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# Prognosis of Rectal Cancer in France

**Guy Launoy, Marc Gignoux, Didier Pottier, Francoise Lefort, Alain Soumrany, Jean Maurel and Arnaud Beck**

**We studied changes in the prognosis of cancer of the rectum (excluding the rectosigmoid junction) from 1978 to 1986 in the French department of Calvados on the basis of the 616 cases in the cancer registry. Taken as whole, survival has improved slightly with time ($P < 0.01$), but the improvement is only significant for men ($P < 0.02$), patients under 70 years ($P < 0.01$) and patients living in urban areas ($P < 0.05$). With regard to tumour characteristics, the improvement was significant only for patients with Dukes' stage C tumours at surgery ($P < 0.02$). To determine the reasons for the improvement in survival, the year of diagnosis and all other prognostic factors were studied in a multivariate model. Diagnostic conditions such as age and tumour stage did not vary from 1978 to 1986; in contrast, the rates of tumour resection and adjuvant radiation therapy increased, possibly explaining at least part of the improvement, particularly for patients with Dukes' stage C tumours.**
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## INTRODUCTION

CANCER OF the rectum is frequent in both France and in Europe as a whole [1]. In France, cancer of the rectum (excluding the rectosigmoid junction), represents about one third of all colorectal cancers [2, 3]. On the basis of registries, the average 5-year survival rate is between 35 and 40% [4, 5]. In the last 10 years, the use of endoscopy has become widespread and attempts to improve survival have involved tumour resection and adjuvant therapy [6–9]. The aim of this study was to assess possible changes in the prognosis of rectal cancer in a well-defined population, together with the impact of changes in medical practice in this setting.

## PATIENTS AND METHODS

Between 1 January 1978 and 31 December 1986, 616 cancers of the rectal ampulla, excluding cancers of the anus and those of

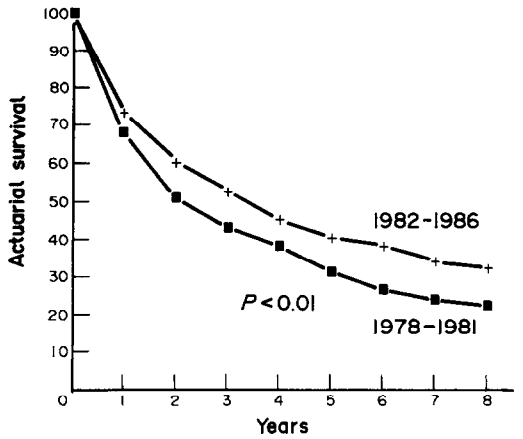


**Fig. 1. Actuarial survival of patients with rectal cancer in Calvados (France) between 1978 and 1982, and 1983 and 1986.**

the rectosigmoid junction, were recorded in the Digestive Tract Tumour Registry of Calvados, a French department. The following information was available for each case: sex, age, home environment (urban/rural), year of diagnosis, locoregional and distant tumour extension, type and place of surgical treatment and use of pre- and postoperative radiation therapy. In the study of survival, conducted in July 1990, the relevant information was obtained in 95% of cases (587/617). The year of diagnosis ranged from 1978 to 1986. Sex, age, home environment and the place of surgery (university hospital or cancer institute/general hospital or private clinic) were treated as qualitative binary variables. Locoregional and distant tumour development were defined according to four modes: the three stages (A, B, C) of Dukes' classification (1932) and metastatic cancer. Surgical treatment was defined according to three modes: no surgery, palliative procedures (including explorative laparotomy, derivations and Hartman's operations) and tumour resection (including Miles' procedure and sphincter-saving resection). Radiation therapy was considered as both absent or present and pre- or postoperative. Figure 1 shows the sociodemographic, clinical and therapeutic characteristics of the population. To explain changes in prognosis, multifactorial analyses of prognostic factors, including the year of diagnosis, were conducted; they included patients who underwent surgery ($n$ = 391) and those who underwent resection of a Dukes' stage C tumour ($n$ = 117).

The survival function was estimated using Kaplan–Meir's method. The Mantel–Cox test was used for the single-factor analyses, while Cox's proportional hazards model was used for the multifactorial analysis. The distribution of qualitative variables was studied with the $\chi^2$ test or Fisher's exact test as appropriate. Calculations were performed using modules 4F, 1L and 2L of the BMDP software package.

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Revised 4 Aug. 1992; accepted 6 Aug. 1992.

## RESULTS

The actuarial survival of the 587 patients was 70.8% at 1 year, 47.9% at 3 years, and 35.5% at 5 years. Survival improved slightly from 1978 to 1986 ($P < 0.01$). By way of an example, Fig. 1 shows the improvement in survival between 1978 and 1981 (257 patients) and 1982 and 1986 (330 patients) ($P < 0.01$). This improvement was associated with both sociodemographic and clinical characteristics. It was significant in men ($P < 0.02$), patients under 70 years ($P < 0.01$) and patients living in the urban environment ($P < 0.05$). With regard to clinical factors, the improvement only concerned patients who underwent surgery ($P < 0.01$); the largest survival increment involved patients with Dukes' stage C tumours at diagnosis ($P < 0.02$). For example, Fig. 2 shows the improvement in survival observed in this subgroup between 1978 and 1981 (52 patients) and 1982 and 1986 (74 patients).

To explain this improvement in survival, the year of diagnosis and other prognostic factors were entered in a multifactorial analysis. Table 2 shows the results for the patients who underwent surgery: neither sphincter preservation nor adjuvant radiation therapy had any influence. The year of diagnosis was not excluded from the model when tumour extension was taken into account, but only when tumour resection was entered.

Table 3 shows the results of the multifactorial analysis for the patients with resected Dukes' stage C tumours: pre-operative radiation therapy was a good prognostic factor, but postoperative radiation therapy had no influence (Fig. 3). Even when the effect of radiation therapy was taken into account the improvement in survival with time remained significant. Similarly, when age was forced into the model, neither of these two variables was excluded.

## DISCUSSION

Very few data are available on recent changes in the survival of well-defined populations of cancer patients. Such studies require continuous and long-term recording of data on incidence, diagnostic conditions, treatment and outcome. Mortality data provide an overall view [10], but they do not allow cancer of the rectum to be distinguished from the cancer of the colon, for example, and must be compared with morbidity data before a valid conclusion can be drawn.

Our data, for the Calvados department in France, show a recent improvement in the survival of patients with rectal cancer.

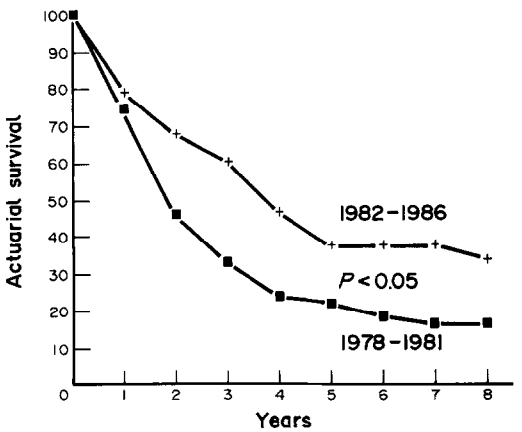


**Fig. 2. Actuarial survival of patients with Dukes' stage C rectal cancer at surgery in Calvados (France) between 1978 and 1982, and 1983 and 1986.**

*Table 1. Distribution of the study population according to sex, age, home environment, diagnosis and treatment of rectal cancers in the department of Calvados* (1978–1986)

| | All cancers ($n$ = 587) | | Surgery ($n$ = 391) | | Excision ($n$ = 335) | |
|---|---|---|---|---|---|---|
| | $n$ | % | $n$ | % | $n$ | % |
| Sex | | | | | | |
| Males | 340 | 57.9 | 243 | 62.1 | 203 | 60.1 |
| Females | 247 | 42.1 | | | | |
| Age at diagnosis | | | | | | |
| Unknown | 43 | | 6 | | 5 | |
| ≤ 70 years | 336 | 61.8 | 262 | 68.1 | 232 | 70.3 |
| > 70 years | 238 | 38.2 | 123 | 31.9 | 98 | 29.7 |
| Home environment | | | | | | |
| Urban | 454 | 77.3 | 305 | 78.0 | 258 | 77.0 |
| Rural | 133 | 22.7 | 86 | 22.0 | 77 | 23.0 |
| Place of treatment | | | | | | |
| Specialised | 306 | 55.5 | 200 | 51.8 | 165 | 49.4 |
| Non-specialised | 254 | 44.5 | 186 | 48.2 | 169 | 50.6 |
| Unknown | 36 | | 5 | | 1 | |
| Surgery | | | | | | |
| None | 196 | 33.4 | 0 | | 0 | |
| Palliative | 56 | 9.5 | 56 | 14.3 | 0 | |
| Resection | 335 | 57.1 | 335 | 85.7 | 335 | 100.0 |
| Tumour extension | | | | | | |
| Unknown | — | | 28 | | 10 | |
| Dukes' A | — | | 73 | 20.1 | 71 | 21.8 |
| Dukes' B | — | | 103 | 28.4 | 99 | 30.5 |
| Dukes' C | — | | 126 | 34.7 | 117 | 36.0 |
| Metastasis | — | | 61 | 16.8 | 38 | 11.7 |
| Adjuvant radiotherapy | | | | | | |
| None | — | | — | | 232 | 69.2 |
| Pre-operative | — | | — | | 21 | 6.3 |
| Postoperative | — | | — | | 71 | 21.2 |
| Time unknown | — | | — | | 11 | 3.3 |

*Table 2. Multi-factorial analysis of the prognosis of rectal cancer following surgery* ($n$ = 391)

| Prognostic factors | Initial model | Final model | Order of importance |
|---|---|---|---|
| Sex | NS | — | |
| Age (≤ 70/> 70) | $P < 0.05$ | $P < 0.10$ | 3 |
| Year of diagnosis | $P < 0.01$ | NS | |
| Tumour extension | $P < 0.0001$ | $P < 0.001$ | 1 |
| Tumour resection | $P < 0.0001$ | $P < 0.001$ | 2 |
| Sphincter-saving procedure | NS | — | |
| | NS | — | |
| Pre-operative radiotherapy | NS | — | |
| Postoperative radiotherapy | | | |

NS= Not significant.

*Table 3. Multi-factorial analysis of the prognosis of rectal cancer following resection of Dukes' stage C tumours*

| Prognostic factors | Initial model | Final model | Order of importance |
|---|---|---|---|
| Sex | NS | — | |
| Age (≤ 70/> 70) | NS | — | |
| Year of diagnosis | $P < 0.05$ | $P < 0.10$ | 2 |
| Postoperative radiotherapy | NS | | |
| Pre-operative radiotherapy | $P < 0.02$ | $P < 0.05$ | 1 |

NS= Not significant.

Between 1978 and 1986, there was no change in either the tumour extension at diagnosis or the mean age at diagnosis. Similar observations have been made on the basis of other cancer registries [11, 12]. The improvement in prognosis was not, therefore, explained by an improvement in diagnostic conditions, as confirmed by our analysis of the subset of patients who underwent surgery. In contrast, treatment changed during the same period, with increases in the rate of surgical resection and sphincter-saving procedures [13], and increased use of adjuvant radiation therapy [14]. This change in treatment explained the overall improvement in the survival of the patients who underwent surgery. It is noteworthy that the sphincter-saving procedure, which has improved patients' quality of life, did not have a negative effect on survival. Chemotherapy was used very little in the study population during this period (4%). In the sub-group of patients with Dukes' stage C tumours at diagnosis (who showed the greatest improvement in survival) pre-operative radiation therapy partly explained the increment. Although care must be taken in interpreting this result because of the retrospective character of the study, our results agree with those of recent randomised trials showing the effectiveness of pre-operative radiation therapy [15–17].

In conclusion, the recent improvement in the prognosis of rectal cancer in the study population is due on the one hand to an increase in the rate of tumour resection and on the other hand to the increased use of adjuvant radiation therapy, particularly prior to surgery. It would be interesting to determine whether a similar improvement in survival has taken place elsewhere in France and in Europe.

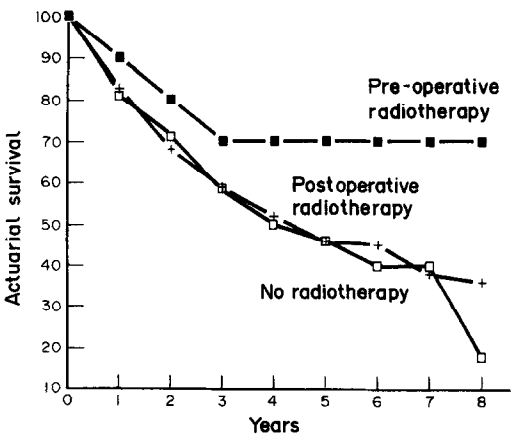


**Fig. 3. Actuarial survival of patients after resection of Dukes' stage C tumours in Calvados (France) according to the type of adjuvant radiation therapy.**

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# Activities of Antioxidant Enzymes and Lipid Peroxidation in Endometrial Cancer

**Reijo Punnonen, Ryuichi Kudo, Kari Punnonen, Eino Hietanen, Tapio Kuoppala, Heikki Kainulainen, Kenichirou Sato and Markku Ahotupa**

**Antioxidant enzyme activities and lipid peroxidation were analysed in normal endometrium and endometrial cancer tissues from Finnish and Japanese patients. The catalase and glutathione peroxidase activities of normal endometrium were significantly lower in Finns than in Japanese. Lipid peroxidation was slightly higher in endometrial cancer as compared with normal endometrium both in the Finns and in the Japanese. When cancer tissues were compared with normal endometrium both in Finns and Japanese the activity of superoxide dismutase was significantly lower in cancer tissue than in normal endometrium. In Finns glutathione S-transferase activity was also lower in endometrial cancer tissue than in normal endometrium, and a similar tendency was also found in Japanese. This study suggests that endometrial cancer tissue is associated with an impaired enzymic antioxidant defence system.**
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## INTRODUCTION

OBESITY IS one of the most important risk factors of endometrial cancer [1, 2]. This has usually been ascribed to the levels of peripheral aromatization of androgens to oestrogens in adipose tissue, which is the major source of oestrogens in postmenopausal women [3]. Several other dietary aspects may also be related to the risk of endometrial cancer. Total fat consumption *per capita* and incidence of endometrial cancer are positively correlated on an international scale [4]. Both the incidence of endometrial cancer and total fat consumption are low in Japan compared with Western countries. In a European case–control study [5] the risk of endometrial cancer was elevated in subjects reporting high fat intake. The basic mechanism by which dietary fats may modulate tumour development remains, however, largely unknown. One of the suggested mechanisms may be increased peroxidation and the production of active peroxides or their decreased inactivation [3, 6, 7].

In this study we have investigated antioxidant enzyme activi-