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To the Editor:

Talamini and colleagues[1] reviewed their 27-year experience of 120 patients with adenocarcinoma of the ampulla of Vater. Despite improvements in care, 5-year survival for this disease remains less than 40%. Talamini and colleagues and others such as commentator Dr. M. Brennan agree that new approaches for the disease are needed. If the cause or causes of adenocarcinoma of the ampulla of Vater are found, then it might be possible to prevent some cases. Here I propose that *Helicobacter pylori*—the curved gram-negative bacterium which is now known to cause virtually all cases of duodenal ulcer and the majority of gastric ulcers, and which may possibly be an agent in gastric adenocarcinoma and MALT lymphomas throughout the length of the gastrointestinal tract[2–4]—may be a cause, or one necessary ingredient, in the pathogenesis of many cases of adenocarcinoma of the ampulla of Vater.

Interestingly, two studies[5,6] have noted a statistically significant association between *H. pylori* infection and adenocarcinoma of the pancreas. In one study,[5] 65% of 92 patients with adenocarcinoma of the pancreas were *H. pylori*-seropositive, while only 45% of 27 controls and 35 patients with colorectal cancer were seropositive ($p = 0.019$). In the other study,[6] 69% of 26 patients with pancreatic cancer seen serially were *H. pylori*-seropositive, but only 39% of 39 matched controls ($p < 0.05$). Furthermore, the proximity of the ampulla of Vater to the duodenum might not be incidental in the pathogenesis of cancer of the ampulla.

Patient material from the study of Talamini et al might still be extant to test for *H. pylori.* It might be possible to organize a prospective study of patients with adenocarcinoma of the Ampulla of Vater using the high sensitivity and specificity ELISA serum antibody test available for *H. pylori,* and compare the incidence of seropositivity to that of appropriate controls. Of course, correlation is not causation. However, an association between *H. pylori* infection and adenocarcinoma of the ampulla of Vater would be interesting. If *H. pylori* is a cause of adenocarcinoma of the ampulla of Vater, then eradication of *H. pylori* (long before any cancer begins to develop) would be a useful prophylactic step against this disease.

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December 10, 1998

To the Editor:

We have read with great interest the paper written by Siewert et al[1] concerning the prognostic factors in gastric cancer. The study prospectively shows that in a large patient population, D2 extended lymphadenectomy can improve survival in gastric cancer patients without affecting the incidence of postoperative complications. Moreover the so-called phenomenon of "stage migration" has been satisfactorily assessed. However, two methodologic aspects of the study should be further stressed.

First, the authors state that "the technique of lymph node dissection was performed according to the recommendations of the JRSGC[2]. . . *en bloc* resection of the stomach with lymph node dissection of compartments I and II was recommended as the procedure of choice. Compartment I comprises all lymph nodes along the major and minor curvature of the stomach (*i.e.*, lymph node stations 1–6 in those undergoing a total gastrectomy and lymph node stations 3–6 in those undergoing a subtotal gastrectomy). Compartment II comprises lymph node stations 7 to 12 in the Japanese classification." According to the Japanese rules, for tumor located at proximal and middle third of the stomach, lymph nodes along the splenic artery (n.11) and at the splenic hilus (n.10) belong to the compartment II and therefore must be dissected to obtain a complete D2 lymphadenectomy. It is well known that to achieve such a dissection, it is necessary to perform a concomitant splenectomy.[3–5] However, if we look at the data, the overall splenectomy rate reported in the paper was 492 cases, whereas the number of tumors located at proximal, middle or entire stomach undergoing extended lymph node dissection was 836. Therefore, even we assume that all the splenectomized patients belong to the extended lymph node dissection group, at least 41% of patients did not undergo a complete D2 dissection, thus leading to a possible misunderstanding of the results.

Second, the cutoff of 25 nodes could not be really effective in differentiating the extent of lymphadenectomy; in actual fact, the mean number of dissected perigastric (n.3, 4), pericardial (n.1, 2), and supra- and infrapiloric nodes (n.5, 6) in patients undergoing total gastrectomy at our Institute during the last year is 36.3 ± 12.8.[6] Therefore, even a D1 lymphadenectomy can lead to a quite large number of dissected nodes. D2 lymphadenectomy can be defined as complete only if all the stations of the second compartment, according to tumor location, have been dissected; the absolute number of dissected nodes is the result and not the limit of dissection.

Despite these two methodologic criticisms, however, the authors should be congratulated because they have definitively demonstrated that extended lymphadenectomy in gastric cancer can be safely and efficaciously performed even by Western surgeons in Western patients.

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April 6, 1999

Author's Reply:

We have enjoyed the letter from Pacelli et al very much and thank the editors for the opportunity to reply. Two questions arise from this letter:

Is a splenectomy necessary to achieve a complete D2 lymphadenectomy? According to our own results, the results of Adachi et al in 1996,[1] and the experience of the National Cancer Center, the answer is clearly: no. It *is* possible to do a D2 lymphadenectomy without splenectomy. According to an analysis of our own data,[2] we were able to excise in standard total gastrectomy without splenectomy a mean of 26.2 ± 1.9 lymph nodes. With a splenectomy, the number of excised lymph nodes was a mean of 29.2 ± 2.3. A higher number of lymph nodes could only be achieved if a left-side pancreatectomy was performed in addition to the splenectomy (39.5 ± 3.6 lymph nodes). Very similar numbers were published by Adachi in 1994.[3]

In conclusion, splenectomy is not necessary for a complete D2 lymphadenectomy. In contrast, the splenectomy should be avoided whenever possible. The splenectomy was the most important risk factor for postoperative complications in the Dutch trial.[4]

The second question refers to the cutoff point of 25 lymph nodes. The problem in all of the published trials is the unclear definition of a D2 lymphadenectomy. We have decided to do this according to the anatomical results published by Wagner.[5] It was clearly demonstrated in this investigation that in compartments I and II, from the anatomic point of view, about 27 lymph nodes can be expected. According to these anatomic results, we have decided to accept only more than 25 excised lymph nodes from the anatomic compartments I and II as a D2 lymphadenectomy. This definition has meanwhile been accepted by the UICC as good clinical practice. In comparison to the British and Dutch trials, this is a more objective and reproducible definition of D2 lymphadenectomy.

In conclusion, the number of 25 lymph nodes as precondition for the acceptance as a D2 lymphadenectomy is not a cutoff point under prognostic aspects but an anatomically given number. In our experience, this is the best way to define a D2 lymphadenectomy.

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April 15, 1999

To the Editor:

We were intrigued by the study by Roder et al[1] on the use of plastic stents for the external drainage of the pancreatic duct at the time of pancreaticoduodenectomy.

Although the development of a pancreatic fistula remains a significant clinical problem after pancreaticoduodenectomy, the incidence of this complication from major centers has significantly decreased in publications within the last decade. Even so, a trial of stent would still appear to have some merit. The trial design was, however, flawed in that it was nonrandomized. Three different methods of pancreatic reconstruction were used and the indications for stenting were not defined. Because four different surgeons took part in the study, and their individual use of stents was not defined, any difference in results could be explained simply by differences in case selection for stenting by individual surgeons or indeed by their dexterity. The overall results clearly indicated a significantly higher pancreatic fistula rate in patients without stents than in those with stents. Fistulae resulted in significant morbidity and mortality, and increased hospital stay. Although the authors emphasize that this shows clear benefit to stenting, the pancreatic fistula rate is considerably higher than that reported from major centers. Indeed,

it would only be within the stented group that the pancreatic fistula rate is similar to that reported in contemporary series without stenting.[2]

No justification or discussion regarding this high fistula rate in the nonstented group is provided. The authors appear to have overlooked one obvious alternative to the techniques described, namely that of an isolated Roux loop pancreaticojejunostomy, despite the report of this technique by Kingsnorth being referenced in the discussion. Kingsnorth reported a low morbidity and mortality with a Roux loop pancreatojejunal anastomosis in a series of 52 patients with no pancreatic fistulae.[3] An absence of pancreatic fistula with this technique has more recently been reported by Papadimitrou and colleagues.[4]

Our experience of the isolated Roux-en-Y pancreaticojejunal anastomosis involves 41 consecutive patients undergoing pancreatoduodenectomy over the last 6 years for both benign and malignant disease (13 periampullary cancer, 17 pancreatic cancer, 5 chronic pancreatitis, 5 neuroendocrine tumors). The average age was 59.7 years (range 29–83 years). There were no pancreatic fistulae and only one death (pancreatic leak rate, 0%; mortality, 2.4%).

We feel the study by Roder and colleagues is fundamentally flawed by the unacceptably high pancreatic fistula rate in the nonstented group. An improved technique should be employed before a randomized prospective trial could be justified.

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Authors' Reply:

We appreciate the opportunity to reply to the letter by Drs. Davidson, Agarwal, and Khan on our paper.

As noted by the authors, our study was indeed not a randomized trial but a prospective evaluation of various reconstruction techniques for pancreatointestinal anastomosis after partial pancreatoduodenectomy at our institution. Although there were a number of potentially confounding parameters with respect to the technique used for reconstruction and the number of surgeons involved in the study, the results of our analysis clearly showed a significant reduction of the prevalence of pancreatic leaks only in the stented patient group irrespective of the other parameters. The rate of pancreatic fistulas observed in the nonstented patient group is well within the range reported from a number of other experienced centers and very similar to the rate of pancreatic leaks observed at our institution before the initiation of the prospective study. This was extensively discussed in the manuscript.

Due to the very favorable results with stented pancreaticojejunostomy in our study, this technique is now routinely employed for reconstruction after partial pancreatoduodenectomy at our institution by all participating surgeons. The results with the procedure obtained after completion of the prospective study in 1997 confirm the data shown in the manuscript, *i.e.*, in a total of an additional 42 partial pancreatoduodenectomies with stented pancreaticojejunostomy, the leakage rate was only 4.7%. Despite the well-realized shortcomings of our prospective study, this observation underlines that at last in our hands a stented pancreaticojejunostomy results in a very low pancreatic fistula rate and a consequently low morbidity and mortality of the procedure.

Nevertheless, we realize that there are numerous techniques for performing the pancreaticojejunostomy, including the well-known technique of an isolated Roux loop pancreaticojejunostomy, with some very favorable results reported by individual authors. As with many other technical modifications, the enthusiastic results reported by some, however, often cannot be reproduced by others. Furthermore, there is obviously no need to change a technique if one has a zero complication rate with it. Our experience shows that for those who do see anastomotic fistula after pancreaticojejunostomy, the use of a pancreatic duct-stent may be an easy way to reduce the prevalence of this serious complication.

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