



Is laparoscopic gastrectomy an oncologically safe procedure in serosa-positive (pT4a) gastric cancer patients?

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Laparoscopic gastrectomy (LG) has been established as a minimally invasive procedure for the management of early-stage gastric cancer, and it has been acknowledged as the standard treatment option for clinical stage I gastric cancer patients as per the Japanese gastric cancer treatment guidelines (1). However, LG has also been used in clinical practice for the management of advanced gastric cancer. Three Asian randomized controlled trials (RCTs) of laparoscopic distal gastrectomy (LDG) and open distal gastrectomy (ODG) had been conducted for locally advanced gastric cancer in Asia (2-6). Short-term advantages of LDG, such as earlier bowel movement, earlier oral intake, or shorter postoperative hospitalization, were shown for both advanced gastric cancer and early-stage disease (2,3). However, whether LDG can reduce postoperative complications is controversial. Only one study showed a significantly lower incidence of overall postoperative complications in LDG, while the other two showed no significant difference (3,4). In view of the oncological safety in advanced stages, disease-free survival was not significantly different between LDG and ODG in any of these studies (4,5).

We had considerable interest in the article by Li *et al.* titled “*Surgical and long-term oncologic outcomes of laparoscopic and open gastrectomy for serosa-positive (pT4a) gastric cancer: A propensity score-matched analysis*” published in the *Journal of Surgical Oncology*. Patients with serosa-positive (pT4a) gastric cancer are considered at high risk for recurrence of peritoneal dissemination and have a poor prognosis. Pneumoperitoneum or contact of the tumor with the forceps

are considered as factors promoting the dissemination of cancer cells from serosa-positive tumors in LG. Therefore, the oncological safety of LG for serosa-positive gastric cancer is controversial. Li *et al.* retrospectively compared short- and long-term outcomes in 202 pairs of LG and OG with D2 lymphadenectomy for pT4a gastric cancer after propensity score matching between 211 LGs and 776 OGs. The incidence of overall postoperative complications was similar between LG (14.4%) and OG (16.3%), and individual complications did not differ significantly. Five-year overall survival and disease-free survival were not significantly different between LG and OG (44.6% *vs.* 42.1%, 40.1% *vs.* 37.6%). Importantly, LG and OG had similar overall survival rates in all pathological stages (IIB, IIIA, IIIB, and IIIC). The incidence of peritoneal recurrence did not differ significantly between LG and OG, with it being 13.4% and 10.9%, respectively. Additionally, the incidence of any other recurrent patterns assessed was similar in the two groups. The authors concluded that LG with D2 lymphadenectomy for patients with pT4a gastric cancer could be a feasible procedure in long-term oncologic outcomes (7).

For patients with advanced gastric cancer, LG appeared comparable with OG in terms of overall survival and disease-free survival. An RCT led by Yu *et al.* distal gastrectomy showed no difference in 3-year disease-free and overall survival between LDG and ODG (4). In accordance, a retrospective matched study by Kinoshita *et al.* showed similar overall, disease-specific, and recurrence-free survivals between LG and OG in patients

with advanced gastric cancer (8). A meta-analysis of retrospective studies also suggested that overall and disease-free survivals were not significantly different between those groups (9). Moreover, recurrent sites were not significantly different in the RCT of LDG versus ODG in a different matched study of LG and OG (4,8). Thus, LG has been considered as an oncologically safe procedure for advanced gastric cancer, although LG could not improve the survival of patients in comparison to OG. However, the incidence of clinical T4 tumors was found to be 41% in the RCT, and 50% in the matched study mentioned above (4,8). The incidence of peritoneal recurrence in the RCT cohort was 22.4% and 18.9% in the LDG and ODG groups, respectively (4), while in the matched study cohort, the incidence was 16.1% and 17.4% (8). Although the study by Li *et al.* included only pathological T4a tumors, it revealed a lower incidence of peritoneal recurrence (13.4% and 10.9% in LG and OG, respectively).

Nevertheless, early diagnosis of peritoneal recurrence is challenging, and the timing of follow-up examination might influence the results. Tumor size is another factor that potentially affects the incidence of peritoneal recurrence. Patients with large type 3 (≥ 8 cm) or type 4 (linitis plastica) tumors are likely to be diagnosed with serosa-invasion and peritoneal recurrence (10). A retrospective comparative study showed that LG had shorter overall survival than OG in type 4 gastric cancer patients alone (8). In the study by Li *et al.*, the low rate (35.6%) of tumors measuring >5 cm might be associated with the lower incidence of peritoneal recurrence (7).

Postoperative adjuvant chemotherapy has been proven to be essential for improved survival of patients at pathologically advanced stages (11). Unfortunately, the effects of postoperative adjuvant therapy were not described in the study by Li *et al.* (7). Postoperative complications have a tremendous impact on patient survival after gastrectomy and often impede postoperative adjuvant chemotherapy. Therefore, minimizing postoperative complications may result in improved survival. Only one RCT suggested the superiority of LG over OG in patients with advanced gastric cancer in terms of the incidence and severity of postoperative complications such as fluid collection and intra-abdominal bleeding, while other studies showed no significant differences (2,3,5). For early-stage patients undergoing LDG, wound-related complications were reported to be significantly decreased in one study but not in another (12,13). It is, therefore, controversial whether LG can reduce severe postoperative

complications and allow patients to receive postoperative adjuvant chemotherapy earlier. Recently, an RCT showed LDG had the benefits of better postoperative safety and adjuvant chemotherapy tolerance compared with ODG for patients with locally advanced gastric cancer who received neoadjuvant chemotherapy (14). Neoadjuvant chemotherapy is promising treatment to prolong survival in patients with advanced gastric cancer (11). However, the RCT was small-scale, single-institutional, and included only distal gastrectomy. The feasibility of LG after neoadjuvant chemotherapy is still unclear. RCTs of LG versus OG after neoadjuvant chemotherapy for advanced gastric cancer will be required in the future.

In conclusion, LG has emerged as a feasible and promising option for patients with advanced gastric cancer. LG is less likely to promote peritoneal dissemination even in patients with a serosa-positive tumor. Ongoing studies on advanced stage patients will prove the feasibility of LG more evidently and confidently. In patients at far advanced tumors (large type 4 tumors or bulky lymph node metastases); however, the oncological safety of LG is still controversial and is yet to be confirmed.

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