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The Kaplan and Meier and the Nelson Estimate for the Probability of Ulcer Recurrence 10 and 15 Years after Parietal Cell Vagotomy

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The use of a nonparametric estimate from incomplete observations is demonstrated on ulcer recurrence 10–15 years after parietal cell vagotomy in 339 patients with duodenal ulcer. The median period of observation was 108 months (range: 1–197 months). Proven recurrent ulcer developed in 62 patients. The life-table method as described by Kaplan and Meier and Nelson's modification are demonstrated. The calculated risk of recurrence after 10 years was 23% (±3.8%) and after 15 years was 27% (±4.3%). The rate of recurrence seemed to decline toward the end of the trial time.

NONPARAMETRIC ESTIMATION from incomplete observation is often used in clinical trials that study time until death (clinical trials of cancer therapy). It is, however, equally relevant to use the estimate in trials that study time until other types of untoward events.

Medical follow-up trials often deal with incomplete follow-up data due to either accidental or controlled losses. Complete follow-up data on all patients is the ideal situation and would give the true rate of the event studied. The major advantage of nonparametric estimation from incomplete observation is that the method makes it possible to use all information from the trial accumulated up to the end of the study.

This paper presents the use of nonparametric estimates from incomplete observation and demonstrates the results from the same study, first followed for 10 years and then again after 15 years.

Patients and Methods

In January 1969, parietal cell vagotomy without drainage was first introduced as the surgical treatment of patients with a duodenal ulcer.[1,2] In 1983, we reported the follow-up results, 2–12 years after surgery, of the patients in the Copenhagen study.[3] In the current study we extended the follow-up period of the same patients, all treated between 1969 and 1979.

Three hundred fifty patients had elective parietal cell vagotomy because of a chronic ulcer located in the duodenal bulb, the pylorus, or the prepyloric area. Information concerning operative technique, acid secretion test,

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TABLE 1. *Example of Formulas Computing the Kaplan and Meier and Nelson Estimates*

Time for Event	Numbers at Risk at t_i	Risk in Interval	Nelson Estimate $\hat{B}(t_i)$	Kaplan Estimate $\hat{S}(t_i)$	SD of $\hat{B}(t_i)$ SD ($\hat{B}(t_i)$)	SD of $\hat{S}(t_i)$ SD ($\hat{S}(t_i)$)
t_i	$N(t_i)$	$1/N(t_i)$	$\sum \frac{1}{N(t_i)}$	$\pi\left(1-\frac{1}{N(t_i)}\right)$	$\sum \frac{1}{N(t_i)^2}$	$\hat{S}(t_i)^*$ SD ($\hat{B}(t_i)$)
1	10	0.1	0.1	0.9	0.1	0.09
5	8	0.125	0.225	0.788	0.16	0.126
9	6	0.167	0.392	0.656	0.23	0.151

distribution of age, sex, and site of ulcer is previously described.[3] All patients without known recurrent ulcer were traced *via* the National Register, and follow-up examination was done between April 1985 and May 1986.

Eleven patients were excluded from the analysis owing to a lack of follow-up information. Thus, a total of 339 patients remained for the analysis. After completion of the follow-up examination, seven patients did not respond, but using the Kaplan and Meier estimate, these patients are included using the previous known time of follow-up examination.

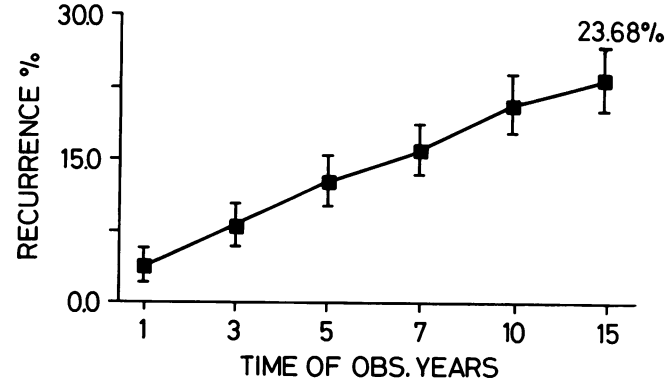

FIG. 1. Probability of ulcer recurrence after parietal cell vagotomy. Kaplan-Meier plots ± 1 SD.

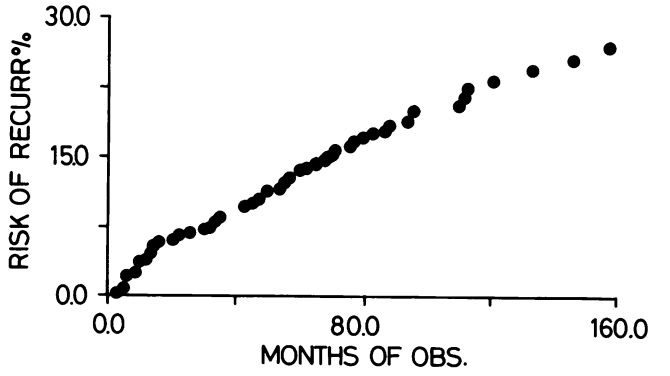

FIG. 2. Integrated recurrence risk after parietal cell vagotomy. Nelson plots ± 1 SD.

Clinical Follow-up

All patients alive without known recurrence with follow-up information of longer than 3 months were sent a similar questionnaire as at the 1981 follow-up examination. Primary nonresponders were sent a additional questionnaire. Secondary nonresponders were, if possible, contacted by telephone. Reports on examinations for ulcer symptoms by general practioners or hospitals were obtained. The median observation time was 108 months (range: 1–197 months).

Statistical Analysis

The ulcer recurrence probability was calculated with due regard to the incomplete follow-up information. The actuarial or life table method as described by Kaplan and Meier[4] was used. Since it is more common to speak of the risk of ulcer recurrence than the freedom from recurrence, data are given as the probability of ulcer recurrence within a given period.

To demonstrate a possible variation in the risk of recurrence over a short period, Nelson's modification of the actuarial method[5] was used. This gives the integrated ulcer recurrence rate as a function of time.

References describing nonparametric estimate for incomplete data are given,[4–7] but to show how simple the analysis is and at the same time perhaps to enable physicians who do not have statistical training to use the method, the method of analysis used for this paper is depicted in Table 1.

TABLE 2. *The Kaplan and Meier and Nelson Estimates for Ulcer Recurrence after Parietal Cell Vagotomy for the 1981 and 1986 Follow-up Study*

	1981	1986
Kaplan and Meier estimate		
10 years	23.76 ± 4.38	20.85 ± 3.03
15 years	?	23.68 ± 3.33
Nelson estimate		
10 years	26.76 ± 5.78	23.31 ± 3.83
15 years	?	26.92 ± 4.37

Results

Of the 339 patients studied, 62 (18.3%) had an ulcer recurrence. The probability of ulcer recurrence, calculated by means of the acturial method, is shown in Figure 1. After 10 years, the risk of recurrence was 20.85% ± 3.03% (mean ± 1 SD), and after 15 years was 23.68% ± 3.33% (mean ± 1 SD).

The integrated estimate for ulcer recurrence is shown in Figure 2. After 10 years, the risk of recurrence was 23.31% ± 3.83% (mean ± 1 SD), and after 15 years was 26.92% ± 4.37% (mean ± 1 SD). There seems to be a higher risk at the beginning, then almost a constant risk and possibly a slight decline in the recurrence risk toward the end of the trial.

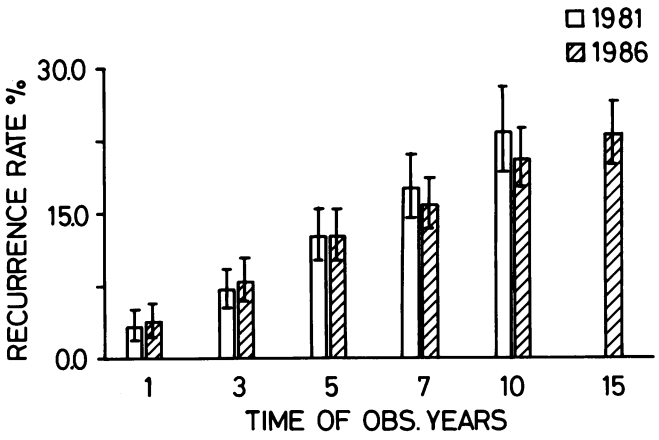

FIG. 3. Probability of ulcer recurrence after parietal cell vagotomy, the 1981 and 1986 follow-up studies. Kaplan-Meier plots ± 1 SD.

Discussion

The 10-year follow-up examination of The Copenhagen parietal cell vagotomy study[3] and the current 15-year follow-up examination were carried out using the exact same method. The results of both the Kaplan and Meier estimate and the Nelson estimate for recurrence after the two follow-up studies are shown in Table 2. Graphic presentation of the Kaplan and Meier estimate for recurrence after the two follow-up studies is shown in Figure 3. The number of recurrences has risen from 42 (13%) to 62 (18%). In the 1981 study, the actuarial probability of ulcer recurrence after 10 years was 23.76% ± 4.38% and the corresponding integrated risk was 26.76% ± 5.78%. In 1981, the Nelson estimation showed a constant monthly risk of 0.23%, and therefore we could expect a probability rate of approximately 37% after 15 years. However, with additional follow-up study from 10 to 15 years, the estimated probability rate showed a rate of 23.68% ± 3.33%.

The median 1981 observation time was 48 months (range: 1–128 months) and the current 1986 observation time was 108 months (range: 1–197 months), which is reflected in the Kaplan and Meier and Nelson estimates giving smaller standard deviation of mean and therefore a higher accuracy of the estimates of recurrence.

The Copenhagen parietal cell vagotomy study has now been followed for a considerably long time. The plot of the Nelson estimates shows the risk of having a recurrent ulcer as a function of time. It seems that the risk is decreasing toward the end of trial time, therefore we can hope that the probability of ulcer recurrence after parietal cell vagotomy without drainage for a chronic duodenal ulcer has reached a stable value of around 25%. However, the final true rate of recurrence can be obtained only with complete follow-up study of all patients. The additional 5 years of trial time from 10 to 15 years has helped us, using the Kaplan and Meier and the Nelson methods to give a more reliable estimate of both the rate and the risk of recurrence.

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