Journal of Gynecology Obstetrics and Human Reproduction 48 (2019) 413–417

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Original Article

Benefits of second-look laparoscopy in the management of pelvic inflammatory disease

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ARTICLE INFO

Article history:
Received 28 November 2018
Received in revised form 13 March 2019
Accepted 20 March 2019
Available online 22 March 2019

Keywords:
Pelvic inflammatory disease
Second look laparoscopy
Fertility

ABSTRACT

Objective: To evaluate the benefits of second-look laparoscopy (SLL) in pelvic inflammatory disease (PID).
Study design: A 5- year retrospective study conducted at Clermont-Ferrand University Hospital and included all patients who had undergone SLL following a PID. Data collection comprised patient and disease characteristics, type of initial medical or surgical treatment, adhesion (AFS) and tubal (MAGE) scores recorded during SLL and outcomes following subsequent pregnancies.
Results: 76 patients who had received SLL were included. A higher rate of severe adhesions was recorded during SLL in patients with stage 3 PID, than for women with stage 1 and 2 (63.6% versus 25%, p = 0.01). A higher rate of Mage scores of 4 were also found in patients with stage 3 PID (25.8% versus 0%, p = 0.001). Multivariate analysis revealed that women at stage 3 are 17 times more likely to have a high level of adhesions than patients at stage 1 (OR [95% CI] = 17.4 [1.7; 1]). A Mage score of 1was found to be associated with higher pregnancy and live birth rates.
Conclusion(s): SLL seems presents benefits for the preservation of fertility in cases of severe PID with tubo ovarian abcess and may be proposed to patients with stage 3 salpingitis and desire for pregnancy. Further prospective randomized study should be done to confirm these results.
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Introduction

Pelvic inflammatory disease (PID) involves deep and severe visceral infections due to bacteria from the endometrium attaining the fallopian tubes following sexually transmitted infection (STI), an endo-uterine maneuver or due to neighboring infection [1]. In France, 200,000 new cases of PID are recorded per year, with 55% of patients aged under 25. These young women are of childbearing age and have a high risk of complications such as chronic pelvic pain, recurrence, ectopic pregnancy and infertility sequelae [2]. Success of PID treatment may not lead to anatomical ad-integrum restitution, and only intra-uterine pregnancy being the best indicator of complete healing.

Treatment involves antibiotics at the acute phase and surgical management may be necessary when imaging reveal tubo-ovarian abscess, in cases of poor clinical tolerance, resistance to medical treatment or unconfirmed diagnosis as specified in French [3,4], European [5] and American [6] recommendations. Surgical management in the acute phase is drainage of the abcess and should be done by laparoscopy or by puncture under vaginal guidance. Using surgical classification, initial management by laparoscopy, makes it possible to determine 3 stages of salpingitis [7] At stage 1 (catarrhal) tubes reveal congestion and hyperemia, stage 2 (parenchymatous) is characterised by increased inflammation levels, and stage 3 (severe salpingitis) by the presence a tubo-ovarian abscess. Second-look laparascopy (SLL) are only reserved for cases of infertility or chronic pelvic pain.

These recommendations favoring medical treatment are based on conclusions from the PEACH study [8,9] which reported that following medical treatment only, 57% of patients conceived and 42% delivered. These encouraging results brought about changes in practice and notably a considerably reduced use of first surgery and of SLL, even though the study only included patients with moderate PID and excluded "tubo-ovarian abscess and surgical abdomens". Furthermore the study reported unacceptably high results for infertility (19%) and subsequent pelvic pain (42%) for patients treated for moderate levels of PID. A comparison of these results with those obtained from systematic surgical management and particularly for acute cases, remains to be carried out. Lastly,

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http://dx.doi.org/10.1016/j.jogoh.2019.03.020
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Table 1
AFS Adhesion score and MAGE score.

Mage Score				
Score	0	2	5	10
Permeability		Phimosis	Hydro-salpinx	
Tubal mucosa	Mucosal folds maintained		Folds diminished	No folds ou synechia
Tubal wall	Normal		Thin	Thick

AFS adhesion Score				
	ADHESIONS	< 1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
OVARY	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
TUBE	R Filmy	1	2	4
	Dense	4*	8*	16
	L Filmy	1	2	4
	Dense	4*	8*	16

Stage 1 [2–5] ***; stage 2*** [6–10] ***; stage 3*** [11–15] ***; stage 4 (>15).***
Stage I : no adhesions, Stage II : mild adhesions [1–6] ***; stage III : moderate adhesions*** [7–15] ***; stage IV : severe adhesions (>15).***
* If the fimbria end of the fallopian tube is completely enclosed, change the point assignment to 16.

no further treatment was proposed to allow evaluation of fertility or reduce risk of complications.

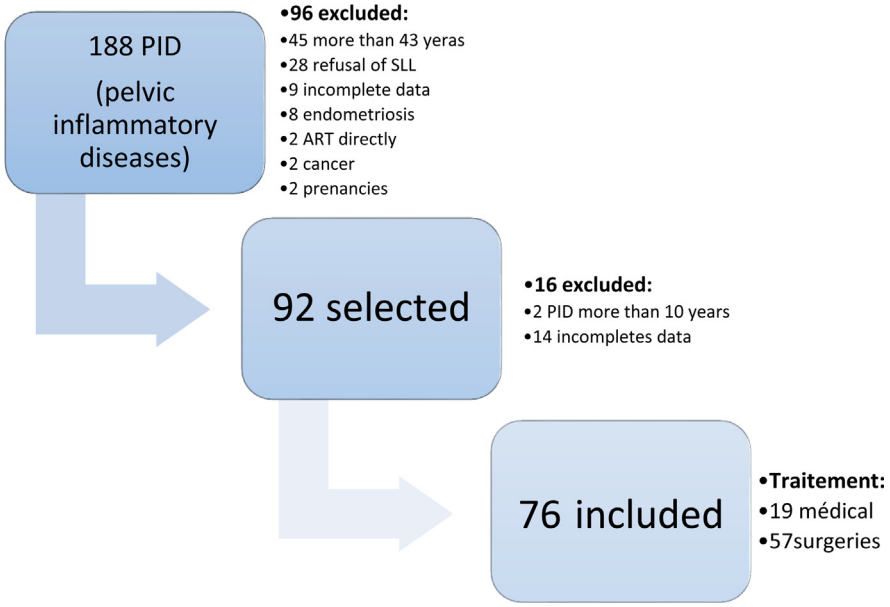
Previously both Bouedec et al. [10] and Raiga et al. [11] had presented results in favor SLL for assessment and restoring of patient fertility. Notably the possibility of obtaining a prognosis concerning fertility, based on the Mage score (grade1 to 4) obtained from tubal evaluation [12] and an adhesion score using the American Fertility Society classification (AFS) [13]. These scores are described in Table 1. This present study aims to evaluate the results and benefits of SLL in cases of PID and to evaluate risk factors that lead to severe complications concerning fertility and which indicate the need for SLL.

Materials and methods

This unicentric retrospective study was carried out at Clermont-Ferrand University Hospital Center over a 5-year period from January 1, 2010 to December 31, 2014. Inclusion criteria concerned all patients who had undergone SLL due to PID initially treated either medically or surgically. A total of 188 patients had received treatment for PID and benefited from a hospital stay (outpatients were not included). Of these, 96 were excluded because they didn't have SLL (age >43 years, associated endometriosis, immediate management for assisted reproductive techniques (ART) and patient refusal) and 16 had SLL but incomplete data (missing data or more than 10 years between initial PID and SLL). A total of 76 patients were finally included as described in the Flow chart (Table 2).

Extensive data collection was carried out to include patient characteristics, clinical and para-clinical characteristics of salpingitis, initial medical and surgical management data, indications and SLL details, and information concerning long-term follow-up notably patient fertility. Two scores relating to fertility were obtained for each surgical intervention: the Mage score (grade1 to

Table 2
Flow chart of the study.



4) for tubal assessment and the AFS classification concerning adhesions (score 0–3). AFS scores 0 and 1 were included in the analyses and so provided increased statistical power.

Statistical analysis was performed using Stata software (version 13, StataCorp, College Station, Texas, USA). All tests were two-sided, with a Type I error set at 0.05. Categorical parameters were expressed as frequencies and associated percentages, and continuous data as mean ± standard deviation or as median [interquartile range], according to statistical distribution. Categorical variables were compared between independent groups (PID stage 1 or 2 vs. PID stage 3, and medical vs. surgical initial management) using the chi-square test or the Fisher exact-test. Quantitative data were compared between groups with the Student *t*-test or with the Mann-Whitney test, as appropriate. The Gaussian distribution was verified by the Shapiro-Wilk test and homoscedasticity by the Fisher-Snedecor test. Furthermore, a multivariable ordinal logistic regression was used to predict AFS stage, using covariates according to univariate results and clinical relevance: age, tubal surgery and PID stage (1 or 2 vs. 3). Because of the small sample (n=57), few variables were included in the model. The results were expressed as odds ratio (OR) and 95% confidence interval.

Results

Our study included 76 patients who underwent SLL post-PID, with an average of 15 per years. General patient characteristics and details of the initial infection episode are summarized in Table 3. When chlamydiae trachomatis has been requested IgG serology was positive in 729%, and PCR in 395%. Other germs were streptococcus, E coli, Neisseiria gonorrhae ans staphyloccoccus aureus. Antibiotic therapy was administered in 100% of cases. Before the french recommandation differents bi ou tri-antibiothérapy were used (amoxicillin and clavulanic acid, levofloxacin, metronidazol and/or ofloxacin). Since 2012 association of Metronidazol and ofloxacin were the reference. Initial surgical management was performed in 57 (75%) patients, the indications were the presence of an abscess confirmed by imaging, uncertain diagnosis and unfavorable clinical evolution in (26.3%). During initial surgery, 57.9% of patients were found to have stage 3 salpingitis. Procedure during initial surgery was adhesiolysis in 93%, salpingectomy in 5.3%, abcess drainage including salpingotomy in 43.9%. Dye tests werent't performed during initial surgery.

Indication of the SLL were pelvic pain (21.1%), hydrosalpinx (18.4%) and others were offered routinely (60.5%). During SLL, 78.9% of patients underwent adhesiolysis and 42.1% tube-related treatment. (19,7% of salpingectomy and 22,4% of neostomy or fimbrioplasty. The median time between initial surgery and SLL was3.5 months [3,5]. An adhesion score was recorded for all patients and the Mage score obtained for 72 patients. 63 patients received long-term follow-up and were contacted by phone, of whom 30 patients (34%) expressed a desire to conceive. We had 23 pregnancies and outcomes were as follows: 16 live births (69.6%), 2 ectopic pregnancy (8.7%), 2 early miscarriage (8.7%) and 3 abortions (13%). Only 5 patients benefited from ART, and two pregnancies were due to IVF. The infertility rate was 23.3%.

Subgroup analyses allowed comparison of SLL characteristics in relation to the PID stage (Table 4) Due to low patient numbers, those with an initial salpingitis stage of 1 and 2 were combined to form a single group of 24 patients, compared to 33 stage 3 patients. At the initial laparoscopy, results revealed 72.7% of severe adhesions at stage 3 as compared to 25% for stages 1 and 2 (p = 0.001). During SLL, more patients in this group received a high adhesions score and a Mage score of 4 (27.3% vs 0%, p = 0.001). Multivariate analysis revealed that stage 3 patients are 8.2 times more likely to have higher adhesion levels than stage 1 or 2 patients (OR [95% CI] = 8.2 [2.2, 30.5], p = 0.02).

Table 3
Patient and PID characteristics, treatment and second-look laparoscopy.

	Total (n=76)
Age (years)	27.6 ± 8.5
Age >37 years	14 (18.4)
Medical history	
Abortion	26 (34.2)
Sexually transmitted infections	7 (9.2)
Abdominal-pelvic surgery	26 (34.2)
Intrauterine device	22 (28.9)
Smoking	43/64 (67.2)
Symptoms	
Pelvic pain	76 (100.0)
Defense	21 (27.6)
Leucorrhoea	40 (52.6)
Fever >38°C	31 (40.8)
Severe sepsis	2 (2.6)
Paraclinical tests	
Normal echography	9/72 (12.5)
Abscess	34/72 (47.2)
Size of abscess (mm)	43.5 ± 14.5
White blood cells (g/l)	13.3 [9.4; 17.8]
C-reactive protein (mg/l)	92.6 [43.9; 171.0]
Chlamydia serology IgG +	35/48 (72.9)
Chlamydia PCR positive	15/38 (39.5)
Initial treatment	
Antibiotic treatment	76 (100.0)
Surgical treatment	57 (75.0)
Adhesiolysis	53/57 (93)
Salpingectomy	3/57 (5.3)
Drainage	25/57 (439)
PID stage	
1	6/57 (10.5)
2	18/57 (31.6)
3	33/57 (57.9)
Second-look laparoscopy	
Indication	
Systematic	46 (60.5)
Pelvic pain	16 (21.1)
Imagery	14 (18.4)
Length of surgery (minutes)	37 [30; 51]
Adhesions score (AFS)	18 (23.7)
Stage I-II (none or small)	25 (32.9)
Stage III (moderate)	33 (43.4)
Perihepatitis (Fitz Hugh Curtis) Stage IV (severe)	8 (10.5)
Tubal score (MAGE)	
Stage 1	52/72 (72.2)
Stage 2	6/72 (8.3)
Stage 3	5/72 (7.0)
Stage 4	9/72 (12.5)
Adhesiolysis	60 (78.9)
Salpingectomy	15 (19.7)
Neostomy or fimbrioplasty	17 (22.4)

Data are presented as frequencies (associated percentage), as mean ± standard deviation, or as median [interquartile range].

Finally, analysis of the relationship between fertility and Mage and adherence scores at SLL was performed by comparing patients who conceived after surgery with those who did not. A total of 30 patients with a childbearing project were selected and included 23 who conceived. Results obtained during SLL allowed the authors to establish a relationship between the pregnancies obtained, their characteristics and fertility scores. Mage scoresof 1 or 2 were found to be associated with a higher pregnancy and birth rate), although this result was not significant. Mage score of 4 was significantly associated with a higher ectopic pregnancy rate. These results are shown in Table 5.

Discussion

The Kreisel study conducted in the US found a4.4% prevalence of PID in sexually active women, this report highlight the magnitude of this public health issue which impacts young women of childbearing age [14]. As explained in the introduction, since 2012 as a result of the

Table 4
Second look laparoscopy (SLL) characteristics depending on initial PID stage (n = 57 patients).

	Stage 1 or 2 (n = 24)	Stage 3 (n = 33)	p-value
Paraclinical tests			
Normal echography	2/21 (9.5)	1/32 (3.1)	0.34
Abscess	6/21 (28.6)	25/32 (78.1)	<0.001
White blood cells (g/l)	10.2 [7.9; 15.3]	15.6 [12.9; 19.2]	0.004
C-reactive protein (mg/l)	90.2 [39.8; 132.0]	91.7 [37.0; 188.0]	0.42
Chlamydia serology IgG	11/14 (78.6)	16/26 (61.5)	0.32
PCR positive chlamydia	8/13 (61.5)	3/14 (21.4)	0.03
Initial surgery			
Severe adhesions (stage IV AFS)	6 (25.0)	24 (72.7)	<0.001
Salpingectomy	0 (0)	3 (9.1)	0.26
Abscess drainage	3 (12.5)	22 (66.7)	<0.001
Second-look laparoscopy			
Adhesions score (AFS)			0.02
Stage I-II (none or small)	6 (25.0)	4 (12.1)	
Stage III (moderate)	12 (50.0)	8 (24.3)	
Stage IV (severe)	6 (25.0)	21 (63.6)	
Tubal score (MAGE)			<0.001
Stage 1	21/23 (91.3)	16 (48.5)	
Stage 2	0/23 (0.0)	6 (18.2)	
Stage 3	2/23 (8.7)	2 (6.0)	
Stage 4	0/23 (0.0)	9 (27.3)	
Adhesiolysis	20 (83.3)	29 (87.9)	0.71
Salpingectomy	1 (4.2)	10 (30.3)	0.02
Neostomy or fimbrioplasty	6 (25)	10 (30.3)	0.66

Data are presented as frequencies (associated percentage), as mean ± standard deviation, or as median [interquartile range].

Table 5
Fertility according to tubal and adhesion score during second-look laparoscopy (n = 30).

	n	Pregnancies	Ectopic pregnancies	Deliveries
Adhesions score (AFS)				
Stage I-II (none or small)	7	5/7 (71.4)	0/7 (0.0)	4/7 (57.1)
Stage III (moderate)	9	8/9 (88.9)	0/9 (0.0)	7/9 (77.8)
Stage IV (severe)	14	10/14 (71.4)	2/14 (14.3)	5/14 (35.7)
p-value		*0.64*	*0.49*	*0.13*
Tubal score (MAGE)				
Stage 1	24	19/24 (79.2)	0/24 (0.0)	15/24 (62.5)
Stage 2	4	2/4 (50.0)	1/4 (25.0)	1/4 (25.0)
Stage 3	0	0	0	0
Stage 4	2	2/2 (100.0)	1/2 (50.0)	0/2 (0.0)
p-value		*0.27*	*0.03*	*0.14*

Data are presented as frequencies (associated percentage).

PEACH study [9], guidelines no longer recommend systematic surgical management, and medical treatment by antibiotics is the first-line therapy [3–6]. But, the conclusions were uniquely based on cases of moderate PID for which complication rates were still high i.e. 19% infertility and 42% chronic pelvic pain. At least, first line antibiotherapy have never shown their efficacity on fertility after PID especially in severe forms [10].

Studies investigating initial surgical management in PID, include the Chayachinda cohort conducted from 2004 to 2011, which reported a low surgical rate of 12.8% for patients with tubo-ovarian abscess (TOA) [15]. Kontoravdis et al, reported a 22.8% rate of surgery for patients with acute pain linked to salpingitis [16]. In our study a higher rate of patients underwent primary laparoscopy (75%), of whom more than half had TOA, our results shows that we probably made two much initial surgery, but the evaluation of the SLL, confirmed that severe PID are more at risk of potential complications like adhesions and tubal infertility and ectopic pregnancies. This is confirmed by the recent French recommendation which support the drainage of tubo-ovarian abcess. This drainage should be realized by vaginal puncture under ultrasound guidance or by laparoscopy, as quickly as possible. Our results, in agreement with this guidelines showed that initial surgery shouldn't by systematic except in severe form with TOA [3,4].

Up to date, in cases of abscess >3 cm, present guidelines advocate drainage by transvaginal route, due to the feasibility and reproducibility of this technique. Granberg et al, in a review of the literature reported a success rate in 77–100% of patients [17] and the French Vermersch study a success rate of 94% [18]. Gjelland, reported complete healing from infection in 93.4% of patients [19]. In a second study, published in 2012, 52.8% of patients who underwent draining and wished to become pregnant, conceived [20]. But patients "who had undergone surgery (after drainage) that made future pregnancy not recommandable" were excluded. Only 38 "good cases" were included and finally only 22 give birth (52%), ... So if vaginal drainage, is efficient on the treatment of the acute phase of PID, we have very poor data about fertility. Moreover, no study to our knowledge has compared efficacy in terms of clinical efficiency and fertility of vaginal vs laparoscopic drainage, data are still missing.

Infertility rates following PID can be high, such as in the USA where rates may vary from21.3%–55.6% [9]. In our study we found a 375% infertility rate, with only 15 out of 24 women desiring to conceive, who delivered. Assessment of fertility in post-PID patients is frequently difficult, requiring long-term follow-up for collection of data on pregnancy and acute episode outcomes. SLL therefore provides a key opportunity to collect validated fertility

scores, specifically MAGE and AFS adhesion scores as previously described. Accordingly Mage et al. (1987) highlighted the relationship between the salpingitis stage, second-look laparoscopy and fertility prognosis, and reported a pregnancy rate that ranged from 58.3% for stage I to 0% for stage IV [12]. These results were confirmed by following studies as Le bouedec (1991), Raiga (1996) Gerber et al. (1996) who performed control laparoscopies and found high rates of adhesions and tubal occlusion [10,11,21]. In a recent retrospective study Chayachinda et al. (2017), used multivariate analysis to show that the presence of a tubo-ovarian abscess is a negative predictor of delivery rate [15]. Finally, Audebert et al. (2014) reported on a more than 10-year follow-up of 434 patients who underwent neosalpingostomy, and consequently advised performing tubal repair in patients selected on the basis of adhesion stage and tubal score [22]. All these results confirmed the interest of a SLL after TOA, and the treatment of the adhesions or the tubal defects. But it's also highlight that no studies and no data are available about fertility post vaginal drainage of TOA, because all SLL were made following laparoscopic intial treatment.

Our study revealed an association between initial infection, secondary adhesions, Mage score and patient fertility. Thus patients with stage3 PID are 8 times more likely to present with a high level of adhesions than stage 1 or 2 patients (OR [95% CI] = 8.2 [2.2, 30.5], p = 0.02). Mage scores of 1 or 2 are associated with higher pregnancy and delivery rates than Mage of 3 or 4 (p = ns), and Mage score of 4 are associated with highly ectopic pregnancies (p = 0.03). These figures correlate with the severity of the initial infection. SLL should therefore be recommended in women who have presented with tubo-ovarian abscess. Some theories estimates that's more the initial infection is severe, more the initial treatment of the tube and its repair in case of damage is quick, more the benefits on the fertility is important [23,24]. We also knows that the infected tubes are also more susceptible to blockage, which if unresolved may lead to hydrosalpinx, a condition resulting in reduced results in IVF as demonstrated by Strandell [25]. This provides further evidence in support of carrying out second look laparoscopy in patients wishing to conceive, usually performed by infertility surgeons, experienced in tubal surgery.

The main limitation of our study concerns its retrospective nature and corresponding issues linked to data collection and reliability. But, our study is the first since the publishing of CNGOF guidelines, to report on fertility following SLL and thus highlight patient groups susceptible to benefit from this technique. For patients, the outcomes of upmost importance is giving birth to a healthy child. Long-term follow-up data is also necessary for assessment of risk of recurrences and pelvic pain. A prospective randomized study about SLL after tubo-ovarian abcess is actually in progress in our center (ClinicalTrials.gov Identifier: NCT03166982).

Conclusion

Over recent years there has been a sharp increase in the incidence of PID in women of childbearing age. Recents guidelines about PID endorse the use of dual-antibiotic therapy, reserving first-line surgery for complicated severe cases and second look laparoscopy (SLL) for selected patients with pelvic pain. Our study, revealed an association between PID initial stages, adhesions, tube- related procedures and patient fertility. While SLL was shown to have little impact on the preservation of fertility in cases of mild to moderate PID, our results find an interest of recommending SLL in women desirous pregnancy and who had a tubo-ovarian abscess at the initial stage. Prospective studies should be done to confirm these results.

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