

Comparative Characteristics of the Direct Results of Extraperitoneal and Transperitoneal Access in the Surgical Treatment of Bladder Cancer

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ABSTRACT

Objective: To compare the results of transperitoneal and extraperitoneal access during radical cystectomy for muscle-invasive bladder cancer to choose the most rational method of surgical treatment.

Materials and methods: The study included 141 patients with muscle-invasive bladder cancer in the T2-3N0-2M0 stage from January 2014 to December 2017. Patients were alternatively divided into groups with transperitoneal access (TPD) n=62, and extraperitoneal access (EPD) n=79.

Results: The average operation time for EPD with ureterocutaneostomy was 142.1 min (range 90-192 min) and for TPD 127.5 min (range 75-180 min), $p < 0.05$, which is not statistically significant, that is the average operation time between the groups showed no differences. The mean estimated blood loss (EPD) was 375 ml (range 210-2800 ml) and 320 ml (range 180-3100 ml) for the DP group ($p = 0.43$). The average hospitalization was 7 (6-14) days for EPD and 12 (9-24) days for PD groups, ($p = 0.48$ with the Mann-Whitney ratio). Postoperative complications were divided into 2 groups: surgical and non-surgical. In total, surgical complications were observed in 36 patients (25.5%), of which 23 (37.1%) were patients with TP, and 13 (16.4%) cases in the group with EPD. Non-surgical complications were observed in 31 (22%) patients, and there was no significant difference between the groups. Pyelonephritis was mainly observed in 21 (14.9%) patients, cardiovascular pathology in 3 (2.1%) patients, and pulmonary embolism (PE) was observed in 7 (4.9%) of the total number of patients studied. Depending on the severity of postoperative complications, we performed the analysis on the Clavien-Dindo scale, according to which in the general study group, postoperative surgical complications developed in 36 of 141 patients, which was 41.8%. At the same time, in the TPD group – 23 37.1%, in the group with EPD-13 (16.4%), $p < 0.05$. Intestinal obstruction developed in 3 and 14 patients in the EPD and TPD groups, respectively ($p = 0.002$); of these, only 4 of the TPD group required repeated surgery. Pelvic

lymphocele (>100 ml) was observed in 5 and 1 patients in the TPD and EPD groups, respectively ($p = 0.13$).

Conclusion Extraperitoneal technique (EPD) with extraperitonealization of the neoplasm is a safe and reliable surgical approach. It has tetrafunctional advantages from the point of view of reduction of intestinal obstruction, frequency of repeated operations, the problems with the stripes and adhesive disease. The extraperitoneal technique with radical cystectomy is comparable in safety and reliability to the transperitoneal surgical approach and gives good peri- and postoperative results according to the parameters studied by us. A significant reduction in postoperative intestinal obstruction and adhesive disease is noteworthy. Thus, EPD is safe both functionally and oncologically.

KEYWORDS: bladder cancer, cystectomy, extraperitoneal surgical approach, transperitoneal access

INTRODUCTION

Transperitoneal radical cystectomy (TPRC) is an established procedure that involves antigrade mobilization and dissection of the bladder, followed by intraperitoneal placement of a new bladder or iliac conduit. Over the past two decades, mortality after radical cystectomy (RC) has reached a plateau (1-3%) [1,2]

Nevertheless, the incidence of muscle-invasive cancer continues to be significant, ranging from 18 to 30% [3], and includes intestinal obstruction, fascial detachment, and urine leakage. In addition, the frequency of early and late re-operations decreased to 5% and 10%, respectively [4]. In order to reduce the incidence, we describe our own method of extraperitoneal radical cystectomy (EPRC). Data from morbidity and pathology outcomes in both groups (EPRC and TPRC) form the basis of this prospective study.

Objective: To compare the results of transperitoneal and extraperitoneal access during radical cystectomy for muscle-invasive bladder cancer to choose the most rational method of surgical treatment.

MATERIALS AND METHODS:

The study included 141 patients with muscle-invasive bladder cancer in the T2-3N0-2M0 stage from January 2014 to December 2017. Patients were alternatively divided into groups with transperitoneal access (TPD) $n=62$, and extraperitoneal access (EPD) $n=79$. Charlson Comorbidity Index [5] (CCI) was used to quantify comorbidity. This study compared TPD and EPD procedures in terms of clinical and pathological characteristics, duration of surgery, blood loss, perioperative complications, 30-day mortality, and cancer outcome after 3 years. The study was approved by the institutional ethics committee.

Informed consent was obtained from all individuals prior to their inclusion in the study. The clinical characteristics of the patients are presented in Table 1

	EPD group N (%)	TPD group N (%)	P value
Age (avarage, range)	63 (57–73)	61 (54–79)	0,77
Charlson mark (mediana, IQR)	4 (3–9)	4 (2-9)	0,83 ^s
Extra weight (BMI> 25)	31 (17,2%)	26 (16,5%)	0,85

EPD was carried out according to the method developed by us. An incision is made from the navel to the symphysis. The abdominal cavity is not opened. the middle line under the navel and the transverse fascia are incised. The peritoneum is being inspected. If there is no germination and/or invasion of the tumor in the peritonium, then by the blunt method it is separated from the bladder. In this case, the peritoneal space is additionally examined. Bilateral pelvic lymphadenectomy is performed from the bifurcation of the common iliac artery along the external iliac artery and vein to the femoral canal distally and the occluding nerve medially. With visual and enlarged lymph nodes, the lymph dissection expands to the level of the inferior mesenteric artery. The bladder is retracted onto the head, and the fibrous-adipose tissue is removed from the behind-symphysis space, exposing the neck of the bladder. The dorsal venous complex is bandaged and separated, and inside the pelvic fascia is cut on both sides. In the process, the prostate is mobilized. The urethra intersects 1-1. 5 cm on distance from the prostate. During the operation, the vascular cruris of the bladder are ligated and retrograde separated. Next, the proximal, paravesical tissues are dissected and the obliterated hypogastric cruris are bandaged and cut. The ureters are the last to be bandaged and cut, and the severed ends are sent for examination. In many cases, the bladder can be removed without opening the peritoneum; if the peritoneum is attached to the bladder dome or when the tumor affects the bladder dome, it can be removed along with the sample. After the sample is removed, the wedges of the bladder neck tissue and the edges of the urethral incision are sent for examination. The ureters are removed to the skin. The technique of transperitoneal surgery was performed in the usual way, as described by Hautmann[6].

Standard dissection of pelvic lymph nodes was performed in both groups in the same way. All patients were given antibiotics during the perioperative period. All patients were observed in the Department of Oncourology of the Republican Specialized Scientific and Practical Center of Oncology and Radiology and were treated in accordance with institutional protocols. Feeding began with the resumption of intestinal movement and gradually increased in accordance with the tolerance of the patient. All drains were removed when the discharge became insignificant (<25-30 ml). All cases requiring treatment or surgery were assessed as complications. Postoperative intestinal obstruction was determined when nausea or vomiting associated with bloating occurred, requiring discontinuation of oral administration and intravenous fluid administration and / or nasogastric tube insertion. The data were collected based on detailed clinical and outpatient follow-up. Patients were examined at intervals of 3 months during the first year after surgery, every six months for the following years.

RESULTS

The average operation time for EPD with ureterocutaneostomy was 142.1 min (range 90-192 min) and for TPD 127.5 min (range 75-180 min), $p < 0.05$, which is not statistically significant, that is the average operation time between the groups showed no differences. The mean estimated blood loss (EPD) was 375 ml (range 210-2800 ml) and 320 ml (range 180-3100 ml) for the DP group ($p = 0.43$). The average hospitalization was 7 (6-14) days for EPD and 12 (9-24) days for PD groups, ($p = 0.48$ with the Mann-Whitney ratio).

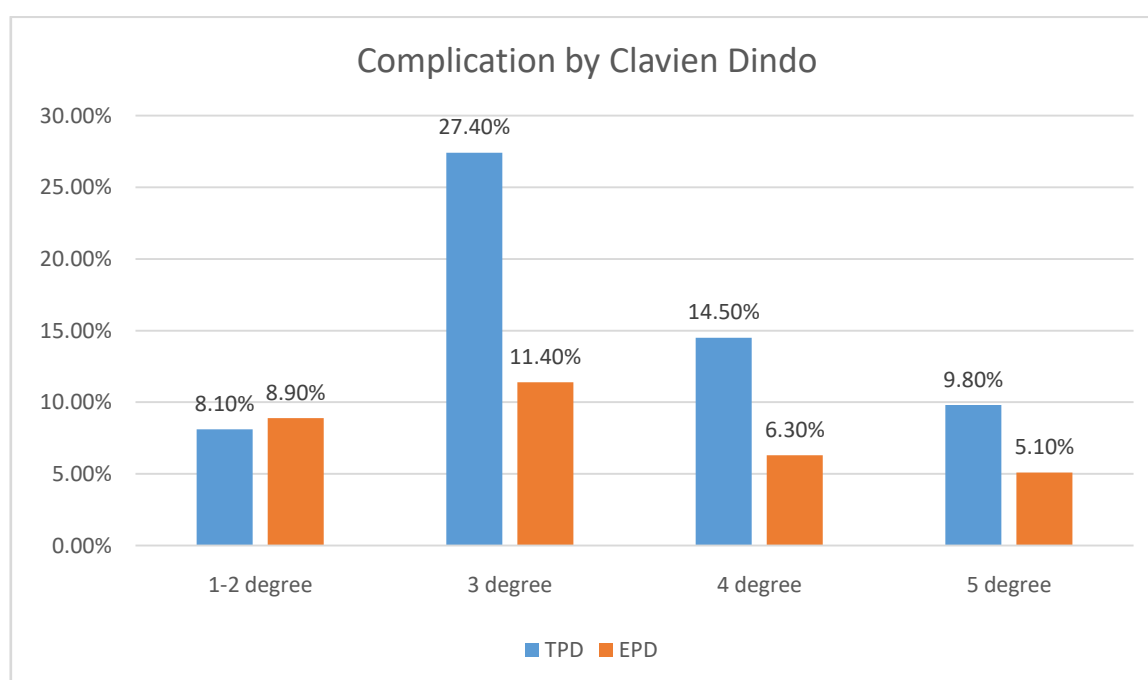
Early complications are shown in Table-2. 1 a patient from the EPD group died from a massive pulmonary embolism. Of the 3 postoperative deaths in the TPD group, 1 had a massive myocardial infarction, and 2 others died from sepsis.

	EPD group Min	TPD group min	P valueMann Whitney
Work time: RCIC (min) Avarage value (range)	142,1 (90-142)	127,5(75- 180)	0,70 *
Calculated blood lost (ml) Avarage value (range)	375 (210–2800)	320 (180- 3100)	0,39 *
Drainage removal (days)	5 (3-8)	9 (6-15)	0,33
Recovering of digestive tract (days)	2,5 (1-4)	5 (5-12)	0,34*
Stay in the hospital (days) mediana (IQR)	7 (6-14)	12 (9-24)	0,49*

The histopathology of the BC sample varied from T2 G3 n0 M0 to pT3aN2M0. Pathologically, 46% of patients in the EPD group and 53% of patients in the TTPD group had organ-limited disease. The volume of the removed lymph nodes was identical in both groups. The average number of removed lymph nodes was 2 (range 2-29) When observed in the EPD group, 4 patients developed local relapse, and 13 patients developed distant metastases. In the TPD group, local relapse developed in 5 patients, and 12 patients developed distant metastases. The difference was not statistically significant.

	EPD group	TPD group	P value in coffecient of Mann Whitney
Duration (months.) Avarage (Range)	71,6 (60-83)	69,9 (62- 78)	0,49 **
Local reccurence	4 (2,2%)	5 (3,2%)	0,59 *
Distant metastasis	13 (7,2%)	12 (7,6%)	0,89 *

Postoperative complications were divided into 2 groups: surgical and non-surgical. In total, surgical complications were observed in 36 patients (25.5%), of which 23 (37.1%) were patients with TP, and 13 (16.4%) cases in the group with EPD. Non-surgical complications were observed in 31(22%) patients, and there was no significant difference between the groups. Pyelonephritis was mainly observed in 21 (14.9%) patients, cardiovascular pathology in 3 (2.1%) patients, and pulmonary embolism (PE) was observed in 7 (4.9%) of the total number of patients studied. Depending on the severity of postoperative complications, we performed the analysis on the Clavien-Dindo scale, according to which in the general study group, postoperative surgical complications developed in 36 of 141 patients, which was 41.8%. At the same time, in the TPD group – 23 37.1%), in the group with EPD-13 (16.4%), $p < 0.05$.



Direct results of treatment of the studied patients in the comparative aspect

Complications	Group with TPD		Group with EPD	
	aŃc	%	aŃc	%
Local purulent septic complications	9	14,5	6	7,6
Peritonitis	4	6,5	2	2,5
Sepsis	1	1,6	0	0
Intra-abdominal bleeding	3	4,8	2	2,5
Stricture	0	0	1	1,3
Festering of incapsulated hematomas	0	0	1	1,3

Adhesive intestinal obstruction	6	9,7	1	1,3
In total	23	37,09±2,7	13	16,4±5,8*
Nonsurgical complications				
Pyelonephritis	10	16,1	11	13,9
Cardiovascular complications	2	3,2	1	1,3
Pulmonary artery thrombosis	3	4,8	4	5,0
In total	15	24,2	16	20,2

Intestinal obstruction developed in 3 and 14 patients in the EPD and TPD groups, respectively ($p = 0.002$); of these, only 4 of the TPD group required repeated surgery. Pelvic lymphocele (> 100 ml) was observed in 5 and 1 patients in the TPD and EPD groups, respectively ($p = 0.13$).

DISCUSSION

TPD using antegradetransperitoneal access is the gold standard in muscle-invasive bladder cancer. This access leads to peritoneal insufficiency in the pelvis and eliminates the natural separation (compartmentalization) between the gastrointestinal tract (GI) and the urinary tract, which leads to impaired peritoneal motility in 25% of patients [7]. Consequently, much attention has recently been paid to re-reperitonealization at the end of cystectomy to maintain gastrointestinal compartmentalization [8].

With this concept in mind, and in order to minimize manipulations with the intestine and eliminate such terrible complications as intestinal obstruction and adhesive disease in the postoperative period, we used extraperitoneal surgical access. Secondly, our technique allowed us to reduce surgical complications by 2 times. Third, due to the fact that we did not perform a laparotomy, there was an early recovery of peristalsis, which reduced postoperative intestinal obstruction.

Our study shows a statistically significant reduction in gastrointestinal complications, such as intestinal obstruction, in the EPRC group ($p < 0.05$). These results coincide with the data of various research groups, which also demonstrated similar results after repeated reperitonealization of the intestinal tract [9,10]

Mattei et al. [11] proved in their studies that colon peristalsis decreases in combination with high creatinine concentrations in the early postoperative phase after radical cystectomy.

Roth et al. [12] described a method for creating dorsolateral peritoneal flaps to restore the peritoneal cover.

Jagdeesh N. Kulkarni in his work showed that, opening the peritoneum at the end of the operation and its early suturing does not give serious complications, but still laparotomy and

contact of the abdominal cavity with air, in the near future is fraught with an adhesive process [13]. However, in our method, no adhesive changes were observed in the abdominal cavity.

Our data suggest that laparotomy of whatever size, the technique we used helps to prevent complications associated with the intestine. Moreover, it helps to reduce respiratory complications in the EPD group (4.4% vs. 8.2% in the TPD group, $p = 0.15$), since the upper half of the abdominal wall is not damaged.

The low rates of intestinal obstruction observed in the EPD group (3.1% vs. 9.7% in the TPD group, $p < 0.05$) can be explained by the fact that the operation was completely extraperitoneal without any effect on the nonperitoneal surface.

The frequency of pelvic lymphocele increased slightly in the EPD group versus in the TPD group, $p = 0.13$. Careful ligation and clipping of lymph vessels during pelvic node dissection has significantly reduced the number of lymphoceles in recent years.

Similar results were obtained in Özkaptan, Orkunt, et al [14] cancer safety has been a major concern for EPD. However, our data show that the frequency of local relapses and distant metastases was comparable between the two groups. The low frequency of metastases in our study can probably be explained by the significant number of patients with pathologically negative lymph node involvement ($> 91\%$ in both groups). Finally, our EPD technique is useful from the point of view that performance is evaluated at an early stage of the procedure, since most tumors are detected in the triangle area.

The overall rate of early complications observed in our study was relatively low. Early complications in different authors range widely from 16% to 66% [15]. The complications published in different studies have been described in detail in different ways, so it is difficult to compare them [16,17]. Our patient population had a relatively high comorbidity with a Charlson index > 3 of 42%, which partially explains the relatively low percentage of overall internal complications.

In the modern era of robotics, it is logical to expect the possibility of a robotic EPD. However, in the current da Vinci systems, the main limiting factor is the small working space in the pelvis, which prevents the movement of several robotic arms. With the future prospects of single-port robots with flexible arms, a robotic EPD, while challenging, may become feasible.

Due to the non-randomized nature of our study, based on a comparison of two cohorts of patients, further prospective randomized trials are needed to prove the real benefit of EPD.

CONCLUSION

Extraperitoneal technique (EPD) with extraperitonealization of the neoplasm is a safe and reliable surgical approach. It has tetrafunctional advantages from the point of view of reduction of intestinal obstruction, frequency of repeated operations, the problems with the stripes and adhesive disease. The extraperitoneal technique with radical cystectomy is comparable in safety and reliability to the transperitoneal surgical approach and gives good peri- and postoperative results according to the parameters studied by us. A significant reduction in

postoperative intestinal obstruction and adhesive disease is noteworthy. Thus, EPD is safe both functionally and oncologically.

Competing interests

The authors state that they have no competing interests.

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