Management of Locally Advanced Rectal Cancer

Yu Jo Chua, MBBS
and David Cunningham, MD, FRCP

Summary

The management of locally advanced rectal cancer remains a challenge because of relatively high local recurrence rates, even with optimal surgery. This chapter reviews the evidence from clinical trials for the use of various perioperative strategies based on radiotherapy, chemotherapy, or both in these patients, as well as discusses how these results may inform clinical practice. In particular, two treatment strategies that have been shown to be beneficial and that are standard treatment options for patients with locally advanced disease are short-course preoperative radiotherapy and long-course preoperative chemoradiotherapy. In clinical trials in which these treatments were used in addition to surgery, improvements in local recurrence rates have been observed, although overall survival has less frequently been prolonged. These patients should also receive postoperative adjuvant chemotherapy.

Other issues that are discussed include the selection of patients with locally advanced disease for treatment, the use of total mesorectal excision as the optimal surgery for these patients, the impact of various preoperative treatments on sphincter preservation rates, and ongoing areas of research in this disease. Although the management of these patients continues to be controversial, it is clear that surgery alone is inadequate for patients with locally advanced rectal cancer and that they are best managed in a multidisciplinary setting.

Key Words: Rectal cancer; locally advanced; radiotherapy; chemoradiotherapy; preoperative treatment.

1. INTRODUCTION

The management of locally advanced rectal cancer is controversial, with opinions and practices varying between and within countries, and particularly between the United States and Europe. Although many clinical trials have explored various strategies for using radiotherapy (RT), chemotherapy, or both
for improving outcomes from surgery, the main therapeutic intervention for these patients, relatively few of these trials have been randomized studies. The interpretation of results and cross-study comparison for the purposes of informing a universally acceptable standard treatment plan have been complicated by issues such as variability in patient selection criteria and technique (e.g., clinical assessment, endorectal ultrasonography [EUS], or magnetic resonance imaging [MRI]), RT techniques (e.g., field techniques and small bowel protection), surgery, and reporting of results. Some of these factors have become less prominent with more consistent use of imaging techniques to aid patient selection, better understanding of the importance of various pretreatment prognostic factors, and improved standardization of RT and surgical techniques.

1.1. Total Mesorectal Excision Surgery

Local recurrence rates of 25–40% have been reported in large series of patients undergoing conventional resections (1,2). An early advance in the treatment of rectal cancer has been that of total mesorectal excision (TME) surgery, which was developed in the United Kingdom in the late 1970s as a response to the poor results with the conventional anterior resections (ARs) and abdomino-perineal resections (APRs) of the time (3). The surgical technique involves the sharp dissection under direct vision of the avascular plane between the mesorectum and the surrounding parietal tissues down to the distal extremities of the pelvis. The resected specimen should ideally have a smooth unbroken surface, a factor in assessing the quality of the procedure performed. In a case series by Heald et al., which included 405 curatively resected patients, the local recurrence rate at 5 and 10 yr was reported to be 3 and 4%, respectively. TME surgery has been widely adopted in Europe as standard treatment for patients with operable rectal cancer. In the United States, TME is regarded by the academic surgical community as appropriate standard treatment; however, actual surgical management of patients in the United States is less standardized, and unfortunately some patients are still receiving substandard surgical procedures.

In two nonrandomized comparisons of the outcomes of patients operated by TME or conventional surgery, it was found that TME was associated with an improved overall survival (OS) and local recurrence rate (1,2). When the results of a Dutch randomized trial that specified that all patients should have TME surgery (4) were compared with those of historical controls from an earlier study of conventional surgery (5), it was found that TME surgery decreased local recurrence rates from 16 to 9% and that the type of surgery (TME vs non-TME) was an independent predictor for local recurrence ($p = 0.002$) (6). Although survival was also higher in the TME cohort (2-yr survival of 86 vs 77% for the non-TME cohort, $p = 0.002$), the risk of distal recurrence was not affected by the type of surgery and was predicted only by the tumor-node