

## The issue of lymphadenectomy during laparoscopic gastrectomy for gastric carcinoma

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surgery, especially for advanced gastric cancer and its impact on both short and long term survival.

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### Abstract

Surgical resection remains the mainstay of treatment for gastric cancer. Laparoscopic assisted gastrectomy has failed to gain universal acceptance as an alternative to the open approach for a number of reasons, one of which includes the issue of oncological radicality in terms of lymph node dissection. Nodal status, which is one of the most crucial and independent predictors of patient survival, therefore has been examined both in single institutional trials and also in randomised controlled trials especially on early gastric cancer. The issue of oncological adequacy for laparoscopic lymph node harvesting for advanced gastric cancer remains a contentious issue because of the unique challenges it poses in terms of complexity, safety and time, and also the lack of randomised controlled trials in this area. It is thus imperative that good quality multicentre randomised controlled trials are designed to investigate the benefits of extended lymphadenectomy in the setting of laparoscopic

Minimal access gastrointestinal surgery for gastric cancer; i.e. laparoscopic distal gastrectomy (LDG), has not achieved universal acceptance by the surgical fraternity although introduced 13 years ago. The reasons are both technical and oncological. Recently, however, there has been a tremendous amount of advancement in the development of laparoscopic instruments which, coupled with increasing experience in the performance of complex laparoscopic gastrointestinal procedures, have led to the expansion of minimal access surgery for both benign and malignant gastric procedures. The following editorial will discuss some of these contentious issues and progress made in this area.

Laparoscopic assisted gastrectomy (LAG) for the management of gastric malignancy is becoming increasingly popular. It was introduced 13 years ago by a group of Japanese surgeons<sup>[1]</sup>. Its wider acceptance, however, as an alternative to the open approach remains a contentious subject, especially because of the technical difficulties involved in achieving an adequate lymph node dissection,

an issue that is viewed differently by Eastern and Western surgeons. Various trials have estimated that there will be lymph node involvement in 3%-5% of gastric cancer cases limited to mucosa only, 11%-25% lymph node involvement if the cancer involves submucosa, 50% lymph node involvement in T2 cancer and 83% lymph node involvement in T3 cancer<sup>[2,3]</sup>. Nodal status, thus, is one of the most crucial and independent predictors of patient survival<sup>[4,5]</sup>. Therefore, the issue of oncology radicality for lymph node harvesting, especially for both early and advanced gastric cancer during LAG, remains hotly debated because of the unique challenge it poses in terms of complexity, safety and time. Many gastrointestinal surgeons, at least in the West, consider laparoscopic D2 lymph node dissection to be tedious, onerous, unnecessary and even unsafe. This assumption is based on a number of randomised controlled trials (level I evidence) comparing open D1 vs D2 lymphadenectomy for gastric cancer, which has shown no long term survival advantage and a higher perioperative complication rate and death in the D2 group<sup>[6,7]</sup>. Furthermore, the cochrane Review<sup>[8]</sup> has confirmed these findings. However, many groups, especially from the East, differ on this issue based on their large retrospective data showing significant benefits and modest morbidity from extended lymph node dissection. Some of the groups with extensive open D2 experience have since consolidated their experience with LAG and have now published randomised controlled trials (RCTs) comparing LDG and open distal gastrectomy (ODG)<sup>[9-12]</sup>. The RCTs have examined the issue of laparoscopic radicality of lymph node dissection mainly in early gastric cancer. To date, all the RCTs (level I evidence) have found lymph node retrieval during a laparoscopic procedure to be not only sufficient but meeting the global standard for adequate staging, emphasizing the oncological radicality of laparoscopic gastric procedures<sup>[13]</sup>. In fact, in none of the RCTs was there any significant statistical difference in lymph node retrieval for the two procedures. However, a recent meta-analysis<sup>[14]</sup>, which pooled together the results of four RCTs, has come to a different conclusion altogether. The authors of this meta-analysis<sup>[14]</sup> have shown that there was a statistically significant reduction in lymph node harvesting for LDG compared to ODG, which may translate into an overall survival disadvantage for patients having LDG. As the long term results for the majority of these trials have not been published, this assumption is difficult to corroborate. However, the long term results are eagerly awaited.

The argument on the merits and risks of extended lymph node clearance for AGC during LAG is additionally controversial because of the absence of level I or II evidence. Hwang *et al*<sup>[15]</sup> reported their experience of LAG for AGC. They compared LAG ( $n = 45$ ) with ODG ( $n = 83$ ) performed between 2004 and 2007 in a non-randomized fashion. These authors found no difference in the mean number of nodes harvested in either group and felt that extended lymphadenectomy for AGC is possible and safe. Furthermore, the authors felt that there was good evidence that LAG was superior in improving the quality

of life. However, the mean follow-up of the patients was around two years and therefore long term results in terms of disease free survival and mortality are not known. Similarly, Kawamura *et al*<sup>[16]</sup> in yet another non-randomized trial comparing LDG ( $n = 53$ ) and ODG ( $n = 67$ ) over a two year period examined the safety and accuracy of D2 dissection for AGC. They concluded that D2 dissection could be performed safely and accurately without undue complications provided the surgical team was skilled in minimally invasive surgical techniques. However, they conceded that no long term results for LDG for AGC are available and therefore the need for an RCT is important to address this issue.

Zhang *et al*<sup>[17]</sup> looked at 10 years of experience in their unit with 391 laparoscopic gastrectomies from 1998 to 2007. In 100 patients (25.6%), the number of lymph nodes retrieved was less than 15. This number is less than one would expect even for D1 lymphadenectomy suggesting that the extent of lymphadenectomy achieved by these authors in a quarter of their patients did not approach the global standard for accurate staging. The findings of this trial suggest that even in experienced hands and in large volume centres, extended lymphadenectomy poses a challenge.

Nodal status, whether in LDG or ODG, remains the most important independent predictor of gastric cancer patient survival. The RCTs comparing LDG versus ODG for early gastric cancer have shown that the extent of lymphadenectomy achieved by current laparoscopic procedures approaches the global standard for accurate staging. Performing extended resection laparoscopically as recommended in Japan remains a challenge and is a time consuming process as evident from the Zhang *et al*<sup>[17]</sup> study. Therefore, laparoscopic gastrectomy for AGC may only be justified under the setting of clinical trials in a high volume centre and in the hands of experienced laparoscopic gastric surgeons. Given the vast difference between Eastern and Western surgeons in surgical experience in gastric cancer surgery, and the difference in the prevalence of gastric cancer between the East and West and a higher rate of complications associated with a more aggressive resection, it is imperative that surgeons in the East take the lead in organising a good quality multicentre randomised controlled trial enrolling a large number of patients to address the issue of LDG versus ODG for the treatment of gastric cancer, with a main emphasis on extended lymph node resection and its impact on both short and long term survival.

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