VIA MEDICA

ORIGINAL ARTICLE

Jolanta Żok[1], Barbara Radecka[2], Krzysztof Adamowicz[3], Jan Korniluk[4], Renata Duchnowska[4]

[1]Department of Oncology and Radiotherapy, PCK Memorial Marine Hospital in Gdynia
[2]Department of the Clinical Oncology, Opole Oncology Centre in Opole
[3]Provincial Oncology Centre in Gdansk
[4]Military Medical Institute in Warsaw

Carcinoembryonic antigen assessment during the perioperative period in patients with colorectal cancer in Poland

Address for correspondence:
Lek. Jolanta Żok
Oddział Onkologii i Radioterapii
Szpital Morski im. PCK w Gdyni
e-mail: kontakt@jolantazok.com

Oncology in Clinical Practice
2016, Vol. 12, No. 6, 201–204
DOI: 10.5603/OCP.2016.0015
Translation: dr n. med. Aleksandra Hołowiecka

ISSN 2450–1654

ABSTRACT

Introduction. Carcinoembryonic antigen (CEA) concentration is often elevated during the course of colorectal cancer. Assessment of the CEA level in this group of patients is recommended pre- and post-surgery, during systemic therapy, and further follow-up. A high preoperative level of CEA is a negative prognostic factor. The aim of the study was to determine the prevalence of CEA evaluation in the perioperative diagnostics in patients with colorectal cancer in Poland.

Materials and methods. The analysis included 620 patients with stage III colorectal cancer, who underwent radical surgery in five Polish oncological centres during 2000–2014. The analysis of the clinical practice concerning the determination of CEA was based on the available medical records involving the pre- and post-operative period.

Results. The determination of the CEA level before the surgery was performed in only 200 patients (32%), and in 528 patients (85%) following resection and before starting the adjuvant systemic chemotherapy. In 74% of patients the preoperative CEA level exceeded 5 ng/mL (median 10.5 ng/mL; standard deviation 4.4–22.5). After the surgical procedure in more than 85% of patients the CEA level was within to the recommended normal value of 5 mg/mL (median 1.9; standard deviation 1.1–3.4).

Conclusions. Preoperative CEA level is scarcely determined in patients with colorectal cancer in Polish centres, which may impede further monitoring of the disease course. These results suggest the need for better adherence to the recommendations concerning the pre- and postoperative diagnostics in this group of patients.

Key words: carcinoembryonic antigen, colorectal cancer

Oncol Clin Pract 2016; 12, 6: 201–204

Introduction

Colorectal cancer (CRC) is one of the most commonly diagnosed malignant neoplasms and one of the main cause of cancer deaths [1]. The morbidity rate of colorectal cancer is gradually increasing in the majority of countries worldwide. This phenomenon may result from aging of population, detrimental diet (high in red meat, animal fats, highly-processed carbohydrates), and obesity [2, 3]. The level of the carcinoembryonic antigen (CEA) is often increased in CRC. CEA is a glycoprotein produced in high amounts by the lining cells of the gastrointestinal tract and of the pancreas during foetal life. After the child's birth the antigen secretion is almost totally discontinued and its concentration in adults'blood is trace [4]. CEA level assessment in patients with CRC is recommended pre- and postoperatively, during systemic therapy, and in long term follow-up [5–8]. The normal CEA level in non-smoking subjects is up to 5 ng/mL (in smokers — up to 10 ng/mL) [5–8]. A high preoperative CEA level is a negative prognostic factor [4–11]. There are no evidence based Polish data concerning the incidence of the pre- and postoperative determination of CEA levels in patients with CRC. The aim of this study

was to evaluate the clinical practice in this scope of diagnostics in a large group of patients treated in several Polish oncological centres.

Materials and methods

The analysis included 620 patients with stage III CRC, who underwent radical surgery in five Polish oncological centres during 2000–2014. This review constitutes part of a bigger scientific programme that aims to evaluate other factors related to the postoperative chemotherapy in CRC. The clinical stage of disease was estimated based on the seventh version of the pTNM (tumour, nodes, metastases) classification, developed by the Union International Cancer Control (UICC) [12]. The CEA level was evaluated by the standard methods used in each specific oncology centre. Data concerning the pre- and postoperative CEA levels were based on the analysis of the available medical records. The influence of the pre- and postoperative CEA level on the overall survival and disease-free survival rates was also assessed. Due to the incomplete data concerning cigarette smoking the upper limit of the CEA level for the whole cohort was determined as 5 ng/mL. The statistical analysis was performed with use of STATA software (version 1.1), based on the data introduced into a specially prepared database. The time of observation was defined in months from the diagnosis of the neoplastic disease to the last information about the patient or death of the patient. The disease-free survival (DFS) time was defined as the period from the first adjuvant chemotherapy course to the progression of the disease (local reoccurrence and/or distant metastases). The overall survival (OS) time represented the period from the start of the adjuvant therapy to the death of patients, regardless of the cause of death, or to the last contact with the patient. In the analysis of our data the level of significance was determined as $p = 0.05$.

Table 1. Clinical characteristics of the analysed group of patients (n = 620)

Clinical feature	n (%)
Age at the time of diagnosis (years)	
Median	62.6
Range	25–85
Sex	
Females	295 (47.6)
Males	325 (52.4)
Localisation of the primary tumour	
Caecum	108 (17.4)
Ascending colon	93 (15.0)
Hepatic flexure	41 (6.6)
Transverse colon	45 (7.3)
Splenic flexure	30 (4.8)
Descending colon	27 (4.4)
Sigmoid colon	275 (44.4)
Non data	1 (0.2)

Table 2. The determination of the carcinoembryonic antigen (CEA) level [ng/mL] pre- and postoperatively

Preoperative CEA concentration [ng/mL]	200 (32.3)
< 5	53 (26.5)
≥ 5	147 (73.5)
No evaluation	420 (67.7)
Postoperative CEA concentration (before the start of chemotherapy) [ng/mL]	528 (85.2)
< 5	450 (85.2)
≥ 5	78 (14.8)
No evaluation	92 (14.8)

Results

The analysed group of 620 patients included 325 females (52%) and 295 males (48%). The range of age at the time of diagnosis was 25 to 85 years (median 63 years). The most common localisation of the tumour was the sigmoid colon (275 patients; 44%). Caecum and ascending colon cancer was diagnosed in 108 (17%) and 93 (15%) patients, respectively. The disease was also localised in transverse colon in 45 patients (7.3%), hepatic flexure in 41 patients (6.6%), splenic flexure in 30 patients (4.8%), and descending colon in 27 patients (4.4%). In one patient the precise localisation of the tumour was not determined.The median observation time from the diagnosis of the neoplastic disease was 52.5 months (range from 36.5 months to 77.6 months). The clinical characteristics of this group are presented in Table 1. Preoperative assessment of the CEA level was done in only 200 patients (32%); and postoperatively, before adjuvant systemic therapy, the test was performed in 528 patients (85%) (Table 2). In 74% of patients the preoperative CEA level did not exceed 5 ng/mL, and the median value was 10.5 ng/mL (standard deviation 4.4–22.5). The postoperative CEA level in more than 85% of patients was within the proposed normal limit of 5 ng/mL (median 1.9; standard deviation 1.1–3.4). In univariate analysis no correlation between the pre- and postoperative CEA level and DFS was observed. On the other hand, the increased CEA level at the beginning of adjuvant chemotherapy correlated with a shorter OS in the univariate analysis [risk score = 1.02 (95% confidence interval 1.01–1.03); $p = 0.0030$]. This correlation was not significant in the multivariate analysis (Fig. 1).

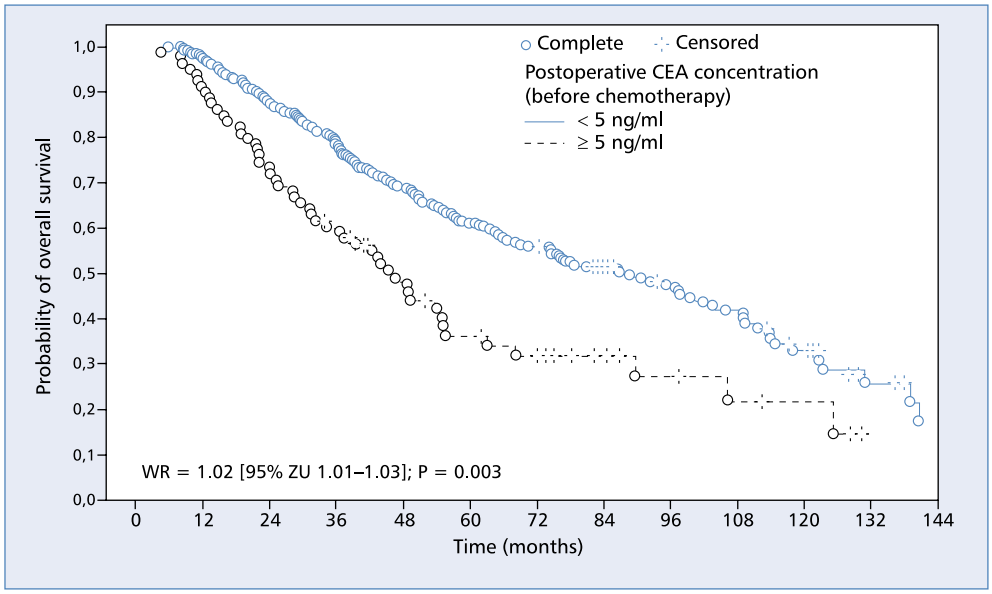

Figure 1. The influence of the carcinoembryonic antigen (CEA) level before the start of adjuvant chemotherapy on the overall survival; univariate analysis

Discussion

CEA is a standard serum tumour marker used in the diagnostics of patients with CRC. The CEA level is strongly associated with tumour burden, which makes this marker useful in the disease monitoring [4, 6, 8–11, 13, 14]. Following Polish and international recommendations, the CEA level assessment should be performed pre- and postoperatively and during the further follow-up phase [5–8, 15]. Due to the insufficient sensitivity and specificity of the CEA test, it is not used as a screening tool for colorectal cancer. A high preoperative and postoperative CEA level is a negative predictive factor [4, 6, 8–11, 13, 16–25].

In the presented paper the CEA level in patients with CRC was determined prior to surgical procedure in only 30% of patients. More frequently (85% of patients) the evaluation was performed after the operative procedure and before adjuvant systemic therapy. Patients with clinical stage III of CRC were included only, because they participated in another scientific project. We can assume, with high likelihood, that these results would be similar in patients in other clinical stages of the disease. A similar situation had been previously reported in some other reviews. As an example, we can cite the results of the analysis of data from the 17th Registry: The Surveillance, Epidemiology, and End Results (SEER) in the United States of America in 2004, which showed that the preoperative CEA level was determined only in 50% of patients [13], and the frequency of the CEA evaluation differed in different states (from 28% in Georgia to 68% in Hawaii) [13]. Our paper includes a numerous group of patients undergoing routine treatment in five Polish oncological centres, but it does not permit us to draw univocal conclusions for the whole population of patients with CRC. Nevertheless, the presented results suggest a need for implementation of mandatory assessment of the preoperative CEA level in patients with CRC admitted to internal diseases departments or to surgical wards.The evaluation of the serum CEA level is a relatively inexpensive test, which is accessible in the majority of diagnostic laboratories.

In this review no correlation between the CEA level and the DFS was shown. The negative correlation of the increased CEA level and the OS reported by the univariate analyses was not confirmed in the multivariate regression model.The lack of these correlations could result from the low power of the applied statistical test due to the relatively low number of patients and the incomplete data concerning the pre- and postoperative CEA evaluation.

Conclusions

In the clinical practice of Polish oncological centres, in nearly 70% of patients with CRC the CEA level is not tested in the preoperative phase, which is inconsistent with national and international recommendations [5–8, 15]. It is advisable to take actions to change this situation. The American Committee on Cancer (AJCC) postulates inclusion of the evaluation of the CEA level into the TNM classification of colorectal cancer [13, 26].

References

1. Ferlay J, Soerjomataram I, Ervik M et al. GLOBOCAN 2012 v1.1. Cancer incidence and mortality worldwide: IARC Cancer Base No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer 2014 (dostęp: 10.10.2016).
2. Haggar FA, Boushey RB. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clin Colon Rectal Surg 2009; 22: 191–197.
3. Didkowska J, Wojciechowska U, Zatoński W. Prognozy zachorowalności i umieralności na wybrane nowotwory złośliwe w Polsce do 2025 roku. Centrum Onkologii — Instytut im. Marii Skłodowskiej-Curie, Warszawa 2009.
4. Perkins GL, Slater ED, Sanders GK, Prichard JG. Serum tumor markers. Am Fam Physician 2003; 68: 1075–1082.
5. Jassem J, Krzakowski M. Nowotwory układu pokarmowego. Praktyczny przewodnik dla lekarzy. Via Medica, Gdańsk 2014.
6. Labianca R, Nordlinger B, Beretta GD et al. ESMO Guidelines Working Group. Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013; 24 (suppl 6): vi64–vi72.
7. www.nccn.org.
8. Locker GY, Hamilton S, Harris J et al. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol 2006; 24: 5313–5327.
9. Strambu V, Iorga C, Radu P et al. Prognostic factors in colorectal cancer evolution. Rom J Morphol Embryol 2011; 52 (suppl 1): 373–377.
10. Zheng CX, Zhan WH, Zhao JZ et al. The prognostic value of preoperative serum levels of CEA, CA 19-9 and CA 62-4 in patients with colorectal cancer. World J Gastroenterol 2001; 3: 431–434.
11. Kim CG, Ahn JB, Jung M et al. Preoperative serum carcinoembryonic antigen level as a prognostic factor for recurrence and survival after curative resection followed by adjuvant chemotherapy in stage III colon cancer. Ann Surg Oncol 2017; 24: 227–235.
12. Sobin LH, Gospodarowicz MK, Wittekind C. TNM — klasyfikacja nowotworów złośliwych. Via Medica, Gdańsk 2010.
13. Thirunavukarasu P, Sukumar S, Sathaiah M et al. C-stage in colon cancer: implications of carcinoembryonic antigen biomarker in staging, prognosis, and management. J Natl Cancer Inst 2011; 103: 689–697.
14. Van Cutsem E, Cervantes A, Adam R et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol 2016; 27: 1386–1422.
15. Herman R, Reguła J, Pałucki J, Polkowski W, Potemski P. Rak okrężnicy. In: Potemski P, Polkowski W (ed.). Nowotwory układu pokarmowego. In: Krzakowski M, Warzocha K (ed.). Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych — 2013 rok. Tom I. Via Medica, Gdańsk 2013; 179–195.
16. 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.
17. Wolmark N, Fisher B, Wieand HS et al. The prognostic significance of preoperative carcinoembryonic antigen levels in colorectal cancer. Results from NSABP (National Surgical Adjuvant Breast and Bowel Project) clinical trials. Ann Surg 1984; 199: 375–382.
18. Duffy MJ, van Dalen A, Haglund C et al. Tumour markers in colorectal cancer: European Group on Tumour Markers (EGTM) guidelines for clinical use. Eur J Cancer 2007; 43: 1348–1360.
19. Chu DZ, Erickson CA, Russell MP et al. Prognostic significance of carcinoembryonic antigen in colorectal carcinoma. Serum levels before and after resection and before recurrence. Arch Surg 1991; 126: 314–316.
20. Harrison LE, Guillem JG, Paty P et al. Preoperative carcinoembryonic antigen predicts outcomes in node-negative colon cancer patients: a multivariate analysis of 572 patients. J Am Coll Surg1997; 185: 55–59.
21. Lucha PA Jr, Rosen L, Olenwine JA et al. Value of carcinoembryonic antigen monitoring in curative surgery for recurrent colorectal carcinoma. Dis Colon Rectum 1997; 40: 145–149.
22. Moertel CG, O'Fallon JR, Go VL et al. The preoperative carcinoembryonic antigen test in the diagnosis, staging, and prognosis of colorectal cancer. Cancer 1986; 58: 603–610.
23. Park YJ, Park KJ, Park JG et al. Prognostic factors in 2230 Korean colorectal cancer patients: analysis of consecutively operated cases. World J Surg 1999; 23: 721–726.
24. Sun LC, Chu KS, Cheng SC et al. Preoperative serum carcinoembryonic antigen, albumin and age are supplementary to UICC staging systems in predicting survival for colorectal cancer patients undergoing surgical treatment. BMC Cancer 2009; 9: 288.
25. Wang JY, Lu CY, Chu KS et al. Prognostic significance of pre- and postoperative serum carcinoembryonic antigen levels in patients with colorectal cancer. Eur Surg Res 2007; 39: 245–250.
26. Amri R, Berger DL. Elevation of pretreatment carcinoembryonic antigen level as a prognostic factor for colon cancer: incorporating a C stage in the AJCC TNM Classification. JAMA Surg 2015; 150: 755–756.