

Randomized controlled trials evaluating laparoscopic vs. open distal gastrectomy for gastric cancer in 2016: a trilogy finally!

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Within the past twenty years, an unmistakable trend towards minimally-invasive surgical approaches has taken the surgical world by a storm. This growing popularity can be seen in the increased demand for laparoscopic resections of gastric cancer, which is swiftly gaining popularity and evidence-based support worldwide. This technically-demanding yet elegant procedure has largely demonstrated equal or superior results compared to conventional open gastrectomy in short- and long-term, large-scale randomized controlled trials (RCT). Increasing numbers of surgeons—especially those in the highly afflicted nations of Japan, China, and Korea—heavily rely on this medium in the surgical management of early and locally advanced gastric cancer patients. A non-exhaustive list of commonly observed benefits includes significantly reduced blood loss, shorter postoperative hospital stay, and improved quality-of-life outcomes (1-3).

Great strides have been taken to standardize laparoscopic procedures and techniques for gastric cancer resections, and a developed story is that of determining the oncologic safety of laparoscopy-assisted distal gastrectomy (LADG) compared to open distal gastrectomy (ODG). Morbidity of laparoscopic gastrectomy ranges between 4.2% to 23.3% (4-10), and a meta-analysis of all randomized controlled trials and high-quality nonrandomized trials comparing

LADG to ODG found an overall favorable response to the former (11).

Recently, Katai and colleagues of the Japan Clinical Oncology Group (JCOG0912) confirmed the non-inferiority and safety of LADG compared to ODG in terms of short-term adverse and clinical outcomes of 912 early gastric cancer patients (LADG: 457 and ODG: 455 patients) (12). The results of this multi-institutional, phase III, RCT demonstrated the following results of LADG *vs.* ODG: longer operative time (278 *vs.* 194 min, $P < 0.001$), less blood loss (38 *vs.* 115 mL, $P < 0.001$), similar in-hospital grade 3–4 complication rates (3.3 *vs.* 3.7%, $P = 0.72$), and higher serum AST/ALT levels (16.4 *vs.* 5.3%, $P < 0.001$); no mortality and grade 3–4 intraoperative complications were reported in either arms. Conversion to open surgery was necessary in 3.5% of patients; the majority was due to technical issues. Time to first flatus and use of analgesics was shorter/smaller for LADG compared to ODG. In the LADG arm, surgical complications increased as body mass index (BMI) increased; whereas, it did not in the ODG arm.

This contribution by JCOG ended a great year of published RCTs on this topic. Earlier in the same year, similar results from the Korean Laparoscopic Gastrointestinal Surgery Study (KLASS-01) and Chinese Laparoscopic Gastrointestinal Surgery Study (CLASS)

groups were published, in which both studies concluded the non-inferiority of laparoscopic surgeries in early and advanced gastric cancer, respectively (13,14).

All studies were able to justifiably advocate for the clinically acceptable status of LADG when compared to ODG. Yet, a peculiar anomaly presented itself in this rather special opportunity to compare results of three parallel studies conducted in the three Far East Asian countries regarding gastric cancer laparoscopic procedure and technique. Although each study appropriately concluded the non-inferiority of LADG, the results leading to this conclusion somewhat contradicted each other. First, the JCOG and CLASS groups found no difference in postoperative complications, whereas the KLASS group found a significantly reduced rate of wound complication rate in the LADG group. Another difference is the number of retrieved lymph nodes, where the JCOG and CLASS groups had similar results between the two arms, and the KLASS group harvested less in the LADG arm compared with ODG.

Several theories can explain these discrepancies. A potential reason is due to a difference in operative extent. D2 gastrectomy was standard for gastric cancer patients during the study period in Japan, whereas either D1+ or D2 gastrectomy is practiced in Korea. This difference in surgical practice can understandably result in a difference in complication rates, since one requires a greater amount of operative time and precision over the other. Also, the laparoscopic surgery education system in these three countries is different. Surgeons in Japan have a more homogenous level of expertise due to a standardized credentialing system, whereas surgeons in Korea and China observe more polarized extremes of competencies due to differing caseloads in high- and low-volume hospitals. Lastly, a difference in the hospital case volumes can produce differing results. The KLASS and CLASS studies were completed in hospitals with huge caseloads, whereas the surgeons in the JCOG study worked in settings with a smaller volume.

These reasons point to an implicit lesson to be learned, and that is of the importance of surgeon's experience. Previous studies argued that this factor plays a defining role in laparoscopic surgery outcomes. A study demonstrated that a plateau in the learning curve—that is, achievement of optimal proficiency—requires approximately 40–90 LADGs with an average of 50 (15–18). Acquiring mastery of LADG requires a substantially steeper learning curve compared to open gastrectomy. Moreover, LADG with extended

lymphadenectomy is considered to be more technically challenging than other laparoscopic procedures—including cholecystectomy, splenectomy, and colorectal resections—because of the extensive lymphatic and blood vasculature of the stomach. A retrospective multicenter study reported that lack of surgeon's experience (defined as less than 50 LADGs) was an independent risk factor for postoperative local complications (1.608 times greater than ODG), reoperation (3.008 times greater than ODG), and longer operative time (18).

The differences observed in the highly controlled settings of the JCOG0912, KLASS-01, and CLASS studies logically imply that these differences are also observed in non-experimental settings. This is alarming, considering this directly impacts patient safety. Studies demonstrating the non-inferiority of laparoscopic gastrectomy can be rendered meaningless unless all surgeons subscribe to the highest standard of expertise, especially in light of the knowledge that this is a challenging skill set to obtain. A potential solution to this problem is two-fold: the international standardization of laparoscopic gastrectomy along with qualification of the surgeons and the effective training of new surgeons by those who are highly experienced and qualified.

Ultimately, the JCOG0912 trial robustly demonstrated the non-inferiority of LADG compared to ODG. The conclusion of this study is externally validated, and JCOG's internationally recognized ability to produce high-quality data is clearly transferred into this study. With this encouraging end to 2016's trilogy of the great LADG *vs.* ODG debate, LADG is expected to become the gold standard for the resection of distal gastric tumors—particularly in Far East Asian nations. An RCT showing similar 5-year overall and relapse-free survival outcomes between these two arms adds fuel to this narrative of LADG's non-inferiority (COACT 0301) (19). The next challenge in the acceptance of this procedure is to train all laparoscopic gastric surgeons to uphold a uniformly high quality of performance. In this way, LADG can become more accessible with an ever-increasing safety profile, so that everyone who needs this procedure can benefit from the advantages it offers over conventional open surgery.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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