum albumin level had no significant effect on evisceration. However, surgery was performed in emergency situations for 80% of cases in Kenig's study and the authors did not mention the rate of oncologic cases (11). In the present study, lower serum albumin level was a predictive factor for evisceration following ORC.

Longer operation time could reflect the surgical difficulty. Prolonged contact of the intestines with air during open surgeries may cause the intestines to lose heat, decrease bowel movements, subileus or ileus. Buchs and colleagues investigated the risk factors for poor wound healing in patients with colorectal surgery, and found that operation time longer than three hours was a predictive factor for poor wound healing (12). Also, Alves et al. showed

Table 2: Comparison of patient demographic data and postoperative results between groups

	Eviscreated N:24	Non eviscreated N:140	P value
Sex			
Female	2 (8.3%)	15 (10.7%)	0.724
Male	22 (91.7%)	125 (89.3%)	
Age (Years)*	63.5±8.0	63.8±8.5	0.860
Presence of Diabetes Mellitus	6 (25.0%)	8 (57.1%)	0.002
Presence of Hypertension	8 (33.3%)	54 (38.6%)	0.625
Presence of Coronary Artery Disease	10 (41.7%)	48 (34.3%)	0.485
Presence of Chronic Obstructive Pulmonary Disease	3 (12.5%)	13 (9.3%)	0.708
ASA Score*	1.9±0.9	1.7±0.7	0.248
Body Mass Index*	28.8±4.2	24.9±4.9	0.001
Pre-operative Hemoglobin (g/dl)*	12.8±2.5	12.9±2.0	0.721
Hemoglobin Decrease (g/dl)*	2.4±1.4	2.4±1.4	0.767
Pre-operative Creatine (g/dl)*	1.0±0.4	1.2±1.3	0.593
Pre-operative Albumin (g/dl)*	3.1±0.6	3.7±0.6	0.001
Operation Time (minute)*	332.5±80.1	268.3±67.3	0.001
Diversion type			
Ileal loop	18 (75.0%)	112 (80.0%)	0.745
Orthotopic neobladder	4 (16.7%)	23 (16.4%)	
Ureterocutaneostomy	2 (8.3%)	5 (3.6%)	
Post-operative intensive care unit	28.0±19.6	26.6±19.7	0.747
Pathology of Cystectomy			
pT0-pT1-pT2	16 (66.7%)	88 (62.9%)	0.720
pT3-pT4	8 (33.3%)	52 (37.1%)	
Lymph node positivity	12 (50.0%)	37 (26.4%)	0.020
Transfusion requirement	9 (37.5%)	65 (46.4%)	0.417

*mean ± standard deviation, ASA: American Society of Anesthesiologists

Table 3: Multivariate analysis of evisceration risk factors

	Odds ratio	%95 CI	P value
Presence of Diabetes Mellitus	7.438	1.535-36.036	0.013
Body Mass Index	0.861	0.748-0.992	0.038
Pre-operative Albumin	3.991	1.575-10.114	0.004
Operation Time	0.992	0.985-0.999	0.036
Lymph node positivity	2.153	0.706-6.564	0.178

the relationship between longer operation time and evisceration (13). In accordance with the aforementioned studies, longer operation time was a predictive factor for abdominal dehiscence following ORC.

The retrospective nature is considered to be a limitation of the study. However, all patient data were recorded in the electronic database system in a prospective manner. Secondly, we are aware of the limited number of patients in our study. In addition, due to working in a university, operations were performed by different surgeons in the same team, which may have affected intraoperative and/ or postoperative outcomes; however, all surgeons had completed their learning curves and performed surgeries with the same technique. Also, the effect of evisceration on patient quality of life and mental health were not evaluated in the present study. Lastly, we did not focus on the cost of evisceration following ORC, which may be the subject of another study.

In conclusion, our study showed for the first time that higher BMI, lower preoperative albumin level, and longer operation time were predictive factors for evisceration following ORC. Additionally, presence of diabetes mellitus was significantly related with evisceration after ORC. Our study findings should be confirmed with randomised clinical research with higher patient numbers and prospective manner.

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