Pergamon

*European Journal of Cancer* Vol. 32A, No. 7, pp. 1156–1161, 1996

Printed in Great Britain
0959–8049/96 $15.00+0.00

PII: S0959-8049(96)00030-5

## Original Paper

# Pre-operative Serum Levels of CA 242 and CEA Predict Outcome in Colorectal Cancer

M. Carpelan-Holmström,[1] C. Haglund,[1] J. Lundin,[1] H. Järvinen[2] and P. Roberts[1]

[1]Fourth and [2]Second Departments of Surgery, Helsinki University Central Hospital, Kasarmikatu 11–13, 00130 Helsinki, Finland

**The prognostic value of the preoperative serum levels of CA 242 and CEA in patients with colorectal cancer was investigated. The serum concentrations of CA 242 and CEA were determined from pre-operative serum samples of 259 patients with colorectal cancer (39 Dukes' A, 100 Dukes' B, 59 Dukes' C and 61 Dukes' D). Survival data of these patients were obtained to the end of 1993. There was a significantly longer survival in patients with a CA 242 level below 20 U/ml compared with patients with an elevated serum level. A difference was seen in overall survival ($P<0.0001$), and in Dukes' B ($P=0.016$) and Dukes' D ($P=0.009$) stages. In Dukes' A and C colorectal cancer, the difference was not significant ($P=0.67$ and $P=0.07$, respectively). When 5 ng/ml was used as cut-off value for CEA, there was a significant difference in overall survival ($P<0.0001$), but not within the different Dukes' stages. The prognosis was considerably worse in patients with concomitant elevation of CA 242 and CEA, compared with the prognosis of patients with normal levels or only one marker elevated ($P<0.0001$). When analysing according to stage, a significant difference was seen in Dukes' B ($P=0.0004$) and Dukes' C ($P=0.0007$) stages. In a multivariate analysis, CA 242 was an independent prognostic factor ($P<0.0001$). CEA was also an independent prognostic factor ($P=0.03$), but only after exclusion of CA 242. Concomitant rise of CA 242 and CEA was found to be a strong independent prognostic factor ($P<0.0001$). This study shows that the pre-operative serum CA 242 level is an independent prognostic factor in patients with colorectal cancer and that the prognosis of patients having a concomitant pre-operative elevation of CA 242 and CEA is poor.** 

**Key words: prognosis, colorectal, neoplasm, tumour marker, CA 242, CEA**
*Eur J Cancer*, Vol. 32A, No. 7, pp. 1156–1161, 1996

## INTRODUCTION

COLORECTAL CANCER is a common cause of death in western countries and different factors have been related to survival. However, the clinical application of many of these prognostic factors is limited, because they are complex or poorly reproducible, or have not been subjected to adequate statistical analysis. A reliable prognostic factor would be of clinical value in planning adjuvant therapies in these patients.

Since CEA was discovered in 1965 [1], it has been the most commonly used tumour marker in colorectal cancer. It has a high sensitivity for recurrent colorectal cancer and is commonly used in the follow-up of surgically treated patients [2–11]. The prognostic value of CEA in colorectal cancer remains uncertain. There are reports supporting a prognostic value of the pre-operative CEA level in colorectal cancer [12–21], while other studies do not [22–27].

The novel tumour marker CA 242 has also shown promising high sensitivity for colorectal cancer, and the concomitant use of CA 242 and CEA increases the sensitivity for early colorectal cancer [3, 28, 29]. CA 242 also seems useful in the follow-up of patients with colorectal cancer [30]. Recently, CA 242 was shown to be superior to CEA as a prognostic factor in colorectal cancer [12].

The aims of this study were to investigate the prognostic value of the pre-operative serum level of CA 242 in patients with colorectal cancer and to compare the results with those of CEA and with the concomitant use of the markers.

## PATIENTS AND METHODS

### *Patients*

Pre-operative serum samples were obtained from 259 patients with clinically diagnosed and histologically verified col-

Correspondence to P. Roberts.
Received 6 Sep. 1995; revised 22 Dec. 1995; accepted 16 Jan. 1996.

orectal cancer at the Fourth Department of Surgery from 1982 to 1989 (157 patients) and Second Department of Surgery from 1987 to 1989 (102 patients). Tumours were classified according to the modified Dukes' classification [31]. 39 patients had Dukes' A, 100 patients Dukes' B, 59 patients Dukes' C and 61 patients Dukes' D colorectal cancer. Colonic and rectal cancer were found in 152 and 107 patients, respectively. There were 137 men (median age 67 years, range 25–89 years) and 122 women (median age 70 years, range 36–88 years). Survival data of the patients to the end of 1993 were obtained from patient records, The Finnish Cancer Registry and the Population Registry. 128 patients died from colorectal cancer during follow-up.

*Assays*

Serum samples were taken pre-operatively and stored at −20°C until analysed. The serum concentrations of CA 242 and CEA were determined by commerically available assays (Wallac Oy, Turku, Finland; Abbott-Diagnostics, Chicago, Illinois, U.S.A.). The CA 242 test is a two-step dissociation enhanced lanthanide fluoroimmunoassay (DELFIA) that uses an antibody against sialylated Lewis[a] as catcher, and CA 242 as the detector antibody. Both CA 242 and CEA were quantitated from the same serum samples. The cut-off values recommended by the manufacturers for diagnostic use are 20 U/ml for CA 242 and 5 ng/ml for CEA.

*Statistical analysis*

Life tables were calculated according to Kaplan and Meier. Deaths were deaths due to colerectal cancer, whereas deaths due to other causes were treated by censoring. Patients were divided into groups having a pre-operative tumour marker value above or below the recommended cut-off levels and their survival was compared. The median survival was calculated including the patients that were censored, using the length of time they were in the study. The statistical significance of the difference in survival of the groups was calculated using the log rank test. When the variable examined had three or more ordered categories, the log rank test for trend was used. Multivariate survival analyses were performed with the Cox proportional hazards model entering the following covariates: age (as a continuous variable), gender (male=0, female=1), Dukes' stage (as nominal groups), location of the tumour (colonic=0, rectal=1), the logarithms of the pre-operative serum CA 242 and CEA levels were entered as continuous variables. Covariates were selected in a stepwise manner (backward to forward), with use of the maximum-likelihood ratio. A *P*-value of 0.05 was adopted as limit for inclusion of a covariate.

## RESULTS

*Survival according stage and localisation of the tumour*

In patients with Dukes' A, B, C and D colerectal cancer, the median survival was 5.8, 5.1, 2.5 and 0.64 years, respectively. The difference in survival between the stage groups was highly significant ($P<0.0001$, trend log rank $\chi^2=142$, df=1). In colonic cancer, the median survival was 4.3 years and in rectal cancer 4.1 years ($P=0.48$, $\chi^2=0.49$, df=1).

*CA 242*

The median survival of 100 patients with serum levels higher than 20 U/ml was 1.5 years compared with 5.0 years of 159 patients with values below that level. The difference between the survival curves was highly significant ($P<0.0001$; Figure 1a, Table 1)

In patients with Dukes' A colorectal cancer, there was no significant difference in survival between patients with pre-operative CA 242 serum levels higher than 20 U/ml (10/39) and patients with serum levels lower than this level (29/39). The median survival was 6.2 years and 5.8 years, respectively ($P=0.7$; Table 1).

In patients with Dukes' B colorectal cancer, the median survival of patients with pre-operative serum levels above 20 U/ml (26/100) was 4.6 years and of those with a lower serum level (74/100) 5.5 years. The difference between the survival curves was statistically significant ($P=0.016$; Figure 1b, Table 1).

In patients with Dukes' C colorectal cancer, the median survival of patients with a pre-operative CA 242 serum level above 20 U/ml (23/59) was 2.2 years compared with 4.3 years of patients with a lower serum level (36/59). The difference between the survival curves approached the borderline of significance ($P=0.07$; Figure 1c, Table 1).

In patients with Dukes' D colorectal cancer, the median survival of patients with a pre-operative serum level above 20 U/ml (41/61) was 0.57 years and of patients with a lower level (20/61) 0.99 years. The difference between the survival curves was statistically significant ($P=0.009$, Figure 1d, Table 1).

*CEA*

The median survival of 112 patients with serum levels higher than 5 ng/ml was 1.6 years and of 147 patients with a lower value, 5.0 years. The difference between the survival curves was highly significant ($P<0.0001$, Table 1).

In patients with Dukes' A colorectal cancer, there was no difference in survival between patients with pre-operative CEA serum levels higher than 5 ng/ml (10/39) and patients with serum levels lower than this level (29/39). The median survival was 6.1 years and 5.8 years, respectively ($P=0.35$; Table 1).

In patients with Dukes' B colorectal cancer, the median survival of patients with pre-operative serum levels above 5 ng/ml (32/100) was 4.6 years and of those with a lower serum level (68/100) 5.4 years. The difference between the survival curves was not statistically significant ($P=0.13$; Table 1).

In patients with Dukes' C colorectal cancer, the median survival of patients with a pre-operative CEA serum level above 5 ng/ml (23/59) was 2.5 years compared to 4.8 years of patients with a lower serum level (36/59). The difference between the survival curves approached the borderline of significance ($P=0.08$; Table 1).

In patients with Dukes' D colorectal cancer, the median survival of patients with pre-operative serum level above 5 ng/ml (47/61) was 0.62 years and of patients with a lower level (14/61) 0.99 years. The difference between the survival curves was not statistically significant ($P=0.17$; Table 1).

*Combination of CA 242 and CEA*

The median survival of 61 patients with concomitant elevation of CA 242 (>20 U/ml) and CEA (>5 ng/ml) was 1.0 year compared with 4.9 years of 198 patients with normal levels or only one marker elevated. The difference between the survival curves was highly significant ($P<0.0001$; Figure 2a, Table 1).

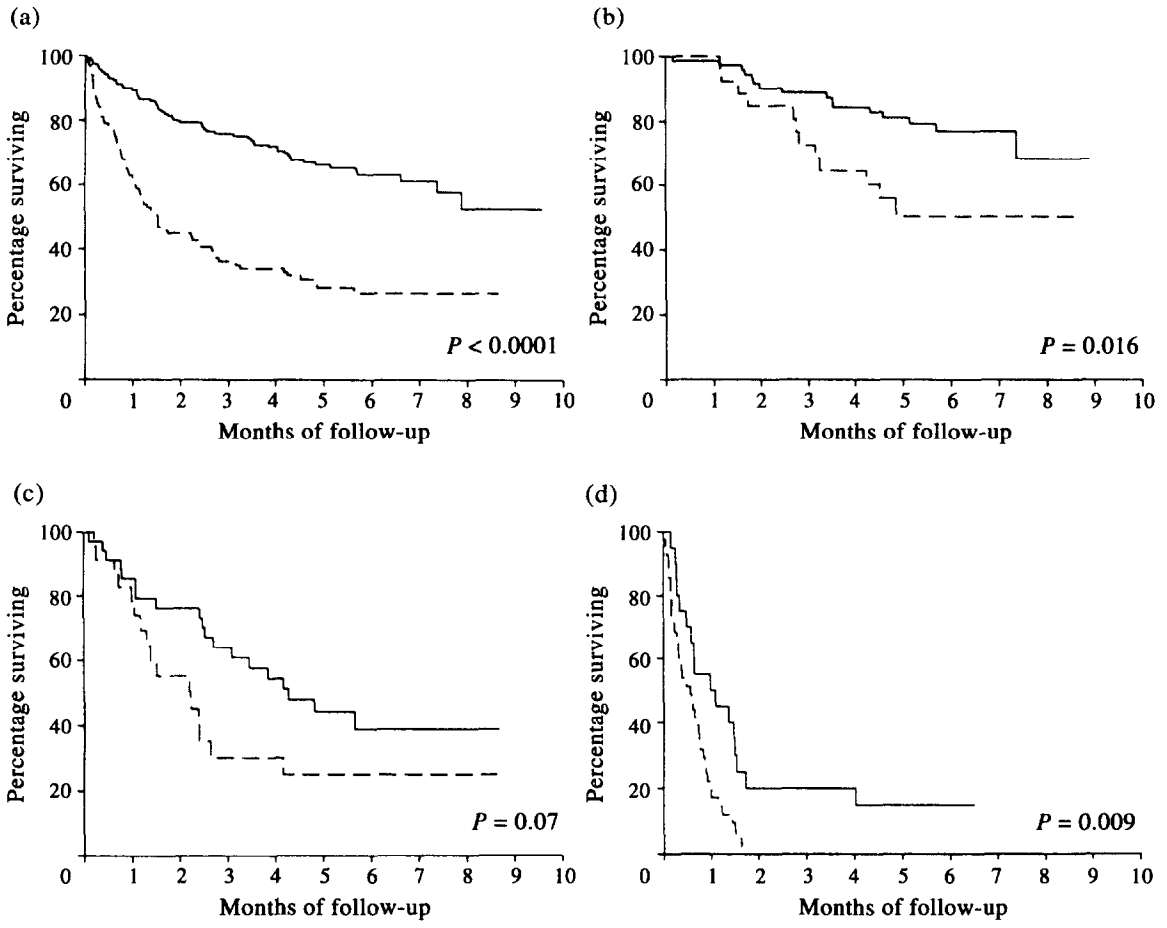


**Figure 1. Life-tables for all the patients with colorectal cancer (a), and in Dukes' B (b), Dukes' C (c), and Dukes' D (d) stages with pre-operative CA 242 below (——) or above (– – –) 20 U/ml.**

In patients with Dukes' A colorectal cancer, there were only 2 patients with both markers elevated, both censored, so a difference in survival between the groups could not be calculated.

In patients with Dukes' B colorectal cancer, the median survival of patients with both markers elevated (12/100) was 3.2 years and that of those with one or no marker elevated (88/100) 5.3 years. The difference in the survival curves was highly significant ($P$=0.0004; Figure 2b, Table 1).

In patients with Dukes' C colorectal cancer, the median survival of patients with both markers elevated (11/59) was 1.4 years compared to 4.3 years of patients with one or no marker elevated (48/59). The difference between the survival curves was highly significant ($P$=0.0007; Figure 2c, Table 1).

In patients with Dukes' D colorectal cancer, the median survival of patients with both markers elevated (36/61) was 0.62 years and of patients with one or no marker elevated 25/61) 0.64 years. The difference between the survival curves was not statistically significant ($P$=0.09; Figure 2d, Table 1).

*Multivariate analysis*

In a multivariate analysis, entering the logarithms of the serum tumour markers as continuous variables, Dukes' stage yielded most prognostic information, followed by CA 242, age and localisaation of the tumour (Table 2). Gender and CEA did not predict prognosis independently at a significance level of 5% (Table 2). If CA 242 was excluded from the Cox model, CEA became an independent prognostic factor ($P$=0.03, data not shown), whereas the localisation of the tumour became non-significant. The maximum likelihood ratio was higher in a multivariate model including Dukes' stage and CA 242 than in a model including Dukes' stage and CEA, $\chi^2$=168 ($P$<0.0001, df=4) versus $\chi^2$=148 ($P$<0.0001, df=4). In a multivariate analysis with both markers elevated or not elevated as covariates, entering the tumour marker levels as below or above the cut-off level (dichotomised), Dukes' stage was the strongest prognostic factor, followed by the combined use of CA 242 and CEA, and then age (Table 3). Localisation of the tumour and gender were not independent prognostic factors.

## DISCUSSION

During the last 20 years, many prognostic factors in colorectal cancer have been evaluated. Unfortunately, the clinical application of many of these variables is limited [32]. Dukes' classification has repeatedly been proven to be strongly correlated with patient survival and is still the gold standard against which all other prognostic factors in colorectal cancer should be assessed [32,33]. However, currently there is also a need to predict outcome within each Dukes' stage, enabling better patient selection for adjuvant treatments. CEA has been in clinical use for decades and the prognostic value of CEA has been investigated in several studies. There are studies supporting the prognostic value of CEA [12–21] and studies that do not [22–27]. In studies where multivariate analysis has been performed, the results have varied. In some of these

*Table 1. Univariate survival analysis of 259 patients with different stages of colorectal cancer according to pre-operative tumour marker level*

| | *n* | Median survival (years) | $\chi^2$ | *P* | RR (CI 95%) |
|---|---|---|---|---|---|
| Overall | | | | | |
| CA 242 ≤20 U/ml | 159 | 5.0 | 40 | <0.0001 | 3.0 (2.1–4.7) |
| CA 242 >20 U/ml | 100 | 1.5 | | | |
| CEA ≤5 ng/ml | 147 | 5.0 | 30 | <0.0001 | 2.6 (1.8–3.79) |
| CEA >5 ng/ml | 112 | 1.6 | | | |
| One or neither elevated | 198 | 4.9 | 82 | <0.0001 | 4.7 (3.2–6.7) |
| Both markers elevated | 61 | 1.0 | | | |
| Dukes' A | | | | | |
| CA 242 ≤20 U/ml | 29 | 5.5 | | 0.67 | 1.4 (0.3–6.0) |
| CA 242 >20 U/ml | 10 | 4.6 | 5.6 | | |
| CEA ≤5 ng/ml | 29 | 6.1 | | 0.35 | 0.38 (0.05–3.1) |
| CEA >5 ng/ml | 10 | 5.8 | 0.88 | | |
| One or neither elevated | 257 | | | | |
| Both markers elevated | 2 | | | | |
| Dukes' B | | | | | |
| CA 242 ≤20 U/ml | 74 | 5.5 | 5.6 | 0.016 | 2.5 (1.2–5.2) |
| CA 242 >20 U/ml | 26 | 4.6 | | | |
| CEA ≤5 ng/ml | 68 | 5.4 | 2.3 | 0.13 | 1.8 (0.83–3.7) |
| CEA >5 ng/ml | 32 | 4.6 | | | |
| One or neither elevated | 88 | 5.3 | 13 | 0.0004 | 4.0 (1.8–9.2) |
| Both markers elevated | 12 | 3.2 | | | |
| Dukes' C | | | | | |
| CA 242 ≤20 U/ml | 36 | 4.3 | 3.2 | 0.07 | 1.8 (0.93–3.6) |
| CA 242 >20 U/ml | 23 | 2.2 | | | |
| CEA ≤5 ng/ml | 36 | 4.8 | 3.1 | 0.08 | 1.8 (0.93–3.6) |
| CEA >5 ng/ml | 23 | 2.5 | | | |
| One or neither elevated | 48 | 4.3 | 12 | 0.0007 | 3.6 (1.6–7.8) |
| Both markers elevated | 11 | 1.4 | | | |
| Dukes' D | | | | | |
| CA 242 ≤20 U/ml | 20 | 0.99 | 6.8 | 0.009 | 2.2 (1.2–3.9) |
| CA 242 >20 U/ml | 41 | 0.57 | | | |
| CEA ≤5 ng/ml | 14 | 0.99 | 1.9 | 0.17 | 1.54 (0.82–2.9) |
| CEA >5 ng/ml | 47 | 0.62 | | | |
| One or neither elevated | 25 | 0.64 | 2.8 | 0.09 | 1.6 (0.92–2.8) |
| Both markers elevated | 36 | 0.62 | | | |

*n*, number of patients; $\chi^2$, chi-square; *P*, *P*-value; RR (CI 95%), relative risk (95% confidence interval).

*Table 2. Stepwise multivariate analysis* of prognostic covariates of survival in 259 patients with colorectal cancer*

| Covariate | P† | RH‡ | CI (95%)§ |
|---|---|---|---|
| Dukes' stage | | | |
| B‖ | NS | 1.5 | 0.69–3.4 |
| C‖ | <0.0001 | 5.2 | 2.4–11 |
| D‖ | <0.0001 | 17 | 7.6–39 |
| CA 242¶ | <0.0001 | 1.8 | 1.4–2.2 |
| Age** | 0.002 | 1.03 | 1.01–1.04 |
| Tumour localisation†† | 0.026 | 1.5 | 1.1–2.1 |
| s-CEA‡‡ | NS | | |
| Gender§§ | NS | | |

*Cox proportional hazards model. †Significance level. ‡Relative hazard. §Confidence interval at 95% level. ‖Dukes' stages entered as nominal groups and compared to Dukes' A. ¶The logarithms of the pre-operative serum levels of CA 242 entered as a continuous variable. **Age was entered as a continuous variable. ††Localisation as category (colonic=0, rectal=1). ‡‡The logarithms of the pre-operative serum levels of CEA entered as a continuous variable. §§Gender as category (male=0, female=1). NS, non-significant.

*Table 3. Stepwise multivariate analysis* of prognostic covariates of survival in 259 patients with colorectal cancer. CA 242 and CEA as one covariate*

| Covariate | P† | RH‡ | CI (95%)§ |
|---|---|---|---|
| Dukes' stage | | | |
| B‖ | NS | 1.4 | 0.6–3.0 |
| C‖ | <0.0001 | 4.6 | 2.1–10 |
| D‖ | 0.0001 | 16 | 7.5–37 |
| CA 242 and CEA ¶ | <0.0001 | 2.2 | 1.5–3.1 |
| Age** | 0.0020 | 1.03 | 1.01–1.04 |
| Tumour localisation†† | NS | | |
| Gender‡‡ | NS | | |

*Cox proportional hazards model. †Significance level. ‡Relative hazard. §Confidence interval at 95% level. ‖Dukes' stages entered as nominal groups and compared to Dukes' A. ¶Pre-operative serum values of elevated CA 242 (>20 U/ml) and CEA (>5 ng/ml)=1, one marker or neither marker elevated=0. **Age was entered as a continuous variable. ††Localisation as category (colonic=0, rectal=1). ‡‡Gender as category (male=0, female=1).

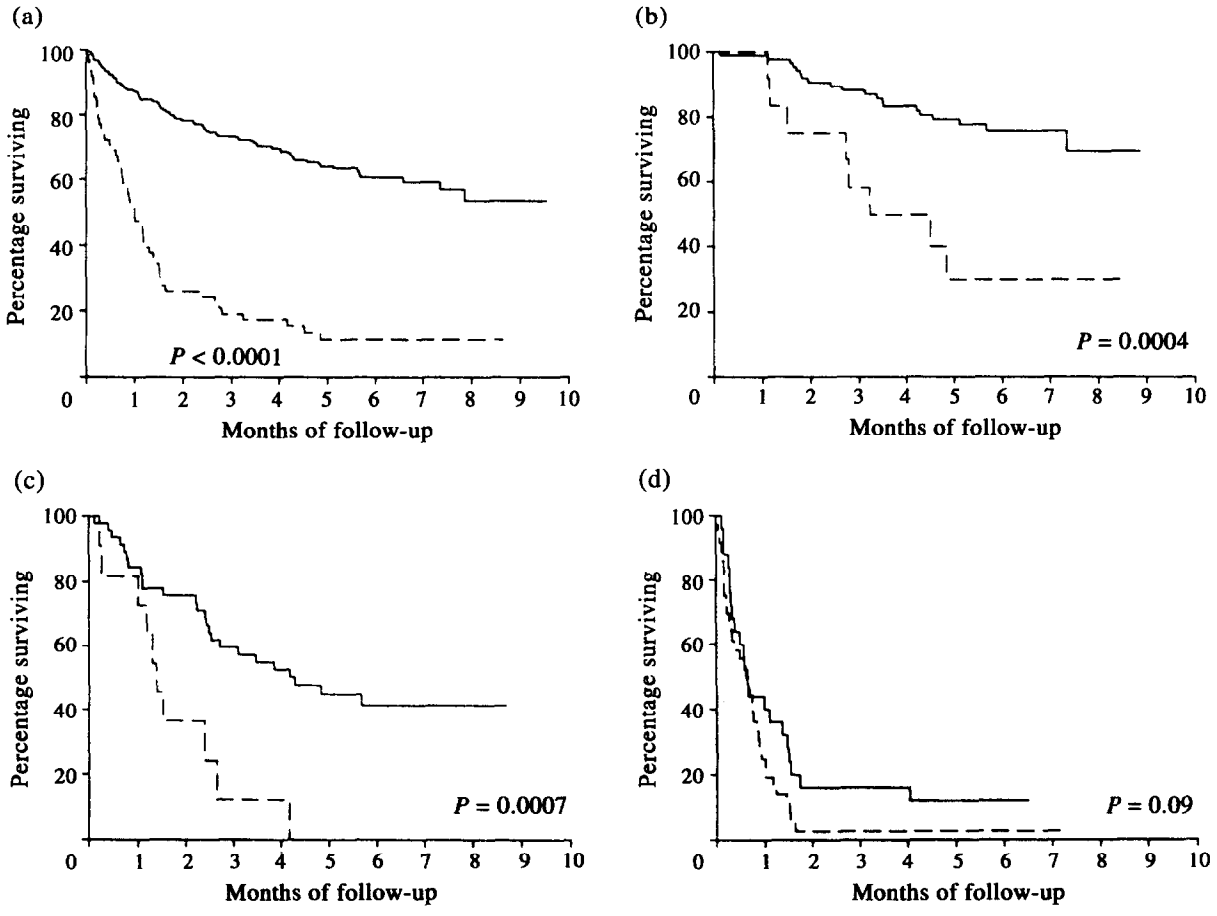


**Figure 2. Life-tables for all the patients with colorectal cancer (a), and in Dukes' B (b), Dukes' C (c), and Dukes' D (d) stages with a pre-operative concomitant elevation of both CA 242 (>20 U/ml) and CEA (>5 ng/ml) (– – –) or with one or no marker elevated (——).**

reports, CEA has been proven to be an independent prognostic factor [12, 15], whereas some reports disagree [23, 24, 27].

In this study, we found a statistically significant difference in survival between patients with a pre-operative CEA level above 5 ng/ml and those with a lower serum level, when all the patients were analysed together and in patients with colonic and rectal cancer, when analysed separately, but not within the different Dukes' stages categories. The difference between the survival curves approached borderline significance in Dukes' C colorectal cancer ($P=0.08$). In a multivariate analysis, excluding pre-operative CA 242, pre-operative CEA was an independent prognostic factor ($P=0.03$).

The novel tumour marker CA 242 has shown promising pre-operative sensitivity in colorectal cancer [3, 28, 29]. In a recent report, the prognostic value of CA 242 was compared with that of other tumour markers [12], and CA 242 was found to be superior to CEA and CA 19-9 in colorectal cancer, but not to CA 50, TPA or TPS. We found a significant difference in overall survival between patients with serum levels above or below 20 U/ml and when divided according to stage: Dukes' B and D colorectal cancer. In Dukes' C colorectal cancer, the difference in survival approached borderline significance ($P=0.07$). In a multivariate analysis, CA 242 was shown to be an independent prognostic factor ($P<0.0001$), while CEA was non-significant.

In pre-operative diagnosis, there is an advantage in combining CA 242 and CEA, as these markers are frequently elevated in different patients, particularly in Dukes' A and B colorectal cancer [28,29]. We therefore studied whether the concomitant use of CA 242 and CEA could be useful in predicting outcome. The greatest difference between patient groups was obtained when comparing patients with a concomitant rise of CA 242 and CEA with patients with no or one marker elevated. The patients with both markers elevated pre-operatively showed a considerably worse prognosis. The differences were highly significant in all the patients and in Dukes' B and C stages ($P<0.0001$, $P=0.0004$ and $P=0.00007$, respectively). In patients with Dukes' B or C colorectal cancer, presumptive prognostic factors may be of utmost importance for patient selection for adjuvant treatments or for predicting surveillance. The prognostic value in the clinical setting of CA 242 and CEA within the stages should be investigated in prospective randomised clinical trials.

1. Gold P, Freedman SO. Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and adsorption techniques. *J Exp Med* 1965, **121**, 439.
2. Hine KR, Dykes PW. Serum CEA testing in the post-operative surveillance of colorectal carcinoma. *Br J Cancer* 1984, **49**, 689–693.
3. Kuusela P, Haglund C, Roberts PJ. Comparison of a new tumour marker CA 242 with CA 19-9, CA 50 and carcinoembryonic antigen (CEA) in digestive tract diseases. *Br J Cancer* 1991, **63**, 636–640.
4. Martin EW, James KK, Hurtubise PE, Catalano P, Minton JP.

The use of CEA as an early indicator of gastrointestinal tumor recurrence and second-look procedures. *Cancer* 1977, **39**, 440–446.
5. Minton JP, Hoehn JL, Gerber DM, *et al.* Results of a 400-patient carcinoembryonic antigen second-look colorectal cancer study. *Cancer* 1985, **55**, 1284–1290.
6. Minton JP, Hoehn JL, Gerber DM, *et al.* Results of a 400-patient carcinoembryonic antigen second-look colorectal cancer study. *Cancer* 1985, **55**, 1284–1290.
7. Northover J. Carcinoembryonic antigen and recurrent colorectal cancer. *Gut* 1986, **27**, 117–122.
8. Quentmeier A, Schlag P, Smok M, Herfarth C. Re-operative for recurrent colorectal cancer: the importance of early diagnosis for resectability and survival. *Eur J Surg Oncol* 1990, **16**, 319–325.
9. Roberts PJ. Tumour markers in colorectal cancer. *Scand J Gastroenterol* 1988, **23**, 50–58.
10. Staab HJ, Anderer FA, Stumpf E, Hornung A, Fischer R, Kieninger G. Eighty-four potential second-look operations based on sequential carcinoembryonic antigen determinations and clinical investigations in patients with recurrent gastrointestinal cancer. *Am J Surg* 1985, **149**, 198–204.
11. Sugarbaker PH, Gianola FJ, Dwyer A, Neuman NR. A simplified plan for follow-up of patients with colon and rectal cancer supported by prospective studies of laboratory and radiologic test results. *Surgery* 1987, **102**, 79–87.
12. Lindmark G, Bergström R, Påhlman L, Glimelius B. The association of preoperative serum tumour markers with Dukes stage and survival in colorectal cancer. *Br J Cancer* 1995, **71**, 1090–1094.
13. Wang JY, Tang R, Chiang JM. Value of carcinoembryonic antigen in the management of colorectal cancer. *Dis Colon Rectum* 1994, **37**, 272–277.
14. Slentz K, Senagore A, Hibbert J, Mazier WP, Talbott TM. Can preoperative and postoperative CEA predict survival after colon cancer resection? *Am Surg* 1994, **60**, 528–532.
15. Wiggers T, Arends JW, Volovics A. Regression analysis in prognostic factors in colorectal cancer after curative resections. *Dis Colon Rectum* 1988, **31**, 33–41.
16. Brummendorf T, Anderer FA, Staab HJ, Hornung A, Stumpf E, Kieninger G. Prognostic value of preoperative serum CEA level compared to clinical staging: III. An approach to scoring of prognostic factors in colorectal cancer. *J Surg Oncol* 1985, **28**, 263–269.
17. Bogenschutz O, Brummendorf T, Staab HJ, Anderer FA, Kieninger G. Prognostic value of preoperative serum CEA level compared to clinical staging IV. Histological grading and tumor type in colorectal and gastric cancer. *J Surg Oncol* 1986, **32**, 165–173.
18. Dhar P, Moore T, Zamcheck N, Kupchik HZ. Carcinoembryonic antigen (CEA) in colonic cancer. *JAMA* 1972, **221**, 31–35.
19. Wanebo HJ, Rao B, Pinsky CM, *et al.* Preoperative carcinoembryonic antigen level as a prognostic indicator in colorectal cancer. *N Engl J Med* 1978, **299**, 448–451.
20. Wolmark N, Fisher B, Wieand HS, Henry RS. The prognostic significance of preoperative carcinoembryonic antigen levels in colorectal cancer. *Ann Surg* 1984, **199**, 375–382.
21. Staab HJ, Anderer FA, Brummendorf T, Stumpf E, Fischer R. Prognostic value of preoperative serum CEA level compared to clinical staging. I. Colorectal cancer. *Br J Cancer* 1981, **44**, 652–662.
22. Filella X, Molina R, Pique JM, *et al.* CEA as a prognostic factor in colorectal cancer. *Anticancer Res* 1994, **14**, 705–708.
23. Moertel CG, O'Fallon JR, Go VLW, O'Connell MJ, Th Y, Thynne GS. The preoperative carcinoembryonic antigen test in the diagnosis, staging, and prognosis of colorectal cancer. *Cancer* 1986, **58**, 603–610.
24. de Mello J, Struthers L, Turner R, *et al.* Multivariate analyses as aids to diagnosis and assessment of prognosis in gastrointestinal cancer. *Br J Cancer* 1983, **48**, 341–348.
25. Steele G, Ellenberg S, Ramming K, *et al.* CEA monitoring among patients in multi-institutional adjuvant G.I. therapy protocols. *Ann Surg* 1982, **196**, 162–169.
26. Goslin R, Steele G, Macintyre J. The use of preoperative plasma CEA levels for the stratification of patients after curative resection of colorectal cancers. *Ann Surg* 1980, **192**, 747–751.
27. Hohenberger P, Schlag PM, Gerneth T, Herfarth C. Pre- and postoperative carcinoembryonic antigen determinations in hepatic resection for colorectal metastases. *Ann Surg* 1994, **219**, 135–143.
28. Carpelan-Holmström M, Haglund C, Kuusela P, Järvinen H, Roberts PJ. Preoperative serum levels of CEA and CA 242 in colorectal cancer. *Br J Cancer* 1995, **71**, 868–872.
29. Nilsson O, Johansson C, Glimelius B, *et al.* Sensitivity and specificity of CA 242 in gastrointestinal cancer. A comparison with CEA, CA50 and CA19-9. *Br J Cancer* 1992, **65**, 215–221.
30. Hall NR, Stephenson BM, Purves DA, Cooper EH. The role of CA-242 and CEA in surveillance following curative resection for colorectal cancer. *Br J Cancer* 1994, **70**, 549–553.
31. Turnball RB, Kyle K, Watson FR, Spratt J. Cancer of the colon: the influence of the no-touch isolation technique on survival rates. *Ann Surg* 1967, **166**, 420–427.
32. Deans GT, Parks TG, Rowlands BJ, Spence RAJ. Prognostic factors in colorectal cancer. *Br J Surg* 1992, **79**, 608–613.
33. Jass JR, Atkins WS, Cuzik J, *et al.* The grading of rectal cancer: historical perspectives and a multivariate analysis of 447 cases. *Histopathology* 1986, **10**, 437–459.

**Acknowledgements**—The authors thank Wallac Oy for kindly supplying the CA 242 test kits assay. This study has been supported by grants from Finska Läkaresällskapet and from Stiftelsen Dorothea Olivia, Karl Walter and Jarl Walter Perkléns minne and from Medicinska Understödsföreningen Liv och Hälsa.