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The Role of Liver-directed Surgery in Patients with Hepatic Metastasis from a Gynecologic Primary Carcinoma

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Abstract

Background—The management of patients with liver metastasis from a gynecologic carcinoma remains controversial, as there is currently little data available. We sought to determine the safety and efficacy of liver-directed surgery for hepatic metastasis from gynecologic primaries.

Methods—Between 1990 and 2010, 87 patients with biopsy-proven liver metastasis from a gynecologic carcinoma were identified from an institutional hepatobiliary database. Fifty-two (60%) patients who underwent hepatic surgery for their liver disease and 35 (40%) patients who underwent biopsy only were matched for age, primary tumor characteristics, and hepatic tumor burden. Clinicopathologic, operative, and outcome data were collected and analyzed.

Results—Of the 87 patients, 30 (34%) presented with synchronous metastasis. The majority of patients had multiple hepatic tumors (63%), with a median size of the largest lesion being 2.5 cm. Of those patients who underwent liver surgery ($n = 52$), most underwent a minor hepatic resection ($n = 44$; 85%), while 29 (56%) patients underwent concurrent lymphadenectomy and 45 (87%) patients underwent simultaneous peritoneal debulking. Postoperative morbidity and mortality were 37% and 0%, respectively. Median survival from time of diagnosis was 53 months for patients who underwent liver-directed surgery compared with 21 months for patients who underwent biopsy alone ($n = 35$) ($p = 0.01$). Among those patients who underwent liver-directed surgery, 5-year survival following hepatic resection was 41%.

Conclusions—Hepatic surgery for liver metastasis from gynecologic cancer can be performed safely. Liver surgery may be associated with prolonged survival in a subset of patients with hepatic metastasis from gynecologic primaries and therefore should be considered in carefully selected patients.

Introduction

Gynecologic cancers affect over 80,000 females per year in the United States, with an annual estimated death rate of over 250,000 [1]. Within this group of cancers of the female genital tract, ovarian cancer is the most common subtype, as 1 in every 70 women in the Western World will develop this form of cancer [1]. While in the majority of cases the disease is limited to the primary gynecologic organ, distant metastasis can develop in up to 40% of patients, in either a synchronous or metachronous fashion [2–4]. Dissemination via the intraperitoneal route is generally considered the most common; however, lymphatic and hematogenous spread of the disease have also been reported [5]. Commonly affected sites include pleura [2, 3], lungs [6, 7], and liver [3]. Rose et al. [5] reported that 48% of gynecologic patients had hepatic metastasis at autopsy, perhaps indicating that liver metastasis from gynecologic primaries may be more common than estimated [8].

Data on management of patients with hepatic metastasis from a gynecologic primary tumor remain scarce. While several series on liver surgery for noncolorectal non-neuroendocrine metastasis have been published [9–12], few included many patients with gynecologic primary cancers. In fact, most—if not all—data on the role of hepatic surgery for gynecologic hepatic metastasis come from either case reports [13–17] or small studies with fewer than 25 patients [9, 18–28]. Due to the limited number of patients in previous studies, the role of liver surgery for hepatic metastasis from a gynecologic primary carcinoma remains ill-defined.

As surgical resection represents the only potentially curative therapeutic option for patients with metastatic disease to the liver, defining the role of hepatic resection for metastatic disease from gynecologic malignancies has important implications. Therefore, the objective of the current study was to assess the safety and efficacy of liver-directed surgery of hepatic metastasis from a gynecologic primary carcinoma. To accomplish this, we utilized a matched-pair analysis to compare outcomes among patients who underwent liver-directed surgery versus biopsy only for hepatic metastasis from a gynecologic primary carcinoma.

Methods

Data on 87 female patients diagnosed with liver metastasis from a primary gynecologic cancer from 1990 to 2010 were identified from our institutional hepatobiliary database. For the purpose of this study, a gynecologic cancer was defined as one of ovarian, cervical, uterine/endometrial, or fallopian origin [29, 30]. Only patients who had biopsy-proven hepatic metastasis from a gynecologic primary were included. Patients who underwent surgery (i.e., resection and/or ablation) for their liver metastasis and patients who underwent a nontherapeutic laparotomy during which liver biopsies were taken were included in the current study. The study was approved by the Johns Hopkins Hospital Institutional Review Board.

Data collection

In addition to standard demographic data, the following data were collected for each patient: primary tumor characteristics (stage, grade, histology, and location of primary tumor), preoperative carbohydrate antigen-125 (CA-125) level, treatment-related variables, and presence and location of any extrahepatic disease. Details on the number, size, and location of the liver metastasis were also recorded. Location of the hepatic metastasis was characterized as “capsular/implant” or “parenchymal” based on re-review of operative notes and all preoperative cross-sectional imaging. Specifically, any lesion noted to be on the capsule of the liver or completely contained within 10 mm from the liver surface was defined as “capsular/ implant” (Fig. 1). Operative information included type of liver-directed therapy (i.e., resection, ablation, both), extent of resection, performance of concurrent procedures, and blood loss during surgery. Liver resection was defined as a minor (<3 segments) or major (≥ 3 segments) hepatectomy. Data on the postoperative course, including length of hospital stay, and perioperative occurrence and Clavien grade [31] of morbidity and mortality were recorded. For all patients, data on vital status and recurrence were noted and defined as intra- or extrahepatic.

Statistical analyses

Summary statistics were obtained using established methods and presented as percentages or median values. The χ^2 test or Kruskal–Wallis test was used to compare categorical data, and the Mann–Whitney *U* test was used for continuous data. Disease-free intervals and survival times were estimated using the Kaplan–Meier method, both from time of surgery (for those patients who underwent hepatic resection) and from time of diagnosis (for all patients) [32]. Differences in survival were examined using the log-rank test. Cox regression analysis was used to identify factors associated with survival [33]. In order to compare the group of patients who underwent liver-directed surgery with those patients who underwent liver biopsy only, a matched-controlled analysis was performed. Specifically, patients were matched for age, primary tumor characteristics, and hepatic tumor burden (number of lesions, size of largest lesion). Hazard ratios and 95% confidence intervals were reported, and $p < 0.05$ was considered significant. All tests were performed using SPSS ver. 18.0 (SPSS, Inc., Chicago, IL).

Results

Patient, tumor, and primary surgery characteristics

The patient and tumor characteristics of the 87 patients who were diagnosed with hepatic metastasis from gynecologic origin and who are included in the current study are detailed in Table 1. Most patients ($n = 67$; 77%) had a primary tumor located in the ovaries and about one half of the patients ($n = 44$; 51%) had stage III disease. All patients underwent surgical therapy of the primary gynecologic tumor, with the majority having a total abdominal

hysterectomy and salpingo-oophorectomy ($n = 71$; 81%). Most patients ($n = 53$; 61%) underwent concurrent lymphadenectomy, of whom 30 (34%) were found to have lymph node metastasis. Of note, 71 (81%) patients had concurrent peritoneal debulking at the time of initial surgery for the primary tumor.

While 30 (34%) patients had synchronous liver disease, 57 (66%) patients developed metachronous liver metastasis after a median disease-free interval of 25 months (95% CI: 19–32) from the time of surgery for the primary gynecologic tumor. Of the 57 with metachronous liver metastasis, 45 patients had postoperative chemotherapy following resection of the primary tumor. Of these 45 patients, 23 underwent subsequent resection of their liver metastasis while 22 patients did not ($p = 0.11$). Of those patients who developed metachronous liver metastasis, 14 (25%) patients underwent surgery for extrahepatic disease during the interval between their primary operation and the diagnosis of liver metastasis.

Overall, most patients ($n = 55$; 63%) had multiple liver lesions, but only 21 (24%) patients had bilobar hepatic metastasis. The median size of the largest lesion was 2.5 cm (range = 0.1–10.5). The majority of patients ($n = 60$; 69%) had deeply situated liver lesions located within the hepatic parenchyma; 27 (31%) patients had liver metastasis characterized as capsular/implant. Most patients ($n = 72$; 83%) had concurrent extrahepatic metastatic disease, with most having peritoneal disease ($n = 71$).

Of the 52 patients who underwent liver-directed surgery, 45 (87%) patients received chemotherapy. Pre- and postoperative chemotherapy was administered to 14 (27%) patients, whereas 31 patients received adjuvant chemotherapy only. All 35 patients who underwent liver biopsy only received systemic chemotherapy. Among the patients who underwent liver-directed surgery ($n = 52$), 30 (58%) patients also received intraperitoneal chemotherapy as part of their therapy.

Details of liver-directed surgery and postoperative course

Of the cohort of 87 patients included in the study, 52 (60%) underwent hepatic surgery for their liver metastasis (Table 2). Of the patients with synchronous liver metastasis ($n = 30$), 24 (80%) patients underwent a simultaneous procedure with hepatic resection at the same time as resection of the primary tumor; the other 6 (20%) patients underwent a staged liver-directed surgery.

The median number of liver lesions treated was 2 (range = 1–8). The majority ($n = 46$; 88%) of patients underwent resection only; radiofrequency ablation only ($n = 2$; 4%) or combined resection and ablation ($n = 4$; 8%) was utilized much less frequently. At the time of liver-directed surgery, most patients ($n = 45$, 87%) also underwent peritoneal debulking. On final pathological analysis of the liver specimen, most patients ($n = 33$; 63%) had a negative hepatic margin (R0), whereas 8 (15%) patients had microscopic disease at the margin (R1) and 1 (2%) patient had macroscopic disease left in situ (R2).

The median postoperative length of stay was 7 days (range = 3–24). There were no postoperative deaths within 90 days of surgery. Nineteen (37%) patients experienced a postoperative complication, most related to wound infection or pulmonary issues. One patient underwent a reoperation for repair of wound dehiscence. No patient had a liver-related complication (i.e., biloma, abscess, liver insufficiency or failure) (Table 2).

Recurrence and overall survival

Following liver-directed surgery ($n = 52$), 39 (75%) patients recurred after a median disease-free interval of 13 months (95% CI: 9–16) (Fig. 2). Among the 39 patients with recurrence, the pattern of recurrence was intrahepatic only in 6 (15%) patients, extrahepatic only in 13

(33%) patients, and intra- and extrahepatic in 18 (46%) patients. In 2 patients (5%), the location of recurrence was unknown. Repeat surgery was undertaken in 3 (8%) patients, all of whom had intrahepatic recurrence only.

Median overall survival from time of diagnosis was 38 months (95% CI: 24–51) for the entire cohort. In order to assess the impact of liver-directed therapy for hepatic metastasis from a gynecologic primary tumor, we then performed a matched-paired analysis. Specifically, patients who underwent surgical therapy of their liver metastasis were matched for age, primary tumor characteristics, and hepatic tumor burden (number of lesions, size of largest lesion) with patients who had biopsy-proven gynecologic liver metastasis disease but did not undergo surgical treatment of their liver disease (Table 3). The median overall survival from time of diagnosis of liver metastasis was 53 months (95% CI: 58–78) for patients who underwent liver-directed surgery ($n = 52$; 60%) compared with 21 months (95% CI: 9–31) for patients who underwent biopsy only ($n = 35$; 40%) ($p = 0.01$) (Fig. 3). Moreover, when calculated from time of surgery ($n = 52$; 60%), the median overall survival was 50 months (95% CI: 24–75), with a 1-, 3-, and 5-year survival of 90, 57, and 41%, respectively (Fig. 1). On univariate analyses, no factor was found to be associated with survival following surgery (Table 4). Location of the primary tumor, histology of the primary tumor, presentation of the liver metastasis, and size, number, and distribution of the hepatic lesions were not found to correlate with survival on univariate analyses (all $p > 0.05$). Specifically, the median survival following surgery was similar for patients with ovarian versus nonovarian primaries (21 vs. 22 months, respectively; $p = 0.53$). While not significant, patients with deeply situated liver lesions (i.e., within the hepatic parenchyma) tended to have a worse survival compared with patients who had liver metastasis characterized as capsular/implant (hazard ratio [HR]: 1.49; 95% CI: 0.90–2.48; $p = 0.12$) (Fig. 4).

Discussion

Although the role of liver surgery in patients with hepatic metastasis from colorectal or neuroendocrine primary tumors is accepted, its role in treating liver metastasis from other primary malignancies is more controversial. Several institutions have reported series of patients who have undergone hepatic resection for noncolorectal and non-neuroendocrine metastases [9–12]. Data have also been published on hepatic surgery for liver metastasis from primary tumors, including sarcoma [34], squamous cell [35], and periampullary [36]. However, few previous studies focused exclusively on the role of hepatic surgery for metastasis derived from primary gynecologic malignancies [9, 13–28]. As such, the role of surgery to treat liver metastasis from gynecologic primary tumors is less clearly defined. The current study is important because it examined whether hepatic resection of metastasis from gynecologic primaries is warranted. Unlike many previous studies, only patients with liver metastasis from gynecologic primary tumors were included. In addition, we compared patients who underwent liver-directed surgery for gynecologic hepatic metastasis with comparably matched patients who underwent biopsy alone to assess the relative benefit of surgical intervention. Our data suggest that in well-selected patients liver-directed surgery for hepatic metastasis from a gynecologic primary can be associated with a 5-year survival of 40%.

An aggressive therapeutic approach that includes primary cytoreductive surgery and debulking procedures is considered part of the standard treatment for many gynecologic malignancies and has been shown to provide a survival benefit [37–39]. In a landmark study in 1975, Griffiths [40] reported on the association between residual tumor burden and patient survival. The inverse relationship between the amount of residual tumor and survival has subsequently been confirmed by other investigators [41–44]. Following cytoreductive

surgery, systemic chemotherapy is typically administered. Most data on combined cytoreduction and chemotherapy have included either patients with stage III disease or those with stage IV disease characterized by peritoneal metastasis [45–47]. Among this group of patients, combined modality treatment of metastatic gynecologic malignancies with cytoreductive surgery and chemotherapy can achieve a median survival in the range of 29–36 months [45–47]. Specifically, patients with metastatic ovarian cancer have a better 5-year survival [48–50] following cytoreductive surgery compared with patients who have advanced metastatic uterine or cervical cancer [51–53]. The role of repeat surgical debulking, however, remains somewhat controversial. The Gynecological Cancer Cooperative Group of the European Organization for Research and Treatment of Cancer (EORTC) examined the role of debulking surgery for metastatic ovarian cancer [54]. In that study, patients who had residual lesions measuring more than 1 cm in diameter after primary surgery were randomized to repeat debulking surgery or no surgery. The authors noted that debulking surgery significantly lengthened progression-free and overall survival with the risk of death being reduced by one third. In a separate study, however, Rose et al. [55] reported no improvement in progression-free survival among patients who had advanced ovarian cancer and residual tumor exceeding 1 cm in diameter after primary surgery who subsequently went on to a secondary cytoreductive surgery. Some investigators [56] have suggested that the reason for the different findings in the two studies may have been related to the increased efficacy of the paclitaxel plus cisplatin regimen in the Rose et al. trial compared to the cyclo-phosphamide plus cisplatin in the EORTC trial, thereby perhaps blunting the effect of the second debulking in the Rose trial. In aggregate, the data suggest that while patients who have had an effective primary debulking operation probably do not benefit from a second operation, those patients whose initial surgical debulking was suboptimal may indeed benefit from a more thorough debulking.

Up to 6–28% of patients with gynecologic malignancies can also develop hepatic metastasis [21, 26]. In general, the development of distant metastatic disease in the lung or liver usually portends a worse prognosis. Several groups, however, have suggested that hepatic resection of liver metastasis from gynecologic malignancies may play a role in the treatment of a subset of patients [7, 18, 19, 26–28, 57]. For patients with liver metastasis, definitive therapy with surgical resection represents the only chance at cure. Despite the liver being the most common site of distant metastasis, resection of metastasis from gynecologic primary tumors is uncommon. In the current study, despite being a major referral center, we were able to amass only 52 patients who underwent surgery for hepatic metastasis from a gynecologic primary carcinoma. Regardless of the relative rarity of this indication for liver surgery, given the expanding indications for hepatic resection of noncolorectal and non-neuroendocrine tumors, data on liver-directed surgery for gynecologic malignancies is important to help inform clinical decision-making. In the current study, we report that liver surgery to treat hepatic metastasis from a gynecologic primary carcinoma was associated with overall 3- and 5-year survival rates of 57 and 41%, respectively. These data are consistent with those reported by Adam et al. [9], who reported a 5-year survival rate of 35–50% for patients who underwent resection of liver metastasis from a gynecologic primary. Other studies [19, 20, 27, 57–59] have reported median survival following liver surgery for gynecologic metastasis ranging from 26 to 62 months, which is similar to the median survival of 53 months that we report here. Unlike other studies, we also performed a matched-paired analysis. When examining patients with hepatic metastasis from gynecologic primary tumors who underwent liver-directed therapy (i.e., resection ± ablation) versus biopsy alone, there was a significant difference in long-term survival. In fact, patients who underwent liver-directed therapy had a near 2.5-fold increase in their median overall survival compared with patients who underwent biopsy alone (Fig. 3). Collectively, data from the current study and from previously published work suggest that liver surgery for hepatic metastasis from a gynecologic primary can result in long-term survival in a subset of patients.

It is important to identify the subset of patients with hepatic metastasis from gynecologic primary tumors who will benefit the most from surgical intervention. In the current study, the majority of patients who underwent liver surgery had a low volume of hepatic disease. In addition, while most patients had extrahepatic disease, the site of the extrahepatic disease was peritoneal in most patients. Although there is considerable data on the benefit of surgery for gynecologic metastasis disseminated via the peritoneal route [60–62], the benefit of surgery in patients with hematogenous spread of metastatic disease is more controversial. Interestingly, in the current study we noted a strong trend in the association between survival and location of the liver metastasis resected. Specifically, patients who underwent liver-directed surgery for metastasis characterized as capsular/implant disease seemingly benefitted more from surgery than patients who had deeply situated/ parenchymal liver metastasis. Other investigators have similarly suggested that location of the liver metastasis (capsular/implant versus parenchymal lesion) may impact outcome following surgery for metastatic gynecologic tumors [63]. These differences in outcome may reflect the underlying differences in prognosis for patients with peritoneal versus hematogenous spread of metastasis.

The current study had several limitations. Despite our institution having one of the largest hepatobiliary experiences in the country, only a small number of patients were included in the current series. This reflected the highly select nature of the cohort of patients with live metastasis from gynecologic primary tumors who were considered for resection. Due to the small sample size, the study had limited statistical power. Like all retrospective studies, selection bias may also have influenced choice of liver-directed surgery versus biopsy only. It is possible that resection/biopsy may simply be a surrogate for tumor biology and/or extent of disease. In turn, it is possible that the benefit of surgery may have been overstated. Causal inferences drawn from the data therefore need to be interpreted in light of these limitations.

In conclusion, resection of hepatic metastasis from gynecologic primary tumors can be performed with zero or near-zero mortality and low perioperative morbidity. Overall, a subset of patients with hepatic metastasis from gynecologic primary tumors can experience a 5-year survival approaching 40%. However, it must be kept in mind that most patients in the current study who underwent liver-directed therapy for gynecologic metastasis had a low burden of hepatic disease and were highly selected. While liver surgery for hepatic metastasis from a gynecologic primary tumor may be warranted and provide a survival benefit, the selection of patients needs to be carefully individualized and incorporated into a multidisciplinary approach.

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Fig. 1. Contrast-enhanced CT scans of a gynecologic primary tumor liver metastasis located (a) on the capsule of the liver (implant) versus (b) lesion situated within the hepatic parenchyma

Fig. 2. Kaplan–Meier curve depicting overall and recurrence-free survival of patients who underwent curative-intent surgery for gynecologic liver metastasis

Fig. 3. Kaplan-Meier curve comparing overall survival of patients who underwent curative-intent surgery for gynecologic liver metastasis with survival of patients who underwent liver biopsy only

Fig. 4.
Kaplan–Meier curve showing overall survival stratified by location of liver metastasis, capsular/implant versus deeply situated/ parenchymal

Table 1

Overall patient and tumor characteristics

Variable	No. of patients (%) (<i>n</i> = 87)
Patient characteristics	
Race, Caucasian	78 (90)
Median age at diagnosis of liver metastasis [range] (years)	60 [31–85]
Primary tumor and surgical details	
Location of primary tumor	
Ovary	67 (77)
Uterus/endometrium	15 (17)
Cervix	3 (4)
Fallopian tube	2 (2)
Stage of primary tumor	
I	7 (8)
II	6 (7)
III	44 (51)
IV	30 (34)
Grade of primary tumor	
Poorly differentiated	50 (58)
Moderately differentiated	15 (17)
Well differentiated	9 (10)
Unknown	13 (15)
Histology	
Papillary serous carcinoma	41 (46)
Endometrioid carcinoma	10 (12)
Papillary serous and endometrioid carcinoma	10 (12)
Adenocarcinoma	10 (12)
Other	16 (18)
Type of primary surgery	
Total abdominal hysterectomy with bilateral salpingo-oophorectomy	71 (82)
Other	16 (18)
Concurrent lymphadenectomy	53 (61)
Concurrent peritoneal debulking	71 (82)
Hepatic metastasis	
Presentation, synchronous	30 (34)
Number of lesions, multiple	55 (63)
Size of largest liver lesion median [range] (cm)	2.5 [0.1–10.5]
Distribution of liver lesions, bilobar	21 (24)
Location of liver lesions	
Capsular/implant	27 (31)
Deeply situated/parenchymal	60 (69)
CA-125, >250 U/ml	36 (41)

Variable	No. of patients (%) (<i>n</i> = 87)
Concurrent extrahepatic disease	72 (83)
Surgical resection of liver metastasis	52 (60)

Table 2

Patient, tumor, liver-directed surgery, and postoperative characteristics of the 52 patients who underwent surgical management of their liver metastasis

Variable	No. of patients (%) (n = 52)
Patient characteristics	
Race, Caucasian	47 (90)
Median age at surgery [range] (years)	60 [40–85]
Hepatic metastasis	
Presentation, synchronous	23 (46)
Number of lesions, multiple	2 [1]
Size of largest liver lesion median [range] (cm)	3 [1–10.5]
Distribution of liver lesions, bilobar	13 (25)
Location of liver lesions	
Capsular/implant	20 (38)
Deeply situated/parenchymal	32 (62)
CA-125, >250 U/ml	15 (29)
Concurrent extrahepatic disease	44 (85)
Details of liver-directed surgery	
Surgical approach	
Open	31 (60)
Laparoscopic	21 (40)
Median number of tumors treated [range]	2 [1–8]
Type of liver-directed therapy	
Resection only	46 (88)
Radiofrequency ablation only	2 (4)
Both	4 (8)
Type of liver resection	
Nonanatomic wedge resection/single segment	30 (58)
Bisegmentectomy	14 (27)
Hemihepatectomy	8 (15)
Extent of resection	
Minor (<3 segments)	44 (85)
Major (≥ 3 segments)	8 (15)
Concurrent lymphadenectomy	29 (56)
Concurrent peritoneal debulking	45 (87)
Median estimated blood loss [range] (ml)	600 [50–2900]
Median units of blood transfusion [range]	2 [0–7]
Margin	
R0	33 (63)
R1	8 (15)
R2	1 (2)
Unknown	10 (19)

Variable	No. of patients (%) (n = 52)
Postoperative course	
Median length of stay median (days)	7 [3–24]
Grade of complications	
None	24 (46)
I	4 (8)
II	5 (10)
III	8 (15)
IV	2 (4)
V	0
Unknown	9 (17)
Perioperative treatment	
Preoperative chemotherapy	14 (27)
Preoperative radiotherapy	0
Postoperative chemotherapy	45 (87)
Postoperative radiotherapy	2 (4)

Table 3

Tumor characteristics for patients who underwent resection compared with patients who underwent a biopsy only

Variable	No. of patients (%) (<i>n</i> = 87)		
	Resection (<i>n</i> = 52)	Biopsy only (<i>n</i> = 35)	<i>p</i>
Primary gynecologic cancer			
Location of primary cancer			
Ovarian carcinoma	42 (81)	25 (71)	0.31
Other gynecologic carcinoma	10 (19)	10 (29)	
Stage at diagnosis of primary tumor			
I/II	4 (8)	9 (26)	0.11
III	31 (59)	13 (37)	
IV	17 (33)	13 (37)	
Grade			
Poorly differentiated	33 (63)	17 (49)	0.35
Moderately/well differentiated	13 (25)	11 (31)	
Unknown	6 (12)	7 (20)	
Histology			
Papillary serous	27 (52)	14 (40)	0.39
Other	25 (48)	21 (60)	
Type of primary surgery			
Total abdominal hysterectomy with bilateral salpingo-oophorectomy	42 (81)	29 (83)	0.81
Other	10 (19)	6 (17)	
Concurrent lymphadenectomy	33 (63)	20 (57)	0.55
Concurrent peritoneal debulking	45 (87)	26 (74)	0.15
Liver metastasis			
Median age at diagnosis [range] (years)	60 [40–85]	58 [31–83]	0.30
Overall presentation, synchronous	23 (44)	7 (20)	0.02
CA-125 at diagnosis ≥ 250 U/ml	17 (33)	10 (29)	0.90
Location of liver lesions			
Capsular/implant	20 (38)	7 (20)	0.07
Deeply situated/parenchymal	32 (62)	28 (80)	
Distribution of liver lesions, unilobar	39 (75)	18 (51)	0.59
Presence of multiple lesions	30 (58)	25 (71)	0.19
Concurrent extrahepatic disease	45 (87)	27 (77)	0.26

Table 4

Univariate analyses of factors proposed to be associated with survival from time of hepatic operation among the 52 patients who underwent liver-directed surgery

Variable	Hazard ratio	95% CI	p
Caucasian race	0.68	0.20–2.53	0.55
Location of primary tumor, ovaries	0.83	0.35–1.96	0.66
Stage at diagnosis of primary			
I/II	<i>Reference</i>		
III/IV	1.56	0.36–6.07	0.55
Grade of primary			
Well/moderate differentiation	<i>Reference</i>		
Poorly differentiated	1.06	0.44–2.56	0.89
Histology			
All other reported histologies	<i>Reference</i>		
Papillary serous	0.76	0.36–1.61	0.48
Type of primary surgery			
Other	<i>Reference</i>		
Total abdominal hysterectomy/bilateral salpingo-oophorectomy	0.82	0.33–2.04	0.67
Lymphadenectomy during primary surgery	0.70	0.57–1.07	0.53
Peritoneal debulking during primary surgery	0.94	0.33–2.70	0.92
Interval surgery	1.37	0.61–3.03	0.44
Synchronous presentation of liver metastasis	0.79	0.37–1.45	0.54
Multiple hepatic lesions	1.61	0.74–3.47	0.23
Size of largest hepatic lesion (cm)	0.91	0.74–1.11	0.36
Presence of concomitant extrahepatic disease	0.72	0.45–1.14	0.16
Location of liver lesions			
Capsular/implant	<i>Reference</i>		
Deeply situated/parenchymal	1.49	0.90–2.48	0.12
CA-125 250 U/ml	0.90	0.34–2.38	0.83
Bilobar distribution	1.05	0.69–1.59	0.83
Major hepatic resection	1.08	0.37–3.16	0.88
Receipt of ablation	0.56	0.13–2.38	0.44
Lymphadenectomy during liver surgery	0.83	0.40–1.75	0.64
Peritoneal debulking during liver surgery	0.53	0.21–1.33	0.18
Positive hepatic resection margin	1.10	0.45–3.23	0.76