Original Article

# Recurrence Rate and Associated Factors of Primary Fallopian Tube Carcinoma in the South of Vietnam

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## Abstract

**Objectives:** This study aimed to determine the recurrence rate and related risk factors of primary fallopian tube cancer (PFTC).
**Materials and Methods:** We conducted a retrospective study of 47 patients with histopathological diagnosis of PFTC treated at Tu Du Hospital between January 1, 2015, and July 31, 2022. The cumulative recurrence rate was estimated using the life table method, and recurrence-associated factors were determined using the Log–rank test and Cox proportional hazard model.
**Results:** The median follow-up period was 40 months (range, 7–96 months). Eight patients (17.0%) experienced recurrence. The cumulative recurrence rate of PFTC patients at 12 months was 4.4% (95% confidence interval [95% CI]: 1.12–16.45), at 24 months was 9.1% (95% CI: 3.52–22.5), at 36 months was 14.9% (95% CI: 6.92–30.41), at 48 months was 19.3% (95% CI: 9.35–37.24), and at 60 months was 25.7% (95% CI: 12.68–47.88). A higher recurrence rate was significantly associated with elevated pretreatment CA 125 level (<35 U/mL vs. ≥35 U/mL, hazards ratio [HR] = 36.9, 95% CI: 1.47–921.37), advanced FIGO stages (Stage I-II vs. stages III, HR = 6.61, 95% CI: 1.18–36.93), and suboptimal debulking surgery (residual disease ≤1 cm vs. residual disease >1 cm, HR = 7.52, 95% CI: 1.47–38.49).
**Conclusion:** The overall recurrence rate of PFTC patients in Southern Vietnam was 17.0%. Appropriate follow-up strategies for patients with high-risk factors are needed for early detection and management of recurrence.

**Keywords:** Cancer of the fallopian tube, hazard ratio, recurrence rate, risk factors

## Introduction

Primary fallopian tube cancer (PFTC) is a rare gynecological cancer, accounting for only 0.14%–1.8% of malignant tumors in the female genital tract.[1] However, epidemiological studies in the past decades have shown an increasing trend in its incidence. In Finland, for instance, the incidence rate increased 4.5 times between 1953 and 1997.[1] Similarly, data from the US National Cancer Institute showed a 4.2-fold increase from 2001 to 2014, with about 300–400 cases reported annually.[2] Although the pathogenesis of PFTC is still not well-understood, recent studies from histology, molecular biology, and genetics suggest that most tumors classified as high-grade pelvic serous carcinomas may originate from the fallopian tubes.[3,4] Therefore, the incidence rate of PFTC may have been underestimated.

While the management of PFTC is generally similar to that of epithelial ovarian cancer (EOC), there is growing evidence to suggest that PFTC is biologically distinct from EOC. PFTC has a higher tendency for microscopic distant metastasis, significantly increasing the risk of recurrence. The recurrence rate of PFTC has been reported to range from

*Article History:*
**Submitted:** 17-Sep-2023
**Revised:** 07-Dec-2023
**Accepted:** 09-Jan-2024
**Published:** 07-Sep-2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/gmit

DOI: 10.4103/gmit.gmit_110_23

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**How to cite this article:** Vo T, Nguyen D, Ho T, Tran H, Nguyen D, Bui T, *et al*. Recurrence rate and associated factors of primary fallopian tube carcinoma in the South of Vietnam. Gynecol Minim Invasive Ther 2024;13:247-52.

31.3% to 64.6%,[5-10] with most recurrences occurring within 3 years after initial treatment and being associated with a poor prognosis.[11] The increasing incidence, high recurrence rates, along with poor prognosis, highlight the critical need to identify factors associated with PFTC recurrence. The identification of such factors would help in providing patients with informed counseling and planning effective treatment strategies to improve clinical outcomes. Nevertheless, factors related to the recurrence of PFTC remain controversial.

Located in Ho Chi Minh City, TuDu Hospital is the largest national-level obstetrics and gynecology hospital in southern Vietnam. The number of PFTC patients diagnosed annually at Tu Du Hospital has been increasing in recent years, with 6 cases in 2015 and 13 cases recorded in 2020. In Southeast Asia, especially in Vietnam, there have been almost no studies on the recurrence rate and related factors of PFTC. The present study aims to determine the recurrence rate and related risk factors of PFTC at TuDu Hospital.

## Materials and Methods

We conducted a retrospective study of patients with PFTC treated at the Gynecological Oncology Department of Tu Du Hospital in Ho Chi Minh City, Vietnam, between January 1, 2015, and July 31, 2022. Patients with histopathological confirmation of PFTC were eligible for the study. Cases were identified following Sedlis diagnostic criteria.[12] Exclusion criteria were secondary fallopian tube carcinoma, low malignant potential tumors, or those who had undergone neoadjuvant chemotherapy. We obtained basic demographic information and clinicopathological data from the medical records. Staging information was derived from surgical notes and pathological reports and was based on the 2009 International Federation for Gynecology and Obstetrics (FIGO) criteria. Histological evaluation was based on the World Health Organization classification of malignant epithelial fallopian tube carcinoma. Suboptimal debulking surgery was defined as residual disease ≤1 cm.

The recurrence of PFTC was defined as cases that had histopathological diagnosis of PFTC were surgically treated, discharged with completed response, and then experienced one of the following: (i) a recurrent increase in CA 125 level according to Rustin's standards,[13] (ii) clinical examination or imaging findings of recurrence disease, or (iii) by histopathological confirmation if the recurrence was surgically treated. Rustin's standards for recurrence based on CA 125 concentration were defined: (i) CA 125 > 2 times the upper normal limit on two occasions at least 1 week apart (in patients with CA 125 in the normal range before treatment, or in patients with elevated CA 125 pretreatment that returned to normal after treatment) or (ii) CA 125 > 2 times the nadir value on two occasions at least 1 week apart (in patients with elevated CA 125 before treatment that never normalizes). At TuDu Hospital, after treatment for PFTC, patients were followed once a month for the first 6 months, once every 2 months for the next 12 months, once every 3 months for the next 18 months, once every 6 months for the next 24 months (i.e., the end of 5 years after treatment), and then once a year. Follow-up information was updated until March 2023, based on a review of medical records and/or telephone contact. Time to recurrence (in months) was defined as the time from treatment completion of PFTC to the time of diagnosed recurrence. The overall follow-up time for nonrecurrences was from the time of treatment completion of PFTC to the time of last follow-up, end of study, or death. Our study was conducted in accordance with the Declaration of Helsinki and was approved by Tu Du hospital's ethics committee (No. 2223/BVTD HDDD November 8, 2022). Informed consent forms were waived because this is retrospective study. Patients' information was not identifiable. Applying sample size formula in survival analysis with HR (hazard ratio) = 9.8 (as per the precedent study by Shamshirsaz *et al*. in 2011), $\alpha = 0.05$, and $1-\beta = 0.90$, the sample size was calculated to be $n = 25$ PFTC cases. The minimal sample size for the recurrent case was 5.

The data were analyzed using Stata 14.2 (StataCorp). Descriptive analyses, including percentages and medians, were performed to examine demographic and clinicopathological characteristics. To investigate the relationship between categorical characteristics and recurrence time, we performed univariate analyses using the log-rank test of equality. We then used Cox proportional hazard regression for multivariate analyses to adjust for potential confounding factors. Variables included in the multivariate models were selected based on their bivariate associations ($P < 0.25$) and prior knowledge. $P < 0.05$ was considered statistically significant.

## Results

During the study period, 56 patients with PFTC were identified. Nine patients were lost to follow-up after surgery, accounting for 16.1% of all included patients [Table 1]. Among the 47 remaining patients, the median age at diagnosis was 54 years (range, 28–72 years). Twenty-seven patients (57.5%) were postmenopausal, and 5 (10.6%) were nulliparous. Preoperative CA125 values were ≥35 U/mL in 25/47 (53.2%) of cases. No bilateral tumors were identified, and in the majority of cases (61.7%), the disease originated on the left side. The main histological subtype was the endometrioid carcinoma (57.5%, 27/47), followed by serous carcinoma (27.7%, 13/47), undifferentiated carcinoma (12.8%, 6/47), and carcinosarcoma (2.1%, 1/47). Forty-five (95.7%) were high grade. According to the 2009 FIGO staging, there were 25 cases (53.2%) were in Stage I, 16 cases (34.0%) were in Stage II, 6 cases (12.8%) were in Stage III, and none were in Stage IV.

Surgery was the initial therapy for all 47 patients. Total hysterectomy with bilateral salpingo-oophorectomy was performed as the initial surgery for all patients, additional omentectomy in 44/47 (93.6%) cases (metastasis detected in 3 cases), pelvic lymphadenectomy in 8/47 cases (17.0%) (metastasis detected in 4 cases), para-aortic

**Table 1: Clinical and histopathologic characteristics of patients with primary fallopian tube carcinoma**

| Characteristics | Total, *n* (%) | Nonrecurrence (*n*=39), *n* (%) | Recurrence (*n*=8), *n* (%) | *P** |
|---|---|---|---|---|
| Age at diagnosis (year old) | | | | |
| <60 | 37 | 30 (81.1) | 7 (19.9) | 0.487 |
| ≥60 | 10 | 9 (90.0) | 1 (10.0) | |
| Postmenopausal period (years) | | | | |
| <10 | 35 | 29 (82.9) | 6 (17.1) | 0.936 |
| ≥10 | 12 | 10 (83.3) | 2 (16.7) | |
| Pretreatment CA125 level (U/mL) | | | | |
| <35 | 22 | 21 (95.5) | 1 (4.5) | 0.039 |
| ≥35 | 25 | 18 (72.0) | 7 (28.0) | |
| Ascites | | | | |
| No | 33 | 28 (84.8) | 5 (15.2) | 0.374 |
| Yes | 14 | 11 (78.6) | 3 (11.4) | |
| Tumor side | | | | |
| Left side | 29 | 24 (82.8) | 5 (17.2) | 0.713 |
| Right side | 18 | 15 (83.3) | 3 (16.7) | |
| Tumor diameter (mm) | | | | |
| <50 | 9 | 8 (88.9) | 1 (11.1) | 0.142 |
| 50–99 | 35 | 29 (82.9) | 6 (17.1) | |
| ≥100 | 3 | 2 (66.7) | 1 (33.3) | |
| Tumor rupture | | | | |
| No | 42 | 36 (85.7) | 6 (24.3) | 0.193 |
| Yes | 5 | 3 (60.0) | 2 (40.0) | |
| Omentectomy | | | | |
| No | 3 | 2 (66.7) | 1 (33.3) | 0.759 |
| Yes | 44 | 37 (84.1) | 7 (15.9) | |
| Lymphadenectomy | | | | |
| No | 42 | 35 (83.3) | 7 (16.7) | |
| Yes | 5 | 4 (80.0) | 1 (20.0) | |
| Debulking | | | | |
| Optimal | 41 | 37 (90.2) | 4 (9.8) | 0.001 |
| Suboptimal | 6 | 2 (33.3) | 4 (66.7) | |
| Histologic subtype | | | | |
| Serous | 13 | 12 (92.3) | 1 (7.7) | 0.510 |
| Endometrioid | 27 | 22 (81.4) | 5 (18.6) | |
| Other | 7 | 5 (71.0) | 2 (28.6) | |
| FIGO stage | | | | |
| I–II | 41 | 36 (87.8) | 5 (12.2) | 0.004 |
| III | 6 | 3 (50.0) | 3 (50.0) | |
| Cycles of chemotherapy | | | | |
| ≤6** | 33 | 28 (84.8) | 5 (15.2) | 0.761 |
| 8 | 14 | 11 (78.6) | 3 (21.4) | |

**P*-value from log-rank test results, **One patient without receiving adjuvant chemotherapy. FIGO: International federation for gynecology and obstetrics

lymphadenectomy in 2/47 cases (4.2%) (metastasis detected in 1 case), and appendectomy in 1 case (no metastasis was found). Forty-one patients (87.2%) underwent complete resection of the tumor, with residual disease no larger than 1 cm. After surgery, 97.9% of patients received adjuvant chemotherapy, which was carboplatin and paclitaxel in all cases. Among them, 69.6% received 6 cycles of chemotherapy, while 30.4% received 8 cycles. Only one patient in stage IA, low-grade serous carcinoma, did not receive adjuvant chemotherapy.

The median follow-up period was 40 months (range, 7–96 months). Eight patients (17.0%) experienced recurrence after a median of 25 months (range, 10–57 months). The recurrence involved the pelvis ($n$ = 2, 25%), retroperitoneal nodes ($n$ = 3, 37.5%), both pelvis and retroperitoneal nodes ($n$ = 2, 25%), and distant sites ($n$ = 1, cervical nodes, 12.5%). At the last follow-up (March 2023), 43/47 (91.4%) patients were alive without evidence of disease, 2/47 (4.3%) were alive with disease, and 2/47 (4.3%) died of disease. The cumulative recurrence rates of PFTC at 12, 24, 36, 48, and 60 months were 4.4%, 9.1%, 14.9%, 19.3%, and 25.7%, respectively [Table 2].

The overall incidence rate was 0.004 person-months (95% confidence interval [CI]: 0.002–0.008). In the preliminary

bivariate analyses and the final multivariate model [Table 3], a higher recurrence rate was significantly associated with elevated pretreatment CA 125 level (<35 U/mL vs. ≥35 U/mL, HR = 36.9, 95% CI: 1.47–921.37), advanced FIGO stages (Stage I-II vs. stages III, HR = 6.61, 95% CI: 1.18–36.93), and suboptimal debulking surgery (residual disease ≤1 cm vs. residual disease >1 cm, HR = 7.52, 95% CI: 1.47–38.49).

## Discussion

In our study, the median follow-up period was 40 months (range, 7–96 months), during which eight recurrences were observed, resulting in an overall recurrence rate of 17.0%. Our study's overall recurrence rate is lower than that reported in previous studies (ranging from 31.3% to 64.6%).[5-10] At the 60-month (5-year) mark, the cumulative recurrence rate in our study was 25.7%, which is similar to the rate reported by Lau *et al*. (26.7%). However, it is still lower than the rates reported in other studies (ranging from 32.7% to 54.8%).[5,6,8-10] These variations between studies may be explained by differences in follow-up duration, the proportion of Stage III-IV patients, and the proportion of patients who underwent optimal debulking surgery, as these are important prognostic factors for PFTC recurrence. Moreover, we noted that 9/56 patients (16.1%) were lost to follow-up in our study, and therefore the actual recurrence rate may be underestimated.

The literature reports that the most common age for PFTC is between 40 and 65 years (with a mean age of 55 years), mostly.[14] Most cases are diagnosed in postmenopausal women and at early stages (Stage I-II) due to the high frequency of symptoms.[15] Histologically, most cases are high grade and serous carcinoma is the most common histological type, accounting for 45%–90% of cases, followed by endometrioid carcinoma and other rare types.[14] Our study supports these findings, with a median age of 54 years (range, 28–72 years), the majority of cases (58.9%) occurring in postmenopausal women, early stages (87.2% with stage I-II), and high grade (94.6%). However, we observed that endometrioid carcinoma is the most common histological type, comprising 58.9% of cases, followed by serous carcinoma (28.6%), undifferentiated carcinoma (10.7%), and carcinosarcoma (1.8%). This suggests that there may be variations in the pathological features of PFTC tumors that were not examined in our study.

In terms of recurrence-associated factors, our study revealed that elevated pretreatment CA 125 level, advanced FIGO stages, and suboptimal debulking surgery were consistently associated with PFTC recurrence. We found that 53.6% of patients had CA 125 levels ≥35 U/mL before surgery, and these levels increased gradually with the stage of the disease, with higher levels in later stages (data not shown). Patients with CA 125 levels ≥35 U/mL before surgery had a 36.9-fold increased risk of recurrence (95% CI: 1.47–921.37) compared to those with CA 125 <35 U/mL. This is in line with previous studies, such as Hefler *et al*. (HR = 2.26, 95% CI: 1.2–3.4)[16] and Shamshirsa *et al*.(HR = 5.31, 95% CI: 1.18–23.93).[17] Our findings are also consistent with many previous studies that have shown advanced FIGO stages and suboptimal debulking surgery are significant prognostic factors for PFTC recurrence.[8,18,19] Overall, these findings emphasize the importance of early detection and effective surgical management of PFTC to improve outcomes and reduce the risk of recurrence.

The role of systematic pelvic and para-aortic lymphadenectomy in the prognosis of PFTC patients is still controversial, despite the strong tendency for lymphatic spread of PFTC. Variations in the surgical approach to lymphadenectomy for PFTC are commonly observed across different institutions and surgeons. Some studies have shown that the 5-year overall survival and 5-year disease-free survival for lymphadenectomy group were significantly higher than that of the group without lymphadenectomy.[19,20] However, most other studies failed to identify a correlation between better prognosis and routine lymphadenectomy.[8,21] In our study, the analysis found no significant difference between this factor and risk of recurrence.

All other factors studied in our research, including age, postmenopausal status, presence of ascites, tumor side, tumor rupture, tumor diameter, histological type, histological grading, and cycles of chemotherapy, showed no significant influence on disease recurrence. These findings are consistent with previous reports in the literature.[19]

**Table 2: Cumulative risk of having primary fallopian tube carcinoma recurrence**

| Month interval | Number of nonrecurrences | Number of recurrences | Number of censored cases | Estimated cumulative risk of recurrences, % (95% CI) |
|---|---|---|---|---|
| 0–12 | 47 | 2 | 3 | 4.4 (1.12–16.45) |
| 12–24 | 42 | 2 | 3 | 9.1 (3.52–22.53) |
| 24–26 | 37 | 2 | 11 | 14.9 (6.92–30.41) |
| 36–48 | 24 | 1 | 9 | 19.3 (9.35–37.24) |
| 48–60 | 14 | 1 | 3 | 25.7 (12.68–47.88) |
| 60–72 | 10 | 0 | 5 | 25.7 (12.68–47.88) |
| 72–84 | 5 | 0 | 4 | 25.7 (12.68–47.88) |
| 84–96 | 1 | 0 | 1 | 25.7 (12.68–47.88) |

CI: Confidence interval

**Table 3: Risk factors for the recurrence of primary fallopian tube carcinoma**

| Factors | Risk time (months) | Recurrence ($n=8$) | | Cox proportional hazards regression, HR (95% CI) | | | |
|---|---|---|---|---|---|---|---|
| | | *n*/ total | Incidence rate (person/1000 months) | Univariate analysis | *P** | Multivariate analysis | *P*** |
| Age at diagnosis (year old) | | | | | | | |
| <60 | 1452 | 7/37 | 4.82 | 1 (reference) | | | |
| ≥60 | 441 | 1/10 | 2.26 | 0.48 (0.06–3.95) | 0.498 | | |
| Postmenopausal period (years) | | | | | | | |
| <10 | 1382 | 6/35 | 1.53 | 1 (reference) | | | |
| ≥10 | 511 | 2/12 | 3.91 | 0.93 (0.19–4.47) | 0.936 | | |
| Pretreatment CA125 level (U/mL) | | | | | | | |
| <35 | 939 | 1/22 | 1.06 | 1 (reference) | | 1 | |
| ≥35 | 954 | 7/35 | 7.34 | 6.69 (0.82–54.7) | 0.076 | 36.9 (1.4–92.3) | 0.028 |
| Ascites | | | | | | | |
| No | 1435 | 5/33 | 3.48 | 1 (reference) | | | |
| Yes | 458 | 3/14 | 6.55 | 1.89 (0.45–7.99) | 0.383 | | |
| Tumor side | | | | | | | |
| Left side | 1307 | 5/29 | 3.83 | 1 (reference) | | | |
| Right side | 586 | 3/18 | 5.12 | 1.31 (0.30–5.74) | 0.714 | | |
| Tumor diameter (mm) | | | | | | | |
| <50 | 335 | 1/9 | 5.39 | 1 (reference) | | | |
| 50–99 | 1463 | 6/35 | 2.52 | 1.45 (0.16–11.29) | 0.790 | | |
| ≥100 | 95 | 1/3 | 13.79 | 4.57 (0.19–52.64) | 0.416 | | |
| Tumor rupture | | | | | | | |
| No | 1703 | 6/42 | 3.52 | 1 (reference) | | 1 | |
| Yes | 190 | 2/5 | 10.12 | 2.76 (0.56–13.75) | 0.214 | 6.39 (0.64–63.84) | 0.114 |
| Omentectomy | | | | | | | |
| No | 180 | 1/3 | 5.56 | 1 (reference) | | | |
| Yes | 1713 | 7/44 | 4.09 | 0.72 (0.09–5.95) | 0.761 | | |
| Lymphadenectomy | | | | | | | |
| No | 1639 | 7/42 | 3.76 | 1 (reference) | | | |
| Yes | 254 | 1/5 | 6.69 | 1.73 (0.34–8.74) | 0.508 | | |
| Debulking | | | | | | | |
| Optimal | 1694 | 4/41 | 2.36 | 1 (reference) | | 1 | |
| Suboptimal | 199 | 4/6 | 20.1 | 7.48 (1.85–30.13) | 0.005 | 7.52 (1.47–38.49) | 0.015 |
| Histologic subtype | | | | | | | |
| Serous | 327 | 1/13 | 3.06 | 1 (reference) | | | |
| Endometrioid | 1332 | 5/27 | 3.75 | 1.22 (0.14–10.90) | 0.858 | | |
| Other | 234 | 2/7 | 8.55 | 2.97 (0.2–33.10) | 0.376 | | |
| FIGO stage | | | | | | | |
| I–II | 1731 | 5/41 | 2.89 | 1 (reference) | | 1 | |
| III | 162 | 3/6 | 18.52 | 6.64 (1.4–39.09) | 0.014 | 6.61 (1.18–36.93) | 0.031 |
| Cycles of chemotherapy | | | | | | | |
| ≤6 | 1094 | 5/33 | 4.57 | 1 (Reference) | | | |
| 8 | 799 | 3/14 | 3.75 | 0.79 (0.18–3.56) | 0.762 | | |

*$P$-value of univariate analysis, **$P$-value of multivariate analysis. CI: Confidence interval, HR: Hazard ratio, FIGO: International federation for gynecology and obstetrics

## Limitations of the study

Our study had some limitations. First, it had a retrospective cohort design with a small sample size and only 8 recurrences, which limited the statistical power for subgroup analyses. Second, due to the retrospective nature of the study, several variables about patients' characteristics and behaviors were not available for analyses. Prospective studies with multiple participation are needed to generate stronger evidence regarding risk factors of PFTC recurrence. Third, the merit of this article is to give the data on fallopian tube cancer in Vietnam in one hospital. This paper may be useful Vietnamese population but may not be suitable for worldwide population. No new intervention was performed.

## Conclusions

Our study found that the overall recurrence rate of PFTC patients in southern Vietnam was moderate (17.0%). Elevated

pretreatment CA 125 level, advanced FIGO stages, and suboptimal debulking surgery were main factors associated with recurrence. Appropriate follow-up strategies (e.g., more regular follow-ups for up to 5 years) are needed for patients with high-risk factors to enable early detection and management of recurrence.

## Author contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Acknowledgment

We are indebted to the participants for making this research possible and to all physicians and staff of the Oncological Gynecology unit of TuDu hospital.

## Data availability statement

Data are available upon request to the corresponding author.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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