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REVIEW ARTICLE

Status for clinically complete remission rectal cancer after concomitant chemo-radiotherapy in Taiwan

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Summary Treatment for Rectal cancer changed after the induction of concomitant chemo-radiotherapy, CCRT. Complete remission of the tumor leads to debate of the necessity of surgical intervention. We evaluate the treatment outcome to know if operation is beneficial to these patients. Patients received long course concomitant chemo-radiotherapy for advanced rectal cancer between 2004 and 2013 in Taiwan were enrolled. Total 2780 patients diagnosed advanced rectal cancer were enrolled. In these patients, 2578 received surgical intervention and 202 were in wait and see for complete remission tumor. Higher local recurrence rate was found with wait and see group (8.9% vs. 2.7%). Also, better overall survival, disease free survival and local recurrence free survival were seen with the surgical intervention group. Surgical intervention may be benefit for some misdiagnosed completed response to CCRT.

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1. Introduction

Colorectal cancer is one of the leading cancers worldwide and surgical resection is the standard treatment. Ever since the introduction of rectal cancer surgery, preservation of anus has remained a major issue and point of debate between surgeons and patients. Surgeons have made suggestions and provided medical service based on the oncologic outcome which has sometimes been opposite to the patients' wish for anal preservation. Initially, many patients find it difficult to accept the destruction of the anus in surgery (abdominal-perineal resection) and the creation of a permanent colostomy. However, the development of chemotherapy and radiotherapy has changed the treatment modality for lower rectal cancer.[1] Although surgical resection remains the standard treatment for rectal cancer with the best possible prognosis, neoadjuvant therapy whether short course radiotherapy or long course concomitant chemo-radiotherapy (CCRT) is also recommended for advanced disease. Meanwhile, the improvement of diagnostic tools provides better evidence on the diagnosis of cancer stage before operation. We follow the treatment guideline but can make modifications based on the clinical information.[2] Surgical resection may not be the only choices now.

Neoadjuvant therapy has been used to reduce the local recurrence rate for advanced tumors. Other possible benefits as to reduce tumor size, downstage disease, increase R0 resection rate, and preserve sphincter are also reported in previous studies.[3,4] Trans-anal surgery is reported in several studies for early stage low rectal cancer.[5,6] These studies also reveal the feasibility of a "wait and see" approach after local excision or chemoradiation for selected early stage rectal cancer.[7–10] Although the latest National Comprehensive Cancer Network (NCCN) guidelines still recommend not to change the policy for rectal cancer resection despite tumor regression after neoadjuvant therapy, modification with individualized therapy is the current trend. Wait and see policy is a typical individual therapy and similar survival results to those for radical surgeries are reported.[11,12] However, the selection criteria remain unclear. The main concern is how to define the clinical T0 rectal cancer. Ultrasound, magnetic resonance imaging (MRI), or fluorodeoxyglucose-positron emission tomography (FDG-PET) is used to carry on the assessment but still limitations are found with each exam.[13–16] Also, selection bias may be seen with the elderly or patients with multiple comorbidities.[17] A larger sample size may be necessary to clarify the impact from CCRT in clinically complete response patients.

In Taiwan, we have more than 10 thousand newly diagnosed colorectal cancers per year with a standardized incidence of 45.1/100,000 in 2012.[18] The number of medical centers in Taiwan is more than 10 and each hospital follows similar guidelines for colorectal cancer treatment. Current policy for advanced low and middle (tumor location within 10 cm from the anal verge) rectal cancer is neoadjuvant therapy first. Radical resection would be arranged within one to two weeks for the patients received short course CCRT. Re-evaluation of the tumor status for the patients after long course CCRT would be arranged six to eight weeks after the completion of radiotherapy. The treatment policy may be modified based on the tumor response to CCRT. Local excision or wait and see may be the option for clinically partial or complete response tumors.

Here, we focus on post neoadjuvant long course CCRT with clinically staged patients who have received different following treatment modality. The main purpose of this study is to clarify the necessity of surgical intervention as the standard procedure and optimal choice for clinical complete response patients. This is a retrospective study in which the data is taken from the Taiwan health insurance database.

2. Patients and method

We traced the data from the Health Promotion Administration, Ministry of Health and Welfare, Taiwan. Patients diagnosed with rectal cancer (within 15 cm from anal verge) and who received neoadjuvant CCRT between 2004 and 2013 were recruited. Pre-treatment diagnostic tools included complete colonoscopy to rule out synchronous colorectal lesion, and MRI or computed tomography (CT) to determine the presence of possible nodal metastasis or distant metastasis. Tissue was obtained during colonoscopy for pathological diagnosis and to confirm the necessity of neoadjuvant therapy. Neuroendocrine tumors, gastrointestinal stromal tumors or other radiotherapy insensitive tumors were excluded. The neoadjuvant therapy was long course radiotherapy (5040 cGy–5400 cGy) with 5-Fu based chemotherapy. After CCRT, repeat exams were arranged and the post-CCRT changes were recorded. Patients were excluded if they were lost to follow up, or if distant metastases were found during CCRT. The remaining patients were divided into two groups, depending on whether they had surgical intervention or not. The available diagnostic tools for the clinical complete response patients included anal digital exam, image study (CT. MRI, or PET), or colonoscopy exam with/without tissue biopsy. The decision for resection or not was based on the clinical findings. Regarding the surgical group, operations were performed 6–8 weeks after the completion of radiotherapy. Tumor size, grade, stage and regression status were recorded by pathologists. Both groups received similar program of follow-up assessment. During follow-up, digital examination, chest radiography, carcinoembryonic antigen (CEA) level determination, CT, PET, abdominal ultrasonography, and colonoscopy were performed to evaluate metastatic or recurrent disease. Recurrence was defined in three categories as local recurrence, regional recurrence, and distant metastasis. Local recurrence means a new tumor lesion was found at an anastomotic site or local excision site for the surgery group and previous tumor location for the non-surgical group. Regional recurrence was diagnosed by studying images including CT/MRI/PET. Tumor or mass lesion was identified within the pelvic area but not linked to previous tumor or anastomotic site were assigned in this category. Distant metastasis was also diagnosed by studying images.

Data were analyzed using SPSS software (version 20, IBM). Comparisons between groups were made using Fisher's exact test. Survival differences were compared using the log-rank test. Statistical significance was set at $P < 0.05$.

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