



Watch and wait approach to the treatment of rectal carcinomas

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During the last decades, the treatment of rectal cancer has developed from only surgical treatment with total mesorectal excision (TME), then surgical treatment with neoadjuvant radiotherapy or radiochemotherapy, and in the last years with total neoadjuvant treatment (TNT) with systemic therapy together with radiochemotherapy before surgery. The surgical treatment, despite precise anatomical dissection, is associated with significant morbidity, with bowel, urinary, and sexual dysfunction and permanent colostomy, impairing patients' quality of life permanently[1]. Around 20% of the patients developed a complete pathological response (pCR) after neoadjuvant treatment[2]. The survival of patients with pCR after neoadjuvant treatment and surgical TME, despite significant morbidity after surgery, is excellent[3]. Excellent survival raises the question of whether surgical treatment is necessary in patients with rectal cancer achieving a pCR after neoadjuvant treatment. The organ preservation in the Watch and wait (W&W) strategy with active surveillance without surgery has become increasingly interesting in patients with a complete or near complete clinical response as an attractive alternative to surgery, even though the local regrowth after cCR is high, reaching about 30%[4]. Patients are often willing to accept potentially worse oncological outcomes to avoid receiving permanent stoma. In strictly selected patients with cCR, the local regrowth occurs mainly in the first 2 years in

the bowel wall, so with the exact surveillance, the local unsalvageable disease after W&W was rare[5]. After local regrowth, the R0 salvage surgery was performed in most of the patients. However, the local failure in patients with local regrowth was high, about 24%, despite the high level of R0 resection, primarily due to patients refusing salvage surgery (9,1%) after local regrowth. Other reasons for local failure were recurrence after salvage surgery (7,8%), distant metastases (4,1%), frailty (2,4%), and unresectable rectal cancer (1.7%)[6]. In patients with a cCR followed by a W&W strategy, the development of local regrowth is also a risk factor for distant metastases. The risk of distant metastases also remains higher for 5 years after the development of local regrowth[7]. Patients with local regrowth from the International Watch and Wait Database with complete clinical response managed by the W&W strategy have a higher risk for distant progression than patients with near complete pathological response (with less than 10% residual cancer cells) after surgical treatment with TME from Spanish rectal Cancer project (VIKINGO). Local regrowth was an independent prognostic risk factor for distant progression[8].

Reducing the oncological risk while maintaining high organ preservation rates in patients using TNT is vital. The occurrence of cCR is a time-dependent phenomenon. The optimal time between

the completion of neoadjuvant radiation therapy and surgery in patients diagnosed with locally advanced rectal cancer is controversial. Assessment at 10 to 16 weeks may detect a minority of patients who achieve complete clinical response after neoadjuvant chemoradiation. Patients suspected of a cCR should be reassessed later [9]. On the other hand, it seems that in patients without pCR in the National Cancer Database, delaying surgery > 12 weeks was associated with reduced overall survival[10].

Many studies analyzing the W&W strategy have several limitations. Most are retrospective, with a limited number of patients included in the studies, high heterogeneity of neoadjuvant treatment, and different radiation techniques. We have only a low number of randomized trials[11].

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