COLOR II – A randomized clinical trial comparing laparoscopic and open surgery for rectal cancer

SUMMARY

Introduction and background

Laparoscopic resection of colorectal malignancies is still controversial, mainly due to initial reports on port-site metastases that caused major concern. Atlhough retrospective studies with large numbers of patients now suggest that the incidence of port-site metastases is comparable to the incidence of wound metastases in open surgery, the pathogenesis of these recurrences remain unclear.

Experimental studies and one randomized clinical trial (Lacy, 2004, New Eng J Med) indicate that laparoscopic surgery might even result in lower recurrence rates. In this trial comparing laparoscopic versus open colectomy for colonic cancer, an improved 3-year survival following laparoscopic resection was found. Results of the COLOR I trial (a comparison between laparoscopic and open surgery in the treatment of colonic cancer) is expected to be available around June 2006.

With ever advancing technique in laparoscopic surgery, the possibilities for longer and more complex operations are expanding. Along with this trend laparoscopic surgeons are performing more demanding surgical procedures, such as Total Mesorectal Excision (TME) for rectal cancer. We believe that the development of laparoscopic TME procedures should be performed in within a trial setting, because long-term results are not established. Within a trial, the technique can be standardized and quality control is assured.

Study design

The COLOR II trial is a randomized, international, multi-center study comparing the outcomes of laparoscopic and conventional resection of rectal carcinoma with curative intent. Clinical and operative data will be collected centrally in the coordinating center in Rotterdam, The Netherlands. Quality of life and costs will be assessed on a national basis. Prior to the start of the COLOR II trial, a feasibility study will be performed. The objective of this feasibility study is to control quality of laparoscopic TME procedures. Per center, five consecutive TME's are peformed, and either recorded or observed by an expert in laparosopic TME. All resected specimens are pathologically analyzed. Furthermore, each participating center should at least send one unedited video of a laparoscopic TME to the monitoring committee for approval.

Endpoints

Primary endpoints of this phase III trial is locoregional recurrence rate 3 years postoperatively. Secondare endpoints are recurrence free and overall survival at three, five and seven years, rate of distant metastases, port-site and wound-site recurrences, microscopic evaluation of the resected specimen, 8-week morbidity and mortality, quality of life and costs.

Statistics

Using log rank statistics with a power of 80% and a type I error of 5%. 1275 patients are needed to detect a difference between both treatment arms of 5% in locoregional recurrence rate 3 years postoperatively, assuming a 10% recurrence rate in the open group. Randomization will be 2:1, laparoscopic versus open resection respectively. Analyses will be on an "intention-to-treat" basis. Randomization is stratified for each participating center, location of the tumor, planned procedure, radiotherapy and gender.

Main selection criteria

Patients with a single rectal cancer at less than 15 cm from the anus at rigid rectoscopy, eligible for surgery with curative intent, can be included. Not included are patients who have local excision of a rectal cancer. Also not eligible are patients with concomitant metastases of other malignancies in their medical history or with signs of acute intestinal obstruction.

Follow-up

Patients will be examined at least once a year for seven years. Every year, up to 7 years after surgery, anamnesis and physical examination are performed. In case of recurrent disease, follow up should be until 3 years from the time of diagnosis of recurrence.