Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2023**; 50(4): 72
https://doi.org/10.31083/j.ceog5004072

Original Research

Association between Serum hCG Level and Persistent Trophoblasts after Laparoscopic Surgery for Tubal Ectopic Pregnancy: A Retrospective Study

Michiko Honda[1], Wataru Isono[1,*], Akira Tsuchiya[1], Asuka Okamura[1], Ako Saito[1], Hiroko Tsuchiya[1], Reiko Matsuyama[1], Akihisa Fujimoto[1], Osamu Nishii[1]

[1]Department of Obstetrics and Gynecology, University Hospital Mizonokuchi, Teikyo University School of Medicine, 213-8507 Kanagawa, Japan
*Correspondence: tetuken2010@gmail.com (Wataru Isono)

Academic Editor: Andrea Tinelli
Submitted: 12 December 2022 Revised: 5 January 2023 Accepted: 30 January 2023 Published: 14 April 2023

Abstract

Background: The use of laparoscopic salpingostomy to treat tubal ectopic pregnancy (TEP) is increasing due to patient preference for subsequent spontaneous pregnancy. However, the incidence of persistent trophoblasts (PT) ranges from 5–29%, although PT rarely occurs after laparoscopic salpingectomy. For this reason, the selection of laparoscopic salpingostomy should be performed carefully. Here, we aimed to identify the risk factors for PT, focusing on serum hCG levels. **Methods**: We reviewed the medical records of 128 patients who underwent laparoscopic surgeries for TEP, including 62 with laparoscopic salpingostomy and 66 with laparoscopic salpingectomy. Among these cases, we identified 13 with PT detected during the postoperative follow-up period. We performed a multivariate logistic regression analysis to assess the influence of each representative factor, particularly serum hCG levels, on the occurrence of PT. We first performed this analysis for 62 cases with laparoscopic salpingostomy and then for all 128 cases. Additionally, we focused on the reduction rates of serum hCG levels after surgery. Based on the scatter plot of the association between the reduction rates and elapsed time after surgery, we tried to create linear regression lines for estimating the appropriate postoperative follow-up period. **Results**: In the multivariate analyses of the 62 cases with laparoscopic salpingostomy, "high hCG", including serum hCG levels of 2000 and 4000 mIU/mL, showed significance. These results were also detected in the analysis of all 128 cases. Next, we obtained the regression lines based on the scatter plots of the association between reduction rates of serum hCG levels and elapsed time after surgery. By referring to the slopes of the regression lines, we could predict 37 and 30 days as the necessary time for serum hCG levels to decrease to one-thousandth in the cases with laparoscopic salpingostomy and salpingectomy. **Conclusions**: Our evaluation of the association between serum hCG level and PT allows us to provide the selection criteria, namely, serum hCG levels over 2000 and 4000 mIU/mL, for laparoscopic salpingostomy. Additionally, our analysis of the association between the reduction rates of serum hCG levels and the elapsed time after surgery allows us to predict the appropriate length for the postoperative follow-up period.

Keywords: tubal ectopic pregnancy; persistent trophoblasts; laparoscopic salpingostomy; laparoscopic salpingectomy; serum hCG level; multivariate analysis; retrospective study

1. Introduction

The incidence of tubal ectopic pregnancy (TEP) is approximately 2% [1,2]. In addition to other fallopian tube-related factors, infertility treatment can increase the risk of TEP [3], and the possibility of encountering TEP in the clinic has been increasing. Recently, laparoscopic surgery, mainly salpingectomy and salpingostomy, has become the gold standard treatment for TEP due to its cost-effectiveness [4]. The choice between these two methods for primary TEP tends to be determined on the basis of both the findings obtained during surgery, such as tubal damage, and the patient's situation, including her parity and future fertility expectations [5]. Some reports have recommended laparoscopic salpingostomy for patients who are unwilling to consider assisted reproductive technology (ART) [5], and recently, the safety of laparoscopic salpingostomy has been verified [6]. The early and accurate diagnosis of TEP before tubal rupture with the combination of imaging by transvaginal ultrasound (TVUS) and the measurement of serum human chorionic gonadotropin (hCG) levels [4,7] has also contributed to this trend. Additional promising markers have also been developed [8]. However, other reports have concluded that post-surgical fertility is not different when cases of ART are included [9,10]. The incidence of persistent trophoblasts (PT) after laparoscopic salpingostomy is thought to be approximately 5–29% [11–14], and the risk of recurrent ectopic pregnancy (REP) increases [15]. Among these two problems, PT is treated as a surgical failure because PT is usually detected within one month after the operation [14] and requires long-term treatment periods. Additionally, according to some reports, the decline in serum hCG levels is slower in patients with PT [12], but the relationship between serum hCG levels and the risk of PT has not been elucidated. Therefore, in this study, after compar-

ing the clinical outcomes of these two operation methods, we aimed to identify the risk factors for PT to provide criteria for selecting laparoscopic salpingostomy or salpingectomy. In particular, because serum hCG levels have been examined many times for both diagnosis and postoperative follow-up in our hospital, we focused mainly on the association between PT and serum hCG levels.

2. Materials and Methods

2.1 Data Collection

This study was reviewed and approved by the Human Ethical Committee of the University of Teikyo Hospital (trial registration number: 20-094). The deidentified medical records of 150 female patients who underwent laparoscopic surgeries, performed after obtaining informed consent, from June 1, 2015 to December 31, 2021, were reviewed retrospectively. In total, 22 cases were excluded for the following reasons: peritoneal ectopic pregnancy (9 cases), miscarriage from the fallopian tube (8 cases), no detection of pregnancy tissue (3 cases), ovarian ectopic pregnancy (1 case) and uterine horn pregnancy (1 case). Since there were relatively few patients in our hospital whose first choice was treatment with intramuscular methotrexate injection (IMI), we did not analyse these cases. We extracted data on representative patient characteristics, such as age, delivery history, presenting symptoms, and physical data, from medical records. In particular, in all patients, serum hCG levels were examined several times, including before and after surgery, and we extracted these data. To evaluate the failure rates of laparoscopic surgeries, we extracted the data on PT (13 cases), in which patients were diagnosed per rising or plateauing serum hCG levels postoperatively and needed to be treated by IMI.

2.2 Laparoscopic Salpingostomy Procedure

The basic procedures of laparoscopic salpingostomy were performed according to the following steps: (1) an umbilical trocar (12 mm) and three lower abdominal trocars (5 mm) were placed in a diamond pattern trocar conformation to access the abdominal and pelvic cavities; (2) diluted vasopressin was injected, and a horizontal incision was made over the ectopic gestation using an ultrasonic scalpel; (3) the products of conception were picked up into a 200-mL MemoBag™ and removed from the umbilical trocar; (4) trophoblastic tissue was verified macroscopically; and (5) the abdominal cavity was washed out with saline.

2.3 Analysis Methods

First, to compare the rates of PT between laparoscopic salpingostomy and salpingectomy, we divided the patients into two groups according to these treatment methods. In our hospital, the choice between these two methods depended largely on the patient's situation, and the numbers were approximately equal. In only 6 cases, tubal pregnancy rupture was detected during surgery. In these two groups, we compared the 19 indexes shown in Table 1 by using Student's *t*-test, Pearson's chi-square test and the Mann–Whitney U test. By referring to a previous study evaluating the influence of the ratio of serum hCG levels before and after laparoscopic salpingostomy on the possibility of PT [12], we also compared this index ("hCG ratio" in Table 1). Second, we tried to evaluate the risk factors for PT, especially to detect the predictive values of preoperative serum hCG levels. Then, four approximate cut-off values were used for serum hCG levels: 2000, 4000, 6000 and 8000 mIU/mL. For each of these four parameters, we performed similar analyses. We first analysed the 62 patients who underwent laparoscopic salpingostomy and then analysed all 128 patients. To control for confounding factors, we divided the patients into two groups according to the presence or absence of each factor and performed multivariate logistic regression analysis. In this analysis, we assessed the influence of the following 14 factors, which were seemed to be related to the conditions of patients and the difficulty of operations: (1) Advanced age, defined as an age $\geq$38 years; (2) High body mass index (BMI), defined as a BMI $\geq$25 (kg/m^2); (3) Nulliparity, defined as no previous delivery; (4) Embryo transfer, defined as cases in which the patients became pregnant after embryo transfer; (5) Abnormal bleeding, defined as patients with abnormal vaginal bleeding caused by TEP; (6) Abdominal pain, defined as patients with abdominal pain caused by TEP; (7) Pelvic haematoma, defined as cases in which pelvic haematoma was detected by TVUS before surgery or during surgery; (8) Foetal heartbeat, defined as cases in which foetal heartbeat was detected by TVUS; (9) Isthmic tubal pregnancy, defined as cases in which isthmic tubal pregnancy was diagnosed during surgery; (10) Abdominal adhesion, defined as abdominal adhesion detected by laparoscopic inspection immediately after the start of surgery; (11) Salpingostomy; (12) High hCG, defined as a serum hCG level $\geq$2000, 4000, 6000, or 8000 mIU/mL; (13) Coexistent leiomyoma, defined as leiomyoma detected by laparoscopic inspection; and (14) Coexistent endometriosis, defined as endometriosis detected by laparoscopic inspection. Since the average age of the patients was 33.4 $\pm$ 4.8 years and since over 40% of the included patients became pregnant after infertility treatments, "Advanced age" was defined as patients aged 38 years or older with reference to a previous report [16]. Statistical analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and JMP version 12 for Windows (SAS Institute, Inc., Tokyo, Japan) to determine the correlations between patient characteristics and the failure of laparoscopic surgery. The odds ratios (ORs) and 95% confidence intervals (CIs) were estimated to determine the strengths of the correlations. $p < 0.05$ was considered statistically significant.

Table 1. Comparison of patient characteristics between laparoscopic salpingostomy and salpingectomy.

	Total	Salpingostomy (n = 62)	Salpingectomy (n = 66)	*p* value
Age	33.4 ± 4.8 (20–44, n = 128)	32.0 ± 4.5 (20–43, n = 62)	34.8 ± 4.7 (22–44, n = 66)	<0.01
BMI	21.3 ± 2.8 (17.1–29.9, n = 128)	21.3 ± 2.9 (17.2–29.9, n = 62)	21.3 ± 2.7 (17.1–28.4, n = 66)	NS
Blood loss	126.4 ± 237.5 (0–1334, n = 128)	104.5 ± 229.3 (0–1334, n = 62)	147.0 ± 245.0 (0–1200, n = 66)	NS
Operation time	54.1 ± 20.1 (25–144, n = 128)	48.6 ± 12.3 (31–100, n = 62)	59.3 ± 24.2 (25–144, n = 66)	<0.01
Treatment period	32.4 ± 17.9 (9–110, n = 128)	37.2 ± 22.4 (9–110, n = 62)	27.8 ± 10.3 (10–66, n = 66)	<0.01
Average hCG	6528.1 ± 11513.8 (2.9–91673.2, n = 128)	3477.4 ± 3493.0 (2.9–18550.1, n = 62)	9393.8 ± 15177.3 (126.2–91673.2, n = 66)	<0.01
Median hCG	2879.5	2117	4093.4	<0.05
hCG ratio	0.38 ± 0.16 (0.10–1.18, n = 121)	0.41 ± 0.18 (0.11–1.18, n = 59)	0.35 ± 0.13 (0.10–0.94, n = 62)	NS
Embryo transfer	23.4% (n = 30/128)	3.2% (n = 2/62)	42.4% (n = 28/66)	<0.01
Nulliparity	72.7% (n = 93/128)	79.0% (n = 49/62)	66.7% (n = 44/66)	NS
Abnormal bleeding	49.2% (n = 63/128)	56.5% (n = 35/62)	42.4% (n = 28/66)	NS
Abdominal pain	36.7% (n = 47/128)	37.1% (n = 23/62)	36.4% (n = 24/66)	NS
Pelvic haematoma	46.9% (n = 60/128)	48.4% (n = 30/62)	45.5% (n = 30/66)	NS
Foetal heartbeat	14.1% (n = 18/128)	8.1% (n = 5/62)	19.7% (n = 13/66)	NS
Isthmic tubal pregnancy	18.8% (n = 24/128)	12.9% (n = 8/62)	24.2% (n = 16/66)	NS
Abdominal adhesion	35.2% (n = 45/128)	32.3% (n = 20/62)	37.9% (n = 25/66)	NS
Persistent trophoblast	10.2% (n = 13/128)	19.4% (n = 12/62)	1.5% (n = 1/66)	<0.01
Coexistent leiomyoma	14.8% (n = 19/128)	6.5% (n = 4/62)	22.7% (n = 15/66)	<0.01
Coexistent endometriosis	7.0% (n = 9/128)	8.1% (n = 5/62)	6.1% (n = 4/66)	NS

After dividing 128 patients into two groups according to laparoscopic surgical methods, we compared 19 representative indexes. In this analysis, eight indexes, namely, “age”, “operation time”, “treatment period”, “average hCG”, “median hCG”, “embryo transfer”, “persistent trophoblast” and “coexistent leiomyoma”, showed significant differences.

Abbreviations: BMI, body mass index; NS, no significance; hCG, human chorionic gonadotropin.

2.4 Serum hCG Level Reduction Rate

To estimate the appropriate postoperative follow-up period, we created linear regression lines based on the scatter plot of the association between reduction rates of serum hCG levels and elapsed time after surgery (laparoscopic salpingostomy: number of spots = 236; laparoscopic salpingectomy: number of spots = 289) by using the ordinary least-squares method with Microsoft Excel. In this analysis, 13 patients with PT were excluded. These plots did not include data below the detection sensitivity (laparoscopic salpingostomy: number of spots = 7; laparoscopic salpingectomy: number of spots = 4). We calculated the indexes as follows: (1) we divided the serum hCG levels postoperatively by these levels immediately before the operation and (2) calculated the Log_{10} values. The formula used was Log_{10} (serum hCG level after/before operation (mIU/mL)). The relationship between this logarithmic index and elapsed time after surgery (days) was plotted. Then, by referring to the slopes of these regression lines, we estimated each required follow-up period for patients with laparoscopic salpingostomy or salpingectomy.

3. Results

3.1 Patient Characteristics

The average age, BMI, operation time, blood loss volume and treatment period of the included patients were 33.4 $\pm$ 4.8 (20–44) years, 21.3 $\pm$ 2.8 (17.1–29.9) kg/m^2, 54.1 $\pm$ 20.1 (25–144) min, 126.4 $\pm$ 237.5 (0–1334) mL and 32.4 $\pm$ 17.9 (9–110) days, respectively. The average and median serum hCG levels just before surgery were 6528.1 $\pm$ 11513.8 (2.9–91673.2) and 2879.5 mIU/mL, respectively. Among these cases, we detected one rare case in which the hCG level of intraperitoneal haematoma was 606.0 mIU/mL and laparoscopic salpingostomy was successfully performed. The average ratio of serum hCG levels before and after surgery was 0.38 $\pm$ 0.16 (0.10–1.18). When the characteristics of the patients with laparoscopic salpingostomy and salpingectomy were compared, significant differences in patient age, operation time, treatment period, the number of patients with embryo transfer, PT and coexistent leiomyoma were detected (Table 1). In the analysis of serum hCG levels, we detected a trend wherein laparoscopic salpingectomy was chosen to treat patients with high serum hCG levels, and the average and median hCG levels were higher in patients with laparoscopic salpingectomy than in those with salpingostomy (9393.8 $\pm$ 15177.3 vs. 3477.4 $\pm$ 3493.0 and 4093.4 vs. 2117.0 mIU/mL). Although laparoscopic salpingostomy tended to be performed for patients with relatively low serum hCG levels, 12 out of the 13 cases with PT were detected among the 62 cases with laparoscopic salpingostomy. Among these 12 cases, PT was detected approximately two weeks after surgery (15.0 $\pm$ 8.8, 3–36 days) by the rebound of decreased serum hCG levels (1304.6 $\pm$ 1177.5, 101.2–3465.3 mIU/mL). In 11 out of 12 cases, we performed IMI once, but in one case, we needed to perform IMI twice. Among patients undergoing laparoscopic salpingectomy, only one was diagnosed with PT and needed IMI 4 days after surgery (serum hCG levels: 456.6 mIU/mL). Next, we compared the serum hCG levels of these 12 PT cases with those of the 50 cases with successive laparoscopic salpingostomy. The average serum hCG level tended to be high among the 12 cases with PT (4635.4 $\pm$ 2401.1 vs. 3199.5 $\pm$ 3672.6 mIU/mL, $p = 0.20$), and the median was more than twice that of the non-PT cases (4627.6 vs. 1899.1 mIU/mL, $p < 0.05$). On the other hand, the ratios of the serum hCG levels before and after laparoscopic salpingostomy were similar (0.45 $\pm$ 0.23 vs. 0.40 $\pm$ 0.17, $p = 0.43$).

3.2 Preparation of Reference Criteria for Serum hCG Levels for Laparoscopic Salpingostomy

To evaluate the association between PT and serum hCG levels, we referred to the aforementioned difference in serum hCG levels between successful and failed cases after laparoscopic salpingostomy. Specifically, we set the cut-off values based on serum hCG levels of 2000, 4000, 6000 and 8000 mIU/mL and performed a multivariate analysis that included an additional 13 factors. First, in this analysis of 62 cases with laparoscopic salpingostomy (Table 2), "high hCG", including serum hCG levels of 2000 and 4000 mIU/mL, showed a significant difference (OR = 14.0, $p < 0.01$ and OR = 6.3, $p < 0.01$), but significance was not apparent for other factors. When focusing on patients whose serum hCG levels were lower than 2000 mIU/mL, we detected few cases with PT after laparoscopic salpingostomy (OR = 0.071, 95% CI: 0.0086–0.60, n = 1/29). Second, as expected, the analysis of all 128 cases showed the following significant factors: "hCG $\geq$2000" (OR = 8.6, $p < 0.01$), "hCG $\geq$4000" (OR = 3.5, $p < 0.01$) and "salpingostomy" (OR = 15.6, $p < 0.01$) (Table 3). In both analyses, two values for serum hCG levels, 2000 and 4000 mIU/mL, were considered to be important. However, other significant predictors could not be detected. From these results, we can provide the following three classifications: (1) for patients whose serum hCG levels are under 2000 mIU/mL, we can safely perform laparoscopic salpingostomy; (2) for patients whose serum hCG levels are over 4000 mIU/mL, we should select laparoscopic salpingectomy to avoid PT; and (3) for patients whose serum hCG levels are between 2000 and 4000 mIU/mL, we should determine the method while considering other patient factors.

3.3 Rate of Decrease in Serum hCG Levels after Laparoscopic Surgery

To estimate the required follow-up period after laparoscopic salpingostomy and salpingectomy, we calculated the rate of decrease in the serum hCG levels by using the logarithmic index (Fig. 1). In this analysis, the slopes of the regression lines in cases with laparoscopic salpingostomy

Table 2. Identification of influencing factors for persistent trophoblasts after laparoscopic salpingostomy.

	Number	OR (95% CI, number)	*p* value
Advanced age	5	1.1 (0.1–10.3, n = 1/5)	NS
High BMI	7	0.7 (0.1–6.1, n = 1/7)	NS
Nulliparity	49	0.8 (0.2–3.3, n = 9/49)	NS
Embryo transfer	2	4.5 (0.3–76.9, n = 1/2)	NS
Abnormal bleeding	35	1.1 (0.3–3.9, n = 7/35)	NS
Abdominal pain	23	1.3 (0.4–4.6, n = 5/23)	NS
Pelvic haematoma	30	1.0 (0.3–3.8, n = 6/30)	NS
Foetal heartbeat	5	1.1 (0.1–10.3, n = 1/5)	NS
Isthmic tubal pregnancy	8	0.6 (0.1–5.0, n = 1/8)	NS
Abdominal adhesion	20	1.7 (0.5–6.1, n = 5/20)	NS
High hCG			
hCG >2000	33	14.0 (1.7–116.9, n = 11/33)	<0.01
hCG >4000	20	6.3 (1.6–24.8, n = 8/20)	<0.01
hCG >6000	11	1.8 (0.4–7.9, n = 3/11)	NS
hCG >8000	4	1.4 (0.1–15.0, n = 1/4)	NS
Coexistent leiomyoma	4	1.4 (0.1–15.1, n = 1/4)	NS
Coexistent endometriosis	5	3.1 (0.5–21.3, n = 2/5)	NS

A multivariate analysis of 62 patients was performed to examine the influence of 13 representative factors that were collected from data in the medical records. The number of patients with each factor, the ORs and 95% CIs for the occurrence of persistent trophoblasts and the *p* values are shown in this table. Only "high hCG" was identified as a significant factor for the occurrence of these complications when the borderline was set to 2000 or 4000 mIU/mL.

Abbreviations: OR, odds ratio; CI, confidence interval; NS, no significance; BMI, body mass index; hCG, human chorionic gonadotropin.

Table 3. Identification of influencing factors for persistent trophoblasts.

	Number	OR (95% CI, number)	*p* value
Advanced age	26	0.3 (0.04–2.4, n = 1/26)	NS
High BMI	15	0.6 (0.1–5.0, n = 1/15)	NS
Nulliparity	93	1.3 (0.3–5.0, n = 10/95)	NS
Embryo transfer	30	0.6 (0.1–2.7, n = 2/30)	NS
Abnormal bleeding	63	1.8 (0.5–5.7, n = 8/63)	NS
Abdominal pain	47	1.6 (0.5–4.9, n = 6/47)	NS
Pelvic haematoma	60	1.0 (0.3–3.1, n = 6/60)	NS
Foetal heartbeat	18	0.5 (0.1–3.9, n = 1/18)	NS
Isthmic tubal pregnancy	24	0.3 (0.04–2.7, n = 1/24)	NS
Abdominal adhesion	45	1.2 (0.4–3.8, n = 5/45)	NS
Salpingostomy	62	15.6 (2.0–124.0, n = 12/62)	<0.01
High hCG			
hCG >2000	79	8.6 (1.1–68.4, n = 12/79)	<0.01
hCG >4000	54	3.5 (1.0–12.1, n = 9/54)	<0.01
hCG >6000	35	0.8 (0.2–3.0, n = 3/35)	NS
hCG >8000	22	0.4 (0.1–3.0, n = 1/22)	NS
Coexistent leiomyoma	19	0.5 (0.1–3.7, n = 1/19)	NS
Coexistent endometriosis	9	2.8 (0.5–15.2, n = 2/9)	NS

A multivariate analysis of 128 patients was performed to examine the influence of 14 representative factors that were collected from medical records. The number of patients with each factor, the ORs and 95% CIs for the occurrence of persistent trophoblasts and the *p* values are shown in this table. "Salpingostomy" and "high hCG" were identified as significant factors for the occurrence of these complications.

Abbreviations: OR, odds ratio; CI, confidence interval; NS, no significance; BMI, body mass index; hCG, human chorionic gonadotropin.

and salpingectomy were –0.092 and –0.11 (R^2 = 0.74 and 0.87), respectively. By using these results, to pursue the decline in serum hCG levels until reaching approximately one-thousandth to one ten-thousandth, we needed follow-up periods of 27 to 36 days after laparoscopic salpingectomy and 33 to 43 days after laparoscopic salpingostomy.

4. Discussion

In total, we detected PT in 13 out of 128 cases approximately two weeks after laparoscopic surgeries and needed to treat them with IMI. Among these 13 cases, patients needed a postoperative follow-up period that was more than twice as long as that of the other 115 successive cases (62.8 $\pm$ 29.0 vs. 26.8 $\pm$ 12.8 days). Only one case with PT was detected after laparoscopic salpingectomy, but 12 out of 62 cases had PT after laparoscopic salpingostomy. Although our sample size was relatively small and this study included 13 PT cases out of a total of 128 cases, this result was roughly similar to that of previous reports, in which researchers reported that the occurrence of PT after laparoscopic salpingostomy ranged from 5 to 29% [11–14]. Next, we analysed 17 representative factors for predicting the occurrence of PT (Table 1). In this analysis, we found that "high hCG", defined as an hCG level above 2000 or 4000 mIU/mL, showed a significant influence on the increase in the possibility of PT. These classifications were almost consistent with those defined in previous reports, namely, an hCG level above 2500, 3000, or 5000 mIU/mL [14,17,18]. From these results, we can simply provide the following criteria for the selection of surgical methods: (1) when the serum hCG level is <2000 mIU/mL, we can positively select laparoscopic salpingostomy, but (2) when the serum hCG level is $\geq$4000 mIU/mL, we cannot strongly recommend laparoscopic salpingostomy. For patients whose serum hCG levels were between 2000 and 4000 mIU/mL, it was difficult to form a definite conclusion. Since some reports pointed out the higher possibility of subsequent intrauterine pregnancy after laparoscopic salpingostomy [5,9], early diagnosis of TEP before reaching relatively high serum hCG levels may become increasingly important. On the other hand, we did not find other significant factors, probably because our sample size was relatively small compared with those of previous reports [9,10,12–14]. Another clear limitation was detected compared with these previous reports [17,18]. We could not collect data on ectopic pregnancy size, since in 36 out of 128 cases, this size could not be measured due to a surrounding haematoma.

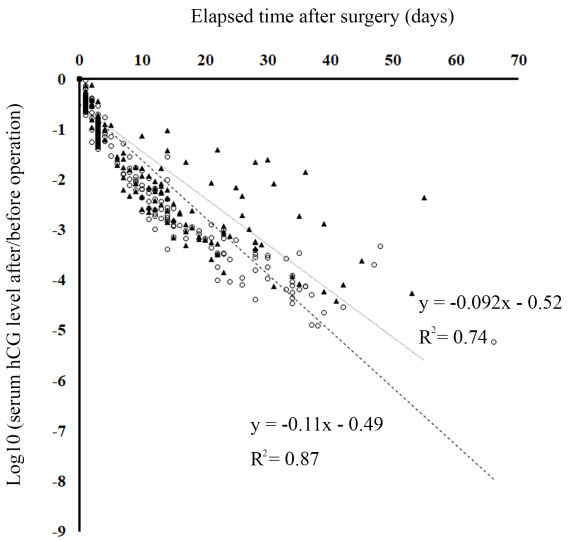

Fig. 1. Reduction rate of serum hCG levels after surgery. The reduction rates of serum hCG levels after laparoscopic salpingostomy (black triangles) and salpingectomy (white circles) are shown with regression lines and R^2 values. X-axis: elapsed time after surgery (days). Y-axis: Log_{10} (serum hCG level after/before operation (mIU/mL)). Abbreviations: Log, logarithm; hCG, human chorionic gonadotropin.

To our knowledge, this is the first study to evaluate the speed of postoperative declines in serum hCG levels after laparoscopic salpingostomy and salpingectomy by plotting the association between the decreasing rate and period (Fig. 1). As expected, according to these linear regression lines, a longer follow-up period was needed after laparoscopic salpingostomy. Considering the average and median serum hCG levels of patients with laparoscopic salpingostomy (Table 1), these patients may need to add approximately one week to the follow-up period to confirm negative serum hCG levels. Due to these difficulties of postoperative management, including the relatively high risk of PT and long follow-up period, the adoption of laparoscopic salpingostomy should be determined carefully.

5. Conclusions

For patients whose serum hCG levels are relatively low, such as below 2000 mIU/mL, we can positively select laparoscopic salpingostomy, but we should select this method carefully for other patients whose serum hCG levels are over 4000 mIU/mL due to the higher risk of PT. This method may demand that we add approximately one week to the follow-up period.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

MH and WI collected and analysed the data and wrote the manuscript. AT and ON supervised the whole study. AT, AO, MH, AS, RM and HT performed medical care on the subjects. AF and ON determined the methods of the operation and supervised all medical procedures. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

This study was reviewed and approved by the Human Ethical Committee of the University of Teikyo Hospital (trial registration number: 20-094).

Acknowledgment

This research was supported by the Mizonokuchi Hospital of Teikyo University with regard to the provision of medical information.

Funding

The author(s) disclose the receipt of financial support from the Japan Society for the Promotion of Conventions (201902081cc) for the research, authorship, and/or publication of this article.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. Human Reproduction. 2002; 17: 3224–3230.

[2] Gingold JA, Janmey I, Gemmell L, Mei L, Falcone T. Effect of Methotrexate on Salpingostomy Completion Rate for Tubal Ectopic Pregnancy: A Retrospective Cohort Study. Journal of Minimally Invasive Gynecology. 2021; 28: 1334–1342.e3.

[3] Marion LL, Meeks GR. Ectopic pregnancy: History, incidence, epidemiology, and risk factors. Clinical Obstetrics and Gynecology. 2012; 55: 376–386.

[4] Hajenius PJ, Mol F, Mol BWJ, Bossuyt PMM, Ankum WM, van der Veen F. Interventions for tubal ectopic pregnancy. The Cochrane Database of Systematic Reviews. 2007; 2007: CD000324.

[5] Ozcan MCH, Wilson JR, Frishman GN. A Systematic Review and Meta-analysis of Surgical Treatment of Ectopic Pregnancy with Salpingectomy versus Salpingostomy. Journal of Minimally Invasive Gynecology. 2021; 28: 656–667.

[6] Poordast T, Naghmehsanj Z, Vahdani R, Moradi Alamdarloo S, Ashraf MA, Samsami A, *et al*. Evaluation of the recurrence and fertility rate following salpingostomy in patients with tubal ectopic pregnancy. BMC Pregnancy and Childbirth. 2022; 22: 2.

[7] Hortu I, Akman L, Akdemir A, Ergenoğlu M, Yeniel O, Sendag F. Management of Ectopic Pregnancy in Unusual Locations: Five-Year Experience in A Single Center. Journal of Clinical and Experimental Investigations. 2017; 8: 90–95.

[8] Sahin C, Uygun ZO, Hortu I, Akdemir A, Kocamanoglu M, Ergenoglu AM, *et al*. Using dynein heavy chain 5 and creatine kinase levels in cervical fluid and blood for early diagnosing of

ectopic pregnancy. The Journal of Obstetrics and Gynaecology Research. 2021; 47: 921–927.

[9] Cheng X, Tian X, Yan Z, Jia M, Deng J, Wang Y, *et al*. Comparison of the Fertility Outcome of Salpingotomy and Salpingectomy in Women with Tubal Pregnancy: A Systematic Review and Meta-Analysis. PLoS ONE. 2016; 11: e0152343.

[10] Mol F, van Mello NM, Strandell A, Strandell K, Jurkovic D, Ross J, *et al*. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. Lancet. 2014; 383: 1483–1489.

[11] Ting W, Lin H, Hsiao S. Factors Predicting Persistent Ectopic Pregnancy After Laparoscopic Salpingostomy or Salpingotomy for Tubal Pregnancy: A Retrospective Cohort Study. Journal of Minimally Invasive Gynecology. 2019; 26: 1036–1043.

[12] Li X, Zhang C, Li Y, Yuan J, Lu Q, Wang Y. Predictive values of the ratio of beta-human chorionic gonadotropin for failure of salpingostomy in ectopic pregnancy. International Journal of Clinical and Experimental Pathology. 2019; 12: 901–908.

[13] Billieux M, Petignat P, Anguenot J, Campana A, Bischof P. Early and late half-life of human chorionic gonadotropin as a predictor of persistent trophoblast after laparoscopic conservative surgery for tubal pregnancy. Acta Obstetricia Et Gynecologica Scandinavica. 2003; 82: 550–555.

[14] Lund CO, Nilas L, Bangsgaard N, Ottesen B. Persistent ectopic pregnancy after linear salpingotomy: a non-predictable complication to conservative surgery for tubal gestation. Acta Obstetricia Et Gynecologica Scandinavica. 2002; 81: 1053–1059.

[15] Ellaithy M, Asiri M, Rateb A, Altraigey A, Abdallah K. Prediction of recurrent ectopic pregnancy: A five-year follow-up cohort study. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2018; 225: 70–78.

[16] Isono W, Wada-Hiraike O, Shirane A, Fujimoto A, Osuga Y, Yano T, *et al*. Alternative strategies to in vitro fertilization/intracytoplasmic sperm injection treatment for aged infertile women. Reproductive Medicine and Biology. 2011; 11: 69–72.

[17] Elito Junior J, Montenegro NAMDM, Soares RDC, Camano L. Unruptured ectopic pregnancy: diagnosis and treatment. State of art. Revista Brasileira De Ginecologia E Obstetricia. 2008; 30: 149–159.

[18] Sivalingam VN, Duncan WC, Kirk E, Shephard LA, Horne AW. Diagnosis and management of ectopic pregnancy. The Journal of Family Planning and Reproductive Health Care. 2011; 37: 231–240.