

Advances and controversies in treatment for locally advanced rectal cancer over the past decades: West meets East

1 | INTRODUCTION

The treatment of locally advanced rectal cancer (LARC) is still challenging and incorporation of new treatment options are being explored and continue to evolve. Total mesorectal excision (TME) with clear circumferential resection margin (CRM) has been accepted as a gold standard of surgery for LARC globally. Complete TME and negative CRM (1 mm) demonstrated improvement of overall survival and reduction in tumor local recurrence with less sexual and urinary dysfunctions.

In this issue of the *Annals of Gastroenterological Surgery*, Kim et al¹ reviewed challenging issues and shifting treatment strategy, and Toiyama et al² reviewed centurial changes in the surgical treatment for LARC. Even though surgery is the mainstay of LARC treatment, the perioperative treatments also have major roles for further improving survival. In the West, the patients with LARC will undergo neoadjuvant chemoradiotherapy (nCRT) or chemotherapy (NAC) followed by TME. However, nCRT contributes to local control significantly but not to overall survival sufficiently and the patients are likely to suffer from various adverse events as a result of the treatment. More recently, induction chemotherapy followed by CRT or upfront CRT followed by consolidation chemotherapy prior to TME, referred to as total neoadjuvant therapy (TNT), has been proposed. TNT, a new paradigm for LARC treatment, is associated with potential efficacy for higher pCR and CRM negative rates compared with nCRT alone or NAC because of greater compliance and earlier administration of full-dose systemic treatment. In addition, a more advanced concept in multidisciplinary treatment – the “watch and wait” strategy – has also developed to minimize long-term morbidity. There are many controversies in these treatments due to a lack of clear evidence regarding treatment protocols including regimens, interval between radiation and subsequent treatment, and adjuvant therapy issues. In Japan, these treatments prior to surgery are not standard until very recently, and lateral lymph node dissection (LLND) has been developed uniquely instead. The NCCN guideline does not recommend LLND unless metastases are clinically suspicious. However, the Japanese trial JCOG 0212 demonstrated the efficacy of LLND in reduction of local recurrence in the lateral pelvic compartment. Taking this result, some Western surgical communities

have been actively expanding this procedure. At the moment, the role of prophylactic LLND vs TNT is still a subject of ongoing debate.

Various international randomized controlled trials (RCTs) have demonstrated that laparoscopic colectomy has superior short-term outcomes and equivalent long-term survival to open resection, while there has been controversy regarding oncological safety of laparoscopic surgery for LARC. The results of several RCTs are inconsistent. The MRC-CLASSIC trial from the UK, the COLOR II trial from Europe, and the COREAN trial from South Korea revealed the equivalence in local recurrence and disease-free survivals. However, two last trials of the ACOSOG-Z6051 in North America and the ALaCaRT in Oceania failed to establish the noninferiority in positive rate of CRM, leading to widespread confusion and debate.³ Laparoscopic rectal cancer surgery with in-line rigid instruments is technically demanding and still highly challenging due to the limited operative field of the narrow pelvis.

Several options have been introduced to overcome the technical limitations of laparoscopic surgery. Transanal TME (TaTME) providing better operative view and less obstructive procedures near the lower rectum is revolutionary. The development of TaTME is expected to improve oncological and functional outcomes and it may play a role as “a trump card” in such difficult cases as obese or male patients with a large tumor or narrow pelvis. The two-team approach is also attractive because of the significant reduction in operative time. However, its technical difficulty sometimes leads to unique complications such as urethral injuries and purse string rupture. It is currently recommended not to perform TaTME in Norway due to clearly higher local recurrence rate. On the other hand, good results have been reported in the Netherlands, suggesting that a rather systematic education is important. These results need confirmation in RCTs, which are currently underway in the GRECCAR 11 trial from France and the COLOR III trial from Europe. International TaTME guidance group including members of the Japan Society for Endoscopic Surgery has just provided a current framework of best practice related to implementation of TaTME.⁴ Robotic-assisted laparoscopic surgery (RALS) providing a stable 3D operating field and intuitive procedures with multiple joints forceps is also extremely innovative. Better ergonomics for the surgeon that make it possible to perform complex procedures precisely is expected to improve the

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quality of TME and reduce autonomic nerve damage. Meta-analysis showed its feasibility despite lack of tactile sensation and higher costs.⁵ However, there is still limited evidence on oncological benefits and safety. The ROLARR trial conducted mainly in the UK failed to reveal the superiority in open conversion, positive CRM, and TME completion rates of RALS, while there is a rapid learning curve and good indications for difficult cases. In Japan, RALS has been covered by insurance for about 2 years which has led it to spread rapidly. Convincing evidence on the safety and oncological benefit of RALS is essential, and two studies in Japan are currently in progress, one is analysis of the National Clinical Database, which is a large-scale nationwide web-based database, and the other is a multicenter prospective phase II study (the VITRUVIANO trial).

I believe now is the time for the West to meet the East.

DISCLOSURE

Conflict of Interest: The author declares no conflicts of interest for this article.

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