Efficacy and safety of consolidation chemotherapy during the resting period in patients with local advanced rectal cancer

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Received February 4, 2018; Accepted September 11, 2018

DOI: 10.3892/ol.2018.9804

Abstract. It remains controversial as to whether a long interval between neoadjuvant chemoradiotherapy (NCRT) and surgery may provide clinical benefits for patients with local advanced rectal cancer (LARC). The addition of consolidation chemotherapy during the resting period was recently considered as a treatment option. The present study aimed to verify the efficacy and safety of consolidation chemotherapy during the resting period in patients with LARC. A total of 156 patients with local advanced stage T3-4N0-2 rectal cancer were enrolled between January 2010 and July 2016. Patients were divided into two groups, those who received consolidation chemotherapy prior to surgery (n=76) and the control group who did not (n=80). Multivariate logistic regression and the Kaplan-Meier method were used to explore the predictors of pathological complete response (pCR) and survival. The demographic and tumor characteristics were comparable between the two groups. The consolidation group yielded significantly higher pCR and near pCR rates compared with the control group (P=0.015). Patients in the consolidation group who also underwent standard adjuvant chemotherapy displayed improved 3-year disease-free survival (DFS) compared with the control group (P=0.036). Notably, the addition of consolidation chemotherapy between NCRT and surgery did not significantly increase the incidence of surgical complications and grade 3 or 4 toxicities when compared with the control group. Consolidation chemotherapy was associated with increased pCR/near pCR rates and improved 3-year DFS, and displayed a manageable safety profile. The present study provided primary evidence for the efficacy and safety of consolidation chemotherapy in LARC. Further prospective studies are warranted in the future to verify these results.

Introduction

Globally, the incidence of colorectal cancer ranks as the fifth highest of all malignant tumor types. Cancer mortality caused by colorectal cancer accounts for the sixth highest cancer mortality rate globally (1). One previous study reported that the incidence of rectal cancer accounts for ~40% of the total incidence of colorectal cancer, and that there is a rising trend (2). Locally advanced rectal cancer constitutes up to 50% of all rectal cancer types and includes nonresectable and borderline-resectable tumor types (3). Currently, neoadjuvant chemoradiotherapy (NCRT) combined with postoperative chemotherapy, or neoadjuvant chemotherapy combined with postoperative chemoradiotherapy, are the standard treatments for local advanced rectal cancer (LARC) in the National Comprehensive Cancer Network (NCCN) guidelines (4).

Pathological complete response (pCR) following NCRT is an important prognostic indicator for patients with excellent treatment outcomes (5,6). Tumor regression occurs slowly. Prolonging treatment intervals in rectal cancer may increase the pCR of the patient, R0 resection, and anus preservation rates (7,8). To achieve an improved pCR rate, a number of studies recommend an interval of 7-8 weeks between NCRT
and surgery (7-9). However, the high pCR rate obtained from long intervals between NCRT and surgery is not associated with a survival benefit, with long and short treatment intervals conferring a similar rate of overall survival (OS) (10-12). Notably, Supiot et al (13) reported that OS and recurrence-free survival (RFS) were slightly lower in the long-interval group compared with those in the short-interval group, which may be due to the prolonged resting period that may increase the probability of distant metastases. This occurrence is more common in ypT3-4N0 and ypT0-4N+ patients who have high risk of distant metastases.

Preoperative chemotherapy may improve patient tolerance to chemotherapy and reduce the incidence of distant metastases. Therefore, theoretically, consolidation chemotherapy between NCRT and surgery may increase the rate of OS and DFS, in addition to distant metastases-free survival (DMFS). Although no corresponding guidelines have been established to date, consolidation chemotherapy is gradually attracting the attention of the research community.

In the present study, the impact of adding consolidation chemotherapy for rectal cancer during the resting period was retrospectively analyzed in order to determine whether consolidation chemotherapy resulted in higher rates of pCR and near pCR and improved survival, and to assess the influence of consolidation chemotherapy on chemotherapy toxicities, surgical outcomes and postoperative complications.

Patients and methods

Patients. A total of 273 patients with cT3-4 N0-2 M0 LARC who underwent neoadjuvant chemoradiation followed by radical resection with total mesorectal excision (TME) at Nanfang Hospital of Southern Medical University (Guangzhou, China) were reviewed. The selection criteria were: i) Age ≤80 years; ii) cT3-4 N0-2 M0 LARC; iii) tumor located 0-10 cm from anal verge; iv) underwent neoadjuvant chemoradiation followed by TME; v) chemotherapeutic regimen was capecitabine, CapeOX or FOLFOX; and vi) dose of radiotherapy was 45-50.4 Gy. Of these patients, 117 were excluded due to age >80 years (n=7), tumor located >10 cm from the anal verge (n=23), or ineligibility due to either chemotherapeutic regimen (n=54) or radiotherapy (n=45-50.4 Gy; n=33). Overall, 156 patients were included in the analysis. Patients were divided into the following two groups according to whether they received chemotherapy or not: Consolidation (n=76) or control (n=80) group (Fig. 1). The following data were reviewed: Sex, age, body mass index (BMI), pretreatment level of carcinoembryonic antigen (CEA), histological type, clinical Tumor, Nodule, Metastasis (TNM) staging, and MRI staging of patients who underwent neoadjuvant chemoradiation followed by TME. The Ethics Committee of Nanfang Hospital of Southern Medical University approved the present study.

Statistical analysis. Continuous variables are expressed as the median and range and were analyzed using two-sample t-tests. Categorical variables are expressed as numbers with percentages and were analyzed using a χ² or Fisher's exact test when appropriate. Univariate analysis was used to preliminarily assess the predictive value of variables for achieving pCR and near pCR. Multivariate analysis was performed on variables with P<0.1 from the univariate analysis to further analyze the independent predictive factors of pCR and near pCR. All analyses were performed using SPSS 21.0 software (IBM Corp., Armonk, NY, USA) for Windows. OS was calculated from the date of surgery to the date of mortality from any cause or the last follow-up visit. Recurrence was determined either via imaging studies or pathological findings. DMFS was defined as the time from surgery to metastasis or mortality, while DFS was defined as the time from surgery to local recurrence, metastasis or mortality. The Kaplan-Meier method was used to analyze the rate of patient survival, and comparisons were performed using the Wilcoxon test. All statistical tests were two-sided. P<0.05 was considered to indicate a statistically significant difference.

Results

Clinicopathological characteristics. Between January 2010 and July 2016, 156 patients with local advanced (cT3-4 and/or cN0-2), low (0-5 cm from the anal verge), and mid- (6-10 cm from the anal verge) rectal cancer were enrolled in the present study. The baseline characteristics of the patients were well balanced between the two groups (Table I). abdominopelvic enhanced magnetic resonance imaging (MRI) was performed on all patients prior to treatment, and 148 (94.8%) patients underwent endoscopic ultrasonography. The median age at diagnosis was 53 years (range, 22-80 years). The majority of the patients were male (69.2%), while females comprised 30.8% of the study population. The majority of tumors were staged as cT4 (76.3%) and III (83.3%). A total of 90 (57.7%) and 60 (42.3%) patients had a tumor located either between 0 and 5 cm, or 6 and 10 cm, respectively, from the anal verge. No differences...
in the consolidation group and nine (11.25%) patients in the control group achieved pCR, while nine (11.84%) patients in the consolidation group and four (5%) patients in the control group achieved near pCR. The rate of pCR and near pCR was significantly higher in patients who underwent consolidation chemotherapy (25/76, 32.8%) compared with that in patients who underwent NCRT only (13/80, 16.25%), (P=0.015). In the univariate analysis, age, sex, differentiation, distance from the anorectal verge, lymphovascular invasion and BMI were not associated with pCR and near pCR rates (P=0.732, 0.780, 0.424, 0.139, 0.250 and 0.919, respectively). Clinical T stage (T3 vs. T4, P=0.002), N stage (N0 vs. N1 vs. N2, P=0.012), AJCC/Union for International Cancer Control (UICC) stage (II vs. III, P=0.005), CEA level (<5 ng/ml vs. ≥5 ng/ml, P=0.014), neural invasion (yes vs. no, P=0.064), interval between NCRT and TME (≥8 weeks vs. <8 weeks, P=0.000), and given consolidation chemotherapy (yes vs. no, P=0.015) were significantly associated with pCR and near pCR rates. Multivariate analysis was performed for the characteristics that had P<0.1 in the univariate analysis (Table II). Aside from neural invasion [OR: 0.447; 95% confidence interval (CI): 0.070-2.838; P=0.393], N stage (OR: 0.729; 95% CI: 0.280-1.902; P=0.518), and AJCC/UICC stage (OR: 0.260; 95% CI: 0.041-1.661; P=0.155), clinical T stage (OR: 0.273; 95% CI: 0.110-0.677; P=0.005), CEA level (OR: 0.378, 95% CI: 0.151-0.944; P=0.037), interval between CRT and TME (OR: 0.263; 95% CI: 0.088-0.785; P=0.017), and given consolidation chemotherapy (OR: 0.378; 95% CI: 0.151-0.944; P=0.037) were factors significantly associated with pCR and near pCR.

Survival. The Kaplan-Meier curves (Fig. 2) demonstrated that the 3-year DMFS (70.72% vs. 74.64%; HR: 1.129; 95% CI: 0.5928-2.162; P=0.70), DFS (70.95% vs. 71.89%; HR: 1.063; 95% CI: 0.5801-1.952; P=0.84), and OS (73.99% vs. 83.40%; HR: 1.286; 95% CI: 0.6300-2.666; P=0.48) did not differ significantly between the two groups. The decision for adjuvant treatment was made on an individual basis according to pathological staging. A total of 69 (44.23%) patients received adjuvant chemotherapy for >3 months, implementing the same regimen used for neoadjuvant chemotherapy (36 in the consolidation group and 33 in the control group). The survival rate of the 69 patients was further analyzed, and distant metastasis was observed in 20 (29.0%) patients [seven (19.4%) in the consolidation group and 13 (39.4%) in the control group]. The estimated 3-year DMFS was 81.91% in the consolidation group compared with 59.66% in the control group (HR: 0.4780; 95% CI: 0.2006-1.162; P=0.10). The 3-year OS was 88.15% in the consolidation group compared with 75.32% in the control group (HR: 0.260; 95% CI: 0.1658-1.594; P=0.25). Although the estimated 3-year DMFS and OS were not significantly different between the two groups, the consolidation group exhibited a higher rate of DMFS and OS. Local recurrence was observed in 7 (10.1%) patients overall [three (8.3%) in the consolidation group and four (12.1%) in the control group]. The estimated 3-year DFS was 85.48% in the consolidation group, and 56.64% in the control group (HR: 0.3992; 95% CI: 0.1752-0.9366; P=0.036, Fig. 3).

Surgical outcome and complications. All patients underwent optimal surgery with TME, among which 56 (73.6%) patients in the consolidation group and 53 (66.2%) patients...
in the control group received a sphincter-saving procedure (P=0.312). A total of 73 (96.1%) patients in the consolidation group and 72 (90.0%) patients in the control group obtained R0 resection of the primary tumor, with negative distal and radial margins. Comparing postoperative pathological findings with clinical status based on imaging prior to NCRT, a higher rate of downstaging for tumor (65.8% vs. 48.6%, P=0.032) and node (55.3% vs. 35%, P=0.011) category was observed in the consolidation group compared with the control group (Table III). No perioperative mortality occurred in this cohort. A total of 25/156 (16.02%) patients developed postoperative complications, including intestinal obstruction (6.5% vs. 7.5%, P=0.822), anastomosis fistula (1.31% vs. 1.25%, P=0.971), infection (6.57% vs. 2.5%, P=0.219), urinary complications

Table I. Summary of patient characteristics.

| Parameter                                      | Total (n=156) | Consolidation group (n=76) | Control group (n=80) | P-value  |
|------------------------------------------------|---------------|----------------------------|----------------------|----------|
| Age, median (range)                            |               | 50 (22-70)                 | 55 (24-80)           | 0.129    |
| Sex                                            |               |                            |                      |          |
| Male                                           | 108 (69.2%)   | 57 (75%)                   | 51 (63.8%)           | 0.128    |
| Female                                         | 48 (30.8%)    | 19 (25%)                   | 29 (36.3%)           |          |
| Clinical T-stage                               |               |                            |                      | 0.130    |
| cT3                                            | 37 (23.7%)    | 14 (18.4%)                 | 23 (28.8%)           |          |
| cT4                                            | 119 (76.3)    | 62 (81.6%)                 | 57 (71.2%)           |          |
| Clinical N-stage                               |               |                            |                      | 0.539    |
| cN0                                            | 26 (16.7%)    | 14 (18.4%)                 | 12 (15.0%)           |          |
| cN1                                            | 49 (31.4%)    | 26 (34.2%)                 | 23 (28.7%)           |          |
| cN2                                            | 81 (51.9%)    | 36 (47.4%)                 | 45 (56.3%)           |          |
| AJCC/UICC stage                                |               |                            |                      | 0.567    |
| II                                             | 26 (16.7%)    | 14 (18.4%)                 | 12 (15%)             |          |
| III                                            | 130 (83.3%)   | 62 (81.6%)                 | 68 (85%)             |          |
| Differentiation                                |               |                            |                      | 0.186    |
| Well differentiated                            | 24 (15.4%)    | 10 (13.2%)                 | 14 (17.5%)           |          |
| Moderately differentiated                      | 89 (57.1%)    | 49 (64.5%)                 | 40 (50%)             |          |
| Poorly differentiated or mucinous adenocarcinoma| 43 (27.5%)    | 17 (22.3%)                 | 26 (32.5%)           |          |
| Distance from anorectal verge                  |               |                            |                      | 0.307    |
| 0-5 cm                                         | 90 (57.7%)    | 47 (61.8%)                 | 43 (53.8%)           |          |
| 6-10 cm                                        | 66 (42.3%)    | 29 (31.2%)                 | 37 (46.2%)           |          |
| Pretreatment with CEA                          |               |                            |                      | 0.312    |
| <5 ng/ml                                       | 88 (56.4%)    | 46 (60.5%)                 | 42 (52.3%)           |          |
| ≥5 ng/ml                                       | 68 (43.6%)    | 30 (39.5%)                 | 38 (47.5%)           |          |
| Neural invasion                                |               |                            |                      | 0.221    |
| No                                             | 146 (93.5%)   | 73 (96.1%)                 | 73 (91.3%)           |          |
| Yes                                            | 10 (6.5%)     | 3 (3.9%)                   | 7 (8.7%)             |          |
| Lymph vascular invasion                        |               |                            |                      | 0.959    |
| No                                             | 152 (97.4%)   | 74 (97.4%)                 | 78 (97.5%)           |          |
| Yes                                            | 4 (2.6%)      | 2 (2.6%)                   | 2 (2.5%)             |          |
| Interval NCRT and TME                          |               |                            |                      | 0.908    |
| ≥8 weeks                                       | 89 (57.1%)    | 43 (56.6%)                 | 46 (57.5%)           |          |
| <8 weeks                                       | 67 (42.9%)    | 33 (43.4%)                 | 34 (42.5%)           |          |
| BMI                                            |               |                            |                      | 0.188    |
| ≥25 kg/m²                                      | 36 (23.1%)    | 21 (27.6%)                 | 15 (18.8%)           |          |
| <25 kg/m²                                      | 120 (76.9%)   | 55 (72.4%)                 | 65 (81.3%)           |          |
| Median follow-up time (months)                 | 30            | 32                         |                      | 0.058    |

AJCC, American Joint Committee on Cancer; UICC, Union for International Cancer Control 2010; CEA, carcinoembryonic antigen; NCRT, neoadjuvant chemoradiotherapy; TME, total mesorectal excision; BMI, body mass index.
Toxicity. The grade 3 or 4 toxicities that developed during neoadjuvant treatment are described in Table V. The rates of hematological toxicity and non-hematological toxicity were not influenced by the administration of consolidation chemotherapy. A total of nine (11.8%) and six (7.5%) patients in the consolidation and control groups had grade 3 or 4 leukopenia, respectively (P=0.358). Grade 3-4 anemia was observed in four patients (5.3%) in the consolidation group.
and in one patient (1.3%) in the control group (P=0.155). Thrombocytopenia was observed in eight patients (10.5%) and six patients (7.5%) in the consolidation and control group, respectively (P=0.509). Overall, grade 3-4 nausea or vomiting, radiation proctitis, diarrhea, dermatitis, hand-foot syndrome, and peripheral neuropathy occurred in two (2.6%), five (6.6%), 15 (19.7%), one (1.3%), five (6.6%), and two (2.6%) patients in the consolidation group and in one (1.3%, P=0.530), four (5.0%, P=0.67), nine (11.3%, P=0.142), one (1.3%, P=0.971), two (2.5%, P=0.219), and zero (0%, P=0.236) patients in the control group, respectively. Neither a life-threatening decrease in blood count nor febrile neutropenia was observed. No other grade 3 or 4 toxicities were recorded.

Discussion

Preoperative 45-50.4 Gy pelvic irradiation combined with fluorouracil or capecitabine monotherapy is the current conventional treatment regimen for LARC. However, a number of studies have reported that this treatment modality yields low pCR rate (12-20%), and this treatment regimen has not significantly improved patients’ survival (5,6). Systemic metastasis is closely associated with long-term survival. However, the majority of patients with rectal cancer may have early micrometastases on initial diagnosis (17,18). Previous studies have revealed that, although preoperative radiotherapy and TME surgery can improve the local control rate, they are inadequate for the treatment of systemic micrometastases (17,18). Previous studies have also demonstrated that the later postoperative systemic chemotherapy was given, the higher the risk of postoperative metastases (19,20). It has also been demonstrated that the addition of chemotherapy either before or following chemoradiotherapy may increase the pCR rate, indicating a synergistic response of additional chemotherapy to standard chemoradiation (8,21). However, few studies regarding consolidation chemotherapy have been published, and even fewer studies concerning the survival of patients who underwent consolidation chemotherapy have been performed to date.

In the present study, a statistically significant increase in the rate of pCR and near pCR in patients administered consolidation chemotherapy compared with those administered conventional neoadjuvant treatment (32.8% vs. 16.25%, respectively), was observed, which largely coincides with the results of previous studies (22,23). Habr-Gama et al (24) first reported the strategy of consolidation chemotherapy in the resting period between the completion of NCRT and surgery. In their cohort, 14 (48%) patients achieved complete clinical response, and five (17%) patients achieved pCR of the primary lesion following surgery. In 2015, Garcia-Aguilar et al (8) published a nonrandomized trial in which the addition of two to six cycles of infusional fluorouracil, leucovorin, and oxaliplatin was associated with an increased pCR rate (18-38%), without increasing complications, compared with the strategy of traditional NCRT in patients with LARC. However, there was a major limitation to this study; as the number of cycles of consolidation chemotherapy increased, the interval between neoadjuvant therapy and surgery also

Table III. Summary of surgical outcome in the consolidation group compared with the control group.

| Parameter                        | Consolidation group, no. (%) | Control group, no. (%) | P-value |
|----------------------------------|------------------------------|------------------------|---------|
| No. of patients                  | 76                           | 80                     | -       |
| pCR + near pCR                  | 25 (32.80)                   | 13 (16.25)             | 0.015   |
| Anal preservation                | 56 (73.60)                   | 53 (66.20)             | 0.312   |
| Resection with negative margins  | 73 (96.10)                   | 72 (90.00)             | 0.140   |
| T downstaging (ypT<ccT)          | 50 (65.8)                    | 39 (48.6)              | 0.032   |
| N downstaging (ypN<ccN)          | 42 (55.30)                   | 28 (35.00)             | 0.011   |

aNear pCR rate being defined by the finding of only isolated residual tumor cells or small groups of residual cancer cells in the rectal wall with no tumor cells in the lymph nodes. pCR, pathologic complete response; T downstaging, tumor downstaging; N downstaging, node downstaging.
increased, which may lead to a high pCR rate. Nonetheless, it has been demonstrated that the increased pCR rate may depend on the timing of response assessment (15). In the present study, the median time interval between the two groups was 8.7 weeks in the consolidation group and 7.4 weeks in the control group (P=0.218). The majority of patients (72%) received two cycles of consolidation chemotherapy, which may reduce the impact of the number of cycles and the treatment interval on pCR and near pCR. Consolidation chemotherapy may improve the pCR rate, and this may be due to numerous reasons. Firstly, extending chemotherapy to the resting period may also allow further exposure of irradiated tumor cells to chemotherapy and eradicate the minimal residual tumor cells (24). Additionally, administering preoperative chemotherapy is conducive to further reducing the tumor burden, as the tumor has a rich blood supply in the preoperative phase, which is beneficial to the distribution of chemotherapy drugs. Lastly, the general condition of the patient is likely to be improved, and thus chemotherapy is better tolerated at this stage.

Data on the impact of consolidation chemotherapy on long-term disease recurrence and survival are limited. The present study has demonstrated an improved DFS (85.48% vs. 56.64%, P=0.036) in patients administered consolidation chemotherapy following stratified analysis by selecting patients with >3 months of adjuvant chemotherapy. OS and DMFS were not significantly different between the two groups, although the consolidation group displayed a higher rate of DMFS and OS (81.91% vs. 59.66%, P=0.010; 88.15% vs. 75.32%, P=0.25) compared with conventional NCRT. The results from the present study verified that consolidation chemotherapy may be associated with improved local control rate and favorable DFS. It may represent a subgroup of LARC with an improved biological behavior. Larsen et al (25) evaluated the prognostic value of CapeOX regimen before, during and after NCRT in LARC and reported a 5-year OS and PFS of 72 and 62%, respectively. Garcia-Aguilar et al (8) recently published a nonrandomized trial in which the addition of 2-6 cycles of FOLFOX was associated with an increased pCR rate (from 18-38%), however the study did not provide evidence of a benefit to long-term survival.

One concern with the use of consolidation chemotherapy is that it may significantly increase toxicity, reduce tolerance and compromise the treatment effect. In the present study, consolidation chemotherapy was well tolerated. Grade 3-4 toxicities were also comparable with those using conventional NCRT (8). This result may be attributed to the following factors: Firstly, modern, highly conformal radiation therapy planning and delivery techniques may potentially reduce the radiation dose to the bowel and pelvis, consequently reducing gastrointestinal side effects and hematological toxicity (26); Secondly, consolidation chemotherapy may be better tolerated.

### Table IV. Summary of complications in the consolidation group compared with the control group.

| Parameter                | Consolidation group, no. (%) | Control group, no. (%) | P-value |
|--------------------------|------------------------------|------------------------|---------|
| No. of patients          | 76                           | 80                     |         |
| Intestinal obstruction   | 5 (6.50)                     | 6 (7.50)               | 0.822   |
| Anastomotic fistula      | 1 (1.31)                     | 1 (1.25)               | 0.971   |
| Infection                | 5 (6.57)                     | 2 (2.50)               | 0.219   |
| Urinary complications    | 0 (0.00)                     | 1 (1.25)               | 1.000   |
| Pelvic fibrosis          | 2 (2.63)                     | 2 (2.50)               | 1.000   |

### Table V. Preoperative chemoradiotherapy grade 3 or 4 toxicities in the consolidation group compared with the control group.

| Parameter                | Consolidation group, no. (%) | Control group, no. (%) | P-value |
|--------------------------|------------------------------|------------------------|---------|
| No. of patients          | 76                           | 80                     |         |
| Hematologic toxicity     |                              |                        |         |
| Leukopenia               | 9 (11.8)                     | 6 (7.5)                | 0.358   |
| Anemia                   | 4 (5.3)                      | 1 (1.3)                | 0.155   |
| Thrombocytopenia         | 8 (10.5)                     | 6 (7.5)                | 0.509   |
| Nonhematologic toxicity  |                              |                        |         |
| Nausea or vomiting       | 2 (2.6)                      | 1 (1.3)                | 0.530   |
| Radiation proctitis      | 5 (6.6)                      | 4 (5.0)                | 0.67    |
| Diarrhea                 | 15 (19.7)                    | 9 (11.3)               | 0.142   |
| Dermatitis               | 1 (1.3)                      | 1 (1.3)                | 0.971   |
| Hand-foot syndrome       | 5 (6.6)                      | 2 (2.5)                | 0.219   |
| Peripheral neuropathy    | 2 (2.6)                      | 0 (0.0)                | 0.236   |
following NCRT, as patients have not been affected by surgical trauma or complications (27).

In the present study, the R0 resection rate of patients in the consolidation chemotherapy group was 96.1%. This corresponds to study of Gao et al (23). Engineer et al (28) previously demonstrated that the addition of chemotherapy following neoadjuvant radiochemotherapy for patients with poor or no response to NCRT may achieve a considerable R0 resection rate (62%). A modest increase in the rate of R0 resection in patients treated with consolidation chemotherapy compared with those treated with traditional neoadjuvant chemoradiotherapy (96.1% vs. 90%, respectively), was observed in the present study; however, it did not reach statistical significance (P=0.14). This may be a result of different attending surgeons and the small sample size of the study. The present study demonstrated an increase in the rate of anal preservation in patients administered consolidation chemotherapy, although the increase also did not reach statistical significance (73.6% vs. 66.2%; P=0.321).

The present study poses a number of limitations. Firstly, as it is a retrospective study, it may have certain disadvantages, including potential selection bias, recall bias and censored data. However, considering the lack of prospectively collected data available, the results may be interpreted as clinically significant. Secondly, owing to the paucity of conclusive data on the use of chemotherapy regimens in patients with stage II/III rectal cancer, FOLFOX, CapeOx, 5-FU/leucovorin or capecitabine are all recommended by the NCCN panel, therefore the protocols of consolidation chemotherapy included in the present study are somewhat heterogeneous. Thirdly, although the results appeared promising, the cohort was too small and the follow-up period too short to confirm whether this strategy yields an improved survival benefit compared with conventional NCRT. Due to the limited sample size and the short follow-up period, it was not possible to adequately analyze all of the results. Therefore, further investigations are required.

In conclusion, this preliminary study revealed that consolidation chemotherapy administered between NCRT and surgery may be associated with improved rates of pCR and near pCR, TN downstaging and DFS. Furthermore, the addition of chemotherapy did not lead to higher toxicity, complications, or worse quality of mesorectal excision. Consolidation chemotherapy is safe and associated with improved oncological outcomes, and may reduce the number of required cycles of postoperative chemotherapy or eliminate the need for such a treatment modality.

Acknowledgements

Not applicable.

Funding

This study was supported by National Natural Science Foundation of China (grant nos. 81672756 and 81472711).

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors’ contributions

HQL and DHW conceived and designed the experiments. HQL and PYL collected the data. JL performed the pathological evaluation. HQL and QZ conducted the clinical follow-up. ZJL and ZYD performed the statistical analyses. HQL and ZYD drafted and revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee of Nanfang Hospital of Southern Medical University (Guangzhou, China) approved the present study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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