A Cohort Study on Second Malignancies in Gastrectomized Patients with Gastric Cancer

I. Second Malignancies Other Than Cancer of the Gastric Remnant

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ABSTRACT: In a retrospective cohort study, a total of 235 (2.32 per cent) second malignancies were clinically observed in 10,138 patients during the average 8.8-year follow-up period. The patients had undergone gastrectomy for gastric cancer during 1960–1975, in seven different institutions. This observed number was smaller than the expected one of 340.9 (p<0.01). Among the 235, cancers of the gastrointestinal tract (111) were the most frequent and followed by respiratory (54) and urogenital (25) cancers. Twelve cases of malignant lymphoma and five of leukemia were also noted. With regard to adjuvant chemotherapeutic agents such as mitomycin-C (MMC), 5-fluorouracil (5FU) or its derivative Tegafur, and cyclophosphamide (EDX), no significant differences in the rate of second malignancies were obtained between the chemotherapy and non-chemotherapy groups. The occurrence rate of second malignancies tended to be higher in the Billroth II group than in the Billroth I, the significance of which is yet to be determined.

KEY WORDS: second malignancies, cohort study, gastric cancer, adjuvant chemotherapy, gastrectomy

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INTRODUCTION

As a consequence of the increased number of cancer patients who survive the disease by combined treatments of surgery, radiotherapy and/or chemotherapy, the occurrence of second malignancies after the first treatment has become a great problem.\textsuperscript{1} Carcinogenesis as a late effect of radiation is now widely recognized, and surgical procedures, e.g., Billroth II method after subtotal gastrectomy, have been given attention as a possible link to these second cancers in the gastric remnant.\textsuperscript{2,3} Anticancer agents themselves may be carcinogenic, as acute leukemia\textsuperscript{4-6} or non-hematopoietic cancers\textsuperscript{7} are among the second malignancies.

In a retrospective cohort study, we analyzed the occurrence of second malignancies in over 10,000 gastrectomized patients, and compared the occurrence rates with regard to both the administration of postoperative adjuvant chemotherapy and the surgical procedures. Second cancers in the gastric remnant following gastric resection will be reported in a succeeding paper.

MATERIALS AND METHODS

All patients with gastric cancer who had undergone gastrectomy in the seven different institutions from 1960 to 1975 were the subjects studied. Those who had died within one year after the operation were excluded from the investigation. A total of 10,138 with the total time at risk being 89,246 person-years (the average follow-up period 8.8 years) were obtained, of which 235 (2.32 per cent) with second malignancies other than cancer of the gastric remnant were clinically observed. The rate of second malignancies was analyzed with regard to the administration of anticancer agents and surgical procedures. Second cancers in the gastric remnant following gastric resection will be reported in a succeeding paper.

The occurrence rate of second cancer in each group was calculated by dividing the actual number of second cancers by the total time at risk (person-years). The $\chi^2$ test was used to determine the statistical significance.

The expected number of second cancers ($E$) in 10,117 patients, ages ranging from 20-84 years was computed for a precise analysis. The expected number of second malignancies in a group can be computed as follows.

Let the age of a patient (x) be i years, and the follow-up period $f_x$ years. Then the expected number of second malignancies ($e_{ix}$) in this “i-year old patient” during the $f_x$ years is written as

$$e_{ix} = R_i + R_{i+1} + \ldots \ldots + R_{i+(f_x-1)} \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ ld