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CLINICAL ARTICLE

Prognostic factors of primary fallopian tube cancer in a single institute in Taiwan

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ABSTRACT

Objective: To improve the understanding of primary fallopian tube carcinoma (PFTC) through an analysis of possible clinical and pathologic determinants of prognosis. *Methods:* A retrospective review of the database of a tertiary hospital in Taiwan for 1978–2007 was conducted to identify patients with a diagnosis of PFTC and to evaluate the clinicopathologic features associated with PFTC outcome. *Results:* Fifty-eight patients (mean age 62.5 years) had a diagnosis of PFTC. Stage III/IV disease (55%) and poorly differentiated tumors (52%) were most common. The median follow-up was 93 months (range, 11–333 months). The 5-year disease-free survival rate was 59%, and the overall survival rate was 64%. Factors important in disease-free and overall survival in univariate analysis included the presence of pelvic and/or para-aortic lymph node metastases, International Federation of Gynecology and Obstetrics stage, high preoperative carbohydrate antigen 125 serum level, completion of optimal debulking surgery, and the use of paclitaxel-based chemotherapy; however, only patients with optimal cytoreduction had a decreased hazard of recurrence (hazard ratio [HR] 0.06; 95% confidence interval [CI] 0.01–0.23) and mortality (HR 0.08; 95% CI, 0.02–0.31) in multivariate analysis. *Conclusion:* Advanced tumor stage, in particular the presence of lymph node metastases, worsened the prognosis of patients with PFTC. However, optimal debulking surgery significantly improved the prognosis, emphasizing the importance of the treatment strategy.

1. Introduction

Primary fallopian tube carcinoma (PFTC) is a very rare gynecologic malignancy with a reported incidence of less than 1% [1]. The most common cell type of PFTC is the serous type. The true incidence of PFTC may have been underestimated as a result of PFTC being incorrectly diagnosed as serous epithelial ovarian carcinoma (EOC) or primary peritoneal serous carcinoma during initial surgery and/or pathologic examination [2]; it is difficult to distinguish these neoplasms [2–4].

As a result of the rarity of PFTC, its optimal management is not well defined [5–9]. However, similar to EOC, PFTC tends to spread intraperitoneally, indicating that the strategy used for the management of EOC might also be appropriate in the treatment of PFTC. An adequate surgical staging and debulking procedure, such as cytology, total hysterectomy, bilateral salpingo-oophorectomy, retroperitoneal lymph node dissection, appendectomy, omentectomy, and excisional biopsy for all suspicious lesions, should be performed initially, followed by multi-agent chemotherapy [3].

In a previous study [8], we reported on 25 patients with PFTC who underwent complete staging surgery followed by multi-agent chemotherapy, but the outcome was very poor. The cumulative disease-free

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survival rate was 36%, even though nearly half (44%) of the patients were diagnosed in the early stage of PFTC and the majority of patients had received postoperative combination chemotherapy [8]. In 2011, an analysis of data from 12 patients with PFTC who were treated with surgery (complete staging surgery in 10 patients) and postoperative multi-agent chemotherapy in southern Taiwan between 1986 and 2005 showed that the 5-year disease-free survival rate was significantly improved (64%) [6]. Further improvement in the management and prognosis of PFTC was seen in a study [5] of 16 patients with PFTC who were treated between 2001 and 2011; in that study, the 5-year disease-free survival rate was over 70%.

This leads to the question of why the prognosis of patients with PFTC in more recent reports [5,6] seems to be better than that in earlier reports [7–9]. To answer this question, we searched PubMed (to November 3, 2013) using the terms "primary fallopian tube tumor" AND "Taiwan" and identified 15 published articles, five of which [5–9] focused on the outcome of patients with PFTC (Table 1). However, the interpretation of these five studies [5–9] is limited by a small number of cases. Therefore, the present study was conducted to investigate a large series of patients with PFTC in Taiwan.

2. Materials and methods

The present study included all women with a diagnosis of PFTC reported at Taipei Veterans General Hospital, Taipei, Taiwan, between January 1, 1978, and December 31, 2007; additional inclusion criteria were a serous histology and treatment with complete staging surgery followed by multi-agent chemotherapy. The study was approved by the Institutional Review Board of Taipei Veterans General Hospital (IRB: 98-11-02). Because the present study was a retrospective chart review, no informed consent was needed.

The diagnosis of PFTC was based on the criteria established by Hu et al. [10] and revised by Sedlis [11,12]: the main tumor arises from the endosalpinx, the histologic pattern reproduces the epithelium of the tubal mucosa, the transition from benign to malignant tubal epithelium is demonstrable, and the ovaries or endometrium are either normal or contain a tumor that is smaller than the tumor in the tube.

The original pathology was reviewed by a gynecologic pathologist (C-R.L.) and an independent colleague. All cases with a controversial diagnosis were excluded from the present study.

Data on the clinical course and long-term follow-up of the women were retrieved from the hospital records. Optimal debulking surgery was defined as residual disease of less than 0.5 cm in diameter. The follow-up period was calculated from the date of the initial surgery to the date of the last follow-up (October 31, 2013) or the time of death.

Cross-tabulations, descriptive statistics, and recurrence data were prepared with SAS version 9.3 (SAS Institute, Cary, NC, USA). The cut-off values for age and the preoperative serum level of carbohydrate antigen (CA) 125 were calculated using receiver operating characteristic curves. Survival curves were plotted by the Kaplan–Meier method and compared with the Mantel–Cox test, using SPSS version 20 (IBM, Amonk, NY, USA). The Mantel–Cox test was also used to select variables to be included in the log-rank analysis. $P < 0.05$ was considered statistically significant.

Table 2
Characteristics of patients with primary fallopian tube carcinoma (n = 58).[a]

Characteristic	Value
Age, y	62.5 ± 9.6
Nulliparity	4 (6.9)
Menopause at diagnosis	49 (84.5)
Symptoms	
Abdominal pain or discomfort	32 (55.2)
Watery discharge	4 (6.9)
Abnormal vaginal bleeding	4 (6.9)
Asymptomatic	18 (31.0)
FIGO stage	
Early (I/II)	26 (44.8)
Advanced (III/IV)	32 (55.2)
Preoperative serum level of CA 125, U/mL	322.9 ± 470.4
Cell grade	
Well and moderately differentiated	28 (48.3)
Poorly differentiated	30 (51.7)
Pelvic lymph node metastases	15 (25.9)
Para-aortic lymph node metastases	4 (6.9)
Retroperitoneal lymph node metastases[b]	15 (25.9)
Optimal debulking surgery	36 (62.1)
Chemotherapy cycles (<6 cycles)	6 (10.3)
Chemotherapy regimen	
Cyclophosphamide-based regimen	32 (55.2)
Paclitaxel-based regimen	26 (44.8)
Recurrence	25 (43.1)
Recurrence site	
Pelvic and abdominal cavity	19 (32.8)
Other	6 (10.3)
5-year disease-free survival	34 (58.6)
Overall survival	37 (63.8)

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; CA, carbohydrate antigen.
[a] Values are given as mean ± SD or number (percentage).
[b] Pelvic and para-aortic lymph node metastases.

3. Results

During the study period, 79 cases of PFTC were reported, 67 of which had a serous histology. Of these, 58 had complete staging surgery followed by multi-agent chemotherapy. These 58 women comprised the study sample.

The mean age of the patients was 62.5 years (range, 41–74 years). Forty-nine patients (84.5%) were postmenopausal, and 4 (6.8%) were nulliparous (Table 2). The most common clinical presentation was abdominal discomfort, fullness, and pain, followed by no symptoms and abnormal vaginal discharge or bleeding. Forty-six (79.3%) patients had an elevated serum level of CA 125 (>35 U/mL). Early-stage PFTC (International Federation of Gynecology and Obstetrics [FIGO] stage I/II) was identified in 26 (44.8%) patients. In more than half of the patients, the tumors were poorly differentiated (Table 2).

Suboptimal debulking surgery was recorded in 22 (37.9%) women, all of whom had advanced cancer; this means that 68.8% (22/32) of the women with FIGO stage III/IV tumors had suboptimal debulking surgery. Only 6 (10.3%) patients received chemotherapy of less than six cycles. Nearly half of the patients were treated with paclitaxel-based chemotherapy; the others were treated with a cyclophosphamide-based combination (Table 2).

Table 1
Studies of primary fallopian tube carcinoma in Taiwan.

Reference	No. of patients (population)	Median duration of follow-up	Most common symptom	5-year disease-free survival rate
Lau (2013) [5]	16 (all stages, all cell types)	40 months	Abdominal pain (37.5%)	73.3%
Ou (2011) [6]	12 (all stages, all cell types)	38 months	Adnexal mass (50%)	64%
Wang (1999) [7]	13 (FIGO III/IV, serous)	38 months	Abdominal pain (69%)	15%
Wang (1998) [8]	25 (all stages, serous)	89 months	Abdominal pain (48%)	36%
Wang (1998) [9]	11 (FIGO I, serous)	69 months	Symptomless (55%)	64%

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.

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