# Optimal timing of surgery after preoperative chemoradiotherapy for rectal cancer

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The optimal timing for rectal cancer surgery after neoadjuvant chemoradiotherapy, in terms of risk of complications or tumour response, remains uncertain.


## Summary

The timing of surgery in rectal cancer treatment after neoadjuvant chemoradiotherapy is debated, mainly because of downsizing and repopulation of tumour cells. The retrospective analysis of prospectively collected data from a series of patients with locally advanced rectal cancer by Lim et al. (**Optimal surgery time after preoperative chemoradiotherapy for locally advanced rectal cancers**. *Ann Surg* 248:243–251) tried to evaluate whether timing of surgery after neoadjuvant chemoradiotherapy has any effect on tumour regression, sphincter preservation, local recurrence rate or overall survival. The study included 397 patients who had received chemoradiotherapy and surgery with different time intervals between the use of these modalities. No differences regarding all four parameters were found in patients with a time interval less or greater than 41 days. Some methodological reasons can be discussed, but the only way to answer the question of timing is, of course, to do a randomised trial.


This article was first published online in ***Nature Clinical Practice Oncology*** 20 January 2009, and is reproduced with permission.
 doi:10.1038/ncponc1325
www.nature.com/clinicalpractice

Surgery is recommended within four to five weeks after chemoradiotherapy for rectal cancer. If the interval is longer there is a risk of repopulation of tumour cells, but the benefit could be increased shrinkage of the tumour. Gradually, on the basis of individual experience, the time span from the end of chemoradiotherapy to surgery has slowly increased – in some cases to a 'wait and watch' approach. The exact timing is not known, but some reports indicate fewer postoperative complications if surgery is postponed for more than six weeks. Lim and colleagues carried out an interesting retrospective study to evaluate the optimum time of surgery after neoadjuvant chemoradiotherapy in patients with locally advanced rectal cancer.[1] A total of 397 prospectively enrolled patients with locally advanced disease was divided into two groups according to the time interval between chemoradiotherapy and surgery: group A (4–6 weeks), and group B (6–8 weeks). Patients with a tumour located at the middle or distal rectum, no previous malignancy and no evidence of distant metastasis were included.

The primary endpoints were whether timing has any effect on downstaging, volume reduction, response rate, sphincter

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preservation, anastomotic-related complication rate, local recurrence survival and overall survival. In this retrospective analysis, five surgeons carried out the surgical procedures. Allocation of patients to surgical procedures was not equal; one surgeon carried out almost half of the procedures and the remaining four carried out the rest – one of these carried out just 2% of the operations.

The mean difference in time period between group A and group B was 15 days, but it is not possible to determine from the paper the median time, which means that the interval between the two groups could be close. One very important difference between the two groups is the chemotherapy regimen, which could be biased in a study such as this one. Patients with delayed surgery have more often been treated with irinotecan hydrochloride and capecitebine (rather than 5-fluorouracil and leucovarin, or capecitabine alone) compared to those with a shorter interval to surgery. However, as this is a retrospective report from a nonrandomised cohort, it is difficult to draw firm conclusions.

Of note, no differences were observed in the response to preoperative chemoradiotherapy between the groups, and there were no differences at all regarding surgical treatment, in terms of sphincter preservation and postoperative, as well as anastomotic, complications. However, a covering ileostomy was performed more often in patients with delayed surgery than in those with a shorter interval to surgery.

From this retrospective analysis of prospectively collected data, it has not been possible to prove any beneficial effects of delaying surgery in patients with rectal cancer after neoadjuvant chemoradiotherapy. The authors of this study concluded that delaying surgery does not improve chemoradiotherapy response or sphincter-preservation rate. The question is, of course, whether or not a delay is beneficial and if so, for how long should one wait? The only way to answer this question is to have strict criteria for the waiting period, with a defined number of weeks, and to test this approach in a randomised trial. Series from hospitals have shown that the longer surgery is delayed, the greater the reduction of the tumour, with a greater effect seen in downsizing, or even an end to the need for surgery at all.[2] The question of sphincter preservation has been addressed in several randomised trials, and no real effect of the timing of surgery has been demonstrated.[3] A study has shown, however, an important time period (around two to three weeks after radiotherapy) when the rate of complications to surgery is high.[4] In this study, short-course radiotherapy was used. Data assessing short-course radiotherapy and delayed surgery indicate a positive effect on downsizing.[5] Preliminary data from an ongoing, randomised, Swedish trial have shown that postoperative complications decrease if the period from radiotherapy to surgery is long.[6]

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