The potential value of bursectomy in operations for trans-serosal gastric adenocarcinoma

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In the current issue, Fujita, Kurokawa, Sugimoto et al. describe interim results of an interesting two-armed non-inferiority trial that was designed to justify the potential elimination of bursectomy (also known as “omentobursectomy”) from a standard D2 operation for advanced gastric cancer. This is probably one of the last purely surgical trials to be reported for advanced disease, given the currently established role for adjuvant therapy [1–3]. The trial was prematurely halted as a result of the convincing S-1 Trial [3], which clearly demonstrated the value of adjuvant therapy in Asian patients following high-quality D2 resection.

The current Osaka Bursectomy Trial illustrates a number of valuable lessons: the way new evidence and clinical trial ethics can upset accrual plans; the value of a strong Data and Safety Monitoring Committee; the value of exploratory subgroup analysis, even in an underpowered prospective randomized clinical trial such as this; and, finally, that even experienced, expert gastric surgeons can occasionally “miss” on their predictions. And indeed, by missing on their initial predictions but subjecting them to an exploratory, non-inferiority randomized test, they have potentially enlightened us all!

The continued practice of bursectomy over the years, despite its unverified therapeutic value, stems from its utility in facilitating: (a) precise, complete resection of disease from the head of the pancreas; (b) complete clearance of the (high-risk) subpyloric station #6 nodes, and; (c) an aesthetic, clean, celiac-based node dissection.

But what about the potential value of bursectomy in eliminating micrometastatic disease in the peritoneum of the lesser sac? For patients with posterior gastric wall trans-serosal (pT3 or pT4) disease, such micrometastases can constitute the seeds of later recurrence. Their early removal might prove beneficial.

Between July 2002 and January 2007, 210 patients with $\geq$ cT2 disease were randomized intraoperatively to receive either bursectomy ($N = 104$) or not ($N = 106$) during their D2 operation. The two groups were generally well balanced with respect to gender (73 vs. 77% male), clinical T stage (61 vs. 67% T2), total gastrectomy (21 vs. 25%), and splenectomy (11.5 vs. 13.2%). R-0 resection was accomplished in almost all patients, and the few R-1 cases (3 vs. 4) were almost all due to positive peritoneal cytology.

The performance of bursectomy was associated with a slightly longer operative time (an additional 27 min on average) and higher blood loss (an additional 125 ml). Interestingly, drain amylase levels on postoperative day 1 were not significantly different between the two groups ($p = 0.543$). Also, node counts did not seem to differ much between the groups, even for the station #6 subpyloric nodes.

In the current report, three-year overall survival rates were 85.6% for the bursectomy group and 79.6% in the non-bursectomy group (HR for death without bursectomy 1.44, $p = 0.443$ for non-inferiority). Analysis of the 48 cases with pathology-proven trans-serosal disease in this trial indicates a biologically reasonable but statistically non-significant advantage to bursectomy. Among the 48 cases with pT3 or T4 disease, three-year overall survival was 69.8% for the bursectomy group and 50.2% for the non-bursectomy group (HR for death 2.16 for the non-bursectomy group; $p = 0.791$ for non-inferiority due to the small sample size). Despite the underwhelming p value,

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Figures 4(b) and 5(b) in the article suggest a possible therapeutic effect. In any case, the authors reasonably concluded that bursectomy should not be abandoned at this time. The hypothesis that it might actually enhance survival should be entertained.

Enhanced accrual to the trial was planned, but owing to the S-1 Trial results, accrual to this “purely surgical” bursectomy trial was closed in 2007. Follow-up continues.

Based on the observations reported in this underpowered trial, the Japan Clinical Oncology Group (JCOG) is now embarking on a 1,000-patient multicenter randomized controlled trial of D2+ bursectomy versus D2 without bursectomy among cT3 and cT4 cases. Adjuvant therapy will be employed routinely for both groups. The primary endpoint will be overall survival. We anxiously await the

results and congratulate our Osaka colleagues for stimulating us in this direction.

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