

Case Analysis

Prognostic Value of Oophrectomy in Colorectal Cancer Patients with Ovarian Metastasis

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Key Words

Colorectal cancer;
Ovarian metastasis;
Oophrectomy

Purpose. Ovarian metastasis was reported to occur in 3~8% female colorectal cancer patients. Improved overall survival has been reported of oophrectomy with curative intent. This study is aimed to investigate the prognosis of surgical treatment for ovarian metastasis from colorectal cancer in our institute.

Methods. Between March 2001 and October 2005, 32 patients receiving oophrectomy due to metastasis from colorectal cancer in VGHTPE were retrieved. The clinicopathologic data and prognosis were analyzed.

Results. The median follow-up duration was 32.6 months (7~72 months). Isolated ovarian metastasis, diagnosed in 8 patients, has a trend toward improved overall survival ($p = 0.128$). Metastatic lesions confined in pelvis and curative operation were associated with improved overall survival significantly ($p = 0.028$ and 0.027 respectively).

Conclusion. Patient who received surgery for ovarian metastases with disease confined to pelvis has better survival than who has associated extrapelvic metastases. Curative resection for ovarian metastasis is effective and could offer potential long-term survival.

[J Soc Colon Rectal Surgeon (Taiwan) 2009;20:94-99]

Colorectal cancer ranks the third leading cause of cancer death in women and causes over 4000 deaths annually in Taiwan.¹ The incidence of metastases to the ovaries from colorectal cancer is relative uncommon and estimated to be 3~8%.²⁻⁵ Most series showed that primary colorectal cancer is the most common nongynecologic malignancy resulting in metastatic tumor to the ovary,⁶⁻⁸ though one series in Japan⁹ revealed that gastric primaries made up 30% of the metastatic primaries to the ovary, followed by breast (21.6%) and colon (6.7%).

When ovarian metastasis is diagnosed, it may be isolated metastatic lesion, part of peritoneal involvement or associated other metastatic lesions. Although there is no definite survival benefit of prophylactic oophrectomy while resection of colorectal cancer,¹⁰⁻¹² improved overall survival has been reported in oophrectomy for patients with direct invasion to ovary or macroscopic ovarian metastasis with curative intent.^{13,14}

This study is aimed to investigate the prognosis of surgical treatment for ovarian metastasis from colo-

Received: March 11, 2009.

Accepted: April 27, 2009.

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rectal cancer in our institute.

Materials and Methods

Patients

From Mar. 2001 till Oct. 2005, a total of 32 patients received oophrectomy due to metastasis from colorectal cancer in the Taipei Veterans General Hospital. The clinical data were prospectively stored in a computerized database.

The surgical specimens were reviewed by specialized gastrointestinal pathologists. In addition to microscopic morphologic difference, immunohistochemistry stain for CK7 and CK20 was used to distinguish metastatic ovarian tumor from primary ovarian carcinoma; CK7(-)/CK20(+) tumors were classified as ovarian metastases from colorectal cancer, whereas CK7(+)/CK20(-) ovarian masses were considered as primary ovarian carcinoma.¹⁵

All patients received 5-FU-based chemotherapy. The follow-up protocol included 3-month-interval visits in the first 2 years, 6-month-interval visits for the next 3 years, and yearly afterward. Follow-up examinations included physical examination, recto-digital examination, CEA levels, chest X-rays, abdominal sonograms, and/or computerized tomography (CT) scan.

The last date of follow up in this study was October 2008 or until patient death. Overall survival was calculated from the date of primary resection of colorectal cancer to the date of death or last follow-up.

Right sided colon tumor was referred to tumor occurred at the cecum, ascending colon, hepatic flexure and transverse colon. Left sided colon tumor was tumor at the splenic flexure, descending colon, sigmoid colon till recto-sigmoid junction. Synchronous ovarian metastases were defined as ovarian metastases diagnosed at the same time or within six months from the operation of the colorectal cancer.

Limited metastasis was defined as the peritoneal seeding confined in pelvis and the extensive metastasis was metastatic involvement beyond pelvis or it associated with other metastasis, such as liver or lung metastasis. Curability is whether R0 or R1 resection is

achieved. If there is macroscopic residual tumor left, it was considered to be non-curative or palliative resection.

Statistical analysis

The statistical analyses were performed by using the SPSS package (version 15.0 for Windows, SPSS, Chicago, IL, USA). Overall survival was evaluated using the Kaplan–Meier method and significant differences between survival curves were evaluated using the Mantel–Cox log rank test. In all cases, *p* values < 0.05 were considered statistically significant.

Results

The median follow-up time was 32.6 months (7~72 months). The incidence of ovarian metastasis in our colorectal cancer series is 4.3% (total 750 female colorectal cancer patients from Mar. 2001 till Oct. 2005). The patient's age ranged from 28 to 82 years old at the time of oophrectomy (mean age 49.9 years old). 18 (56.2%) patients were younger than 50 years old at the time of presentation of ovarian metastasis. (Table 1).

Anatomic location of the primary tumor was as follows: right-sided colon in 14 patients (43.7%), left-sided colon in 14 patients (43.7%), and rectum in 4 patients (12.5%).

Three patients (9.4%) have no locoregional lymph node involvement, 10 patients (31.2%) have 1-3 positive lymph nodes and 13 patients (40.6%) have more than 4 lymph nodes involvement (Table 2) in primary colorectal lesion.

Synchronous ovarian metastases occurred in 15 patients (46.9%), and metachronous ovarian metastases occurred in 17 patients (53.1%).

Bilateral ovarian involvement was noted in 13 patients. 24 patients had other combined metastases at the presentation of ovarian metastasis and peritoneal involvement is the most common associated lesion (Table 3). Thirteen patients received synchronous oophrectomy while resection of primary colorectal cancer. Two patients received oophrectomy previous to colorectal cancer resection. In the 17 metachronous

Table 1. Clinical characteristics of all 32 colorectal cancer patients with ovarian metastasis as prognostic factors for overall survival

| Characteristic | No. of patients | % | p value |
|-------------------------------|-----------------|------|---------|
| Age | | | 0.220 |
| Mean \pm S.D. | 49.9 \pm 11.6 | | |
| < 50 | 18 | 56.2 | |
| \geq 50 | 14 | 43.8 | |
| Location | | | 0.592 |
| Right sided colon | 14 | 43.7 | |
| Left sided colon | 14 | 43.7 | |
| Rectum | 4 | 12.5 | |
| Pre-op CEA level | | | 0.642 |
| < 6 ng/ml | 10 | 31.2 | |
| \geq 6 ng/ml | 22 | 68.7 | |
| Pre-op CA-125 level | | | 0.268 |
| < 35 U/ml | 3 | 9.4 | |
| \geq 35 U/ml | 15 | 46.8 | |
| N.A. | 14 | 43.8 | |
| Ovarian metastasis | | | 0.879 |
| Synchronous | 15 | 46.9 | |
| Metachronous | 17 | 53.1 | |
| Bilateral ovarian involvement | | | 0.913 |
| Unilateral | 19 | 59.4 | |
| Bilateral | 13 | 40.6 | |
| Associated metastasis | | | 0.128 |
| Isolated | 8 | 25.0 | |
| Combined | 24 | 75.0 | |
| Extend of metastasis | | | 0.028 |
| Confined in pelvis | 13 | 40.6 | |
| Beyond pelvis | 19 | 59.4 | |
| Curability of operation | | | 0.027 |
| Curative | 14 | 43.8 | |
| Palliative | 18 | 56.2 | |

N.A.: not available

ovarian metastasis patients, time interval between primary colorectal cancer resection and oophorectomy ranges from 5 to 36 months (mean 18.9 ± 8.2 months).

Of the 32 patients, isolated ovarian metastasis was diagnosed in 8 patients. In the initially isolated ovarian metastasis group, most patients (7/8) received synchronous oophorectomy while resection of primary colorectal cancer. There were 13 patients whose metastatic lesions confined in pelvis and 14 patients received curative operation for ovarian metastasis with/out associated metastatic lesions. In the curative resection group, 5 patients received unilateral salpingo-oophorectomy and one of them developed ovarian metastasis during follow-up and she received second

Table 2. Pathological characteristics of all 32 colorectal cancer patients with ovarian metastasis as prognostic factors for overall survival

| Characteristic | No. of patients | % | p value |
|--------------------|-----------------|------|---------|
| T stage | | | 0.361 |
| T3 | 18 | 56.2 | |
| T4 | 8 | 25.0 | |
| N.A. | 6 | 18.8 | |
| N stage | | | 0.267 |
| N0 | 3 | 9.4 | |
| N1 | 10 | 31.2 | |
| N2 | 13 | 40.6 | |
| N.A. | 6 | 18.8 | |
| Mucinous component | | | 0.291 |
| < 50% | 21 | 65.6 | |
| \geq 50% | 3 | 9.4 | |
| N.A. | 8 | 25.0 | |

N.A.: not available

Table 3. Associated metastasis patterns while presentation of ovary metastasis

| Associated metastasis patterns | N = 24 | % |
|------------------------------------------------------|--------|------|
| locally advanced | 2 | 8.3 |
| liver metastasis | 11 | 45.8 |
| lung metastasis | 3 | 12.5 |
| peritoneum seeding | 18 | 60.0 |
| retroperitoneal or para-aortic lymph node metastasis | 1 | 4.2 |

salpingo-oophorectomy 3 years after first salpingo-oophorectomy.

Median overall survival of all 32 colorectal cancer patients with ovarian metastasis was 43.4 ± 6.4 months (Fig. 1). In the series, isolated ovarian metastasis has a trend toward improved overall survival ($p = 0.128$) (Fig. 2). Metastatic lesions confined in pelvis and curative operation were associated with improved overall survival significantly ($p = 0.028$ and 0.027 respectively) (Figs. 3 & 4).

Discussion

The incidence of metastases to the ovaries from colorectal cancer is estimated to be 3~8%.²⁻⁵ In the present study, the incidence of colorectal cancer with ovarian metastasis is 4.3%.

The mean age of colorectal cancer patients with

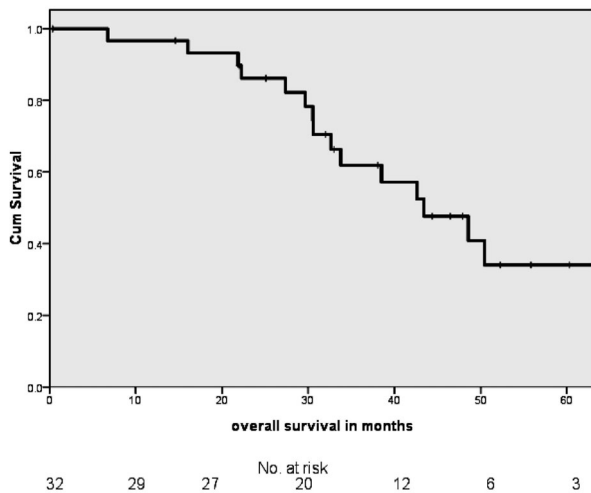


Fig. 1. Survival curve for all 32 colorectal cancer patients with ovarian metastasis (median survival: 43.4 ± 6.4, 1-, 3- and 5-year survival of all the 32 patients was 96.7%, 61.9% and 34.0%, respectively)

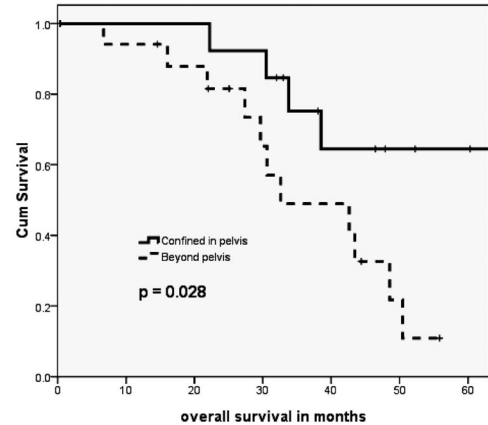
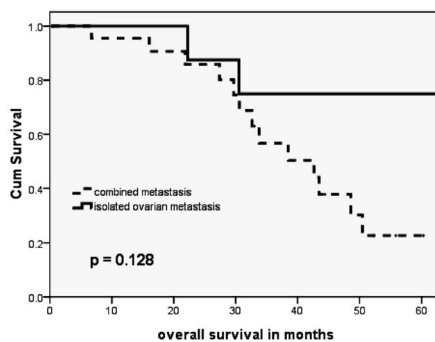
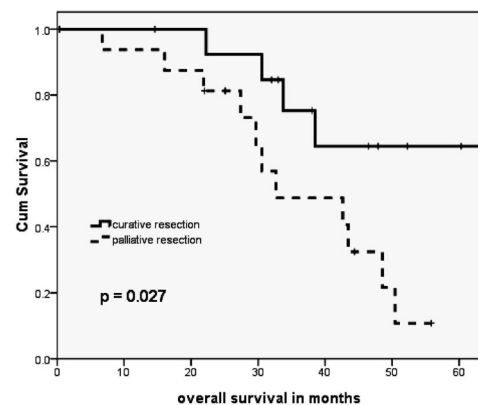


Fig. 3. Metastasis that confined in pelvis is significant prognostic factor for overall survival (median survival: 72.4 months vs. 32.6 months)



| | | | | | | |
|-----------------------------|----|-------------|----|---|---|---|
| | 24 | No. at risk | 13 | 8 | 4 | 1 |
| combined metastasis | | 21 | 19 | | | |
| isolated ovarian metastasis | 8 | 8 | 8 | 7 | 4 | 2 |

Fig. 2. Isolated ovarian metastasis has trend toward better overall survival (median survival: 72.4 months vs. 42.6 months)



| | | | | | | | |
|----------------------|----|----|-------------|----|---|---|---|
| | 14 | 14 | No. at risk | 12 | 6 | 4 | 3 |
| Curative resection | | | 14 | | | | |
| Palliative resection | 18 | 15 | 14 | 8 | 6 | 2 | 0 |

Fig. 4. Curative resection for ovarian metastasis is significant prognostic factor for improved overall survival (median survival: 72.4 months vs. 32.6 months)

ovarian metastasis is 49.9 years old. It consists with previous study that the incidence of colorectal ovarian metastatic disease is greater in younger menstruating women.^{8,12} This is compatible with the theory of hematogenous spread of ovarian metastasis, that is, a functional ovary is more vascularized than the post-menopausal ovary. Therefore, all ovaries should be inspected carefully while operation for colorectal cancer, especially in young-aged women patients and these women should be followed up regularly by transvaginal ultrasonography to detect such meta-

stases as early as possible.¹³

In the database, 13 patients (40.6%) developed bilateral ovarian metastasis at the time of presentation. In the curative resection group, 5 patients received unilateral salpingo-oophrectomy and one of them developed ovarian metastasis during follow-up. Therefore, management of ovarian metastasis should included bilateral salpingo-oophrectomy, even if only one ovary grossly abnormal, to avoid a second laparotomy for metachronous recurrence.

This study showed that clinical characteristics, such as age, location of primary tumor, pre-operative CEA or CA-125 level, synchronous or metachronous metastasis, unilateral or bilateral ovarian involvement and pathological characteristics, such as depth of primary tumor invasion, locoregional lymph node status, and mucinous component, do not have significant effect on overall survival. In a clinicopathologic analysis of 103 patients with ovarian metastasis from colorectal cancer,¹⁴ they found that bilaterality of ovarian metastases is independent significant poor prognostic factors of survival (hazard ratio, 2.08; 95 percent confidence interval, 1.156-3.758; $p = 0.015$).

The limitation of current study is the small sample size that precluded a reliable multivariable analysis. Another limitation is that some pathology reports associated with operations conducted at other hospital were insufficient to describe the clinical and pathologic status of the primary tumors. The last one is the relatively short follow-up duration.

In the current study, metastatic lesions confined in pelvis rather than isolated ovarian metastasis is favorable prognostic factor for overall survival of colorectal cancer patients with ovarian metastasis. Isolated ovarian metastasis is diagnosed in only 8 patients in this series, that is, it merely yielded the trend of better survival. Surgery for patients with disease confined to the pelvis render curative operation possible and it does provide possible long-term survival (median survival after curative operation is estimated to be 72.4 months). This suggests that a more aggressive surgical approach may be warranted for women with disease confined to the pelvis.

Conclusion

Ovarian metastasis from colorectal cancer is uncommon and has decreased overall survival. Patient who received surgery for ovarian metastases with disease confined to pelvis has better survival than who has associated extrapelvic metastases. Curative resection for ovarian metastasis is effective and could offer

potential long-term survival.

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病例分析

結腸直腸癌併卵巢轉移的病人 接受卵巢切除手術治療的預後

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目的 結腸直腸癌女性病患約百分之 3~8 會發生卵巢轉移。根除性卵巢切除已被報告可以增加病人整體存活率。此篇研究是爲了研究本院針對結腸直腸癌併卵巢轉移的病人手術治療的預後。

方法 從 2001 年三月到 2005 年十月共有 32 位結腸直腸癌病人在本院接受卵巢切除手術。這些病人的臨床及病理的資料與預後的關係將予以分析。

結果 這些病人的追蹤時間中位數爲 32.6 個月。單純只有卵巢轉移的病人有 8 位，這類病人有較好的預後，但未達顯著差異。不過，如果是轉移的病灶只發生在骨盆腔或是病人可以接受完全根除性手術，則明顯有較好的預後。

結論 結腸直腸癌併卵巢轉移病人如果轉移的病灶只發生在骨盆腔比轉移超過骨盆腔的病人有較好的預後。根除性手術對結腸直腸癌併卵巢轉移的病人是有效的，甚至可能有長期存活的可能。

關鍵詞 結腸直腸癌、卵巢轉移、卵巢切除手術。