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Research Paper

Application of Clavien-Dindo Classification System in the Early Complications of Radical Cystectomy in Al-Yarmook Teaching Hospital

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ABSTRACT:

BACKGROUND:

The most effective treatment for muscle-invasive bladder cancer and non-muscle invasive bladder cancer with highest risk of progression, is Radical cystectomy and urinary diversion. This operation carries a high risk of complications of multiple types that can affect not only the urinary system but also other systems.

OBJECTIVE:

This study analyzes the early complications (within 30 days) of Radical
Cystectomy and urinary diversion, using a standardized classification system i.e. Clavien-Dindo classification system.

PATIENTS AND METHODS:

This is a combined retrospective and prospective study analyzing the early complications of RC. We review the early (30 days) post-operative period retrospectively for the previous cases and monitor this period, prospectively, for the coming cases at Al-Yarmook teaching hospital in Baghdad, Iraq from October 2017, to October 2019. We record the preoperative variables and postoperative complications in a systematic method using Clavien-Dindo classification system and the relationship between them.

RESULTS:

Twenty three patients are included in the study with a mean age 65.1 year. Urinary diversion types are cutaneous ureterostomy (9 patients) ileal conduit (10 patients) and orthotopic bladder (4patients). Most of the postoperative complications are minor (CD grade I and II) (73.3%).
The predominant grade of complications are grade II (46.4%), while the least grades are grade IVb (3.5%) and grade V (3.5%).

CONCLUSION:

Radical cystectomy and urinary diversion for urinary bladder cancer carries a high risk of complications, but fortunately, most of these complications are minor and of low grade according to Clavien-Dindo classification system. Applying this classification system in the early complications of radical cystectomy allows rapid review of complications by researchers.

KEYWORDS: Bladder cancer, Radical cystectomy, Complications, Clavien-Dindo.

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INTRODUCTION:

Optimal treatment of muscle-invasive bladder cancer MIBC requires a multidisciplinary approach incorporating urologic oncologists, medical oncologists, and radiation oncologists with support from the pathologist, radiologist, and cancer specialist nurse [(1,2)]. The gold standard therapy for organ-confined muscle-invasive bladder cancer is radical cystectomy with neoadjuvant cisplatin-based chemotherapy [(1,2,3)].

Radical cystectomy (RC) is a complex procedure involving not only the genitourinary but also the gastrointestinal tract for urinary diversion.

In addition to this complexity, patients are frequently elderly and have significant comorbidities.

Although major complications are infrequent, any complication remains common with the most frequent being gastrointestinal (29%) or infectious (25%). Postoperatively, efforts are necessarily to be directed at minimizing the possibility of these complications and maximizing the return of normal physiology [4]. Complications of radical cystectomy and urinary diversion are common, and many are severe and potentially life-threatening. Early complications, including hemorrhage, thromboembolic events, infection, and cardiovascular and pulmonary complications, are not directly related to the urinary diversion and do not appear to be different in patients undergoing different types of diversion, while late morbidity was usually linked to the type of urinary diversion [3,5].

The Clavien classification system for surgical complications was originally developed in 1992 [6] and modified by Dindo et al. in 2004 [7]. This is composed of five grades ranging from simple deviation from the anticipated course to death, the first two grades are minor and the remaining are major [7].

PATIENTS AND METHODS:

This is a combined retrospective and prospective study, analyzing the early complications of Radical cystectomy (RC) at Al-Yarmook teaching hospital in Baghdad, Iraq from October 2017, to October 2019.

During this two years, 25 patients had been prepared for radical cystectomy. Cystectomy had been done in twenty-three patients, the remaining two patients had frozen pelvis with failure to do cystectomy and only urinary diversion had been done, so, they were excluded from this study. For that, 23 patients had been involved in this study, 14 of those are retrospective while 9 are prospective.

Retrospectively, the data has been collected from the hospital information system. While prospectively, the data have been collected directly by following up those patients.

The data include: the preoperative age, sex, occupation, comorbidities (history of hypertension and diabetes mellitus), history of smoking, and alcohol consumption.

The patients have been evaluated with detailed medical history, physical examination, complete blood picture, blood biochemistry tests, serum minerals, renal function tests, liver function tests, urinalysis, PSA, urinary system ultrasound and staging computed topography and/or magnetic resonant imaging.

Physical status according to American Society of Anesthesiologists, Body Mass Index (BMI) in kilogram per square meter, and the performance status according to Eastern Cooperative

Oncology Group (ECOG) performance scale was recorded.

Postoperatively, complications (up to 30 days) has been detected and classified into five grades according to the Clavien-Dindo classification system and studied in correlation to the preoperative assessments.

Mechanical and chemical bowel preparations have been routinely administered two days before the surgery. Elastic compressive stocking and low molecular weight heparin (LMWH) have been used in all the patients as Deep vein thrombosis (DVT) prophylaxis, the LMWH has been continued for 28 days postoperatively. All RCs have been done with open approach, though a lower midline laparotomy incision, and standard steps of surgery have been followed. All uretero-intestinal and uretero-cutaneous anastomoses have been stented regardless of the type of urinary diversion for at least 3 weeks.

Three types of diversion have been used: ureterocutaneous (UC), ileal conduit (IC) and orthotopic bladder (OB). Nine patients underwent UC, 10 of them underwent IC while only 4 underwent OB.

Analysis of data was carried out using the available statistical package of SPSS-25 (Statistical Packages for Social Sciences- version 25). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of difference of different means (quantitative data) were tested using ANOVA test for difference among more than two independent means. The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (□2-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05 [8].

RESULTS:

Twenty three patients were included in our series with a mean age 65.1±8.0 (49-79) years. Nineteen patients of them were males and four were females.

Table (1) shows the preoperative patients' distribution according to the age, history of comorbidities and ASA score, while table (2) shows the preoperative hemoglobin and renal function.

Table 1: Preoperative variables of the patients.

		No	%
Age (years)	<60 y	4	17.4
	60-69	12	52.2
	≥70 y	7	30.4
	Mean±SD (Range)	65.1±8.0	(49-79)
Comorbidities	Hypertension	7	30.4
	Diabetes mellitus	6	26.1
	Obesity (BMI≥30)	8	34.8
	Smoking	14	60.9
American Society of Anesthesiologists ASA score	ASA 1	2	8.7
	ASA 2	20	87
	ASA 3	1	4.3
	ASA 4	0	0
	ASA 5	0	0
	ASA 6	0	0

Table 2: Preoperative hemoglobin level and renal function parameters.

	Mean±SD
Haemoglobin (g/dl)	12.42±1.18
Blood urea (mg/100ml)	1.57±20.69
Serum creatinine (mg/100ml)	1.39±0.53

The urinary diversion was three types: cutaneous ureterostomy (9 patients), ileal conduit (10 patients) and orthotopic bladder (4 patients).Table (3) shows the analysis for complications of any grade in the whole patient variables.

No variables evaluated predicted complications except ASA score (P value= 0.018) which showed statistical significance.

Table 3: Patient demographics and characteristics according to the different types of urinary diversions.

		Diversion type						P value
		CU (n=9)		IC (n=10)		OB (n=4)		
		N	%	N	%	N	%	
Age (years)	<60 y	1	11.1	2	20.0	1	25.0	0.815
	60-69y	6	66.7	4	40.0	2	50.0	
	≥70 y	2	22.2	4	40.0	1	25.0	
	Mean±SD (Range)	64.7±6.6 (55-76)		67.0±9.3 (49-79)		61.3±8.2 (51-71)		
Gender	Male	7	77.8	8	80.0	4	100.0	0.596
	Female	2	22.2	2	20.0	-	-	
Hypertension	Yes	5	55.6	1	10.0	1	25.0	0.095
	No	4	44.4	9	90.0	3	75.0	
Diabetes mellitus	Yes	3	33.3	2	20.0	1	25.0	0.803
	No	6	66.7	8	80.0	3	75.0	
Smoking	Yes	5	55.6	6	60.0	3	75.0	0.800
	No	4	44.4	4	40.0	1	25.0	
Obesity	Obese (BMI=>30Kg/m2)	5	55.6	3	30.0	-	-	0.139
	No	4	44.4	7	70.0	4	100	
ASA score	1	-	-	-	-	2	50.0	0.018*
	2	8	88.9	10	100	2	50.0	
	3	1	11.1	-	-	-	-	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.
CU: Cutaneous ureterostomy. IC: ileal conduit. OB: orthotopic bladder. BMI: body mass index. ASA: American society of anesthesiologists.

Patients who underwent cutaneous ureterostomy as a type of diversion had higher mean BMI and poorer renal function as compared with other types of diversion. These results were statistically insignificant as in table (4).

Table 4: Relationship between the BMI and serum creatinine with the diversion type.

	Diversion type			P value
	CU (n=9)	IC (n=10)	OB (n=4)	
BMI (Kg/m2)	28.92±4.60 (22.0-35.0)	26.27±4.81 (16.7-33.0)	26.88±1.84 (24.5-29.0)	0.424
Serum creatinine (mg/100ml)	1.59±0.53 (0.90-2.30)	1.31±0.54 (0.70-2.20)	1.15±0.51 (0.80-1.90)	0.343
-Data were presented as Mean±SD (Range)				

*Significant difference among three independent means using ANOVA test at 0.05 level. CU: Cutaneous ureterostomy. IC: ileal conduit. OB: orthotopic bladder. BMI: body mass index. SD: standard deviation.

All the patients had complications which differ from patient to patient. The total number of complications were 56 complications, 41 (73.3%) of them are minor complications (Clavien-Dindo grade I and II, 26.7% and 46.4% respectively) while 15 (26.7%) were of major grade (CD grade IIIa, IIIb, IVa, IVb and V, 5.3%, 5.3%,8.9%,3.5% and 3.5% respectively). As in figure (1):

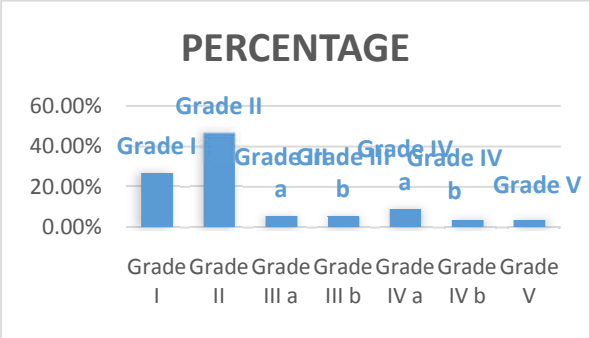

Figure 1: The percentage of the grades of complications according to the Clavien-Dindo CD score from the total number of complications.

The predominant type of complications was hematological which constitute 35.7% of the whole complications. The second most common was infectious (19.6%) then gastrointestinal (19.4%) complications. Anemia was the most common hematological complication. Superficial surgical site infection and chest infections represented in 10.7%, 8.9% of the complications, respectively, as infectious complications. Gastrointestinal complications mostly consisted of ileus (16%) that needs potassium supplementation of the patents. 5.3% of complications required intervention under general anesthesia. Death rate was 3.5%. As in table (5)

Table 5: The number of complications that developed with its percentage from the total number of complications.

		No	%
Grade I:	Paralytic ileus need K	9	16
	Superficial Surgical site Infection	6	10.7
Grade II:	Blood transfusion	20	35.7
	Chest infection	5	8.9
	GIT fistula treated with TPN	1	1.7
Grade IIIa:	Wound closure under LA	1	1.7
	IVU or descending pyelogram	2	3.5
Grade IIIb:	Missed bowel injury needs exploration	1	1.7
	Wound closure under GA	2	3.5
Grade IVa:	Dialysis	2	3.5
	CVA	1	1.7
	Respiratory failure & ETT	2	3.5
Grade IVb:	Multi-organ failure	2	3.5
Grade V:	Death	2	3.5
Sum		56	~100

K: Potassium, TPN: Total Parental Nutrition, LA: Local anesthesia, IVU: Intra venous Urography, GA: General anesthesia, CVA: Cerebro vascular Accident, ETT: Endo tracheal Tube.

When comparing all the three types of urinary diversion for complication rates and grades, the result was statistically insignificant. As in table (6):

Table 6: Complications of radical cystectomy according to the type of urinary diversion and grade of complications.

		Diversion type						P value
		CU (n=9)		IC (n=10)		OB (n=4)		
		No	%	No	%	No	%	
Grade I	Yes	5	55.6	7	70.0	-	-	0.058
	No	4	44.4	3	30.0	4	100.0	
Grade II	Yes	9	100.0	8	80.0	4	100.0	0.241
	No	-	-	2	20.0	-	-	
Grade IIIa	Yes	2	22.2	1	10.0	-	-	0.509
	No	7	77.8	9	90.0	4	100.0	
Grade IIIb	Yes	1	11.1	1	10.0	1	25.0	0.735
	No	8	88.9	9	90.0	3	75.0	
Grade IVa	Yes	2	22.2	2	20.0	-	-	0.596
	No	7	77.8	8	80.0	4	100.0	
Grade IVb	Yes	-	-	1	10.0	1	25.0	0.330
	No	9	100.0	9	90.0	3	75.0	
Grade V	Yes	-	-	1	10.0	1	25.0	0.330
	No	9	100.0	9	90.0	3	75.0	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level. CU Cutaneous ureterostomy. IC ileal conduit. OB orthotopic bladder.

DISCUSSION:

The most effective treatment for muscle-invasive bladder cancer and non-muscle invasive bladder cancer with highest risk of progression is Radical cystectomy and urinary diversion [1].This operation carries a high risk of complication that need to be studied in a systematic method.This study has revealed that the age and gender had insignificant statistical effect (p value= 0.815,0.596, respectively) on the complication rate and grade, as Donat et al showed in their thesis that older patients with bladder cancer provides similar disease control and survival outcomes with risks of high grade perioperative morbidity comparable to those in younger patients [8].

While Takada et al showed that age (P = 0.019) and gender (P = 0.007) were significant predictors of any grade complications [9]. Hypertension has been found in 30.4% of our patients with no significant effect on the complication rate (p value= 0.095). While Novara et al [10] study showed 44% of patients were hypertensive with no significant effect on the complication rate (p value=0.669). These are incompatible with Patidar et al [11] study which showed a significant effect of hypertension on the complication rate (p value =0.001). The hypertensive patients in Patidar et al study was 43.3%.

Diabetes mellitus is recognized in 26.1% of patients with no significant effect on the complication rate (p value= 0.803). While Novara et al [10] study showed 14% of patients were diabetic with no significant effect on the complication rate (p value= 0.341). These are mismatched with Patidar et al [11] study which showed a significant effect of diabetes mellitus on the complication rate (p value =0.031). The diabetic patients in patidar et al study was 43.3%. Smoking has been found in 60.9% of our study patients with no significant effect on complication rate (p value =0.800). While Patidar et al study showed that 43.8% of the patients were smoker with significant effect on the complication rate (p value < 0.001) [11].

The mean Body Mass Index (BMI) was 27.41kg/m2 with 34% of patients were obese (BMI ≥30 kg/m2), but there is no significant effect of

obesity (p value= 0.139) and higher BMI on the complication rate. Novara et al [10] and Takada et al [9] studies also showed insignificant effect of BMI with p value (0.822 and 0.209, respectively) and their mean BMI was 26.5 kg/m2 and 23 kg/m2, respectively. This difference in the mean BMI may be due to different race in Takada et al group (Japan) [9].

The physical status assessment according to American Society of Anesthesiologists (ASA) score revealed that 87% of patients in our study were ASA II and only 4.3% were ASA III and no one was > ASA III. While Novara et al study concluded that ASA I were 10%, ASA II were 53%, ASA III were 35% and 2% were ASA IV [10]. This is may be due to patients with high ASA score have high perioperative risk of morbidity and mortality, and most of those patients did not accept the risk of that intervention and referred for oncology department for other options of treatment with less risk. This study shows that the only variable that significantly affect the overall early complications rate is ASA score (p value 0.018) which is consistent with Hautmann et al and Shabsigh et al studies [12,13]. But these studies and other showed that there were other variables that significantly affect complication rate. This can be explained by the larger sample of patients by other studies.

Mean serum creatinine is 1.39mg/dl in this study, which has no significant statistical effect on complication rate (p value= 0.343). Novara et al [10] study showed that the mean serum creatinine was 0.97 mg/dl with no statistical effect on the complication rate (p value=0.355).

Regarding Clavien-Dindo score whether major or minor complications, our study revealed that most of the complications (73.3%) were classified as minor complications (Clavien-Dindo grade I and II), that was comparable to Patidar et a, Schiavina et al and Roghmann et al studies that showed minor complications in 71.9%, 66.5% and 66,8%, respectively[11,14,15]. But these results discordant with Novara et al study which showed that the minor complications were the most predominant type of complication (87%) [10].

Regarding the grade of complications, the most frequent grade in our study, according to Clavien-Dindo score was grade II (about 46.4% of the whole complications) and the least frequent was grade IV b and grade V (3.5% of the whole complications). These result were comparable to Patidar et al study, which was done in India, that showed that grade II was the most frequent (48.9%) and the least was grade IV b and grade V (2.7%) [11]. Blood transfusion is classified as grade II complication, and that made this grade the most frequent grade of complications because most of the patients need at least one unit of blood transfusion post operatively.

This study showed that the most common type of complication was hematological (35.7%) then infectious (19.6%) and gastrointestinal (19.4%), which was comparable to Patidar et al and Roghmann et al in their studies which showed predominant hematological complications as 28.4% and 25%, respectively[11,15]. The cause of the predominant of hematological complications in our study as well as these studies was the blood transfusion for blood loss and anemia, as this operation carries high risk of blood loss that needs replacement.

According to the type of urinary diversion, there is no significant difference observed between the three types of diversion, in our study like Patidar et al, De Nunzio et al and Abe et al studies [11,16,17]

CONCLUSION:

Radical cystectomy and urinary diversion for urinary bladder cancer carries a high risk of complications, but fortunately, most of these complications are minor according to the Clavien-Dindo classification system. Applying this classification system in the early complications of radical cystectomy is feasible and allows rapid review of complications by the surgeons and researchers.

RECOMMENDATIONS:

The limitation of this study is that the sample size. So, I highly recommend to do other prospective studies over one or two years on multiple centers in Iraq. This will provide longer time of follow up of these patients and recording the complications not only for 30 days, but also for longer period. Also, the prospective study allows to review measures that can affect the rate of complications e.g. enhanced recovery program.

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