Chinese-German J Clin Oncol
DOI 10.1007/s10330-014-1331-2
July 2014, Vol. 13, No. 7, P309–P315

Five-year oncologic outcomes and prognostic factors for locally advanced low rectal cancer after low anterior resection

Bo Yao, Yadi Wang, Na Lu

Department of Radiation Oncology, The Military General Hospital of Beijing PLA, Beijing 100700, China

Received: 12 May 2014 / Revised: 25 May 2014 / Accepted: 10 June 2014

Abstract ***Objective:*** The aim of the study is to investigate the long- term oncologic outcomes including local recurrence, distant metastases and overall survival (OS) for patients with low rectal cancer underwent low anterior resection (LAR) with total mesorectal excision (TME), and to analyze the prognostic factors for them. ***Methods:*** Between January 2001 and December 2009, 147 patients with clinical stage II and III rectal cancers located 3-6 cm from the anal verge underwent LAR with TME without temporary diverting stoma. The median distal resection margin (DRM) was 1.0 (range, 0.3–5) cm. Anastomostic leakage occurred in 29 (19.7%) patients. Thirty patients received surgery alone, 20 patients received preoperative chemoradiotherapy (CRT), 43 patients received postoperative CRT, and adjuvant chemotherapy was administered for 108 patients. The median cycle of adjuvant chemotherapy was 6 (range, 2–20) cycles. The median follow- up was 74.8 (range, 30.1–146.3) months. ***Results:*** In all patients, 5-year recurrence-free survival (RFS), disease-free survival (DFS) and OS were 70.4%, 54.2% and 60.5%, respectively. Forty-three (29.3%) patients suffered local recurrence. Patients received preoperative CRT with a downstaging yp0/I who had a better 5-year RFS, DFS and OS, which were 100%, 90.9%, and 90.9%, respectively. For patients with pathologic stage II and stage III, the 5-year RFS, DFS, and OS were 79.2% and 60.1%, 67.9% and 39.1%, 72.1% and 48.2%, respectively. On multivariable analysis, RFS was associated with anostomostic leakage, DFS was associated with anastomostic leakage and pathologic N stage, and OS was associated with anastomostic leakage, pathologic N and T stage. For patients with anastomostic leakage, the 5-year RFS, DFS, and OS were 51.7%, 32.4%, and 38.3%, respectively, which were worse than that for patients without anastomostic leakage, the latter were 75.2%, 59.7%, 65.7%, respectively ($P < 0.05$). DRM and radiotherapy were associated with RFS on univariable analysis ($P < 0.05$), but not on multivariable analysis. Tumor grade was prognostic factors for RFS and OS on univariable analysis, but not on multivariable analysis. The other factors including sex, age, tumor size and adjuvant chemotherapy were not associated with RFS, DFS and OS on univariable analysis. ***Conclusion:*** For patients with low rectal caner underwent LAR and TME, the long-term oncologic outcomes were satisfactory for patients with stage yp0/I, but not for patients with pathologic stage III. Anastomositic leakage negatively affect long-term oncologic outcomes. Radiotherpy, adjuvant chemotherapy and distal resection margin were not associated with long-term outcomes.

Key words low rectal cancer; sphincter-preserving surgery; long-term outcomes; prognostic factors

Although abdominoperineal resection is still the most common operation in patients with tumors less than 6 cm from the anal verge, more and more patients received sphincter-preserving surgery in recent decades [1–6]. Many studies have confirmed that distal intramural spread of microscopic tumor cells is rarely present beyond 1 cm from gross tumor margin [1, 7]. Some studies have showed distal resection margin (DRM) 1 cm or less produced similar oncologic outcomes to greater than 1 cm [3–6]. Based on these data, a DRM of 1 cm became an accepted standard in low rectal cancer patients treated with sphincter-preserving surgery [1–6]. In recent studies, using different kinds of sphincter-preserving surgery standardization including low anterior resection (LAR) and inter-sphincteric resection (ISR) in different low or ultralow rectal cancers, there were no differences or even better in local control and overall survival compared to abdominoperineal resection (ARP) [4, 8–12]. So sphincter-preserving surgery combined with total mesorectal excision (TME) has become the treatment of choice for low rectal cancer patients [4, 9–11]. However, the long-term oncologic outcomes continue to be unclear, especially, the influence of clinical or treatment characteristics on that remains controversial. Herein, we reported the long-term follow-

Correspondence to: Bo Yao. Email: yaobo898@sina.com

Table 1 Clinical characteristics of all patients

Characteristics	No. of patients	%
Gender		
Male	91	61.9
Femal	56	38.1
Age (years)		
Median (range)	57 (20-86)	
p tumor stage (AJCC)		
p 0/I	11	7.5
p II	58	39.5
p III	78	53.1
T stage		
pT0	8	5.4
pT1	2	1.4
pT2	0	7.5
pT3	102	69.4
pT4a	24	16.3
N stage		
N0	69	46.9
N1	46	31.3
N2	32	21.8
Tumor size (cm^2)		
Median (range)	15 (1.5–70.5)	
Tumor grade		
Well differentiated	20	13.6
Moderately	91	61.9
Poorly	36	24.5
DRM (cm)		
Median (range)	1 (0.3–5)	
Radiotherapy		
No	84	57.1
Preoperative	20	13.6
Postoperative	43	29.3
Adjuvant chemotherapy		
No	39	26.5
1–3 cycles	17	11.6
4–6 cycles	61	41.5
> 6 cycles	30	20.4

up of this patient cohort in order to study the oncologic outcomes and prognostic factors on survival, local recurrence and distant metastases.

Materials and methods

Between January 2001 and January 2011, 147 patients with rectal cancer treated at the Military General Hospital of Beijing PLA (China), the median distance from the anal verge was 4 (range, 3–6) cm. All patients underwent sphincter-preserving surgery with TME. The inclusion criteria for the study were: (1) histologically confirmed adenocarcinoma; (2) clinical TNM stage was stage II–III before surgery. We excluded those who had clinical stage T4b and located at less than 3 cm from the anal verge cases with stage II–III who underwent APR. Informed consent was obtained from each individual before treatment. All patients had the following examinations: clinical examination included digital rectal examination, a colonoscopy with a biopsy, a CT scan of the thorax, abdomen and pelvis and 98 patients had a pelvis of MRI. The precise level of the lower edge of the tumor from the anal verge was assessed by the surgeon. Staging was based on the criteria of the American Joint Committee on Cancer (AJCC), seventh edition. Pathological stage was performed after surgery for all patients (Table 1).

Surgery

All patients underwent TME and low LAR. Coloanal was performed in all patients, and hand-sewn anastomosis was performed in 83 patients before 2007 and after that stapled anastomosis was performed by a double-stapling technique in 64 patients. All of patients had presacral drainage without protective temporary diverting stoma. Symptomatic anastomotic leakage in this study was defined as peritonitis caused by leakage, pelvic abscess, and discharge of feces, pus, or gas from pelvic drainage which was confirmed by abdominopelvic CT scan and rigid sigmoidoscopy. Twenty-nine (19.7%) patients suffered anastomostic leakage. The median DRM was 1 (range, 0.3–5) cm.

Radiotherapy (RT) and concurrent chemoradiotherapy (CRT)

Sixty-three patients underwent pre- or postoperative RT combined with concurrent chemotherapy. Table 2 showed the comparisons between the patients with and without radiotherapy.

Twenty patients underwent concurrent CRT preoperatively and then surgery was performed 4–6 weeks after CRT. Among of them, 8 patients had pathological complete regression, 3 had downstaging yp I diseases. Forty-three patients had postoperative CRT. In all 63 patients, the median radiotherapy dose was 50 (range, 45–52) Gy in 25–28 fractions for tumor or tumor bed plus regional lymph nodes, and 10 of those patients received a boost of 5.4 to 9 Gy delivered to the tumor or tumor bed. Thirty-seven patients used three-dimensional conformal RT and 26 patients used intensity-modulated RT. Concurrent chemotherapy consisted of 5-Fluorouracil (5–FU) leucovorin (LV) in 23 patients or capecitabine taken orally alone in 40 patients.

Adjuvant chemotherapy

Adjuvant chemotherapy was administered for 108 patients, and the median cycle was 6 (range, 2–20) cycles, and chemotherapy regimens included 5-FU plus LV in 2 patients, capecitabine alone in 6 patients, 5-FU/LV/oxaliplatin in 92 patients, 5-FU/LV/irinotecan in 2 patients, or capecitabine/oxaliplatin in 6 patients.

Table 2 The comparisons between patients with radiotherapy and without radiotherapy

	With RT (*n* = 63)		Without RT (*n* = 684)		χ^2	*P*
	n	%	*n*	%		
Gender					2.945	0.086
Male	44	69.8	47	56.0		
Female	19	30.2	37	44.0		
Age (years)					12.651	0.000
< 70	60	95.2	61	72.6		
≥ 70	3	4.8	23	27.4		
Clinical TNM stage					1.782	0.182
II	34	54.0	36	42.9		
III	29	46.0	48	57.1		
Tumor grade					2.959	0.228
High	7	11.1	13	15.5		
Median	44	69.8	47	56.0		
Low	12	19.0	24	28.6		
Distal resection margin (cm)					0.433	0.510
< 1	14	22.2	15	17.9		
≥ 1	49	77.8	69	82.1		
Adjuvant chemotherapy					8.481	0.004
Yes	54	85.7	54	64.3		
No	9	14.3	30	35.7		
*Long-term complications					8.167	0.004
Yes	15	23.8	6	7.1		
No	48	76.2	78	92.9		
Anastomostic leakage					1.035	0.309
Yes	10	15.9	19	22.6		
No	53	84.1	65	77.4		
Local recurrence					3.956	0.047
Yes	13	20.6	30	35.7		
No	50	79.4	54	64.3		

*, including ileus, anal fistula, and anal stenosis

Statistical analysis

The Statistical Package for the Social Sciences (SPSS version 15.0) was used for data management and statistical analyses. Pearson chi-square or fisher's exact test was used to evaluate the difference between patients with and without radiotherapy. Local recurrence was defined as the presence of any anastomosis, pelvic, regional lymph nodes, or perineal recurrence documented by either clinical or pathological examination. The overall survival (OS), disease-free survival (DFS), and recurrence-free survival (RFS) were calculated using Kaplan-Meier survival analysis, and Log-rank test was used to compare groups. Covariates including all the significant factors with $P < 0.05$ were included in multivariable model by using Cox regression with enter method. Two-sided *P* values less than 0.05 were considered statistically significant and with 95% confidence intervals (CIs).

Results

The median follow-up time was 74.8 (range, 30.1-146.3) months. In all patients, 5-year RFS, DFS and OS were 70.4%, 54.2% and 60.5%, respectively. Forty-three (29.3%) patients suffered local recurrence. The local recurrence were none patients, 10 (20.4%) patients, 2 (22.2%) patients, 2 (22.2%), 17 (33.3%) patients and 12 (66.7%) patients for pathologic stage 0/I, IIA, IIB, IIIA, IIIB and IIIC, respectively. The most commonest recurrent location was anastomosis that occurred in 36 (24.5%) patients. The other recurrent locations including presacral area in 21 (14.3%) patients, the primary tumor bed and its proximal mesorectum in 22 (15.0%) patients, and the lateral pelvis lymph nodes in 12 (8.2%) patients. Fifty-five patients had distant metastases including 31 patients had liver metastasis, 31 patients had lung metastases, 16 patients had bone metastases, and 11 patients had the other metastases. Twenty-one patients had long-term complications including ileus, anal fitula or anal stenosis.

Table 3 Oncologic outcomes of univariable Cox regression analysis

Variables	RFS 5-year rate (%)	*P* value	DFS 5-year rate (%)	*P* value	OS 5-year rate (%)	*P* value
Gender		0.490		0.761		0.565
Male	72.2		54.8		62.0	
Female	67.4		53.5		58.1	
Age (years)		0.163		0.554		0.704
≥ 70	57.7		46.2		64.2	
< 70	73.4		57.5		59.8	
pTNM		0.007		0.001		0.005
0/I	100		90.9		90.9	
II	79.2		67.9		72.1	
III	60.1		39.1		48.2	
pT stage		0.040		0.006		0.007
T0–1	100		100		100	
T2	80		72.7		90.9	
T3	71.5		53.9		59.4	
T4a	49.0		25.3		36.7	
pN stage		0.001		0.000		0.000
N0	82.6		71.8		75.1	
N1	66.5		52.6		64.0	
N2	49.8		18.8		24.3	
Anastomostic leakage		0.007		0.009		0.016
Yes	51.7		32.4		38.3	
No	75.2		59.7		65.7	
DRM		0.025		0.312		0.572
< 1	55.2		48.3		54.4	
≥ 1	74.2		55.7		62.0	
Tumor size (cm^2)		0.177		0.112		0.261
< 17	74.1		59.4		64.4	
≥ 17	64.8		46.6		54.1	
Adjuvant chemotherapy		0.815		0.767		0.576
Yes	70.0		56.8		63.4	
No	71.8		51.5		52.8	
Cycles of Chemotherapy		0.907		0.502		0.293
No	71.8		46.8		52.8	
< 6 cycles	67.0		51.0		54.5	
≥ 6 cycles	71.7		60.5		64.5	
Radiotherapy		0.047		0.203		0.751
Yes	79.1		61.0		61.3	
No	64.2		49.7		60.3	
Tumor grade		0.044		0.076		0.026
Well	95.0		75.0		79.7	
Moderate	65.6		53.4		61.8	
Poor	68.8		43.4		47.2	

Table 3 summarized the univariable analyses of the association between patients clinical and treatment characteristics with RFS, DFS and OS. The common significant factors affected RFS, DFS and OS including the pathologic T stage, N stage and TNM stage, and anastomotic leakage ($P < 0.05$). Radiotherapy and distal resection margin were the significant prognostic factors for RFS ($P < 0.05$), rather than for the DFS and OS. Tumor grade was the associated with RFS and OS, but not for DFS.

The significant univariables were selected to be analyzed by using Cox regression test. Table 4 showed the multivariate analyses results. Anastomostic leakage was the only common associated factor with RFS, DFS and OS ($P < 0.05$). Pathological stage T was the prognostic factor for OS ($P < 0.05$). Pathological stage N was the prognistic factor for DFS and OS ($P < 0.05$). Radiotherapy, distal resection margin and tumor grade were not prognostic factors for RFS, DFS or OS.

Table 4 Multivariate analyses of association between patient, treatments and tumor factors with RFS, DFS and OS

	RFS			DFS			OS		
	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
pTNM: 0/I vs II vs III	1.554	0.49–4.86	0.448	0.79	0.32–1.97	0.611	0.61	0.22–1.68	0.339
pN: N0 vs N1 vs N2	1.495	0.76–2.94	0.244	2.39	1.37–4.19	0.002	2.56	1.39–4.72	0.003
pT: T0/T1/T2 vs T3/T4a	2.758	0.65–11.77	0.170	3.38	0.99–11.46	0.051	5.64	1.27–25.09	0.023
Anastomostic leakage: Yes vs no	2.89	1.47–5.65	0.002	2.16	1.23–3.76	0.007	1.823	1.03–3.23	0.040
DRM: < 1 vs ≥ 1	0.529	0.27–1.04	0.065	0.909	0.50–1.65	0.754	1.21	0.64–2.29	0.553
Tumor grade: High/moderate vs low	0.907	0.45–1.83	0.785	1.31	0.76–2.26	0.336	1.44	0.83–2.50	0.192
Radiotherapy: Yes vs no	0.615	0.31–1.20	0.156	0.81	0.48–1.37	0.428	1.08	0.63–1.86	0.783

Discussion

In the present study, 5-year RFS, DFS and OS were 70.4%, 54.2% and 60.5%, respectively in all patients. These results are worse than some studies [11–14], but similar to the reports from Valentini V *et al* [13], which showed in patients with low rectal cancer (≤ 5 cm from the anal verge) received LAR, the 5-year local control, distance control, and OS were 86.0%, 64.3%, and 64.7%, respectively. Meanwhile, other studies using ISR showed better local control and survival [8, 14, 15].

In multivariable analysis, anastomostic leakage was the only common significant factor with RFS, DFS and OS. Apart from that, pathologic N stage was associated with DFS and OS, pathologic T stage was associated with OS, however, radiotherapy or chemotherapy was not prognostic factors for long-term outcomes, although radiotherapy had an affect on RFS in univariable analysis. Therefore, the extent of tumor progression combined with surgery techniques were the main factors of long-term outcomes for low rectal cancers. Akagi Y *et al* [14] reported 124 patients with low rectal cancer located at 1–4 cm from the anal verge had ISR and no patients received pre- or post-operative radiotherapy, and 46.8% patients with risk factors (pT4, vascular invasion, perineural invasion, and perforation) had postoperative chemotherapy, and had lower local recurrence rate (4.7%, 4.9% and 5.0% for stage I, II and III), and better OS (90.5%, 91.0% and 83.6% at each stage).

In this study all patients with low rectal cancer underwent LAR with TME without temporary diverting stoma. The rate of anastomostic leakage (19.7%) was higher than other studies (4–15%) which had diverting stoma [16–19]. Unfortunately, anastomostic leakage was associated with RFS, DFS and OS in the multivariable analysis in the study. The effect of anastomostic leakage on the log-term outcomes remains controversial, Dulk MD *et al* [18] proved that was prognostic factors for OS, but others not proved [16, 19]. To prevent anastomostic leakage, temporary diverting stoma was generally used in low rectal cancer patients, and be confirmed that significantly reduced the incidence of anastomostic leakage [16–18].

Pre- or post-operative CRT is part of the standard treatment of locally advanced rectal cancer, and has been proved to improve local control but not to affect long-term survival. Compared with postoperative CRT, preoperative CRT was superiors in local control, toxicity, sphincter-preserving [12, 20, 21]. Nevertheless, in practise a substantial number of patients with stage II/III rectal cancers did not receive any pelvic irradiation, especially in elderly patients [5]. In our study, 42.9% patients received pre- or postoperative CRT, however, only 20 patients received preoperative CRT among them. Of the patients received preoperative CRT, 11 with a downstageing yp 0/I had a significantly better 5-year RFS, DFS and OS (100%, 90.9% and 90.9%, respectively) compareing to the patients with pathologic stage II/III cancers. In the present, CRT significantly improved RFS in univariable analysis, but not in multivariable analysis. Moreover, patients with CRT had higher rate of long-term complications including ileus, fistula and anal stenosis than patients without CRT. Other studies [22, 23] also showed surgery with radiotherapy increased risk and severity long-term toxicities and reduced quality of life, and so recently, some authors considered not all the patients with stage II–III in the TME era have to receive CRT [14, 24–26]. Frasson M *et al* [25] confirmed patients with cT3N0 or cT2N+ received TME alone without pre- or postoperative CRT had a low 5- year local recurrence (9.5%). So the author suggests CRT may be unnecessary for patients with stage II/III if the circumferential resection margin (CRM) is free. The report from Akagi Y *et al* [14], mentioned above, showed although no patients received pre-or post-operative radiotherapy, the long-term oncologic results were good in patients underwent ISR alone. For patients either with LAR or ISR, preoperative chemoradiotherapy was identified to be a risk factor of anal function [27]. For some patients without high risk factors, whether radiotherapy should be omitted, that needs to be studied prospectively in the future.

The median DRM was 1 (range, 0.3–5) cm in the present study, although which was associated with RFS in univariable analysis, not in multivariable analysis. The optimal DRM for low rectal cancers remains unclear. Nash GM *et al* [1] showed close DRM was a risk factor for

local control, however, more and more studies confirmed that a DRM of 1 cm was safe not to negatively affect the local control and OS [2, 4, 5].

In the present study, 73.5% patients received adjuvant chemotherapy after surgery, and chemotherapy regimens and cycles were heterogenetic. Only 20.4% patients received chemotherapy 6 cycles or more. Although there was no association between adjuvant chemotherapy and RFS, DFS and OS, owing to the heterogeneity mentioned above, the power of statistics was reduced, so whether the patients benefited from adjuvant chemotherapy not be answered in this study. Although there has been no conclusive evidence to define optimal adjuvant chemotherapy regimen or the most optimal subgroups of patients to be treated, adjuvant chemotherapy was recommended routinely for patients with locally advanced rectal cancer [13, 28, 29].

This study is limited by the retrospective analysis of database, heterogeneity in chemotherapy and RT dose. Especially, CRM was not routinely reported in our hospital, however, some authors [25, 30] have shown low rectal cancers had a higher frequency of CRM involvement compared to tumors situated over 5 cm from the anal verge, so CRM was the most important factor for the risk of local recurrence, more relevant than the DRM.

In conclusion, from the results of the patient cohort with low rectal caner underwent LAR with TME and without temporary diverting stoma, we learned the long-term oncologic outcomes were satisfactory for patients with downstaging yp0/I, but unsatisfactory for patients with pathologic stage III. We confirmed anastomositic leakage negatively affect long- term oncologic outcomes, pathologic T and N stage were associated with DFS or OS. Although radiotherapy and DRM were the prognostic factors for RFS on univariable analysis, but not on multivariated analysis, therefore, in the future that needs to be further evaluated prospectively. Surgery techniques and experiences should be further improved, and a diverting stoma may be reduce the leakage rate.

References

1. Nash GM, Weiss A, Dasgupta R, *et al*. Close distal margin and rectal cancer recurrence after sphincter-preserving rectal resection. Dis Colon Rectum, 2010, 53: 1365–1373.
2. Kiran RP, Lian L, Lavery IC. Dose a subcentimeter distal resection margin adversely influence oncologic outcomes in patients with rectal cancer undergoing restorative proctectomy? Dis Colon Rectum, 2011, 54: 157–163.
3. Kim YW, Kim NK, Min BS, *et al*. Factors associated with anastomostic recurrence after total mesorectal excision in rectal cancer patients. J Surg Oncol, 2009, 99: 58–64.
4. Rullier E, Denost Q, Vendrely V, *et al.* Low rectal cancer: calssification and standardization of surgery. Dis Colon Rectum, 2013, 56: 560–567.
5. Fitzgerald TL, Brinkley J, Zervos EE. Pushing the envelope beyond a centimeter in rectal cancer: oncologic implications of close, but negative margins. J Am Coll Surg, 2011, 213: 589–595.
6. Park IJ, Kim JC. Adequate length of the distal resection margin in rectal cancer: from the oncological point of view. J Gastrointest Surg, 2010, 14: 1331–1337.
7. Shirouzu K, Ogata Y. Histopathologic tumor spread in very low rectal cancer treated with abdominoperineal resection. Dis Colon Rectum, 2009, 52: 1887–1894.
8. Martin ST, Heneghan HM, Winter DC. Systematic review of outcomes after intersphincteric resection for low rectal cancer. Br J Surg, 2012, 99: 603–612.
9. Lim SB, Heo SC, Lee MR, *et al*. Changes in outcome with sphincter-preserving surgery for rectal cancer in Korea, 1991-2000. Eur J Surg Oncol, 2005, 31: 242–249.
10. Jarry J, Faucheron JL, Moreno W, *et al.* Delayed colo- anal anastomosis is an alternative to prophylactic diverting stoma after total mesorectal excision for middle and low rectal carcinomas. Eur J Surg Oncol, 2011, 37: 127–133.
11. Gerard JP, Chapet O, Nemoz C, *et al.* Improved sphincter preservation in low rectal cancer with high- dose preoperative radiotherapy: the Lyon R96-02 randomized trial. J Clin Oncol, 2004, 22: 2404–2409.
12. Crane CHH, Skibber JM, Feig BW, *et al.* Response to preoperative chemoradiotherapy increases the use of sphincter-preserving surgery in patients with locally advanced low rectal carcinoma. Cancer, 2003, 97: 517-524.
13. Valentini V, Stiphout R, Lammering G, *et al.* Nomograms for predicting local recurrence, distant metastases, and overall survival for patients with locally advanced rectal cancer on the basis of european randomized clinical trials. J Clin Oncol, 2011, 29: 3163–3172.
14. Akagi Y, Shirouzu K, Ogata Y, *et al*. Oncologic outcomes of intersphincteric resection without preoperative chemoradiotherapy for very low rectal cancer. Surg Oncol, 2013, 22: 144–149.
15. Chamlou R, Parc Y, Simon T, *et al.* Long-term results of intersphincteric resection for low rectal cancer. Ann Surg, 2007, 246: 916–922.
16. Smith JD, Paty PB, Guillem JG, *et al*. Anastomostic leakage is not associated with oncologic outcome in patients undergoing low anterior resection for rectal cancer. Ann Surg, 2012, 256: 1034–1038.
17. Bennis M, Parc Y, Lefevre JH, *et al*. Morbidity risk factors after low anterior resection with total mesorectal excision and coloanal anastomosis. Ann Surg, 2012, 255: 504–510.
18. den Dulk M, Marijnen CA, Collette L, *et al*. Multicentre analysis of oncological and survival outcomes following anastomostic leakage after rectal cancer surgery. Br J Surg, 2009, 96: 1066–1075.
19. Lee WS, Yun SH, Roh YN, *et al.* Risk factors and clinical outcome for anastomostic leakage after total mesorectal excision for rectal cancer. World J Surg, 2008, 32: 1124–1129.
20. Sauer R, Liersch T, Merkel S, *et al.* Preoperative versus postoperative chemoradiotherapy for locally advanced rectal cancer: results of the German CAO/AROAIO-94 randomized phase III trial after a median follow- up of 11 years. J Clin Oncol, 2012, 30: 1926–1933.
21. Atif E, Sakr H, Teama S, *et al*. Effect of radical surgery combined with pre- or postoperative radiotherapy in treatment of resectable rectal cancer. Chinese-German J Clin Oncol, 2012, 11: 384–390.
22. Emmertsen KJ, Laurberg S; Rectal Cancer Function Studr Group. Impact of bowel dysfunction on quality of life after sphincter- preserving resection for rectal cancer. Br J Surg, 2013, 100: 1377–1387.
23. Bruheim K, Guren MG, Skovlund E, *et al*. Late side effects and quality of life after radiotherapy for rectal cancer. Int J Radiat Oncol Biol Phys, 2010, 76: 1005–1011.

24. Baek SJ, Kim SH, Kwak JM, *et al*. Selective use of preoperative chemoradiotherapy for T3 rectal cancer can be justified: analysis of local recurrence. World J Surg, 2013, 37: 220–226.
25. Frasson M, Granero EG, Roda D, *et al*. Preoperative chemoradiotherapy may not always be needed for patients with T3 and T2N + rectal cancer. Cancer, 2011, 117: 3118–3125.
26. Fucini C, Pucciani F, Elbetti C, *et al*. Preoperative chemoradiotherapy in T3 operable low rectal cancers: a gold standard? World J Surg, 2010, 34: 1609–1614.
27. Ito M, Saito N, Sugito M, *et al*. Analysis of clinical factors associated with anal function after intersphincteric resection for very low rectal cancer. Dis Colon Rectum, 2009, 52: 64–70.
28. Bosset JF, Collette L, Calais G, *et al*. Chemotherapy with preoperative radiotherapy in rectal cancer. N Engl J Med, 2006, 355: 1114–1123.
29. Collette L, Bosset JF, den Dulk M, *et al*. Patients with curative resection of cT3–4 rectal cancer after preoperative radiotherapy or radiochemotherapy. Dose anybody benefit from adjuvant fluorouracil-based chemotherapy? A trial of European Organization for Research and Treatment of Cancer Radiation Oncology Group. J Clin Oncol, 2007, 25: 4379–4386.
30. Nagtegaal ID,Velde CJH, Marijnen CAM, *et al*. Low rectal cancer: a call for a change of approach in abdominoperineal resection. J Clin Oncol, 2005, 23: 9257–9264.

《中德临床肿瘤学杂志》2014年征稿启事

《中德临床肿瘤学杂志》是由中华人民共和国教育部主管，华中科技大学同济医学院主办的医学肿瘤学学术期刊（全英文月刊），已先后被中信所科技核心数据库、中国期刊全文数据库、万方数据资源系统数字化期刊群、维普资讯网科技期刊数据库、中国学术期刊综合评价数据库、EMBASE、Index Copernicus等国内外重要检索系统收录。国际、国内刊号为：ISSN 1610-1979（纸质版），1613-9089 (网络版)；CN 42-1654/R，邮发代号：38-121。

本刊主要刊登世界各国作者，特别是中国作者在肿瘤学领域的优秀科研成果和临床诊疗经验，包括与临床肿瘤学密切相关的基础理论研究等成果，并全文以英语发表，在国内外公开发行。辟有述评、专家笔谈、论著、临床研究、实验研究、综述、病例报道、人物专栏等栏目。

本刊具有编审效率高、出版周期短、学术价值高、临床实用性强、印刷精美等特点。承诺将一如既往地以广大作者为依托，积极为作者和读者服务，严格做到对所有来稿处理及时、审稿认真、退修详细、发稿迅速。对具有国际领先水平的创新科研成果及国家重点项目开辟“绿色通道”，审稿迅速，刊登及时。

欢迎全国各级肿瘤学医务工作者踊跃投稿、组稿！

《中德临床肿瘤学杂志》2014年重点专栏报道计划如下：

1，肺癌；2，肝癌；3，胰腺肿瘤；4，胃肠肿瘤；5，乳腺肿瘤；6，甲状腺癌；7，骨肿瘤；8，泌尿生殖系肿瘤；9，脑肿瘤；10，血液系统疾病；11，妇科肿瘤；12，耳鼻喉科肿瘤；13，皮肤肿瘤；14，肿瘤诊断学（特别是肿瘤影像诊断学）；15，肿瘤化疗；16，肿瘤放疗；17，肿瘤转化医学；18，肿瘤心理学；19，其他。

敬请您关注！具体投稿和联系方式请参见杂志版权页。

《中德临床肿瘤学杂志》编辑部