Total pelvic exenteration for rectal cancer: outcomes and prognostic factors

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Background: To perform complete resection of locally advanced and recurrent rectal carcinoma, total pelvic exenteration (TPE) may be attempted. We identified disease-related outcomes and prognostic factors.

Methods: We conducted a single-centre review of patients who underwent TPE for rectal carcinoma over a 10-year period.

Results: We included 28 patients in our study. After a median follow-up of 35 months, 53.6% of patients were alive with no evidence of disease. The 3-year actuarial disease-free and overall survival rates were 52.2% and 75.1%, respectively. On univariate analysis, recurrent disease, preoperative body mass index greater than 30 and lymphatic invasion were poor prognostic factors for disease-free survival, and only lymphatic invasion predicted overall survival. Additionally, multivariate analysis identified lymphatic invasion as an independent poor prognostic factor for disease-free survival in this patient population with locally advanced and recurrent rectal carcinoma.

Conclusion: Despite the significant morbidity, TPE can provide long-term survival in patients with rectal carcinoma. Additionally, lymphatic invasion on final pathology was an independent prognostic factor for disease-free survival.

Contexte : Pour pratiquer une résection complète du cancer du rectum avancé au stade local et récidivant, on peut tenter une exentération pelvienne totale (EPT). Nous avons déterminé des résultats liés à la maladie et des facteurs de pronostic.

Méthodes : Nous avons procédé à une étude unicentrique portant sur des patients qui ont subi une EPT pour un cancer du rectum au cours d'une période de 10 ans.

Résultats : Nous avons inclus 28 patients dans notre étude. Après un suivi médian de 35 mois, 53,6 % des patients étaient vivants et ne présentaient aucun signe de maladie. Les taux actuariels de survie sans maladie et de survie globale à 3 ans s'établissaient à 52,2 % et 75,1 % respectivement. Une analyse unidimensionnelle a révélé que la maladie récidivante, un indice de masse corporelle préopératoire de plus de 30 et l'envahissement du système lymphatique étaient des facteurs de pronostic médiocre de survie sans maladie et seul l'envahissement du système lymphatique prédisait la survie globale. En outre, l'analyse multidimensionnelle a déterminé que l'envahissement du système lymphatique constituait un facteur indépendant de pronostic médiocre de survie sans maladie dans cette population de patients atteints de cancer du rectum avancé au stade local et récidivant.

Conclusion : En dépit de la morbidité importante, l'EPT peut assurer une survie à long terme chez les patients atteints de cancer du rectum. De plus, l'envahissement du système lymphatique au moment de l'examen pathologique final constituait un facteur indépendant de pronostic de survie sans maladie.

Rectal carcinoma is a major cause of cancer-related death in Canada.[1] Although most cases of rectal carcinoma are now diagnosed at an earlier stage, partially owing to screening efforts, about 18% of cases are clinically diagnosed as locally advanced with evidence of tumours beyond the confines of the bowel wall.[2] In addition, about 5% of rectal carcinoma tumours are found to invade the urinary tract.[3] With the advent of total mesorectal excision for rectal carcinoma, several studies have demonstrated that negative surgical margin status is the most important prognostic factor for disease-free survival.[4–6] Patients with operable locally advanced or recurrent rectal carcinoma involving contiguous pelvic organs are considered for en-bloc excision of pelvic viscera "total pelvic exenteration" (TPE) to obtain negative margin

status in the hopes that the same impact on disease-free survival will be observed.

Total pelvic exenteration was first described in 1948,[7] and it involves the en-bloc removal of the pelvic viscera in patients with advanced pelvic malignancy. As a consequence, most patients postoperatively have 2 ostomies, 1 for stool and 1 for urine, although surgical reconstruction of the gastrointestinal and/or genitourinary tract to eliminate ostomies has been described in this population.[8,9] Perioperative mortality rates historically were as high as 20%–30%,[10,11] but more recent reports demonstrate rates less than 10%,[12,13] likely owing to improved health care and surgical technology. Despite reductions in mortality, postoperative morbidity is high, ranging from 22%[14] to 78%[12] in recent series. Although highly efficacious,[15–17] it is controversial whether the increased use of neoadjuvant chemoradiation therapy in locally advanced operable rectal carcinoma contributes significantly to postoperative morbidity.[18,19] In the face of disparate data regarding the morbidity associated with this procedure, we wanted to provide detailed analysis of morbidity and survival of patients with rectal carcinoma who underwent TPE. We sought to identify disease- and patient-specific factors that might indicate what patients would receive maximal benefit from such aggressive treatment.

Methods

We reviewed the cases of patients who underwent TPE for locally advanced or recurrent rectal carcinoma at our centre between October 1997 and December 2007. Instead of a general review of all patients with locally advanced and recurrent rectal carcinoma who may have underwent other extirpative surgeries, we focused on the patients undergoing TPE specifically because we wanted to highlight the complications and clinical outcomes unique to this procedure. After obtaining institutional ethics review board approval, we conducted a retrospective review of patient medical records, focusing on patient demographics, operative findings, pathological findings, postoperative morbidity, perioperative (30-d) mortality, and disease-free and overall survival.

Statistical analysis

We performed statistical analyses using SPSS software version 16.0 (SPSS Inc.). Noncategorical variables were analyzed and compared using the Student *t* test, and categorical variables were analyzed and compared using the χ^2 test. We calculated cumulative survival rates according to the Kaplan–Meier method, and we performed univariate analyses using the log-rank test. Variables tested in univariate analysis included recurrent versus primary disease, age older than 55 years, BMI greater than 30, tumour size greater than 5 cm, preoperative stage, use of neoadjuvant therapy, surgical margin status and lymphatic invasion on final pathology. Multivariate analyses involved forward conditional stepwise Cox regressional analysis. Only variables statistically significant on univariate analysis were included in the multivariate equation (recurrent disease, lymphatic invasion and BMI > 30).

Results

Participants

During the study period, 28 patients underwent TPE for locally advanced or recurrent rectal carcinoma at our centre. Patient demographic and clinical characteristics are outlined in Table 1. The median patient age at time of TPE was 61 (range 34–77) years. Comorbidities included hypertension (25.0%), diabetes (10.7%), obesity (BMI > 30; 25.0%) and positive smoking history (35.7%). All patients were evaluated with history; physical examination; routine blood work, including liver function tests and carcinoembryonic antigen levels; chest radiography; colonoscopy with biopsy; and computed tomography (CT) scanning of the abdomen and pelvis to determine the patient's pretreatment

Table 1. Clinical characteristics of 28 patients who underwent total pelvic exenteration for colorectal cancer

Characteristic	No. (%)
Age, yr	
≤ 55	9 (32.1)
> 55	19 (67.9)
Sex	
Male	25 (89.3)
Female	3 (10.7)
Tumour status	
Primary	24 (85.7)
Recurrent	4 (14.3)
Tumour location (primary only)	
Upper rectum	11 (45.8)
Mid rectum	7 (29.2)
Lower rectum	6 (25.0)
Pretreatment clinical stage	
II	21 (75.0)
III	5 (17.9)
IV	2 (7.1)
Pathological tumour size, cm	
≤ 5	10 (35.7)
> 5	18 (64.3)
Neoadjuvant chemoradiation	
Yes	23 (82.1)
No	5 (17.9)
Preoperative comorbidities	
Hypertension	7 (25.0)
Diabetes	3 (10.7)
Smoking	10 (35.7)
Obesity (BMI > 30)	7 (25.0)

BMI = body mass index.

clinical stage. The location of the primary tumour was recorded based on the preoperative opinion of the surgeon. Cystoscopy, magnetic resonance imaging (MRI) and positron emission tomography were performed on a case-by-case basis.

The pretreatment clinical stage was consistent with locally advanced rectal carcinoma in 24 patients and the remaining 4 patients had locally recurrent disease. Two patients had documented liver metastatases before TPE and underwent concomitant liver metastectomy along with TPE. Neoadjuvant chemoradiation therapy was administered in 23 (82.1%) patients. Nineteen (67.9%) patients had adjuvant chemotherapy at some time during their treatment course.

Operative findings

The mean operative time required for TPE was 503 (standard deviation [SD] 115) minutes. The mean operative time in obese (BMI > 30) patients was not statistically different than that in nonobese patients (mean 509 [SD 141] min v. mean 500 [SD 109] min). The mean blood loss was 1405 (SD 895) mL, with 7 (25.0%) patients having lost less than 1000 mL of blood during the procedure. For urinary diversion, an ileal conduit was created in 23 (82.1%) patients and a colon conduit was created in the remaining 5 (17.9%) patients. All patients had construction of a colostomy.

Pathological findings

Of the 24 patients who had a primary carcinoma, 17 (70.8%) had ypT4, 5 (20.8%) had ypT3 and 2 (8.3%) had ypT2 lesions on pathological analysis. The 2 patients with ypT2 lesions had significant tumour downsizing after neoadjuvant chemoradiation therapy, in which pretreatment MRI demonstrated infiltration into the adjacent seminal vesicles and bladder, respectively. Analysis of all patient specimens demonstrated a mean tumour size of 6.1 cm. All tumours were adenocarcinomas with the following histologic subtypes: 3 (10.7%) specimens were well differentiated, 14 (50%) moderately differentiated, 6 (21.4%) poorly differentiated and 5 (17.9%) were mucinous. Pathological invasion of the genitourinary organs was seen in 17 (60.7%) specimens, lymphatic invasion was demonstrated in 8 (28.6%) and negative surgical margins were achieved in 21 (75.0%) specimens. Five (17.9%) patients had regional lymph node metastases.

Table 2. Comparing patient, disease and treatment factors for primary versus recurrent disease

Variable	Recurrent disease, $n = 4$	Primary disease, $n = 24$	p value
BMI, mean (SD)	28.9 (6.6)	26.2 (4.3)	0.29
Tumour size, mean (SD)	5.1 (3.2)	6.2 (3.1)	0.51
Preoperative stage IV	1/4	1/24	0.13
Neoadjuvant chemoradiation	4/4	19/24	0.31
Positive surgical margins	1/4	6/24	1.00

BMI = body mass index; SD = standard deviation.

Comparing patient, disease and treatment factors for primary versus recurrent disease

There were no statistically significant differences in mean preoperative BMI, mean tumour size, presence of metastases preoperatively, use of neoadjuvant chemoradiation therapy or surgical margin status between patients with primary or recurrent rectal cancer (Table 2).

Morbidity

Total pelvic exenteration was associated with significant postoperative morbidity (Table 3). Ten patients required at least 1 subsequent operative procedure (excluding percutaneous drains) for postoperative complications; 2 patients required 3 surgeries each and 3 patients required 2 surgeries each. We noted that patients with a BMI greater than 30 had a statistically higher rate of wound dehiscence (2 of 7 obese patients v. 0 of 21 nonobese patients, $p = 0.010$) and exhibited a trend toward estimated blood loss greater than 1000 mL (7 of 7 obese patients v. 14 of 21 nonobese patients, $p = 0.08$). No other postoperative morbidities were observed with increased frequency in the obese patient population. There was 1 perioperative (30-d) death due to sepsis and multiple system organ failure.

Follow-up and survival

At a median follow-up of 35 (range 1–147) months after TPE, 15 (53.6%) patients had no evidence of disease; 4 (14.3%) were alive with disease recurrence, and 9 (32.1%)

Table 3. General and urologic morbidities among 28 patients who underwent total pelvic exenteration for colorectal cancer

Morbidity	No. (%)	No. procedures required
General		
Wound infection	10 (35.7)	1 surgery
Small bowel obstruction	9 (32.1)	4 surgeries
Pelvic abscess	7 (25.0)	1 surgery, 6 drains
Perineal fistula	4 (14.3)	2 surgeries
Wound dehiscence	2 (7.1)	2 surgeries
Delayed mesenteric bleed	1 (3.6)	1 surgery
Urologic		
Recurrent UTIs/pyelonephritis	17 (60.7)	0 procedures
Urostomy stenosis	3 (10.7)	1 surgery
Urine leak (conduit)	3 (10.7)	2 surgeries, 1 drain
Urine leak (ureterointestinal anastomosis)	2 (7.1)	1 surgery, 1 drain
Ureteric stricture	2 (7.1)	2 surgeries

UTI = urinary tract infection.

patients had died due to progression of rectal cancer. In the 2 patients with a documented liver metastasis and metastectomy at the time of TPE, 1 was recurrence-free after 17 months of follow-up and 1 was alive but had new liver metastases 20 months after resection. Our actuarial 3-year disease-free survival rate was 52.2% and the 3-year overall survival rate was 75.1% (Fig. 1).

Prognostic factors for disease-free and overall survival

Univariate analysis demonstrated 3 statistically significant poor prognostic factors for disease-free survival: TPE for recurrent disease (p = 0.010; Fig. 2), BMI greater than 30 (p = 0.035) and lymphatic invasion on final pathological analysis (p < 0.001; Fig. 3). Only lymphatic invasion was statistically significant as a poor prognostic factor for overall survival on univariate analysis (p = 0.012). Multivariate analysis identified only lymphatic invasion (p < 0.001, hazard ratio 7.9, 95% confidence interval 2.4–26.7) as an independent poor prognostic factor for disease-free survival. Clinical stage, surgical margin status, time period (1997–2001 v. 2002–2007) and use of neoadjuvant or adjuvant therapies did not have a statistically significant impact on prognosis in this study.

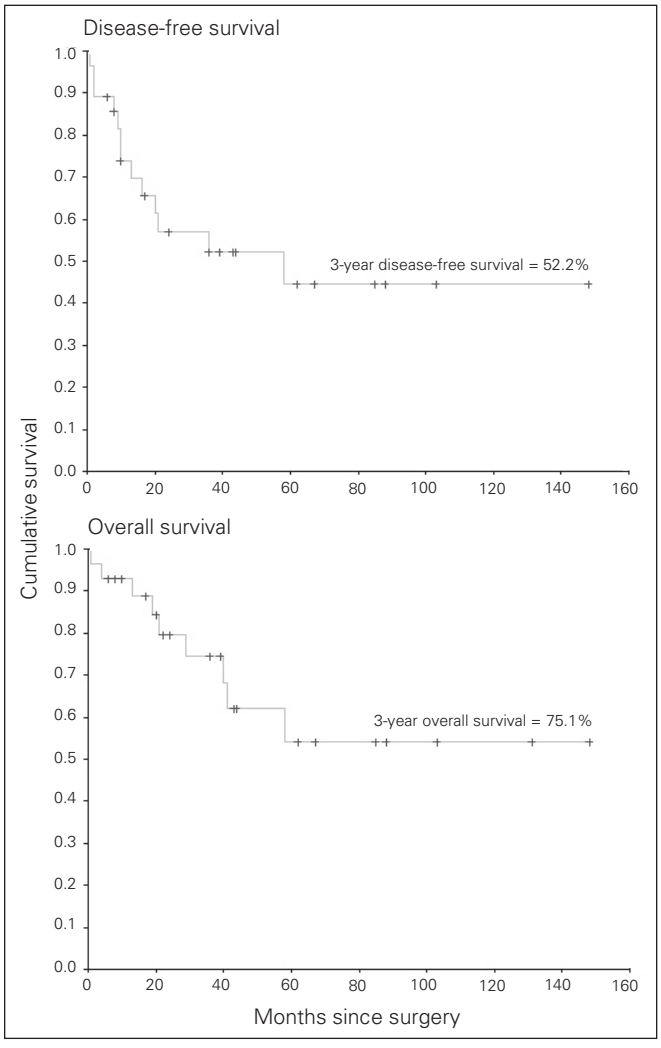

Fig. 1. (**A**) Cumulative disease-free survival for the entire cohort (n = 28) treated with with total pelvic exenteration (TPE). (**B**) Cumulative overall survival for the entire cohort (n = 28) treated with TPE.

Discussion

Total pelvic exenteration was first developed mainly for palliation of advanced pelvic malignancy but now exists within the armamentarium of the gynecologist, urologist and general surgeon alike. In tertiary care centres, these procedures are often performed by multidisciplinary

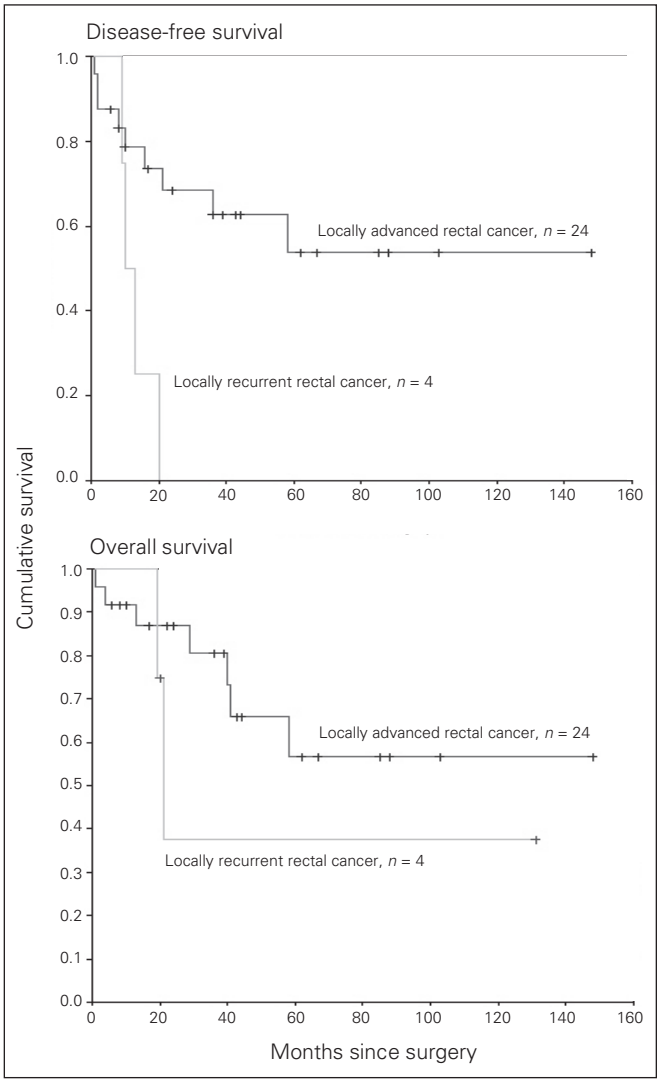

Fig. 2. (**A**) Disease-free survival in patients with locally recurrent (n = 4) and locally advanced (n = 24) rectal cancer. Patients with locally advanced rectal cancer had improved disease-free survival on univariate analysis (p = 0.010). (**B**) Overall survival in patients with locally recurrent and locally advanced rectal cancer with no statistically significant differences identified between the groups.

pelvic oncology teams, whereby subspecialization and collaboration have been shown to be very successful for a variety of pelvic malignancies.[20] When first described by Brunschwig in 1948,[7] the perioperative mortality for TPE was more than 23%, and there were no long-term survivors. Over the last 60 years, important health care advances have made TPE and other procedures for rectal carcinoma much safer and efficacious.[21] Reviewing contemporary studies of patients undergoing TPE for locally advanced or recurrent rectal carcinoma (Table 4) demonstrates this trend, with low perioperative mortality and greatly improved survival rates. Our perioperative mortality of 3.6% and 3-year disease-free and overall survival rates of 52.2% and 75.1%, respectively, are comparable to those reported in the literature and reiterate the potential for long-term survival and cure with this surgery despite its inherent morbidity.

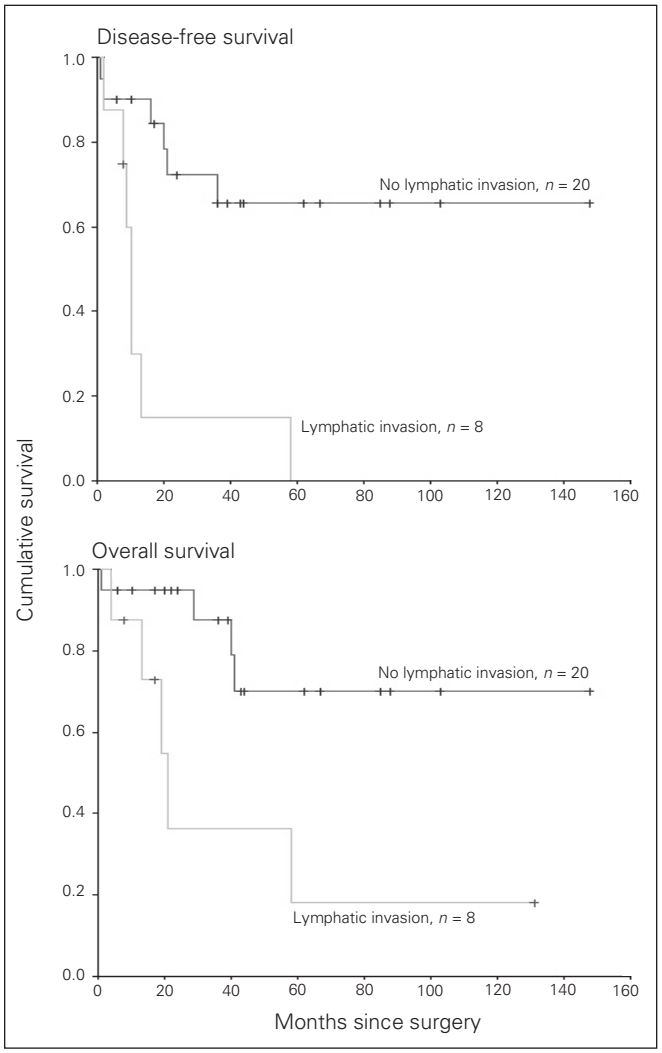

Fig. 3. (**A**) Disease-free survival in patients with (n = 8) and without (n = 20) lymphatic invasion on final pathology. Patients without lymphatic invasion had improved disease-free survival on univariate ($p < 0.001$) and multivariate analysis ($p < 0.001$). (**B**) Overall survival in patients with and without lymphatic invasion on final pathology. Patients without lymphatic invasion had improved overall survival on univariate analysis ($p = 0.012$).

Morbidity, particularly morbidity requiring a subsequent surgical procedure, was substantial in our patient population undergoing TPE. Ten (35.7%) patients required a subsequent surgical intervention for a postoperative complication, which may be explained by the inclusion of remote complications in our analysis (e.g., the requirement of a laparotomy for a small bowel obstruction owing to intra-abdominal adhesions). This rate is somewhat higher than that reported in the literature, although a similar recent study noted a surgical reintervention rate of 27% owing to complications.[29] The practice at our centre is for both the colorectal surgeon and urologist to follow patients postoperatively. The continuing urologic care is important to screen for complications associated with urinary diversions, such as silent urinary obstruction and deterioration in renal function. Even with this diligent follow-up, the postoperative urologic complication rate was similar to that reported in a larger series from the Memorial Sloan–Kettering Cancer Center, where the reported rate of significant urologic complications following TPE was 17%.[23] Patients with rectal carconima who require removal of the bladder have higher complication rates, as outlined by Fujisawa and colleagues,[30] whose patients underwent bladder-sparing surgery for locally advanced rectal carcinoma and had a postoperative morbidity of 10.5%; the rate increased to 58.3% if cystectomy was required.

Even with advances in diagnostics and neoadjuvant therapies, the final decision to proceed with an exenteration can only be made at the time of laparotomy when it is still often impossible to distinguish between inflammatory and

Table 4. Contemporary series of total pelvic exenteration for rectal cancer

Study	No.	Primary or recurrent	Perioperative mortality, %	Survival, %
Jimenez et al.[12]	55	Both	5.5	40.0 (5-yr DFS)
Hida et al.[14]	50	Primary	6.0	64.0 (5-yr OS)
Meterissian et al.[22]	40	Both	0	49.0 (5-yr OS)
Russo et al.[23]	47	Both	2.0	34.0 (3-yr DFS)
Ike et al.[24]	45	Recurrent	13.0	14.0 (5-yr OS)
Ike et al.[25]	71	Primary	1.4	
T3				66.0 (5-yr OS)
T4				39.0 (5-yr OS)
Takeuchi et al.[26]	15	Primary	N/A	54.7 (5-yr OS)
Vermaas et al.[27]	35	Both	3.0	
Primary				52.0 (5-yr DFS)
Recurrent				32.0 (3-yr DFS)
Gannon et al.[34]	72	Both	0	48.0 (5-yr OS) 38.0 (5-yr DFS)
Wells et al.[28]	52	Recurrent	0	41.0 (4-yr OS) 27.0 (4-yr DFS)
Present study	28	Both	3.6	75.1 (3-yr OS) 52.1 (3-yr DFS)

DFS = disease-free survival; N/A = not available; OS = overall survival.

malignant adhesions between organs. In these cases, intraoperative frozen-section analysis may be misleading, especially in patients who have previously undergone pelvic radiation.[31] Our study demonstrated that about 40% of patients undergoing TPE did not have histologic tumour infiltration of adjacent genitourinary organs owing to the uncertainty of being able to fully resect the tumour safely or to the risk of tumour spill. This finding is consistent with the literature, which reports that 20%[14]–56%[32] of TPE tumour specimens did not infiltrate the genitourinary organs.

Determining which patients with locally advanced rectal carcinoma will benefit from TPE has remained a challenge. Multiple retrospective studies have identified prognostic factors associated with improved outcomes in patients undergoing TPE that are mainly consistent with the known prognostic factors for rectal cancer in general, including tumour stage,[25] presence of nodal metastases[25,33] and positive surgical margins.[12,27] Our study did not identify these factors as statistically significant, possibly owing to inadequate sample size or bias in this or other studies. For example, in the study by Ike and colleagues,[25] all patients underwent an extended lymphadenectomy, and about 60% of the patients undergoing TPE had positive lymph nodes; this rate is substantially higher than that in our study and may have biased the results.

We identified 3 poor prognostic factors for disease-free survival by univariate analyses: recurrent disease, preoperative BMI greater than 30 and lymphatic invasion.

Patients undergoing TPE for recurrent disease were shown to have worse outcomes in 3 previous studies.[12,27,34] These 3 studies included a greater percentage than ours of patients who required reoperation owing to recurrent disease, but statistical significance was still demonstrated despite our small sample size. In addition, the patients with recurrent rectal carcinoma were similar to those with primary disease with respect to many other known prognostic factors, indicating that the difference in disease-free survival is not likely accounted for by other factors. Despite this finding, aggressive surgical approaches to resect locally recurrent rectal carcinoma should be undertaken in properly selected patients. The University of Toronto cancer centres recently published their series focusing on this patient population.[28] They demonstrated that en-bloc resection (including sacrectomy in 54% of patients) provided a 4-year overall survival rate of 48% in patients who underwent resection with curative intent. Their patients with a negative margin had statistically significant improvement in disease-free survival.

Interestingly, a BMI greater than 30 was also a poor prognostic factor on univariate but not multivariate analysis. A large prospective trial has linked obesity with a 1.5- to 1.8-fold increased risk of colorectal cancer (colorectal carcinoma) mortality.[35] Conversely, a recent prospective randomized chemotherapy trial of 1053 patients with stage-III colorectal carcinoma demonstrated that neither BMI nor weight change was associated with an increased risk of cancer recurrence or death.[36] Interestingly, poor prognostic associations between obesity and other types of tumours have been established.[37–39] Although our study was not designed to assess the association between elevated BMI and worse locally advanced rectal cancer treatment outcomes, the controversial effects of obesity and outcomes of colorectal carcinoma treatment requires further study.

Lymphatic invasion was the strongest poor prognostic factor identified in our study, with statistical significance for disease-free survival (univariate and multivariate analyses) and overall survival (univariate analysis). Defined as a "category I" prognostic factor by the College of American Pathologists,[40] lymphatic invasion is a known prognostic factor in the colorectal carcinoma population.[41–43]

Limitations

Our study has limitations, including its retrospective nature, relatively small sample size and the heterogeneous inclusion of patients with primary and recurrent rectal carcinoma and 2 patients with liver metastases who underwent metastectomy. In addition, pathological analysis was performed by multiple pathologists over the 10-year study period. A recent study by Harris and colleagues[44] demonstrated that there may be significant interobserver variability in the interpretation of lymphatic invasion, although the future use of monoclonal antibodies to D2–40, a specific lymphatic endothelial marker, may improve the sensitivity of determining lymphatic invasion in pathological specimens.[45] Nevertheless, the standard pathological techniques for diagnosing lymphatic invasion in this study have demonstrated a dramatic difference in outcomes between patients with and without lymphatic invasion.

CONCLUSION

Although TPE is associated with significant morbidity, many patients with advanced rectal carcinoma who undergo the procedure can have substantially increased disease-free survival. In our series, the absence of lymphatic invasion on final pathology was identified as a prognostic factor for disease-free and overall survival.

Competing interests: None declared.

Contributors: Drs. Domes and Colquhoun designed the study. Drs. Domes, Colquhoun, Izawa and Luke acquired and analysed the data. Drs. Taylor and House also analysed the data. Drs. Domes and Izawa wrote the article. All authors reviewed the article and approved its publication.

References

1. Canadian Cancer Society/National Cancer Institute of Canada. Canadian Cancer Statistics 2009, Toronto, Canada, 2009.
2. O'Connell JB, Maggard MA, Liu JH, et al. Are survival rates different for young and older patients with rectal cancer? *Dis Colon Rectum*

2004;47:2064-9.
3. McNamara DA, Fitzpatrick JM, O'Connell PR. Urinary tract involvement by colorectal cancer. *Dis Colon Rectum* 2003;46:1266-76.
4. Tzardi M. Role of total mesorectal excision and of circumferential resection margin in local recurrence and survival of patients with rectal carcinoma. *Dig Dis* 2007;25:51-5.
5. den Dulk M, Marijnen CA, Putter J, et al. Risk factors for adverse outcome in patients with rectal cancer treated with an abdominoperineal resection in the total mesorectal excision trial. *Ann Surg* 2007;246:83-90.
6. Glynne-Jones R, Mawdsley S, Novell JR. The clinical significance of the circumferential resection margin following preoperative pelvic chemo-radiotherapy in rectal cancer: why we need a common language. *Colorectal Dis* 2006;8:800-7.
7. Brunschwig A. Complete excision of pelvic viscera for advanced carcinoma. *Cancer* 1948;1:177-83.
8. Koda K, Tobe T, Takiguchi N, et al. Pelvic exenteration for advanced colorectal cancer with reconstruction of urinary and sphincter functions. *Br J Surg* 2002;89:1286-9.
9. Goluboff ET, McKiernan JM, Todd G, et al. Reconstruction of urinary and gastrointestinal tracts in total pelvic exenteration: experience at Columbia-Presbyterian Medical Center. *Urology* 1994;44:666-70.
10. Boey J, Wong J, Ong GB. Pelvic exenteration for locally advanced colorectal carcinoma. *Ann Surg* 1982;195:513-8.
11. Lopez MJ, Kraybill WG, Downey RS, et al. Exenterative surgery for locally advanced rectosigmoid cancers. Is it worthwhile? *Surgery* 1987;102:644-51.
12. Jimenez RE, Shoup M, Cohen AM, et al. Contemporary outcomes of total pelvic exenteration in treatment of colorectal cancer. *Dis Colon Rectum* 2003;46:1619-25.
13. Law WL, Chu KW, Choi HK. Total pelvic exenteration for locally advanced rectal cancer. *J Am Coll Surg* 2000;190:78-83.
14. Hida J, Yasutomi M, Maruyama T, et al. Results from pelvic exenteration for locally advanced colorectal cancer with lymph node metastases. *Dis Colon Rectum* 1998;41:165-8.
15. Theodoropoulos G, Wise WE, Padmanabhan A, et al. T-level downstaging and complete pathologic response after preoperative chemoradiation for advanced rectal cancer result in decreased recurrence and improved disease-free survival. *Dis Colon Rectum* 2002;45:895-903.
16. Chari RS, Tyler DS, Anscher MS, et al. Preoperative radiation and chemotherapy in the reatment of adenocarcinoma of the rectum. *Ann Surg* 1995;221:778-86.
17. Mohiuddin M, Marks J, Marks G. Management of rectal cancer: short vs. long-course preoperative radiation. *Int J Radiat Oncol Biol Phys* 2008;72:636-43.
18. Horisberger K, Hofhernz RD, Palma P, et al. Tumor response to neoadjuvant chemoradiation in rectal cancer: predictor for surgical morbidity. *Int J Colorectal Dis* 2008;23:257-64.
19. Valenti V, Hernandez-Lizoain JL, Baixauli J, et al. Analysis of early postoperative morbidity among patients with rectal cancer treated with and without neoadjuvant chemoradiotherapy. *Ann Surg Oncol* 2007;14:1744-51.
20. Nguyen DQA, McGregor AD, Freites O, et al. Exenterative pelvic surgery-eleven year experience of the Swansea Pelvic Oncology Group. *Eur J Surg Oncol* 2005;31:1180-4.
21. Vergara-Fernandez O, Swallow CJ, Victor JC, et al. Assessing outcomes following surgery for colorectal cancer using quality of care indicators. *Can J Surg* 2010;53:232-40.
22. Meterissian SH, Skibber JM, Giacco GG, et al. Pelvic exenteration for locally advanced rectal carcinoma: factors predicting improved survival. *Surgery* 1997;121:479-87.
23. Russo P, Ravindran B, Katz J, et al. Urinary diversion after total pelvic exenteration for rectal cancer. *Ann Surg Oncol* 1999;6:732-8.
24. Ike H, Shimada H, Ohki S, et al. Outcome of total pelvic exenteration for locally recurrent rectal cancer. *Hepatogastroenterology* 2003; 50:700-3.
25. Ike H, Shimada H, Yamaguchi S, et al. Outcome of total pelvic exenteration for primary rectal cancer. *Dis Colon Rectum* 2003;46:474-80.
26. Takeuchi H, Ueo H, Haraoka M, et al. Surgical results of total pelvic exenteration for locally advanced colorectal adenocarcinoma. *Hepatogastroenterology* 2005;52:90-3.
27. Vermaas M, Ferenschild FT, Verhoef C, et al. Total pelvic exenteration for primary and locally recurrent rectal cancer. *Eur J Surg Oncol* 2007;33:452-8.
28. Wells BJ, Stotland P, Ko M, et al. Results of an aggressive approach to resection of locally recurrent rectal cancer. *Ann Surg Oncol* 2007; 14:390-5.
29. Oledzki J, Chwalinski M, Rogowski W, et al. Total cystectomies in the surgical treatment of rectal cancer with prior chemoradiation: analysis of postoperative morbidity and survival. *Int J Colorectal Dis* 2004;19:124-7.
30. Fujisawa M, Nakamura T, Ohno M, et al. Surgical management of the urinary tract in patients with locally advanced colorectal cancer. *Urology* 2002;60:983-7.
31. Luna-Perez P, Barrientos H, Delgado S, et al. Usefulness of frozen-section examination in resected mid-rectal cancer after preoperative radiation. *Am J Surg* 1990;159:582-4.
32. Lehnert T, Methner M, Pollok A, et al. Multivisceral resection for locally advanced primary colon and rectal cancer: an analysis of prognostic factors in 201 patients. *Ann Surg* 2002;235:217-25.
33. Nakafusa Y, Tanaka T, Tanaka M, et al. Comparison of multivisceral resection and standard operation for locally advanced colorectal cancer: analysis of prognostic factors for short-term and long-term outcome. *Dis Colon Rectum* 2004;47:2055-63.
34. Gannon CJ, Zager JS, Chang GJ, et al. Pelvic exenteration affords safe and durable treatment for locally advanced rectal carcinoma. *Ann Surg Oncol* 2007;14:1870-7.
35. Calle EE, Rodriguez C, Walker-Thurmond K, et al. Overweight, obesity and mortality from cancer in a prospectively studied cohort of US adults. *N Engl J Med* 2003;348:1625-38.
36. Meyerhardt JA, Niedzwiecki D, Hollis D, et al. Impact of body mass index and weight change after treatment on cancer recurrence and survival in patients with stage III colon cancer: findings from cancer and leukemia Group B 89803. *J Clin Oncol* 2008;26:4109-15.
37. Dawood S, Broglio K, Gonzalez-Angulo AM, et al. Prognostic value of body mass index in locally advanced breast cancer. *Clin Cancer Res* 2008;14:1718-25.
38. Spangler E, Zeigler-Johnson CM, Coomes M, et al. Association of obesity with tumor characteristics and treatment failure of prostate cancer in African-American and European American men. *J Urol* 2007;178:1939-44.
39. Gong Z, Agalliu I, Lin DW, et al. Obesity is associated with increased risks of prostate cancer metastasis and death after initial cancer diagnosis in middle aged men. *Cancer* 2007;109:1192-202.
40. Compton CC, Fielding LP, Burgart LJ, et al. Prognostic factors in colorectal cancer. College of American Pathologists Consensus Statement 1999. *Arch Pathol Lab Med* 2000;124:979-94.
41. Michelassi F, Black GE, Vannucci L. A 5 to 21 year follow-up and analysis of 250 patients with rectal adenocarcinoma. *Ann Surg* 1988; 208:379-89.
42. Krebs B, Kozelj M, Kavalar R, et al. Prognostic value of additional pathological variables for long-term survival after curative resection of rectal cancer. *World J Gastroenterol* 2006;12:4565-8.
43. Matsumoto K, Nakayama U, Inoue Y, et al. Lymphatic microvessel density is an independent prognostic factor in colorectal cancer. *Dis Colon Rectum* 2007;50:308-14.
44. Harris EI, Lewin DN, Wang HL, et al. Lymphovascular invasion in colorectal cancer: an interobserver variability study. *Am J Surg Pathol* 2008;32:1816-21.
45. Kalof AN, Cooper K. D2-40 immunohistochemistry—so far! *Adv Anat Pathol* 2009;16:62-4.