



# Comparison between laparoscopic and open surgery in stage II and III colorectal cancer using propensity score matching

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It is a great honor to comment on the article entitled “Propensity score-matched study of laparoscopic and open surgery for colorectal cancer in rural hospitals” by Nakao and his colleagues in the *“Journal of Gastroenterology and Hepatology”* (1).

This retrospective study compared the short- and long-term outcomes between laparoscopic surgery (LAP) and open surgery (OP) for stages II and III colorectal cancer, especially in middle-volume hospitals in rural areas of Japan. They defined a middle-volume hospital as a hospital that has more than 200 beds and less than 200 colorectal cancer operations per year. The study included patients who underwent colorectal surgery from January 2004 to April 2009. A propensity score-matched case-control study of colorectal cancer patients was conducted, and 261 patients were included in each cohort. Overall survival (OS), disease-free survival (DFS), and postoperative complications of LAP and OP were compared, and they concluded that LAP may be a feasible option for stages II and III colorectal cancer.

In detail, as for short-term outcomes, the blood loss was significantly less in LAP than in OP ( $P < 0.01$ ), wound infection and ileus occurred less frequently ( $P < 0.01$ ,  $P = 0.01$ ) after LAP. Median postoperative hospital stay was 12 *vs.* 18 days, which was significantly shorter in the LAP group ( $P < 0.01$ ). There were no significant differences in the number of harvested lymph nodes, severity of postoperative complications, and mortality within 30 days postoperatively. As for long-term outcomes, the 5-year DFS was 81.8% and 77.8%, and the 5-year OS was 90.3% and 88.8% for LAP and OP, respectively, with no significant difference.

LAP for colon cancer has become common nowadays. Several randomized studies have reported not only its short-term benefits (i.e., decreased pain, improved postoperative pulmonary function, reduced postoperative ileus, improved incidence of wound infection, faster recovery, and shorter hospital stay) (2-7), but also its noninferiority in terms of long-term outcomes (i.e., morbidity, DFS, and OS) (4,8-12). The results shown in the article followed these previously reported findings. In fact, in Japan, 38,992 of the total 54,169 patients with resected colorectal cancer underwent laparoscopic surgery in 2015. This accounted 72% of all resected cases (13).

According to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines published in 2016 (14), it is recommended that careful consideration is necessary in adaption of LAP in stages II and III disease as it requires D3 lymphadenectomy. The concept of D3 lymphadenectomy in colorectal cancer is almost identical to that for mesocolic resection, which is widespread in the West. Many past randomized trials have excluded transverse colon cancer because of its anatomic complexity and difficulty (2,14,15). LAP for rectal cancer still is recommended to be performed as a “clinical trial” at this time (6,9), since it not only requires more advanced skills but also is unclear in oncologic safety (16,17). The guideline also refers to cases that need careful LAP adaption. High body mass index (BMI) and history of past laparotomy may lead to prolonged operation time, higher laparotomy conversion rate, and mortality (18-22). Therefore, the guideline recommends each hospital to determine their

adaptation criteria by their learning level and individual surgeon's skill.

The latest article by the Japan Clinical Oncology Group (JCOG) reported that the survival outcomes following LAP versus OP D3 dissection for Stage II or III colon cancer (JCOG 0404) were similar (23). It is a phase 3, randomized controlled trial, accomplished under strict quality control. Also, uniform surgical procedure, including D3 lymph node dissection with intraoperative photographs assessed by the quality control committee, was demanded. Uniform adjuvant chemotherapy was given to patients with stage III disease with fluorouracil (500 mg/m<sup>2</sup> by bolus intravenous infusion on days 1, 8, 15, 22, 29, and 36) and leucovorin 250 mg/m<sup>2</sup> by 2-hour drip intravenous infusion on days 1, 8, 15, 22, 29, and 36).

In this study, 1,057 patients were assigned randomly to either OP (n=528) or LAP (n=529). Transverse colon cancer was excluded. The 5-year OS was 90.4% for OP and 91.8% for LAP, and noninferiority was not demanded because the number of events observed was insufficient. The group previously reported short-term outcomes of this study that showed LAP was more beneficial than OP (7). As a whole, they concluded that LAP D3 surgery could be an acceptable treatment option for patients with stage II or III colon cancer.

Nakao *et al.* (1) mentioned that the surgical procedure and postoperative chemotherapies were performed in accordance with the JSCCR guidelines (14) and the standards of the participating institutions. However, the detailed surgical procedure, especially the extent of lymphadenectomy, is not mentioned. There were 16 (6.1%) transverse colon cases in the LAP group and 15 (5.8%) in the OP group, and 37 cases (14.2%) of rectal cancer in both groups. These cases may require more advanced surgical skills, leading to higher morbidity rates. The conversion rate in LAP was 8.4%, higher compared to the JCOG 0404. Therefore, it may be better to exclude these cases when analyzing the data for comparison to previous randomized controlled trials (RCTs). On the other hand, the median numbers of harvested lymph nodes were 12 in LAP and 14 in OP, much less than 21 and 22, respectively, in the JCOG 0404 study. Still, the 5-year OS rate was 90.3% and 88.8% for LAP and OP, respectively, similar to that of 91.8% for LAP and 90.4% for OP in the JCOG 0404.

The regimen of adjuvant chemotherapy is not introduced in this study by Nakao *et al.* (1). They have noted these points as limitations of this study and mentioned that

further accurate investigation is required. I strongly agree with the authors because the level of lymphadenectomy and adjuvant chemotherapy regimen may have substantially influenced the long-term outcomes. Since the rectal cancer cases were included, the ratio of simultaneous covering stoma also is a point of interest.

This article has focused on the LAP for colorectal cancer cases in rural middle-volume hospitals in Japan. It may be the first article to assess the practical surgery performed in such hospitals, as no similar studies have been published previously in Japan as far as we searched. It is interesting to see and compare the practical clinical data between rural middle-volume hospitals and high volume-centered hospitals. The results of this study may be highly suggestive, but we always must have knowledge of the latest and standard guidelines to make a proper judgment.

In conclusion, the results of the present study were comparable to those of the JCOG 0404 study, demonstrating the safety of the laparoscopic approach in stages II and III colorectal cancer in middle-volume hospitals in Japan. As for rectal cancer, careful indication of laparoscopic surgery still is regarded.

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