

ORIGINAL ARTICLE

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Prognostic influence of delays between exploratory and definitive laparotomy in the treatment of malignant ovarian tumors

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Abstract Background: The aim of this retrospective study was to evaluate whether a delay between a preliminary exploratory laparotomy and a definitive staging laparotomy and interval chemotherapy between the two operations affected the prognosis of ovarian cancer. Methods: Of 504 patients with malignant tumors of the ovary who were treated at the Department of Obstetrics and Gynecology between 1980 and 1993, there were 24 who had a delayed definitive staging laparotomy. Results: Sixteen patients did not have chemotherapy between their two operations. After definitive laparotomy, 13 patients (54.2%) were free of disease and 11 patients had residual disease (45.8%). Conclusions: The value of chemotherapy between preliminary and definitive laparotomy in halting tumor growth was not demonstrated by the results of our analysis.

Keywords Delayed definitive laparotomy in ovarian cancer

Introduction

Adequate surgical treatment of malignant ovarian tumors at primary surgery is not always possible. The reasons for this include ovarian carcinoma being an incidental

finding, inadequate preoperative investigation, the unavailability of intraoperative frozen-sections, false-negative reports on frozen sections or a lack of patient consent for radical surgery.

Studies examining the effects of delays between initial and definitive cancer surgery are only available for breast and colorectal carcinomas. Prechtel et Hallbauer 1979 found that the survival of breast cancer patients is compromised when the definitive surgical procedure is delayed for more than 7 d.

We evaluated whether a delay between primary diagnostic-exploratory laparotomy and definitive staging laparotomy had an impact on the prognosis of malignant ovarian neoplasms.

Materials and methods

Of 504 patients with malignant tumors of the ovary who were treated at the Department of Obstetrics and Gynecology between 1980 and 1993, we studied those who for various reasons had a preliminary and then a definitive laparotomy. The following data were recorded: date of birth, menopausal status, preoperative ultrasonographic findings, including the morphologic characteristics of the mass in question (cystic, solid, septae, unilocular, presence of adhesions), tumor marker, and clinical findings.

With regard to the preliminary laparotomy, the presence of ascites or adhesions, and the surgical procedures undertaken were recorded, the timing of the definitive laparotomy, the final FIGO stage, histologic findings at the time of second laparotomy, including tumor grade were recorded. The medical records were reviewed for details of postoperative chemotherapy and follow-up.

The patients were also divided into those who did and do not have chemotherapy between the first and the second laparotomy.

Results

Twenty-four of the 504 patients had a second laparotomy including radical surgery (4.7%). Of those, 16 patients did not have chemotherapy between their first and second operations.

Table 1 summarizes the demographic data and the intraoperative management during initial laparotomy.

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Table 1 Patients

	No chemotherapy <i>n</i> =16		Adjuvant chemotherapy <i>n</i> =8	
	Delay 42 d Or less	Delay >42 d	Delay 269.5 d Or less	Delay >269.5 d
Mean age [a]	37	41	56	56
Premenopausal	4	4	1	1
Postmenopausal	4	2	3	3
Surgical technique during initial laparotomy				
Diagnostic laparotomy	2	2	–	–
Operative laparotomy	6	6	4	4
Biopsy ^a	2	1	3	2
Ovarectomy/adnexectomy ^a	4	5	1	2
Puncture of a cyst ^a	1	3	–	–
Rupture of a cyst ^a	1	1	–	–

^a More than one procedure/
incident per patient possible

Table 2 FIGO stage and tumor grade at the time of second laparotomy

	No adjuvant chemotherapy		Adjuvant chemotherapy	
	Delay 42 d (<i>n</i> =8)	Delay >42 d (<i>n</i> =8)	Delay 269.5 d (<i>n</i> =4)	Delay >269.5 d (<i>n</i> =4)
Stage			n	
Ia	2	6	–	–
Ia	2	–	–	–
III	2	1	1	–
IIIb	1	–	–	1
IIIc	1	1	3	2
IV	–	–	–	1
Grade				
Grade 0/1	4	4	–	–
Grade 2	2	3	1	1
Grade 3	2	1	3	3

Table 2 presents the staging and grading of the tumors and their FIGO stage at second laparotomy. Table 3 shows the histologic classification. At definitive laparotomy, 13 patients (54.2%) were free of disease and 11 patients had residual disease (45.8%). A total of 17 (70.8%) patients had chemotherapy after the second laparotomy.

In the patients who did not receive chemotherapy (*n*=16), the median interval between the two operations was 42 days (range, 2–194 d). And they were subdivided into those who had their second operation within 42 days of explorative laparotomy (*n*=8) and those in whom the delay was longer (*n*=8). In the patients who had chemotherapy (*n*=8), the definitive laparotomy was performed within a median of 269 d (range, 175–918 d) of initial laparotomy. The median duration of follow-up for all patients was 22.7 months (range, 4–94 months). In 11 patients (45.8%), the tumor recurred after a mean of 14.7 months (range, 1–60 months) after the second laparotomy.

Survival data is shown in Table 4 and progression in staging in Table 5.

Table 3 Histological classification

Histologic type	<i>n</i>	%
Borderline tumor	1	4.2
Serous adenocarcinoma	10	41.7
Mucinous adenocarcinoma	6	25
Endometrioid ovarian carcinoma	1	4.2
Malignant germ cell tumor	2	8.3
Undifferentiated carcinoma	3	12.5
Krukenberg's tumor	1	4.2

Discussion

Because in the past many gynecology departments were not staffed and equipped for frozen sections [5] and immediate radical operations, we expected a large number of ovarian cancer patients to be referred to the University of Vienna for further treatment after a preliminary laparotomy. However, among the 504 patient histories reviewed, only 24 cases of delayed definitive laparotomy were identified. Delays between exploratory and definitive laparotomy are probably rather rare

Table 4 Table showing a "trend" for longer survival time in the group with earlier definitive surgery

Stage	Earlier definitive surgery No chemotherapy <i>n</i> =16			Later definitive surgery Chemotherapy <i>n</i> =8		Total no of patients who survived	
			Survival time [months]			Survival time [months]	
Ia	No deaths	8	27	–	–	8	–
Ila	2 deaths	2	12	–	–	0	–
III	Ideath	3	25	1 died	–	2	22
IIIb	No deaths	1	22	1 died	–	1	62
IIIc	1 deaths	2	20	1 died	–	5	13
IV	–	–	–	1 died	–	0	11

Survival time in month

Table 5 Stage at first and second operations

Stage at first surgery	Stage at definitive surgery												
	I	a	b	c	II	a	b	c	III	a	b	c	IV
I abc		8				2							
II abc													3
III abc									4		2		4
IV													1

Numbers in shaded area indicates those who slipped a stage between operations (*n*=5)

because ovarian cancer is usually diagnosed at an advanced and symptomatic stage.

Two studies strongly suggest that delays in laparotomy after laparoscopic excision of an ovarian mass subsequently found to be malignant result in an increase in the number of advanced tumors, thus compromising ultimate patient prognosis [3, 4]. Wallwiener et al. [8] also reported three patients in whom ovarian cancer was unexpectedly found at the time of laparoscopy and showed that the prognosis may be worsened when definite laparotomy is delayed. In one of his patients, a 35-d delay between laparoscopic cystectomy and definite laparotomy was associated with extensive metastatic spread. Likewise, Kindermann et al. [3] showed that a delay in definitive laparotomy of only 8 d after laparoscopy is associated with advances in tumor stage and concluded that delays between laparoscopy and laparotomy adversely affect prognosis.

This may also hold for delays between exploratory and definitive laparotomy, regardless of whether or not chemotherapy is used in the interval [1, 2, 7]. The rational approach of administering chemotherapy between exploratory and definitive laparotomy is not supported by the results of our analysis.

The median delay between exploratory and definitive laparotomy in patients receiving chemotherapy was markedly longer than that in patients not treated with chemotherapy (269.5 vs. 42 d). The mean age of patients not receiving chemotherapy was considerably lower than that of patients receiving chemotherapy. Whereas the proportion of FIGO stage Ia ovarian cancers was high among patients not receiving chemotherapy in whom laparotomy was delayed for more than

42 d, FIGO stage III–IV ovarian cancers were frequent among patients treated with chemotherapy. It is likely that there was bias in the decision to use chemotherapy based on the fact that most of the induction patients had advanced stage, high grade disease while patients with lower stages of the disease did not receive any therapy. Seven of the patients not receiving chemotherapy were tumor-free at the time of definitive staging laparotomy. Therefore, it would appear that the timing of staging laparotomy does not have an influence on the prognosis if all the tumor has been removed at initial laparotomy.

This article represents an examination of the possible influence of delayed treatment after a preliminary diagnostic laparotomy. Definitive conclusions cannot be drawn because of small numbers. But we would suggest that time delay influences the stage of disease and survival time (Table 4) and strict preoperative protocols should be in place to ensure that an absolute minimum number of patients with ovarian cancer have a first preliminary and then a second definitive laparotomy.

References

1. Burg ME van, Lent M van, Buyse M, et al. (1995) The effect of debulking surgery after induction chemotherapy on the prognosis in advanced ovarian cancer. Gynecologic Cancer Cooperative Group of the European Organization for Research and Treatment of Cancer. *N Engl J Med* 332:629–634
2. Chambers JT, Chambers SK, Voynick IM, Schwartz PE (1990) Neoadjuvant chemotherapy in stage X ovarian carcinoma. *Gynecol Oncol* 37:327–331

3. Kindermann G, Maaßen V, Kuhn W (1995) Laparoscopic preliminary surgery of ovarian malignancies. Experiences from 127 German gynecologic clinics. *Geburtshilfe Frauenheilkd* 55:687–694
4. Maiman M, Seltzer V, Boyce J (1991) Laparoscopic excision of ovarian neoplasms subsequently found to be malignant. *Obstet Gynecol* 77:319–321
5. Menzin A, Rubin SC, Noumoff JS, LiVolsi V (1995) The accuracy of a frozen section diagnosis of borderline ovarian malignancy. *Gynecol Oncol* 59:183–185
6. Prechtel K, Hallbauer M (1979) On the prognosis of carcinoma of the breast following a two-stage operation. *Geburtshilfe Frauenheilkd* 39:187–194
7. Schwartz PE, Chambers JT, Makuch R (1994) Neoadjuvant chemotherapy for advanced ovarian cancer. *Gynecol Oncol* 53:33–37
8. Wallwiener D, Diel IJ, Sohn C, et al. (1996) Laparoscopy in apparently benign ovarian tumors between benefit and catastrophe and the deceptive safety of laparoscopy lap sacs. *Zentralbl Gynaecol* 118:53–61