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PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

A retrospective study of patients reported to the Danish Cancer Registry in a five-year period

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Abstract

Fifty-two patients with carcinoma of the fallopian tube diagnosed and treated during a 5-year period in Denmark were reviewed. The median age of the patients was 60 years. No patients had a preoperative diagnosis. History and clinical findings were similar to previously reported series. Treatment consisted of hysterectomy and bilateral salpingo-oophorectomy, often succeeded by postoperative whole pelvic irradiation. Five-year survival was 37.4%, depending on stage. In stage I+II the survival rates were similar regardless of whether postoperative radiation therapy had been given or not. Little is known about the patterns of spread. The relatively bad prognosis for stages I and II after radical surgery indicates early undetected metastases and the need for more aggressive adjunctive therapy.

Key words: Fallopian tube carcinoma, cancer registry material, stage, treatment, survival.

Every year 10 to 12 cases of primary carcinoma of the fallopian tube are diagnosed and reported to the Danish Cancer Registry. These patients account for 0.5% of all gynaecologic malignancies in Denmark equal to a standardized incidence rate of 0.29/100000. The appearance of 4 cases within 5 years at the Department of Gynecology, Fredericia Hospital, provoked a further interest in this uncommon tumour. The present paper reports a retrospective study of 52 proved cases diagnosed in Denmark during a 5-year period from June 1st 1978 till May 31st 1983.

Material and Methods

We obtained the data of 59 registered women with cancer of the fallopian tube from the Danish Cancer Registry and collected clinical records and histologic slides of these cases from departments all over Denmark. To confirm the diagnosis all specimens were reexamined by a pathologist (FA), without knowledge of the previous diagnosis. The original 59 patients were hereby reduced to 52, the diagnoses being changed to ovarian cancer in 5 patients, to leiomyosarcoma in 1 patient and to carcinosarcoma of the fallopian tube in 1 patient. The pathology data together with information from the clinical records made it possible to characterize the material with respect to the stage of the cases (Table 1). The staging system used was a simplification of the FIGO (International Federation of Gynaecologists and Obstetricians) staging system (1). It was chosen since the study was retrospective and since only few patients had extended surgery of the type sometimes used in ovarian cancer.

All information was thoroughly updated and the vital status of the patients on December 1st, 1985 was checked with a national population registry. Death certificates and, if possible, autopsy reports were obtained for deceased patients. Information about patients still alive was obtained from the physicians treating the patients.

Survival curves were determined using Kaplan-Meier plots and curves were statistically compared by the log-rank test. Survival was calculated from the date of diagnosis to the date of last observation or to the date of death.

Results

The most frequent presenting symptoms were lower abdominal pain (n=36), abnormal bleeding/postmenopausal bleeding (n=32) and watery vaginal discharge (n=30). The classical triad consisting of these 3 symptoms was

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found in 7 patients (13%) only. Less common but not rare symptoms were abdominal discomfort, distension and alterations in the patterns of defecation and urination. The often mentioned syndrome 'hydrops tubae profluens' (2), characterized by a pelvic mass that disappears in association with profuse vaginal discharge and colicky abdominal pain, was not noted in any patient.

None of the patients were correctly diagnosed preoperatively. Thirty-six (70%) patients were postmenopausal. Fifteen patients (28%) were nullipara. The available information about the 52 patients was incomplete as far as previous hormonal therapy was concerned, and so the possible importance of this factor could not be studied. One patient had an oestrogen-producing ovarian tumour removed 2 years prior to the diagnosis of fallopian tube carcinoma.

A large pelvic or lower abdominal mass was a common clinical finding. Gynaecological examination in advance of surgery revealed a tumour in 12 of the 19 patients in stage I and in all the patients in stages III and IV. At surgery a palpable tumour in stage I or II often turned out to be a large sactosalpinx which revealed malignant tumour.

Four out of 10 patients had pathological vaginal cytology; in 2 of these subsequent curettage revealed adenocarcinoma of the endometrium, whereas in the other 2 repeated curettages yielded normal findings.

None of the patients with stage I or II tumours had ascites. One patient only had a history of hysterectomy.

Bilateral tumours were found in 4 of 35 cases in stages I and II. The remaining 31 patients had unilateral tumours which were about equally distributed between right and left sides.

If possible, the surgical treatment consisted of total abdominal hysterectomy and bilateral salpingo-oophorectomy either initially or, if there was no peroperative suspicion of the malignant diagnosis, in a following operation. All patients with stages I and II tumours underwent radical surgery, while tumour tissue was often left in stages III and IV. Only 2 patients underwent the type of extended surgery often employed in ovarian cancer, including omentectomy, appendectomy, resection of the lymph nodes and assessment of peritoneal washings.

The stage distribution of the 52 patients is shown in Table 2. The diagnoses of the cases were fairly uniformly distributed throughout the 5-year period studied, with the shortest observation time after treatment being 30 months. The median age was 60 years, with a range from 37 to 79 years (Table 3).

Postoperative radiotherapy was given to 5 patients with stage III or IV disease. Of the 35 patients with stage I and II tumours 17 received postoperative megavoltage irradiation. The radiotherapy was in all cases limited to the pelvic area, with doses ranging from 45 Gy to 55 Gy given in 4 to 6 weeks. No patients received para-aortal or whole abdomino-pelvic postoperative irradiation.

Survival curves for patients in stages I and II (all operated by hysterectomy and bilateral salpingo-oophorectomy) according to initial treatment are shown in Fig. 1. No statistically significant difference was found between patients treated with surgery alone and patients treated with surgery and primary postoperative irradiation ($p>0.5$). Five patients in stage III or IV were given postoperative chemotherapy and had a median survival of 19 months. Five patients were given chemotherapy when relapse was found. One patient had a complete surgico-

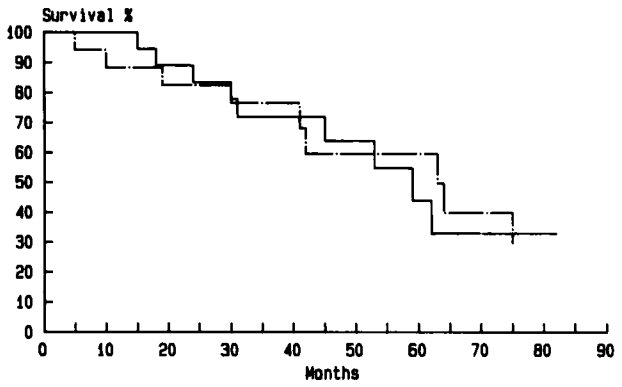

Fig. 1. Kaplan-Meier estimate of survival in 35 patients in stage I or II according to initial treatment. Surgery ——, surgery and radiotherapy –·–·–. $p>0.6$.

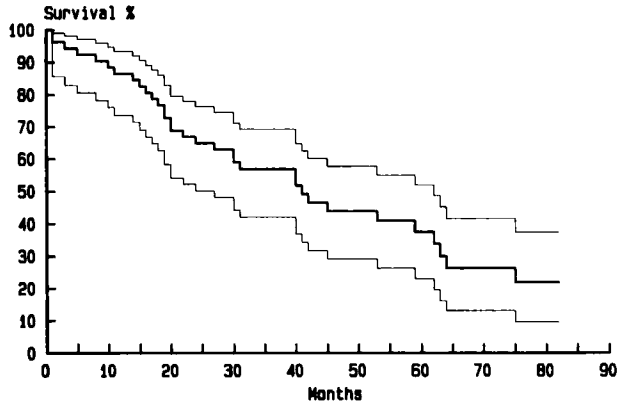

Fig. 2. Kaplan-Meier estimate of survival in 52 patients with fallopian tube carcinoma diagnosed in Denmark 1978–1983, all stages (95% confidence intervals).

Table 1

Staging of fallopian tube carcinoma

Stage I	Tumour limited to the tube(s), no penetration through the serosa
Stage II	Tumour penetrates the serosa of the tube and may involve the ovary and/or the uterus
Stage III	Tumour invading other organs in the pelvis
Stage IV	Tumour spread outside the pelvis and/or tumour cells in the ascites fluid

Table 2

Primary carcinoma of the fallopian tube reported to the Danish Cancer Registry June 1, 1978 to May 1, 1983. Status on December 1, 1985

	Stage (No. of patients)				
	I	II	III	IV	Total
Alive and well	9	5	1	0	15
Alive with metastases	0	1	1	0	2
Dead	10	10	2	13	35
Total (%)	19 (36)	16 (31)	4 (8)	13 (25)	52 (100)
5-year survival rate	64%	40%	6%		37.4%

Table 3

Age distribution of 52 patients with carcinoma of the fallopian tube

Age	n
<40	0
40–44	4
45–49	4
50–54	5
55–59	10
60–64	9
65–69	11
70–74	7
>74	2
Total	52

Table 4

Fifty-two patients with carcinoma of the fallopian tube. Distribution of the histological appearance in each stage

	Stage I	Stage II	Stage III+IV	Total
Grade				
1	3	7	2	12
2	10	6	7	23
3	6	3	8	17
Nuclear polymorphy				
Mild	11	12	11	34
Severe	8	4	6	18
Mitoses				
0–25	2	3	5	10
26–75	11	6	6	23
>75	6	7	6	19
Lymphocytic reaction				
Mild or absent	12	15	12	39
Moderate	7	1	5	13
Vascular invasion				
Not identified	11	7	2	20
Suspected	5	7	9	21
Proved	3	2	6	11
Total	19	16	17	52

pathological response lasting for more than 24 months following treatment with cisplatinum and cyclophosphamide.

No patients received intraperitoneal radionuclides for therapeutic purpose.

As will be seen in Fig. 2, the prognosis as a whole was poor (5-year survival rate 37.4%). In this material (Table 2) 35 patients died after a median survival of 22 months (range 0–76 months). Seventeen patients were alive on December 1st, 1985 with a median survival time of 46 months (range 30–93 months).

The 52 histologic slides were examined by a skilled pathologist (FA) and grouped according to histological grading, nuclear polymorphy, number of mitoses per 10 high power fields (400 times magnification), lymphocytic reaction and vascular invasion. Table 4 shows these histological parameters in relation to clinical stage. Only invasion of blood or lymph vessels seemed to influence survival in the early stages. Out of 18 patients without signs of vascular invasion 15 obtained 5-year survival compared to only 5 out of 17 with proved or suspected vascular invasion. All in all, the number of patients is too small for more extensive conclusions.

In order to find other useful prognostic criteria we studied the history of the patients, including age, menstrual status, previous hormonal treatment and parity, but we could not establish any factor associated with the prognosis.

By contrast, we found an obvious relationship between survival and stage (Fig. 3). Patients in stages I (5-year survival rate 64%) and II (5-year survival rate 40%) had a significantly higher survival rate ($p<0.005$) than patients in stages III+IV (5-year survival rate 6%). The difference between stage II alone and stages III+IV was also significant ($p<0.005$).

Discussion

In contrast to other malignant gynaecologic tumours no constantly used international staging exists for carcinoma of the fallopian tube. Several staging systems have

been proposed (3–6). In most recent works the patients have been classified by a modification of the staging system for ovarian cancer (1, 7) used by FIGO. In accordance with Benedet et al. (3) we propose the staging system shown in Table 1. We believe that patients with tumour cells in ascites are in an advanced stage. Podratz et al. (8) found that the presence of exfoliated cells in ascites correlated with the survival; the 5-year survival rate was 67% for patients with negative cytologic findings and only 20% for those with positive cytologic findings. Eddy et al. (9) found that patients with ascites or positive peritoneal cytology had a median survival of 24 months, which was similar to the median survival for all patients.

In our material ascites was only reported in patients with wide-spread abdominal disease.

Data on natural history of the disease are in our series fairly similar to those described in previous reports (2, 7, 9–11). Our study suggests, as do some previous reports, that patients with fallopian tube carcinoma more often than expected tend to be nullipara.

Hysterectomy plus bilateral salpingo-oophorectomy has long been regarded as the treatment of choice. This is based on the fact that the tumour is quite often bilateral and disseminated to the uterus and/or ovaries. This might be due both to direct extension of the tumour and to spread through the vascular or lymphatic system (2, 8, 9, 12, 13). A multifocal tumorigenesis in the Müllerian epithel has also been reported (14).

The surgical treatment is sometimes succeeded by radiotherapy. Concerning the early cases (stages I and II) we found, in agreement with some authors (2, 9) but in contrast to others (1, 3–5, 15), no difference in survival rates between patients receiving or not receiving postoperative pelvic irradiation (Fig. 2). It can, of course, not be excluded that the patients receiving postoperative irradiation represented a prognostically less favourable group. We did not, however, find any indication of this in the records and the decision about postoperative irradiation seems to have mainly depended upon prejudices within the local radiotherapy department. The postoperative radiotherapy did not seem to influence the prognosis. The reasons for this might have been insufficient radiation doses, low radiosensitivity of the tumours or early spread beyond the irradiated volume. It should be mentioned, however, that in single cases both partial and complete responses to radiotherapy have been reported (7, 9). Although few data exist on the use of whole abdominopelvic irradiation, some authors have reported encouraging results (12, 16, 17).

During recent years a rising number of cases with complete response after chemotherapy judged by second-look laparotomy has been reported (8, 9, 18). In 1978 one patient in our material with a primary fallopian tube carcinoma stage II was operated by hysterectomy and bilateral salpingo-oophorectomy without any adjuvant therapy. She was checked at regular intervals, and at second-look laparatomy in 1982 a relapse was verified. She was treated with cisplatinum and cyclophosphamide. In 1984 at a third-look laparotomy a complete surgico-pathological response, lasting at least 24 months, was verified and at the last check-up in 1985 (93 months after the initial diagnosis) the patient was still in good health without evidence of disease.

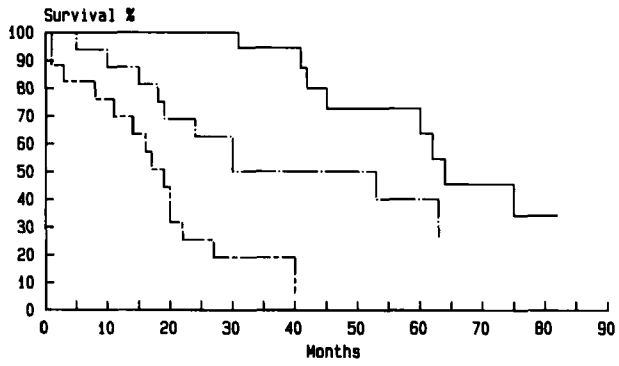

Fig. 3. Kaplan-Meier estimate of survival in 52 patients with fallopian tube carcinoma according to stage. Stage I — (n=19). Stage II –·–· (n=16). Stage III+IV ———— (n=17). $p<0.001$.

The reason for the bad prognosis of patients in stages I and II, primarily operated by apparently complete resection (Fig. 1), is probably that unknown metastases are left at surgery.

The need for meticulous surgical staging is obvious. It should be of interest to employ more radical surgical procedures, as in ovarian cancer, involving total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, cytologic assessment of peritoneal washings, pelvid and para-aortal node sampling and multiple peritoneal biopsies from suspicious areas.

If such extended surgery were performed on all patients in stages I and II, the knowledge of the dissemination pattern could be increased and an improved basis obtained for early postoperative treatment.

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