Primary carcinoma of the fallopian tube
A retrospective analysis of 47 patients

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Summary
Background: Fallopian tube carcinoma is a rare disease, and few data about prognostic factors are available in the literature.

Patients and methods: The medical charts of 47 patients with primary carcinoma of the fallopian tube treated at our institution between 1982 and 1994 were reviewed. Age, stage, histologic grade, residual disease after surgery, peritoneal cytology and lymph-node involvement were evaluated for their prognostic impact in a univariate analysis.

Results: The mean age of the patients was 57.5 years and 19 of them (40%) had early-stage disease. Poorly differentiated tumors were diagnosed in 64% of the patients. Eleven of 20 patients (55%) submitted to surgical evaluation of lymph-nodes had retroperitoneal involvement. Thirty-three patients received CAP chemotherapy following surgery, and the overall clinical response rate was 80%. Sixteen patients (34%) had recurrences within 8 to 50 months from diagnosis. Twenty patients (42.6%) are alive without disease, one patient is alive with tumor, and 26 patients (55.3%) died of the disease. The median survival for the group as a whole was 44 months, and the actuarial 5-year survival was 29%. In univariate analysis stage (I+II vs. III+IV), grade (G1+G2 vs. G3) residual disease after surgery (less than 2 cm vs. greater than 2 cm), peritoneal cytology (negative vs. positive) and lymph-node metastases were all factors significantly affecting survival.

Conclusions: Aggressive cytoreductive surgery followed by platin-based chemotherapy offer the possibility of long-term control of primary tubal carcinoma.

Key words: fallopian tube carcinoma, survival analysis

Introduction
Primary carcinoma of the fallopian tube is a rare disease, accounting for less than 1% of all malignant tumors of the female reproductive tract [1].

Due to the low number of cases, heterogeneous staging systems [2–4] and different methods of post-operative treatment, comparative analyses among series reported in the literature is limited and difficult [5].

In order to evaluate the prognostic factors and the effectiveness of different treatment modalities we retrospectively reviewed the clinico-pathologic characteristics of 47 patients treated for primary carcinoma of the fallopian tube at our institution during a 13-year period.

Patients and methods
Medical records of 47 patients treated for primary carcinoma of the fallopian tube at the III Department of Obstetrics and Gynecology, University of Milan, San Gerardo Hospital, Monza, between 1982 and 1994, were reviewed. Fallopian tube carcinoma was diagnosed using pathologic criteria proposed by Sedlis [6]. Representative histologic sections of the primary lesions were available in all cases and were reviewed. Grading was performed by applying the criteria used for epithelial ovarian cancer. Tumor staging was based on the FIGO Gynaecology Oncology Committee staging classification for fallopian tube malignancy [7].

Twenty-three patients were initially treated in our institution and 24 were referred to us after primary surgery performed in other hospitals. For patients undergoing primary surgery in our institution, standard surgical management included, when feasible, total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and cytoreduction in an attempt to maximally debulk any metastatic lesion. Patients without macroscopic peritoneal disease after debulking surgery were submitted, to systematic or selective pelvic and para-aortic lymphadenectomy. The CAP regimen (cyclophosphamide 500 mg/m², adriamycin 50 mg/m² and cisplatin 50 mg/m² every four weeks) was used as first-line treatment for 33 patients requiring chemotherapy. Different antibiotic agents, alone or in combination, were administered as second-line treatment. Between 1982 and 1986, stages I and II patients received whole pelvic irradiation following surgery. The total delivered doses ranged from 4000 to 5500 rads, but fractionation schedule, and field arrangement were variable during the study period.

Age, clinical stage, grade, peritoneal cytology, residual disease after primary surgery, depth of tubal invasion and lymph-node involvement were evaluated for their prognostic impact. Cross-tabulated data were subjected to the chi-square test with Yates correction. Survival curves were obtained by the Kaplan–Meier method [8], and the median survival times were compared by the Mantel–Haenszel log-rank test [9]. Values of P < 0.05 were considered to be statistically significant.

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Results

The mean age of the population studied was 57.5 years, ranging from 38 to 76 years. Evaluation of age by decade showed a peak frequency during the sixth decade. Five patients were nulliparous, while 34 (72%) were multiparous. Thirty-six patients (77%) were postmenopausal. Four patients had family histories of ovarian cancer and one of breast cancer. The most common presenting symptoms were vaginal bleeding (16 patients) and abdominal pain or pressure (13 patients). In four patients the diagnosis of fallopian tube carcinoma was incidental, at pathologic examination, and not recognized at the time of laparotomy for benign disease. No patient was correctly diagnosed preoperatively. Sixteen of the 27 patients (59%) for whom preoperative serum CA-125 determination was available had high levels (exceeding 40 U/ml) of this antigen (median 238 U/ml; range 64-3200 U/ml). The most common physical findings before surgery were pelvic or abdominal mass and ascites. One patient presented with left groin node enlargement.

Surgical procedures performed as primary treatment are listed in Table 1. Stage, grade, amount of residual disease after primary surgery, histology and peritoneal cytology are summarized in Table 2. Twenty patients underwent surgical removal of lymph-nodes (6 pelvic and para-aortic systematic lymphadenectomy and 14 lymph-node sampling), and 11 (55%) of them were found to have lymph-node metastases (3 patients pelvic; 4 para-aortic; 3 pelvic plus para-aortic; 1 groin node). Four additional patients had diagnoses of retroperitoneal involvement made by lymphangiography or CT scan, and confirmed by fine-needle biopsy.

The postoperative management of 19 patients with early (I-II) stage disease included: no-treatment (n = 9), chemotherapy (n = 5) and radiotherapy (n = 5). Recurrence rates and median survivals were significantly different (P = 0.02) among patients submitted to radiotherapy (80% recurrence rate, 12 months' median survival), no-treatment (44% recurrence rate, 33 months' median survival) and chemotherapy (20% recurrence rate, 72 months' median survival).

Thirty-three patients (1 stage I, 4 stage II, 26 stage III and 2 stage IV) received postoperative chemotherapy with the CAP regimen. A mean 6 cycles (range 4 to 9) were administered. Nine patients without gross residual disease after cytoreductive surgery were not evaluable for response. Of the remaining 24 patients, 15 had clinical complete responses (CR), 4 had partial responses (PR), 3 had stable disease (SD) and 2 had progressive disease (PD) to chemotherapy. The overall clinical response rate (CR + PR) was 80%. Twenty-one patients were submitted to second-look operation (SLO); 13 (62%) of them were found free of disease, in pathologic complete response (pCR), seven had macroscopic persistent disease and one had tumor cells only in the peritoneal washing. Four pCR patients relapsed, and two of them died despite second-line treatment. Nine patients who achieved PR, SD and PD after first-line chemotherapy were further treated (chemotherapy = 5, radiotherapy = 2, progesteron = 2), but none of them responded to second-line treatment and all of them died (median survival 9 months). The patients who achieved pathologic complete responses had significantly (P = 0.02) better survivals than those with persistent disease at second-look operation (median survival 64 months vs. 18 months).

Sixteen patients (34%) experienced recurrences within 8 and 50 months after diagnosis (median 19 months). Ten patients had local recurrences, 4 had dis-

<table>
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<tr>
<th>Extent of surgical treatment</th>
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<tr>
<td>T.A.H./B.S.O.</td>
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<tr>
<td>+ Omentectomy</td>
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<td>T.A.H./B.S.O. + Omentectomy</td>
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<td>T.A.H./B.S.O. + Omentectomy + Lymphnode sampling</td>
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<td>B.S.O. + Omentectomy</td>
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B.S.O. = bilateral salpingo-oophorectomy; T.A.H. = total abdominal hysterectomy.

Table 2. Clinical and pathologic features of 47 patients with tubal carcinoma.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Patients (%)</th>
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<tbody>
<tr>
<td>I</td>
<td>10 (21.3)</td>
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<tr>
<td>II</td>
<td>9 (19.1)</td>
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<tr>
<td>III</td>
<td>26 (55.3)</td>
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<tr>
<td>IV</td>
<td>2 (4.3)</td>
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<tr>
<th>Grading</th>
<th>Patients (%)</th>
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<tbody>
<tr>
<td>G1</td>
<td>6 (12.8)</td>
</tr>
<tr>
<td>G2</td>
<td>11 (23.4)</td>
</tr>
<tr>
<td>G3</td>
<td>30 (63.8)</td>
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<tr>
<th>Residual disease after surgery</th>
<th>Patients (%)</th>
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<tbody>
<tr>
<td>Absent</td>
<td>24 (51.1)</td>
</tr>
<tr>
<td>&lt; 2 cm</td>
<td>6 (12.8)</td>
</tr>
<tr>
<td>&gt; 2 cm</td>
<td>17 (36.1)</td>
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<table>
<thead>
<tr>
<th>Histology</th>
<th>Patients (%)</th>
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<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>28</td>
</tr>
<tr>
<td>Serous-Papillary</td>
<td>13</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>3</td>
</tr>
<tr>
<td>Squamous</td>
<td>1</td>
</tr>
<tr>
<td>Adenosquamous</td>
<td>1</td>
</tr>
<tr>
<td>Clear cell</td>
<td>1</td>
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<tr>
<th>Peritoneal cytology</th>
<th>Patients (%)</th>
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<tbody>
<tr>
<td>Positive</td>
<td>15 (37.5)</td>
</tr>
<tr>
<td>Negative</td>
<td>25 (62.5)</td>
</tr>
<tr>
<td>Peritoneal washing</td>
<td>19</td>
</tr>
<tr>
<td>Ascites</td>
<td>6</td>
</tr>
</tbody>
</table>

G1 = well differentiated; G2 = moderately differentiated; G3 = poorly differentiated.
tant metastases and 2 had local and distant recurrent
disease.

Twenty patients (42.6%) are alive without evidence
disease, 1 patient is alive with tumor, and 26 patients
(55.3%) have died of their disease. The median survival
for the group as a whole was 44 months (range 5–139),
and their actuarial 5-year-survival was 29% (Figure 1).
Almost all patients achieving long-term survival (more
than 60 months) had received extensive surgical stag-
ing, optimal cytoreductive surgery and full-dosage
platin-based chemotherapy.

Univariate analysis of different prognostic factors
revealed that stage (I + II vs. III + IV), grade (G1 + G2
vs. G3), residual disease after primary surgery (less
than 2 cm vs. greater than 2 cm), peritoneal cytology
(negative vs. positive), and lymph-node metastases
were all factors significantly affecting survival (Table 3).

Discussion

Primary carcinoma of the fallopian tube is a rarely
diagnosed tumor. Most reports describe small, retro-
spective series of patients collected over several years
[10–12], and the literature does not offer valid informa-
tion regarding the distribution of prognostic factors or
the value of different treatment modalities for the dis-
ease.

In the current study, the median age of the patients
at presentation and the nulliparity rate were similar to
those in previous reports of tubal carcinoma [11, 13,
14]. Two-thirds of the patients in our study and in pre-
vious studies were postmenopausal [10, 15]. Although
the symptomatology of tubal carcinoma is not specific,
serum CA-125 determination, cytology and transvagi-
nal ultrasound might promote correct preoperative
diagnosis in early-stage disease [16].

Sixty percent of the patients in our series had ad-
vanced stage (III and IV) disease. Tubal carcinoma is
usually considered to present at an earlier stage be-
cause of abdominal pain secondary to tubal distension
[15, 17]. However, the true incidence is probably
underestimated, as many cases are incorrectly diag-
nosed as ovarian cancer [11, 12]. The observation of an
apparent increase in late-stage presentation in recent
decades may reflect improving staging techniques [18].
In the current series, as in previous studies [2–4, 10, 15,
17], when different staging systems were adopted, a
significant relation between stage and survival has been
noted.

In this report and in others in the literature [1, 10],
most of the tumors were poorly-differentiated, and
grade was significantly related to survival. In contrast to
ovarian and endometrial cancer some studies have
failed to demonstrate a correlation between histologi-
ical grade and prognosis [14, 15].

As previously reported [12, 19], in our series the
depth of tubal invasion was not prognostic of survival.
Schiller and Silverberg [4] staged patients according to
modified Duke’s colonc cancer staging that used both
depth of invasion and distant disease. More recently,
Peters et al. analyzed stage I patients and found that
depth tubal invasion was the only significant prognostic
variable [15]. Therefore, the prognostic significance of
the depth of invasion remains controversial.

Recent studies have highlighted the potential for
nodal metastases as an important factor limiting long-
term survival in patients with tubal cancer [19–21]. In
this study, 55% of patients submitted to surgical re-

![Figure 1. Overall survival of 47 patients with fallopian tube carci-
noma.](image-url)