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RESEARCH ARTICLE

Pelvic Exenteration for Recurrent Rectal Cancer: A Single Institution Experience

Rekürren Rektal Kanserlerde Pelvik Ekzantrasyon: Tek Merkez Deneyimi

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ABSTRACT

Aim: Rectal cancer is an important cause of cancer-related deaths worldwide (1-2). Although rectal cancers can be diagnosed earlier nowadays due to the development of screening programmes, 18% of patients have a locally advanced stage at the time of diagnosis (3). Despite the improvements in total mesorectal excision and oncological treatments, the locoregional recurrence rates vary between 6-10% in rectal cancer patients (4-5).
Method: The data of patients who underwent pelvic exenteration for recurrent rectal cancer in our clinic between January 2015 and December 2019 were retrospectively analysed.
Results: It was found that the patients with lymphovascular invasion (LVI) and perineural invasion (PNI) showed statistically poor survival rates (p=0.038/0.022). Two of the patients had a positive surgical margin and two others had a positive radial margin. There was no statistically significant difference between surgical margin positivity and prognosis (p>0.05). The mean number of metastatic lymph nodes was 4.0 (0-12), and the total number of lymph nodes was 12.35 (2-27). There was no statistically significant difference between patients with lymph node metastasis in terms of survival (p=0.079). Seven of the patients (41.1%) received systemic treatment before the surgery. It was statistically determined that the patients who received this treatment showed better survival rates (p=0.045).
Conclusion: It was found that pelvic exenteration had a positive effect on survival and local recurrence in recurrent rectal cancer, and that neoadjuvant therapy increased survival rates.
Keywords: Complication, pelvic exenteration, rectal cancer, recurrence, survival

ÖZ

Amaç: Rektal kanser tüm dünyada kansere bağlı ölümlerin önemli bir nedenidir (1-2). Günümüzde gelişen tarama programları ile birlikte rektal kanserlere daha erken tanı konulabilse de tanı anında hastaların %18'i lokal ileri evrededir (3). Total mezorektal eksizyon ve onkolojik tedavilerdeki gelişmelere rağmen rektum kanserli hastalarada lokorejyonel rekurrens oranları %6-10 arasında değişmektedir (4-5).
Yöntem: Kliniğimizde Ocak 2015-Aralık 2019 tarihleri arasında nüks rektum kanseri nedeniyle pelvik ekzantrasyon yapılan hastaların verileri retrospektif olarak inceledi.
Bulgular: Patoloji raporları incelendiğinde hastaların 10'unda (%58,8) lenfovasküler invazyon, 10'unda (%58,8) perinöral invazyon vardı. lenfovasküler invazyon ve perinöral invazyon olan hastaların istatistiksel olarak kötü sağkalım gösterdikleri saptanmıştır (p=0,038/0,022). Hastaların 2'sinde cerrahi sınır pozitif gelmiş olup, 2'si de radyal sınır pozitifliğiydi. Cerrahi sınır pozitifliği ile prognoz arasında istatistiksel olarak anlamlı fark yoktu (p>0,05). Metastatik lenf nodu sayısı ortalama 4,0 (0-12), toplam lenf nodu sayısı ortalama 12,35 (2-27) olarak bulunmuştur. Lenf nodu metastazı olan hastalarda sağkalım açısından istatistiksel olarak fark bulunmamıştır (p=0,079). Hastaların 7'si (%41,1) operasyon öncesi sistemik tedavi almıştır. Sistemik tedavi alan hastaların daha iyi sağkalım gösterdiği istatistiksel olarak saptanmıştır (p=0,045).
Sonuç: Nüks rektum kanserinde pelvik ekzantrasyon ve neoadjuvan tedavinin sağ kalımı artırdığı lokal nüksü azalttığı gözlenmiştir.
Anahtar Kelimeler: Komplikasyon, pelvik ekzantrasyon, rektum kanser, nüks, sağkalım

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Introduction

Rectal cancer is an important cause of cancer-related deaths worldwide.[1,2] Although rectal cancers can be diagnosed earlier nowadays due to the development of screening programmes, 18% of patients have a locally advanced stage at the time of diagnosis.[3] Despite the improvements in total mesorectal excision and oncological treatments, the locoregional recurrence rates vary between 6%-10% in rectal cancer patients.[4,5] Invasion to the genitourinary organs occurs in some patients with pelvic recurrence.[6,7] Pelvic recurrences may present with symptoms such as pain, tenesmus, dysuria and fistula that cannot be controlled by treatment.[8] The procedure of removing all tumour tissues in order to achieve negative surgical margins in the pelvis is called pelvic exenteration, which significantly contributes to survival in well-selected patient groups with a multidisciplinary approach.

This study aimed to present the outcomes of our patients who underwent pelvic exenteration for locoregional recurrence and to determine the prognostic factors.

Materials and Methods

Data of patients who underwent pelvic exenteration for recurrent rectal cancer in our clinic between January 2015 and December 2019 were retrospectively analysed. Patients with a pelvic recurrence who developed systemic metastasis were not operated. The site of local recurrence and presence of a distant metastasis in all patients were evaluated by magnetic resonance imaging (MRI) and computed tomography (CT). Preoperative colonoscopy was performed on the patients to locate the tumour site, and cystoscopy was performed on patients with suspected bladder invasion. A total of 17 patients who met these criteria were included in the study. The patients' surgery types and pathology reports, demographic features, length of hospital stay, reasons for re-admission, postoperative complications, postoperative mortality, total and disease-free survival were examined. The radiological examinations (chest X-ray, CT, ultrasonography, endoultrasonography, MRI, positron emission tomography) were reviewed by retrospectively scanning the patients' data. The 8th edition of the TNM classification was used for staging. Ethics committee approval was obtained from our institute. All patients were operated by the same surgical team. Informed consent was obtained from the patients in the preoperative period. The patients underwent bowel cleansing using laxatives and enemas a day before the surgery, and a single-dose prophylactic antibiotic (cefazolin 2 gr) was administered preoperatively. The patients underwent total pelvic exenteration (TPE). TPE is defined as the removal of the genitourinary and reproductive organs including the rectum, distal colon, distal ureters and the lymph nodes draining these, as well as the pelvic peritoneum, and this procedure can be performed in combination with sacrectomy. Afterwards, reconstructions such as lower anastomoses instead of permanent ileostomy, new vagina due to sexual dysfunction, urinary diversion (new bladder or supravesical urinary diversion) and flap-grafts to close the pelvic floor defects can be performed in order to increase the quality of life.

Statistical Analysis

Data analysis was done using SPSS 11.5 software. For descriptive statistics, quantitative variables were presented as mean ± standard deviation and median (minimum-maximum), and qualitative variables were presented as number of patients (percentage). A survival analysis was performed using the Kaplan-Meier method through qualitative and quantitative variables and the log-rank test was used to determine significant differences between the groups. The level of statistical significance was set at 0.05.

Results

Of the patients, 9 (52.9%) were females and 8 (47.1%) were males. The mean age of the patients was 53.4±10.1 years. TPE was performed on all the patients, of whom, 6 (35.3%) had lower, 7 (41.2%) had middle, and 4 (23.5%) had upper rectum localisation, and there was no significant correlation between the survival of the patients and tumour localisation ($p>0.05$). We had performed a low anterior resection for all patient for the initial surgery and all surgical margins were clear. Of the patients, 12 (70.5%) had taken neoadjuvant chemoradiotherapy before the initial surgery. When classified according to T-stage, three patients were T2 (11.7%), five patients were T3 (29.4%), three patients were T4a (11.7%) and six patients were T4b (35.2%). It was observed that survival decreased as the T-stage increased ($p<0.001$). N was positive in 11 (64.7%) and N was negative in 6 (35.3%) patients. Mortality was found to be high in patients with N positive results and was statistically significant ($p<0.05$). There was no statistical significance in terms of overall survival, disease-free survival and deficit conversion ($p>0.05$). The mean follow-up duration was 16 months (1-50 months), and considering overall survival, 8 (47.1%) of 17 patients survived, while 9 (52.9%) died. The mean survival time was 23.8 months. Three of the patients (11.7%) developed recurrence, and all recurrences occurred in the pelvic region as a local recurrence. The mean length of hospital stay was 18.1±11.5 days. The patient characteristics are shown in Table 1.

The surgical indication was vaginal invasion in 5 (29.4%) patients, bladder invasion in 11 (64.7%) patients and uterine

invasion in 1 (5.8%) patient. The mean operative time was 200.8±9.2 min. Of the patients, five developed an infection, one developed an ileal conduit leak and one developed postoperative early bleeding. There was no statistically significant correlation between complication development and survival in the patients (p>0.05). Only the patient who developed an ileal conduit leak required reoperation, while the other patients were treated conservatively. Seven patients were readmitted to the hospital for infection, one patient for acute renal failure and three patients for deterioration of the general condition, and the causes of infection were pyuria[2], intra-abdominal collection[4] and wound infection.[1]

When the pathology reports were examined, 10 (58.8%) of the patients had lymphovascular invasion (LVI) and 10 (58.8%) had perineural invasion (PNI). It was found that the patients with LVI and PNI showed statistically poor survival rates (p=0.038/0.022). Of the patients, two had a positive surgical margin and two had a positive radial margin. There was no statistically significant difference between surgical margin positivity and prognosis (p>0.05). The mean number of metastatic lymph nodes was 4.0 (0-12), and the total number of lymph nodes was 12.35 (2-27). There was no statistically significant difference between patients with lymph node metastasis in terms of survival (p=0.079).

Seven of the patients (41.1%) received chemoradiotherapy before pelvic exenteration. In accordance with the multidisciplinary team decision, 10 (58.9%) of the patient did not receive chemoradiotherapy before pelvic exenteration. It was statistically determined that the patients who received this treatment showed better survival rates (p=0.045).

According to the Kaplan-Meier analysis, the one-year and 2-year survival rate was 74% and 26%, respectively. It was statistically shown that the patients who had 12 months or less between the initial operation and pelvic recurrence had worse survival rates than those who had more than 12 months between the initial operation and pelvic recurrence (p=0.001). Table 2 presents the univariate analysis results that were suggested to affect survival, and the probability of the 1- and 2-year survivals related to these results.

Table 1. Patient characteristics

Age	**53.47±10.16**	
Total number of lymph nodes removed	12.35±1.77	
Number of metastatic lymph nodes	4.00±0.94	
Survival time (months)	23.83±5.07	
Lymphovascular invasion	Yes	10 (58.8)
	No	7 (41.2)
Perineural invasion	Yes	10 (58.8)
	No	7 (41.2)
Recurrence	Yes	3 (17.6)
	No	14 (82.4)
Operative time (min)	200.88±9.27	
Preoperative systemic treatment	Yes	7 (41.2)
	No	10 (58.8)
Length of hospital stay (days)	18.12±2.80	
Reason for re-admission	Infection	7 (63.8)
	ARF	1 (9)
	Deterioration of general condition	3 (27.2)

Min: Minimum, ARF: Acute rheumatic fever

Table 2. Survival analyses

		1 year (%)	2 years (%)	Survival time	p
Overall		74.0	26.9	23.83±5.07	-
Neoadjuvant therapy	No	63.5	19.5	14.06±2.77	0.045
	Yes	85.7	64.3	36.64±7.74	
LVI	No	80.0	80.0	41.20±7.87	0.038
	Yes	70.0	16.7	14.70±2.55	
PNI	No	83.3	83.3	42.66±6.69	0.022
	Yes	57.1	15.2	14.32±2.56	
Metastatic lymph node	No	75.0	50.0	39.00±9.52	0.079
	Yes	72.7	13.6	17.18±3.15	
Sex	Female	55.6	27.8	21.52±6.52	0.507
	Male	27.8	0	20.66±2.37	

PNI: Perineural invasion, LVI: Lymphovascular invasion

Discussion

Pelvic exenteration was first described in 1948 in Brunschwig pelvic malignancies as the en bloc resection of pelvic organs.[9] Although the mortality rates have been shown to be 20-30% for many years, this rate has dropped to <10% due to the improvements in the surgical technique, intensive care and anaesthesiology.[10,11,12,13]

Rectal cancer surgery is particularly challenging in lower rectal tumours and in patients having a narrow pelvis. Despite all the advances in the surgical technique, the locoregional recurrence rates in colorectal cancer vary between 6%-10%.[4,5] The vast majority of recurrences occur within the first three years after surgery, and when these patients are left untreated, the prognosis varies between 6-8 months.[14] Patients whose tumour is limited to the pelvis and who do not have distant metastasis are eligible for pelvic exenteration. However, pelvic exenteration can be performed in combination with metastasectomy in a group of patients with resectable distant liver and lung metastases.[7,15,16] Resectability should be determined by preoperative imaging, including CT, MRI and positron emission tomography. Siatic nerve invasion, external iliac artery invasion, paraaortic lymph node involvement and lymphoedema as a finding of venous or lymphatic infiltration in the lower extremity are considered contraindications for pelvic exenteration.[17] TPE is defined as the removal of the genitourinary and reproductive organs including the rectum, distal colon, distal ureters and the lymph nodes draining them as well as the pelvic peritoneum and can be performed in combination with sacrectomy. Anterior pelvic exenteration is the resection of the reproductive organs, upper rectum and bladder by preserving the lower part of the rectum. Posterior pelvic exenteration is defined as the resection of the rectum and reproductive organs by preserving the bladder. In our study, all of the patients underwent TPE.

Despite the high mortality and morbidity rates, pelvic exenteration is associated with increased survival in recurrent rectum tumours. In their systemic review, Heriot et al.[18] showed that pelvic exenteration increased survival with an acceptable morbidity rate and found that the cancer-specific survival rate was increased and local recurrence was significantly reduced by neoadjuvant or adjuvant chemoradiotherapy. Domests et al.[19] found a 30-day mortality rate of 3.6%, 3-year disease-free survival rate of 52.2% and 3-year overall survival rate of 75.1%. In our study, the 30-day mortality rate was 5.8%, 1- and 2-year overall survival rates were 74% and 26.4%, respectively. Our 1- and 2-year disease-free survival rates were 67.3% and 40.4%, respectively. We think that the reason for the lower survival time in our study is due to the inclusion of only patients who developed recurrences, the short follow-up period and small number of patients.

In the literature, many factors such as positive surgical margin, neoadjuvant therapy, number of metastatic lymph nodes, lymphovascular invasion and perineural invasion have been identified to be effective in determining survival after pelvic exenteration, and among these, R0 resection has been shown to be the most important prognostic factor.[19,20,21,22,23] However, in their study, Kakuda et al.[24] found no difference between patients who underwent R1 resection and those who underwent R0 resection in terms of overall survival rates (23-18 months p=0.67). In our study, the radial surgical margin was positive in two patients and the effect of surgical margin positivity on survival could not be demonstrated (p>0.05). While the effect of lymph node positivity on survival has been demonstrated in many studies[22,23,24,25], the effect of lymph node positivity on survival could not be demonstrated in the present study. We think that the reason for this is our small number of patients and short follow-up time. In our study, the factors affecting survival rates were found to be the time from the initial operation to pelvic recurrence, lymphovascular invasion, perineural invasion and neoadjuvant therapy (p=0.001, p=0.038, p=0.022, p=0.045).

In patients undergoing pelvic exenteration, a second surgery may be required for reasons such as adhesion due to primary surgery and fibrosis due to radiotherapy, resulting in the prolongation of the operative time, increase in postoperative complications and prolonged length of hospital stay. In a systemic review including 23 studies, the researchers found the complication rates after pelvic exenteration as 37%-100%.[26] In our study, the complication rate was 41.1%, and most of these patients developed wound infection. Reoperation was performed on one patient for postoperative bleeding and in one patient for ileal conduit leak. In the literature, there are prolonged operative times.[20] In our study, the mean operative time was recorded as 200.88±9.27 min. We think that the operative time in this study is shorter than those reported in the literature because all the surgical interventions were performed by the same team of experienced professionals.

Radiological studies are unable to determine whether invasion to the genitourinary organs is due to inflammation or tumour invasion in 20%-56% of patients undergoing pelvic exenteration.[27,28] In our series, 29.4% of the patients did not show tumour invasion to the genitourinary organs.

Although pelvic exenteration provides a high level of local control in recurrent rectal cancers, the rate of recurrence after pelvic exenteration ranges from 4.8%-61% (average 22%) in the literature.[26] In our study, three of all patients developed local recurrence (11.7%), which is consistent with the literature.

Conclusion

In conclusion, it was found that pelvic exenteration had a positive effect on survival and local recurrence in recurrent rectal cancer, and that neoadjuvant therapy increased survival rates.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, approval was obtained from the Ethics Committee of Ankara Dr. Abdurrahman Yurtaslan Oncology Health Application and Research Center (decision no: 95, date: 27.05.2020).

Informed Consent: Obtained.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Concept: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Design: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Data Collection or Processing: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Analysis or Interpretation: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Literature Search: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Writing: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D.

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