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Oophorectomy during surgery for colorectal carcinoma

Abstract Background The purpose of the study is to identify the effect of synchronous prophylactic oophorectomy in women undergoing colorectal cancer surgery on long-term survival, recurrences and sites of failure. **Patients and methods** From 1987 to 2003, 124 women, mean age 69 ± 10 (35–91) years, with colorectal carcinoma were retrospectively reviewed. In 70 (56.5%) women the ovaries were preserved during surgery and 54 (43.5%) women underwent synchronous prophylactic oophorectomy during primary tumour resection. Univariate and multivariate analysis were used to assess the effect of oophorectomy on long-term survival, recurrences and sites of failure. **Results** By univariate analysis it was demonstrated that synchronous oophorectomy had no effect on long-term survival ($p=0.7294$). By multivariate analysis it was demonstrated that stage was the only factor independently influencing survival ($p=0.0061$). Twenty-eight patients (23%) developed recurrence and 10 of them developed locoregional recurrence. By univariate analysis it was demonstrated that the number of recurrences was not different between women with or without oophorectomy ($p=0.259$). Distant and locoregional recurrences were not different between women undergoing resection of primary colorectal carcinoma with or without oophorectomy ($p=0.611$). **Conclusions** Oophorectomy does not appear to influence long-term survival, the total number of recurrences or the sites of failure.

Key words Colorectal cancer • Oophorectomy

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Introduction

The reports about oophorectomy during surgery for colorectal carcinoma are retrospective. The incidence of synchronous ovarian metastases in patients with colorectal carcinoma is approximately 2–8% [1–3]. In one-third gross inspection of the ovaries may not reveal the presence of implants and only histologic examination may confirm diagnosis [4]. There is no prospective randomised trial with high statistical power about the role of prophylactic oophorectomy during surgery for colorectal carcinoma. As a consequence there is no consensus about oophorectomy during surgery for colorectal cancer. The purpose of the study is to compare long-term survival, recurrences and the sites of failure retrospectively between women undergoing oophorectomy and those with preservation of the ovaries during colorectal cancer surgery.

Patients and methods

The data from 124 women, mean age 69±10 (35–91) years that underwent surgery for colorectal cancer from 1987 to 2002 were retrieved and analysed. The patients did not have distant metastases at the time of initial diagnosis. In group A (54 women, 43.5%), oophorectomy with or without hysterectomy was performed in addition to colorectal cancer resection. In group B (70 women, 56.5%), only resection of the primary tumour was performed and the ovaries were left intact. The groups were compared for tumour location, type of surgery, extent of lymph node resection, T, N, stage (TNM classification), residual tumour, hospital morbidity and mortality, treatment with adjuvant systemic chemotherapy and early postoperative intraperitoneal chemotherapy, adjuvant postoperative radiotherapy, recurrences and the pattern of recurrences. The end points of the study were overall survival, recurrences and the failure sites.

Statistical analysis was made using SPSS (Statistical Package for Social Sciences). The study of relationships between variables was made using χ^2 (Pearson's correlation). Survival analysis was performed using the Kaplan–Meier method and comparison of curves with the log-rank-test. Cox regression analysis made possible multiple analysis of survival and logistic regression analysis was used to calculate the clinical factors related to recurrence. p values ≤0.05 were considered significant. The postoperative deaths were not excluded from the survival analysis.

Fig. 1 Overall survival

64% ($p=0.7294$) (Fig. 1). By Cox-regression analysis it was demonstrated that stage was the single clinical factor independently influencing survival ($p=0.0061$). By logistic regression analysis it was demonstrated that stage was the single clinical factor independently influencing recurrence ($p=0.0000$).

Results

The majority of patients were postmenopausal and there were 4 premenopausal women in each group ($p>0.05$). Three patients in group A and 8 in group B died in the immediate postoperative period ($p=0.254$). Twelve patients in group A and 17 in group B had complications ($p=0.34$). The groups were comparable for age, T, N, stage and residual tumour. Five patients with rectal cancer in group A and 2 in group B received postoperative radiotherapy ($p=0.129$). Seven women in group A and 11 in group B received early postoperative intraperitoneal chemotherapy ($p=0.649$). Thirty-seven women in group A and 34 in group B were treated by systemic adjuvant chemotherapy ($p=0.019$). The number of women with right-sided colon cancer was higher in group B ($p=0.004$) and as a consequence the number of right colon resections was also higher in group B ($p=0.026$). The number of radical lymph node resections was also higher in group A ($p=0.044$). Fifteen women in group A (27.8%) and 13 in group B (19.1%) had tumour recurrence ($p=0.259$). Nine patients in group A were recorded as having distant metastases and 6 were recorded with locoregional metastases. Nine patients in group B were recorded as having distant metastases and 4 were recorded with locoregional metastases ($p=0.611$).

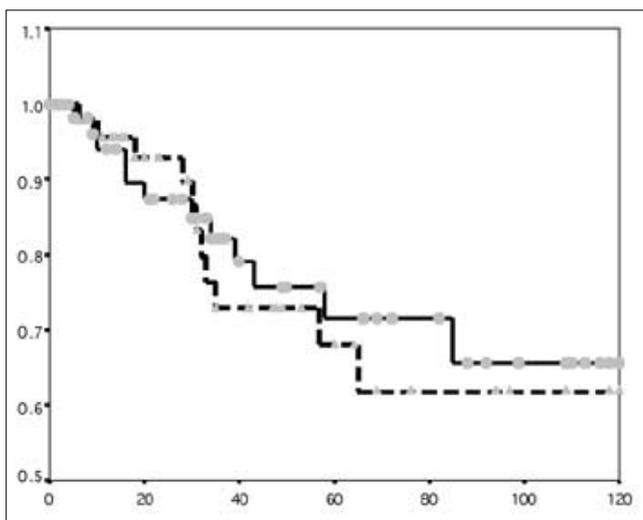Five-year survival rate for both groups was 63%. Five-year survival rate for group A was 62% and for group B

Discussion

The role of prophylactic oophorectomy in colorectal cancer surgery has been under debate since the 1970s. In addition it has not been clear whether both ovaries with or without hysterectomy should be removed. In many studies prophylactic oophorectomy during surgery for colorectal cancer has been advocated, particularly in postmenopausal women [1, 5–7]. In a few studies oophorectomy is recommended as an integral part of colorectal cancer surgery regardless of the patient's age [2, 8]. Other studies do not support aggressive resection of the ovaries because they have found that the true incidence of synchronous or metachronous metastases is very low [9] or because they believe that in postmenopausal women oophorectomy is not optimal [10]. It has been demonstrated that even if bilateral prophylactic oophorectomy has been performed, long-term survival is not affected [11, 12]. In one study it was demonstrated that there was no impact on survival although a 5% improvement in survival favoured the oophorectomy group [13]. In others it has been emphasised that macroscopic metastatic disease to the ovaries is a poor prognostic factor in colon cancer [14]. Although there is no survival benefit associated with resection of occult microscopic disease, long-term survival is possible if patients are rendered surgically disease-free [15]. The guidelines of the National Cancer Institute of the USA

emphasise that there is no data supporting prophylactic oophorectomy [16]. One prospective randomised trial has been published about the role of prophylactic oophorectomy during surgery for colorectal carcinoma. The study had very small statistical power and could not document any benefit in survival in 155 women with stage B and C tumours of the colon and rectum [17].

The results of the present study demonstrated that overall survival was the same in both groups. It was also demonstrated that the total number of recurrences was similar and there was no difference in pattern of recurrence. Although a large prospective study with high statistical power is warranted to demonstrate the possible difference between women undergoing oophorectomy and no oophorectomy, there is much evidence that ovarian secondaries is not dependent on the preservation of the ovaries themselves. In fact, ovarian secondaries of colorectal cancer origin progress from cancer cells exfoliated from the primary tumour during surgery that are later entrapped because of gravity in the milky spots of the perigonadal fat [18] or at the pelvic peritoneum when the ovaries have been removed by prior surgery [19–21]. As a consequence, development of locoregional recurrences that are part of iatrogenic intraoperative dissemination does not seem to be prevented by oophorectomy.

References

1. Cutait R, Lesser M, Enker W (1983) Prophylactic oophorectomy in surgery for large-bowel cancer. Dis Colon Rectum 26:6–11
2. O'Brien P, Newton B, Metcalf J, Rittenbury M (1981) Oophorectomy in women with carcinoma of the colon and rectum. Surg Gynecol Obstet 153:827–830
3. Birkrant A, Sampson J, Sugarbaker P (1986) Ovarian metastasis from colorectal cancer. Dis Colon Rectum 29:767–771
4. Young R, Scully R (1987) Metastatic tumors of the ovary. In: Kurman R (ed) Blauenstein's pathology of the female genital tract, 3rd Edn. Springer, New York, pp 743–768
5. Graffner H, Alm P, Oscarson J (1983) Prophylactic oophorectomy in colorectal carcinoma. Am J Surg 146:233–235
6. McGill F, Ritter D, Richard C, Kaleya R, Wadler S, Greston W, O'Hanlan K (1999) Krukenberg tumors: can management be improved? Gynecol Obstet Invest 48:61–65
7. Mrad K, Marice P, Fabre A, Pautier P, Lhomme C, Duvillard P, Sabourin J (2000) Krukenberg tumor: a clinico-pathological study of 15 cases. Ann Pathol 20:202–206
8. Tunca J, Starling J, Hafez G, Buchler D (1983) Colon carcinoma metastatic to the ovary. J Surg Oncol 23:269–272
9. Blamey S, Mc Dermott F, Pihl E, Hughes E (1981) Resected ovarian recurrence from colorectal adenocarcinoma: a study of 13 cases. Dis Colon Rectum 24:272–275
10. Becker S, Tomacruz R, Kaufman H, Brislow R, Montz F (2002) Gynecologic abnormalities in surgically treated women with stage II or III rectal cancer. J Am Coll Surg 194:315–323
11. Sielezneff I, Salle E, Antoine K, Thirion X, Brunet C, Sastre B (1997) Simultaneous bilateral oophorectomy does not improve prognosis in postmenopausal women undergoing resection for cancer. Dis Colon Rectum 40:1299–1302
12. Shofield A, Pitt J, Biring G, Dawson P (2001) Oophorectomy in primary colorectal cancer. Ann R Coll Surg Engl 83:81–84
13. Ballantyne G, Reitel M, Wolff B, Ilstrup D (1985) Oophorectomy and colon cancer. Impact on survival. Ann Surg 202:209–214
14. Miller B, Pittman B, Wan J, Fleming M (1997) Colon cancer with metastasis to the ovary at the time of initial diagnosis. Gynecol Oncol 66:368–371
15. Huang P, Weber T, Mendoza C, Rodriguez-Bigas M, Petrelli N (1999) Long-term survival in patients with ovarian metastases from colorectal carcinoma. Ann Surg Oncol 6:322
16. Nelson H, Petrelli N, Carlin A et al (2001) Guidelines 2000 for colon and rectal cancer surgery. J Natl Cancer Inst 93:583–596
17. Young-Fadok T, Wolff B, Nivatvongs S, Metzger P, Ilstrup D (1998) Prophylactic oophorectomy in colorectal carcinoma: preliminary results of a randomized, prospective trial. Dis Colon Rectum 41:277–283
18. Hagiwara A, Takahashi T, Sawai K et al (1993) Milky spots as the implantation site for malignant cells in peritoneal dissemination in mice. Cancer Res 53:687–692
19. Sugarbaker P, Averbach A (1996) Krukenberg syndrome as a natural manifestation of tumor cell entrapment. In: Sugarbaker PH (ed) Peritoneal carcinomatosis: principles of management. Kluwer Academic Publishers, Boston, pp 163–191
20. Kanellos I, Zacharakis E, Demetriades H, Betsis D (2003) Surgical management of colorectal cancer. Medimond Int Proc 4:275–277
21. Kanellos I, Demetriades H, Zintzaras E, Mandrali A, Mantzoros I, Betsis D (2003) Incidence and prognostic value of positive peritoneal cytology in colorectal cancer. Dis Colon Rectum 46:535–539