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Review Article

# Primary fallopian tube cancer: Domestic data and up-to-date review

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ABSTRACT

Primary fallopian tube carcinoma (PFTC) is a rare gynecological malignancy with the following characteristics: its preoperative diagnosis is easy to miss or delay because of a lack of specific symptoms and signs; it is difficult to distinguish from serous epithelial ovarian cancer or primary peritoneal serous carcinoma during or even after operation because they have the same histopathological features; and there is uncertainty regarding the optimal management because of the lack of available standard guidelines. All of these factors contribute to the major challenge of undertaking a comprehensive study of this disease. To improve our understanding of this rare disease, the domestic data were summarized first. We searched PubMed on this topic, using the term "primary fallopian tube tumor and Taiwan" (from January 1, 1990 to November 3, 2013) and identified 15 published articles, but only 11 studies focused on the outcome of patients with PFTC in Taiwan. These limited data were not enough to increase our knowledge in dealing with this disease; therefore, the addition of large series or published review articles addressing this topic was needed. According to these reports, we concluded: (1) the main type of PFTC was serous type, often poorly differentiated; (2) the diagnosis of PFTC is frequently missed or delayed; (3) PFTC is often of an earlier International Federation of Gynecology and Obstetrics (FIGO) stage than is epithelial ovarian cancer (EOC), because of the appearance of earlier but nonspecific symptoms or signs, such as abdominal pain, vaginal bleeding, and watery discharge or mass; (4) the most important clinicopathological prognostic factor was FIGO stage; (5) the therapeutic strategy is still uncertain, but is often based on the guidelines for treating EOC. An intensive surgical effort such as a complete surgical resection or optimal cytoreduction surgery with a minimal residual tumor followed by a platinum-paclitaxel combination chemotherapy with/without targeted therapy (for example, antiangiogenesis agents) may provide the best possibility of disease-free or overall survival.


## Introduction

Primary fallopian tube carcinoma (PFTC) is a very rare gynecologic malignancy, even though its true incidence may be

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underestimated as a result of its having the same surgical findings or pathological features as serous-type epithelial ovarian carcinoma (EOC) or primary peritoneal serous carcinoma (PPSC) [1,2]. Treatment is normally based on the same guidelines as those used for EOC, because PFTC tends to spread intraperitoneally. However, there is no doubt that the optimal management of PFTC is still uncertain, because of the rarity of the disease. Although PFTC is very similar to serous-type EOC, there are still a few differences between the two. For example, PFTC tends to recur in the retroperitoneal nodes and distant sites more than does EOC [3]. PFTC is more frequently found at an early stage, but EOC is often diagnosed at an advanced stage [1]. Abdominal pain is often found in patients with PFTC, because tubal distension may result in this nonspecific symptom [1]. The shorter history of symptoms in PFTC than in EOC allows detection at an earlier stage in patients with PFTC [4]. PFTC shows a propensity for microscopic distant metastases, compared with the macroscopic intraperitoneal metastasis of EOC [5].

Similar to EOC [6,7], complete surgical staging in early-stage [International Federation of Gynecology and Obstetrics (FIGO) stage I/II] PFTC and extensive and optimal debulking surgery in late-stage (FIGO III/IV) PFTC, including cytology, total hysterectomy, bilateral salpingo-oophorectomy, retroperitoneal lymph node dissection, appendectomy, omentectomy, and excisional biopsy for all suspicious lesions, provided the best chance of cure. However, because of the propensity of PFTC for microscopic distant metastases and the relatively high risk of recurrence despite complete tumor excision in the early stage, postoperative chemotherapy was highly recommended [8,9], although some opposed this suggestion [1].

In an earlier report [9], we found that two Stage IA patients without adjuvant chemotherapy had died of the disease: one experienced recurrence 765 days after completion of the surgery and the other, 1012 days postsurgery. Although complete and thorough surgical intervention for Stage I PFTC is important, some authors did not favor the use of postoperative adjuvant therapy, especially in Stages IA and IB disease without tumor infiltration of the serosa or without pre- or intra-operatively ruptured tumors [1]. Even so, we suggest that postoperative adjuvant chemotherapy may play a crucial role in the successful management of surgicopathological Stage I PFTA, even in Stage IA cases; especially if the tumor size is $> 2$ cm in diameter [8]. Another study included 25 patients with complete staging for PFTC, followed by multiagent chemotherapy [9]. In that report, even though 44% of patients with PFTC ($n = 11$) were early stage and more than 90% of patients ($n = 9$) received postoperative combination chemotherapy [cyclophosphamide, adriamycin, and cisplatin], the prognosis was still poor. The cumulative disease-free survival rate was only 36% [9]. Because of the poor outcomes and the rarity of PFTC, we believe it is necessary to review this topic to improve our understanding of this rare disease. We summarized all domestic data and updated the information as a reference for future management of this rare but relatively lethal disease.

## Literature review

We searched PubMed on this topic, using the term "primary fallopian tube tumor and Taiwan" (from January 1, 1990 to November 3, 2013), and identified only 15 published articles [9–23]; however, 11 studies discussed patients with PFTC in Taiwan [9–19]. In addition, only three papers showed a series of case studies [10–12], with patient numbers ranging from 12 to 25. To further update our knowledge of this rare disease, other large series were also included in this review [4,8,24–48].

The domestic data, including the three papers, were obtained from two institutions, and data from larger series of patients with PFTC ($>$ 30 patients), including published review articles, are summarized in Table 1.

## Clinical presentation

Because PFTC is often asymptomatic, a specific preoperative diagnosis is extremely difficult, and the usual clinical diagnosis is an ovarian tumor or pelvic inflammatory disease (PID) [1]. The most common symptoms and signs are abdominal pain, which may be colicky as a result of forced tubal peristalsis or dull as a result of tubal distension, and vaginal bleeding or watery discharge [1]. These symptoms or signs might allow for an earlier stage of PFTC to be diagnosed. In addition, in patients who complain of lower abdominal pain in association with vaginal bleeding and/or watery discharge (16.7%) or tubo-ovarian abscess (25%), the possibility of PFTC should be considered [11]. However, the incidence of PID is definitely far higher than that of PFTC, and PID is a medical illness usually treated conservatively with antibiotics, not surgery [49,50].

The domestic data (Table 1) showed that although abdominal pain might be one of the most frequently noted symptoms ($>$ 50%), fewer than 50% of all patients with PFTC were found at an earlier stage (FIGO I/II) [9]. By contrast, abdominal pain, vaginal bleeding or discharge, or even a pelvic mass seemed to be similarly frequently reported in studies from Western countries (Table 1), but in more than 50% of patients with PFTC the diagnosis was made at an earlier stage (FIGO I/II). The Latzko triad of symptoms, including an intermittent, profuse, serosanguinous vaginal discharge, a colicky pain, often relieved by the discharge, and abdominal or pelvic masses, has been reported in $\leq$ 15% of patients with PFTC [1].

An early cervicovaginal cytological diagnosis in cases of silent PFTC is a more difficult issue [51], although cervicovaginal smears might reveal cases of otherwise unsuspected PFTC. The anatomical site of PFTC allows an early diagnosis by cervicovaginal smear, because the malignant cells, which may exfoliate from the primary tumors, migrate through the fallopian tube and are deposited in the vaginal pouch or cervix canal. Some characteristic features of cervicovaginal smears might suggest the possibility of PFTC; these include the clean background, which disappears when liquid-based cytology is used, the small number of malignant cells, and the papillary grouping of overlapped neoplastic cells [52]. Moreover, the lack of tumor diathesis appears to be an intriguing and almost constant, although nonspecific, finding [50].

## Imaging evaluation

Imaging routinely carried out for any suspicious gynecologic cancers includes ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) [53]. PFTC is difficult to diagnose radiologically, and most cases are preoperatively diagnosed as ovarian carcinomas [54]. Several single case reports in the literature [55,56], including ours [17], describe the ultrasound, CT, and MRI findings of PFTC.

Ultrasound is an essential imaging technique in the diagnostic workup of patients with gynecological lesions, including PFTC. Anechoic or low-level echoes with papillary projections or intraluminal masses revealed on ultrasound is an indication of PFTC; however, most of the echographic appearances of the fallopian tube are nonspecific, mimicking other pelvic diseases such as tubo-ovarian abscess, ovarian tumor, and ectopic pregnancy [53]. The appearance of PFTC is usually based on the dominant component—the solid tumor or the hydrosalpinx, which may be altered with serial imaging, reflecting the change in the amount of serous fluid within the tube. The former appears as a sausage-shaped adnexal mass and the latter appears as a fluid-filled tubular adnexa structure, containing nodular or papillary solid components, or a multilocular cystic mass with a cog-and-wheel appearance [57].