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Stump Cancer Following Gastric Surgery

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This paper reviews the literature regarding the development of gastric cancer in the stomach remnant following gastric resection. Although there is as yet little supporting experimental evidence, clinical studies suggest that the risk of developing gastric cancer is increased, perhaps as much as 6-fold, following partial gastrectomy for benign lesions. It also appears that the risk of developing cancer is greatest if the lesion for which the gastrectomy was originally performed was a gastric ulcer rather than a duodenal ulcer. The type of gastrectomy does not seem to influence this increased risk. Hypotheses are reviewed concerning the role of changes in gastric morphology following partial gastrectomy in the development of cancer.

In the early 1950's, cases of carcinoma developing in the gastric remnant following partial gastrectomy began to appear in the literature [1]. This condition soon was termed "stump carcinoma," but the number of cases remained small and so it did not excite much interest. Over the last few years, an increasing number of patients has been reported with this condition, as a result of which its appearance is beginning to pose some questions of fundamental importance.

It is necessary to follow the progress of large numbers of patients over a period of many years to obtain enough information on this subject, since the appearance of the cancer is usually delayed for many years (the average time interval being around 20 years in most series). Because of this difficulty, a prospective series is unlikely ever to give absolute answers to the questions posed by this unusual complication. It is important to ascertain whether gastric stump carcinoma appears with greater frequency than anticipated and, if so, whether its occurrence is related to any particular type of operation. Although Peters [2] collected 1,410 cases reported in the world literature between 1930 and 1970, he was still unable to reach definite conclusions.

There seems little doubt that benign gastric ulcers may become malignant, and that a relationship exists between intestinal metaplasia of the gastric mucosa, gastritis, and gastric carcinoma [3]. Similarly, mucosal changes following gastric surgery have been demonstrated in animals [4] and man [5], but their relationship to the development of carcinoma has not been fully established. Changes in mucosal morphology that may be induced by partial gastrectomy may play a significant part in the subsequent development of a carcinoma and, thus, it is important to investigate the original mucosal pathology. Establishment of this condition as a real clinical entity will assist the experimental pathologist in the interpretation of his findings. Therefore, we must try to answer the questions of whether the risk of development of gastric malignancy is increased or decreased by partial gastrectomy, and whether this risk is influenced by the original lesion for which the operation was undertaken, or by the type of anastomosis constructed during the gastrectomy.

A retrospective study of the cases of stump carcinoma seen in the gastroenterologic clinic of St. James' Hospital, London, was undertaken in 1973 [6]. It was based upon a search of the records of 5,115 patients who underwent partial gastrectomy for peptic ulceration and other benign disorders in the 24-year period from 1940 through 1963 and 1,473 patients with gastric cancer diagnosed since 1940. Patients with peptic ulceration treated other than by partial gastrectomy were excluded. From this search, 36 patients were found to have developed a stump carcinoma, representing 2.4% of all gastric cancer patients. Of these, 8 had had their original operation at other hospitals, and so were not in-

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cluded in the main analysis, since the original pathology could not be confirmed. In such a large series of cases spread over many years, it is obviously not possible to undertake a review of all patients, so that the incidence of stump carcinoma of 0.55% is certain to be an underestimation. However, the study had the virtue of knowing for certain the original pathology (with histologic reappraisal in many cases), the type of operation undertaken, and the full clinical details of the patients. In addition, our unit was aware of this complication following the original report of 4 cases [7], and there was particular interest in establishing the diagnosis at an early stage.

Of the 5,115 patients who underwent partial gastrectomy, 50% had had the operation for duodenal ulcer, 33% for gastric ulcer, 10% for combined duodenal and gastric ulcers, and 7% for other indications. In contrast, there was a very different frequency distribution of the indications for partial gastrectomy among the 28 patients who later developed stump carcinoma: duodenal ulcer in only 11%, gastric ulcer in 78%, combined ulcers in 3.5%, and other lesions in 7.5%. The preponderance of gastric ulcer as the original pathology persisted even when all cases occurring within 3 years of the original operation were excluded, representing 70% of cases.

When the type of operation was considered, more were found to have had a Polya type of resection than a Billroth I procedure (13:7), but this figure did not reach statistical significance. Many more operations of the Polya type were performed in the whole series since, in the early years under review, this was the standard operation for gastric, as well as duodenal ulcers, and only later did the Billroth I procedure become standard for gastric ulcers. The time interval for appearance of the stump carcinoma was found to average 11.3 years from the original operation.

Many other series of cases have been reported but, as in our study, any conclusions must be tempered by the difficulties in obtaining accurate data. In Norway, Helsingen and Hillestad [8] undertook a careful follow-up of 222 patients who had a partial gastrectomy in a 25-year period, of which 11 developed a stump cancer. The average time interval for appearance of the cancer was 20 years. Another Norwegian series reported 84 cases found at autopsy among an unselected group of patients [9]. In the U.S.A., Morgenstern [10] reported 22 patients who were found to have stump carcinoma at a time that averaged 24 years after the initial gastric resection. Swiss workers reported that 2.7% of their gastric cancer patients had surgery for an earlier ulcer [11], with an average interval of 19 years. Again, the total number of patients undergoing ulcer surgery was unknown, so that the frequency of this complication was impossible to assess. Hofstetter et al. [12] reported 27 cases and assessed the frequency as 4% of all gastric cancer patients. The mean interval between surgery and cancer diagnosis was 20 years. Debray et al. [13], reporting from Paris, found 11 patients who presented to their unit, and collected another 102 cases from the European literature. They also noted an incidence of 5.9% in 50,000 autopsies. Lastly, de Jode [14] documented 19 cases presenting to the London Hospital in a 10-year period, with presentation from 2 to 37 years after the original surgery. All of these studies highlight the need for long-term follow-up of patients undergoing gastric surgery, if this complication is to be defined accurately.

It can be concluded that 2 to 5% of gastric cancer patients will have had previous surgery for a benign gastric disease. However, this does not help determine the cancer risk of partial gastrectomy, since it was found in a population survey in the London area that 1.1% of all people over the age of 45 years had previously undergone surgery for peptic ulcer [15]. The difficulties of following up a large series of patients over many years are obvious, so that the 0.55% incidence of stump carcinoma in the St. James' series is an underestimate. Therefore, this series was examined in relation to the expected incidence of carcinoma of the stomach, based on death rates from the disease in England in 1970 (Office of Population Censuses and Surveys, 1970). The frequency of death from stomach cancer increased markedly with age, being only 1 in 8,451 between the ages 25 to 54 years, but rising to 1 in 437 for the age group 65 to 74 years. The numbers of patients in the series in various age groups were too small to be assessed separately but, with a mean age of 61 years, the expected frequency of cancer of the stomach for this age was 1 in 1,033. However, the actual frequency in the St. James' series was 1 cancer for every 183 patients having previous gastric surgery, which suggests a significant increase above the expected rate.

The increased risk of gastric cancer following gastric resection suggested by the data of the St. James' series has been confirmed by other investigators. Helsingen and Hillestad [8] assessed the risk at 3 times the expected incidence, based on a similar method of calculation, when the surgery had been undertaken for gastric ulcer. Hilbe et al. [16], using a statistical study of autopsies, found a rate of gastric cancer of 8.2% in patients who had gastric surgery, as opposed to 5.9% in nonoperated upon patients. Saegesser and James [11] stated that the risk of malignant degeneration of a gastric stump was higher than the risk of cancer of the stomach in

a group of comparable subjects in the general population. Stalsberg [17] estimated that the relative risk of developing gastric cancer increased 8 times that of the general population after 35 or more years following gastric resection, and that previous operations were nearly 3 times as common among patients with gastric cancer than among controls [18]. Hofstetter et al. [12] also found the incidence to be "notably" elevated over the incidence in a comparable group of subjects who had not had previous gastric surgery. Morgenstern et al. [10] suggested that the increasing number of cases being reported reflects an increased incidence, especially in view of the decreasing overall incidence of gastric cancer. Thus, there would appear to be considerable evidence that surgery for benign gastric conditions increases the risk of gastric cancer. This risk may be even greater than is apparent when it is considered that at least half of the cancers in the general population occur in that portion of the stomach that is normally resected by partial gastrectomy.

The more difficult questions to answer are whether the increased risk of gastic cancer is influenced by the type of operation performed and by the original pathologic lesion. The reconstruction following partial gastrectomy results in the gastric mucosa being subjected to a new environment, since it is bathed by a juice of different composition. There is almost certainly a greater exposure of the gastric mucosa to intestinal juice in the Polya gastrojejunal anastomosis than in the Billroth I gastroduodenal type anastomosis, but a change in gastric mucosa is likely to follow either procedure. In fact, this has been demonstrated experimentally when reflux of duodenal contents into the stomach was shown to lead to all of the changes of chronic gastritis [4]. Intestinal metaplasia of the gastric mucosa is a change that has been attributed to reflux, and it has been suggested to also have an association with carcinoma [3, 19, 20]. If a causal relationship between these changes and carcinoma exists, it might be expected that some of the previously described studies would demonstrate it. In fact, Morgenstern et al. [10] found that 91% of the stump cancers in their series occurred around the stoma, and they attributed this to the associated mucosal changes. However, others [13, 21] have found a high incidence of stump cancers occurring around the cardia, and Taksdal and Stalsberg [9] found no real histologic differences between patients with and those without previous gastric surgery. They also made the observation that intestinal metaplasia and gastritis were no more prominent in the primary resected stomachs of 16 patients who later developed stump carcinoma. This latter piece of evidence is important, for it does not support a concept that the state of the original gastric mucosa is related to the subsequent development of carcinoma.

Clinical evidence that the original lesion for which partial gastrectomy is done influences the development of stump cancer is strong, but by no means conclusive. Most authors have found that, in absolute numbers, most stump carcinomas develop following surgery for duodenal ulcers, but there may be 2 reasons for this. Firstly, duodenal ulceration develops at an earlier age than gastric ulceration, so that operations for duodenal ulcer are performed in a younger age group. As a result, there is a longer time interval in which cancer may appear and, as mentioned previously [17], the time interval is important. Secondly, in all series of gastric resection, operations for duodenal ulcer are more common than operations for gastric ulcer [6, 8, 11]. However, when the expected incidence of cancer was related to the original pathology in the St. James' series, it was found that 1 in 865 patients who had a duodenal ulcer developed cancer, whereas 1 in 120 of those who had a gastric ulcer later presented with cancer. The incidence of gastric cancer developing in the duodenal ulcer group was close to the expected incidence of gastric cancer in the general population. Similar data have been reported from Norway where the incidence of stump cancer was 3 times the expected incidence of gastric cancer in patients who had a gastric ulcer originally, but was not greater than expected in the patients who had a duodenal ulcer originally. It was concluded that the type of operation was not an influential factor, but that the original disease was a determining factor in the development of stump cancer.

Other authors have reached conclusions from their studies, but few are supported by statistical data. Peters et al. [2] evaluated the possible etiologic and pathologic factors, especially the role of chronic atrophic gastritis, and concluded that the presence of preoperative gastritis may be important in the subsequent development of stump cancer. Debray et al. [13] concluded that the type of gastrectomy does not appear to influence the frequency of stump cancer, a conclusion supported by the St. James' data. Both Saegesser and James [11] and Stalsberg [18] believe that the gastritis induced by the establishment of a gastrojejunostomy may act as a carcinogenic influence over a long period of time. It might be possible to correlate these divergent experimental and clinical conclusions by postulating that the stomach with a gastric ulcer has a mucosa already showing such a degree of "gastritis" that, given the altered stimulation following gastrojejunostomy, the development of frank carcinoma is likely to occur in time. At present, however, there

is no direct evidence to support this concept. Montgomery and Richardson [22] summarized this problem by stating: "In a sense partial gastrectomy for a benign ulcer postpones the risk of gastric carcinoma, but may ultimately increase it."

Résumé

Revue de la littérature concernant le développement d'un cancer dans le moignon gastrique après gastrectomie subtotale. Malgré l'absence de preuve expérimentale, les études cliniques suggèrent que le risque d'apparition d'un cancer est accru, peut-être jusqu'à 6 fois, après gastrectomie pour lésion bénigne. Le risque semble être également plus élevé après gastrectomie pour ulcére gastrique que pour ulcère duodénal. Le type de résection gastrique n'a aucune influence. Diverses hypothèses ont été émises concernant les altérations postopératoires de la morphologie gastrique et leur rôle possible dans le développement du cancer: ces hypothèses sont revues.

References

1. Freeman, M.A., Berne, C.J.: Gastric carcinoma of gastrojejunal stoma. Gastroenterology *27*:210, 1954
2. Peters, H., Schubert, H.J., Reifferscheid, M.: Das carcinoma in Restmagen nach Resektion wegen gutartiger Befunde. Langenbecks Arch. Chir. *336*:219, 1974
3. Reynolds, K.W., Johnson, A.G., Fox, B.: Is intestinal metaplasia of the gastric mucosa a pre-malignant lesion? Clin. Oncol. *1*:101, 1975
4. Lawson, H.H.: Effect of duodenal contents on the gastric mucosa. S. Afr. J. Surg. *3*:79, 1965
5. Gough, D.C., Craven, J.L.: Presentation to British Society of Gastro-enterology. Gut *16*:843, 1975
6. Nicholls, J.C.: Carcinoma of the stomach following partial gastrectomy for benign gastroduodenal lesions. Br. J. Surg. *61*:244, 1974
7. Swynnerton, B.F.A., Tanner, N.C.: Chronic gastric ulcer—a comparison between a gastroscopically controlled series treated medically and a series treated by surgery. Br. Med. J. *2*:841, 1953
8. Helsingen, N., Hillestad, L.: Cancer development in the gastric stump after partial gastrectomy for ulcer. Ann. Surg. *143*:173, 1956
9. Taksdal, S., Stalsberg, H.: Histology of gastric carcinoma occurring after gastric surgery for benign conditions. Cancer *32*:162, 1973
10. Morgenstern, L., Vamakawa, T., Seltzer, D.: Carcinoma of the gastric stump. Am. J. Surg. *125*:29, 1973
11. Saegesser, F., James, D.: Cancer of the gastric stump after partial gastrectomy for ulcer (Billroth II principle) for ulcer. Cancer *29*:1150, 1972
12. Hofstetter, J.R., Realini, S., Fasel, J., Arnold, J., Saegesser, F.: Cancer du magnon gastrique après resection pour ulcère bénin. Praxis *64*:1472, 1975
13. Debray, V.C., Bouvry, M., Roches, P.: Stump carcinoma after gastric resection for ulcer. Schweiz. Med. Wochenschr. *88*:631, 1958
14. De Jode, L.R.: Gastric carcinoma following gastroenterostomy and partial gastrectomy. Br. J. Surg. *48*:512, 1961
15. Doll, R., Avery-Jones, F., Buchatzsch, M.M.: Special report to Ser. Med. Res. Council, London. No. 276, 1951
16. Hilbe, G., Salzer, G.M., Hussl, H., Kutschera, H.: The incidence of cancer in the gastric remnant after subtotal gastric resection. Arch. Klin. Chir. *323*:142, 1968
17. Stalsberg, H.: Stomach cancer and previous gastric surgery. Gastroenterology *62*:1276, 1972
18. Stalsberg, H.: Stomach cancer following gastric surgery for benign conditions. Lancet *2*:1175, 1971
19. Skinner, J.M., Heenan, P.J., Whitehead, R.: Atrophic gastritis in gastrectomy specimens. Br. J. Surg. *62*:23, 1975
20. Duplessis, D.J.: The distribution of gastritis in carcinoma of the stomach. Br. J. Surg. *61*:521, 1974
21. Lagache, G., Vankemmel, M.: Cancer of the gastric stump following gastrectomy for ulcer. Arch. Chir. *20*:618, 1966
22. Montgomery, R.D., Richardson, B.P.: Gastric ulcer and cancer. Q. J. Med. *44*:591, 1975

Invited Commentary

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Nicholls has admirably summarized the world literature on carcinoma of the gastric stump. Extrapolating from the review of Peters et al. [1] and our own literature review [2], I would estimate that the total number of cases reported to date numbers well over 2,000. Despite this large number of reported cases, valid statistical conclusions regarding incidence, etiology, and even pathology are hard to come by. I will not compound the statistical complexities so well described by Nicholls by adding my own interpretation of the heterogeneous statistical studies. Instead, I should like to give my partially subjective, partially objective, views after more than 2 decades of "stump" watching for carcinoma.

1. There is little doubt that the condition is increasing in frequency. Hardly an Index Medicus goes by without one or more reports of stump carcinoma, alone or in series.

2. The crescendo in incidence quite naturally followed the ascendancy of gastric resection for the