

# Clinical Presentation of Paraovarian Cysts

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**ABSTRACT** **Background:** A paraovarian cyst (POC) is located between the ovary and the fallopian tube. In many cases POCs are diagnosed and managed as ovarian cysts. But since POC are a distinct entity in their clinical presentation and surgical intervention, they should be better defined.

**Objectives:** To describe the clinical perioperative and operative characteristics of patients with POCs in order to improve pre-operative diagnosis and management.

**Methods:** A retrospective cohort study of patients with an operative diagnosis of POC between 2007 and 2019 in a single university-affiliated tertiary care medical center was included. Demographic characteristics as well as symptoms, sonographic appearance, surgery findings, and histology results were retrieved from electronic medical records.

**Results:** During the study period 114 patients were surgically diagnosed with POC, 57.9% were in their reproductive years and 24.6% were adolescents. Most presented with abdominal pain (77.2%). Preoperative sonographic exams accurately diagnosed POC in only 44.7% of cases, and 50.9% underwent surgery due to suspected torsion, which was surgically confirmed in 70.7% of cases. Among women with confirmed torsion, 28.9% involved the fallopian tube without involvement of the ipsilateral ovary. Histology results showed benign cysts in all cases, except two, with a pathological diagnosis of serous borderline tumor.

**Conclusions:** POC should always be part of the differential diagnosis of women presenting with lower abdominal pain and sonographic evidence of adnexal cysts. If POC is suspected there should be a high level of suspicion for adnexal torsion and low threshold for surgical intervention, especially in adolescent, population who are prone to torsion.

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**KEY WORDS:** adnexal cysts, adolescents, isolated fallopian tube torsion, paraovarian cysts (POC), torsion

A paraovarian cyst (POC) is located between the ovary and the fallopian tube [1,2]. The terms paraovarian cyst and paratubal cyst are used interchangeably depending on their proximity to the ovary or fallopian tube. When a paratubal cyst is pedunculated and located near the fimbria of the fallopian tube, it is referred to as a hydatid cyst of Morgagni, which is usually smaller than 2 cm [3]. POCs develop either from the mesothelium of the broad ligament (68%), from paramesonephric remnants (30%), and rarely from mesonephric remnants (2%) [1]. POCs are generally benign while borderline or even malignant paraovarian tumors are rarely encountered [4].

The exact incidence of POC is unknown, presumably due to their frequent asymptomatic presence. In previous studies, estimated incidence was 3–20% of all adnexal masses [5]. POCs have been reported in all age groups, from premenarchal girls to menopausal women [5,6].

A sonographic misdiagnosis of POCs as ovarian cysts or other cystic finding is common. In more than half of the cases the accurate diagnosis of POCs is not achieved preoperatively [6–8]; therefore, these cases are managed as presumed ovarian cysts. Since POCs are a distinct entity from ovarian cysts in their clinical presentation and surgical intervention, they should be better defined. In this study, we aimed to improve POC diagnosis and management by better describing the clinical profile, sonographic appearance, and complications.

## PATIENTS AND METHODS

A retrospective cohort study was conducted in our hospital during a 12-year period (2007–2019). Data were retrieved from electronic medical records of patients with an operative diagnosis of POC. The study was approved by the Yitzhak Shamir Medical Center ethics committee (#220/13; approved on 13/01/16). Due to the retrospective nature of the study, informed consent was not required.

Demographic characteristics including age, reproductive status, parity, and gravidity were collected. Data regarding associated symptoms, such as abdominal pain, duration and location,

nausea, vomiting, and peritoneal irritation signs were obtained.

Blood tests including a complete blood count and ovarian tumor markers were obtained. Sonographic evaluation including cyst location, size, echogenicity, presence of septations, and/or papillary projections were recorded. Indication for surgery, type of operative procedure, operative findings, and complications, such as adnexal torsion and blood loss, were obtained from the operative records. Final histopathology reports were included in final analysis.

Cyst measurements included the largest cyst diameter. Duration of abdominal pain was calculated from the medical records based on patient descriptions at the onset of pain prior to emergency department (ED) visit.

Sonographic appearance of a simple cyst is defined as an enclosed thin walled sac containing clear content with either one or two loculations. In contrary to a complex cyst that contains either a solid component, septations, or papillation.

Histologic findings were defined as simple or neoplastic according to tissue origin. Simple POCs originate from embryonic remnants of the urogenital system or from the invagination of fallopian tubes serosa creating a mesothelial cyst. Neoplastic POCs originate from a neoplastic transformation of a paraovarian simple cyst or from the adjacent ovary [9].

The World Health Organization's upper age cutoff for adolescence (age 19 years) was used.

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 24 (SPSS, IBM Corp, Armonk, NY, USA). Descriptive variables are presented as the mean  $\pm$  standard deviation. Frequencies are presented as percentages. One-way ANOVAs and Fisher's exact tests were employed as appropriate. *P* value  $< 0.05$  was considered statistically significant.

## RESULTS

Our study comprised 114 patients who were surgically diagnosed with POCs between the years 2007 and 2019.

Their demographic characteristics as well as clinical presentation and indications for surgery are presented in Table 1.

The mean age of the patients was 30.7 years (range 11–81 years). Most were in the reproductive age group (57.9%). Three of the patients were pregnant. Adolescents composed 24.6% of the patients while none were found to be premenarchal. More than half of the women were nulliparous (57.9%). Most POC cases (77.2%) presented with abdominal pain. A little less than a quarter (21.9%) reported abrupt onset of pain in the last 24-hours prior to emergency room arrival, while about half (55.9%), had onset of abdominal pain several days or more before admission. 50.9% of the women underwent operation due to suspected torsion, and in about 70.7% of them the diagnosis was confirmed. In 77.2% of cases, abdominal pain, acute or chronic, was the reason for surgery, with one-third also reporting nausea and

**Table 1.** Clinical characteristics of women with paraovarian cysts

	Absolute number	Frequency %
Mean age, years	30.7	
<b>Age distribution</b>		
Premenarchal	0	0
Adolescents	28	24.6
Reproductive age	66	57.9
Pregnancy	3	2.6
Menopause	17	14.9
<b>Clinical presentation</b>		
Abdominal pain	88	77.2
Abdominal pain >24h	63	55.3
Abdominal pain <24h	25	21.9
<b>Location of pain</b>		
One sided	46	40.4
Diffused	42	36.8
Nausea/vomiting	32	28.1
Asymptomatic	26	22.8
<b>Surgical indication</b>		
Suspected torsion	58	50.9
Part of abdominal pain workup	30	26.3
Part of sonographic finding workup	26	22.8

vomiting. The remaining surgeries were performed with the sonographic appearance as the indication.

Table 2 shows the sonographic findings before the surgery.

Approximately one-third (31.6%) of sonographic examinations were conducted abdominally since the patients were virgins. In more than half of the cases (55.3%) sonographic evaluation did not accurately diagnose POC; 39.5% were misdiagnosed as ovarian cysts, and in 15.8% the exact location of the cyst was not indicated. Bilateral POCs were diagnosed in 4.4% of the cases. POC median size was 65 mm. Most of the cysts (77.2%) had a simple sonographic appearance-unilocular without solid components. Tumor markers were missing in most of the patients.

Only 44.7% of the women had an accurate diagnosis of POC made by ultrasound prior to surgery. No significant difference was found in the accuracy of diagnoses made by abdominal compared to vaginal sonographic approach. This finding was also true regarding the location, side of the cysts, and the presence of torsion. The side and measurement of the cysts described by sonograms performed prior to surgery and the surgery findings were comparable.

Table 3 details surgery data and histologic findings.

In our population, 5% underwent laparotomy and the rest

**Table 2.** Ultrasound findings

	Absolute number	Frequency %
<b>Ultrasound approach</b>		
Vaginal	78	68.4
Abdominal	36	31.6
<b>Cystic location</b>		
Separately from ipsilateral ovary-correct diagnosis	51	44.7
Integral part of ovary, misdiagnosis	45	39.5
Not described	18	15.8
<b>Cyst side</b>		
Right	52	45.6
Left	57	50
Bilateral	5	4.4
<b>Cystic size (mm)</b>		
Median	65	
< 50	33	30.2
50-100	55	50.5
> 100	21	19.3
<b>Cyst features</b>		
Simple cyst	88	77.2
Multi-loculated cyst without	10	8.8
Solid component	6	5.3
Presence of pappilations	7	6.1
Not indicated by u/s	1	0.9

had laparoscopies. Left sided cysts were more common, but not significantly (50% vs. 45.6%); 39.5% of the patients were operatively diagnosed with torsion. In 71.1% adnexa were found to be twisted around itself and the rest had only the tube twisted. Most of the women underwent cystectomy. In four patients cystotomy was performed, mostly due to concern about damage to the fallopian tube and future fertility. Unilateral or bilateral salpingo-oophorectomy was performed exclusively in postmenopausal women. Salpingectomy was performed on an individual basis in cases where significant damage to the fallopian tube could not be avoided, or in women who completed their fertility plan. In addition, 57% of the cysts were simple and 36.8% were neoplastic. All the cysts were benign except two that were serous borderline tumor (1.8%), found in a 22-year-old and a 75-year-old woman. The 22-year-old patient was admitted and operated with the suspicion of adnexal torsion. Malignancy was not suspected during sonographically or during the surgery.

**Table 3.** Surgery and histology findings

	Absolute number	Frequency %
<b>Cystic size (mm)</b>		
< 50	23	20.2
50-100	56	49.1
> 100	32	28.1
<b>Laterality</b>		
Right	52	45.6
Left	57	50
Bilateral	5	4.4
<b>Torsion</b>		
Confirmed torsion	45	39.5
Number of twists, mean ± SD	3.0 ± 1.49	
Torsion of whole adnexa	32	28.1
Torsion of tube alone	13	11.4
<b>Procedure</b>		
Fenestration of the cyst	7	6.1
Cystectomy	82	71.9
Salpingectomy	2	1.8
Salpingoophorectomy	23	20.2
Blood loss (ml)	10-200	10 (median)
Length of surgery (min)	20-120	55 (median)
<b>Histology results</b>		
Simple cyst	65	57
Benign neoplasia	42	36.8
Borderline neoplasia	2	1.8
Missing histology	5	4.4

The 75-year-old patient was operated on due to the sonographic appearance of a complex adnexal mass.

Table 4 shows the comparison of characteristics of women with and without torsion.

Women with torsion were significantly younger than women without torsion. Accordingly, the age group distribution of patients with torsion varied significantly, with more adolescents and reproductive age women compared with postmenopausal women. There was no significant difference in cyst size between women with and without torsion. Women with torsion had a significantly higher rate of sudden onset of pain (under 24 hours), localized abdominal pain, and higher leukocytes counts.

In 58 women the indication for surgery was suspected torsion. In 70.7% (41 women) the surgery confirmed this suspicion. Four patients demonstrated adnexal torsion without preoperative suspicion. Three of these cases had adnexal torsion and in one patient only the tube was involved. The time from

**Table 4.** Analysis of torsion patients with paraovarian cysts (n=114)

	Torsion (n=45)	No torsion (n=69)	P value*
Mean age ± SD) year	25.6 ± 12.9	34.1 ± 18.3	<b>&lt; 0.01</b>
<b>Age group</b>			
Adolescent, year (%)	14 (31.1)	14 (20.3)	
Reproductive, year (%)	29 (64.4)	40(58.0)	
Menopause, year (%)	2 (4.4)	15 (21.7)	
Mean cyst size, mm	74	77	0.647
Torsion of adnexa, number	32	-	
Torsion of tube, number	13	-	
Number of twists, mean ± SD	3.0 ± 1.49	-	
Abdominal pain	44 (97.8%)	44 (63.8%)	<b>&lt; 0.01</b>
Pain duration < 24 hour	21 (46.7)	4 (5.8)	<b>&lt; 0.01</b>
Localized pain	31 (68.9)	9 (13.0)	<b>&lt; 0.01</b>
White blood cells	10,779 (3998)	8,361 (2708)	<b>&lt; 0.01</b>

\*Bold indicates significance

admission to operation was significantly shorter in women with surgically confirmed torsion.

In the torsion group there were more women with acute abdominal pain and nausea than chronic abdominal pain (51.2% vs. 23.5%  $P = 0.018$ ). Correlation between duration of pain and the number of twists was not found.

## DISCUSSION

In this study we summarized 12 years of surgeries for POCs at our medical center. To the best of our knowledge, this is the largest study to date regarding this entity. The main focus of this study was to better characterize the clinical manifestations of POCs in order to improve diagnosis and management.

In our study, most POC cases were not accurately recognized before surgery. This finding is supported by previous studies by Muolokwu et al. [6] and Darwish et al. [7], demonstrated that POC were often preoperatively diagnosed as ovarian cysts, hydrosalpinx, and peritoneal inclusion cysts. POCs sonographic characteristics are variable; therefore, it is essential to consider POC as part of the differential diagnosis.

Savelli et al. [10] reported that dissociation of the cyst from the ovary when pushing the vaginal ultrasound probe is a useful diagnostic sign, referred to as split sign, for discriminating paraovarian masses.

In our study the majority of women were in their reproductive years with a large proportion of them being adolescents, but none were premenarchal. This finding is consistent with previously published studies [3,11-13]. Conversely, in a study by Muolokwu and colleagues [6] composed of 110 adolescents with POC,

12.6% were found to be prepubertal. The age reported in that study ranged from 1 to 19 years old, but the distribution of ages was not reported. We suspect that at least some of the girls were in fact babies still under their mother's hormonal influence or premenarchal girls after onset of puberty. Nevertheless, those study authors and others [14] hypothesized that POCs increase in size with hormonal activity [6]. In addition, in histological and immune-profile studies of 25 Wolffian adnexal tumors, the neoplasm was believed to originate from Wolffian remnants. Hormone receptors were demonstrated in all cases [15]. The age distribution and the histological findings in our study suggest that POCs are affected by the hormonal milieu. This raises the question whether combined oral contraceptive therapy could prevent the growth and potentially take a part in the management of POCs.

It seems that POC rarely cause symptoms and are therefore often incidental findings. Symptoms probably occur in cases of excessive growth or when hemorrhage, rupture, or torsion occurs. Considering the high rate of torsion in our cohort (40%), which concurs with previous studies [6,11], the question of preventive laparoscopic cystectomy is raised. Until now, there has been no clear recommendation for cystectomy to prevent torsion neither for ovarian masses nor for POC. The correlation between cyst size and the risk of torsion varies among studies. Although no clear size cutoff exists, most studies refer to 5 cm diameter as the deflection point from which the risk for torsion increases [16,17]. In mature teratomas  $\geq 5$  cm in diameter, a prophylactic removal is usually recommended [18]. However, our study did not demonstrate a correlation between cyst size and torsion. It seems that when POCs grow, symptoms occur, and preventive cystectomy to prevent torsion may be considered, especially in adolescents who are most prone to torsion.

In our study, torsion was confirmed in about 70% of the women who underwent surgery due to suspected torsion. In previous studies regarding adnexal torsion, the diagnosis was confirmed intraoperatively in only about 50% of the cases [19]. Our study design makes it hard to determine whether the positive predictive value for torsion based of clinical findings is higher in POC than in ovarian masses. However, we hypothesized that once POC become symptomatic, the risk of torsion is increased and we should be more liberal to perform surgery.

In 30% of the cases demonstrating torsion, only the tube had rotated without involvement of the ipsilateral ovary. No cases were found where only the ovary was twisted. Isolated fallopian tube torsion (IFTT) is a very rare gynecological diagnosis [20]. Shevach et al. compared adnexal torsion to IFTT. They found that both groups present primarily with abdominal pain, but women with IFTT presented with less pain, usually no peritoneal signs, and longer duration of pain. POC was the most common finding in IFTT [21]. Therefore, it is important to assess abdominal pain with POC with high level of suspicion for torsion. Surgery should be performed without delay when indicated and before irreversible damage to the tube occurs.

**LIMITATIONS**

Our study is limited by its retrospective design and potential for underreporting, which could be very important in the effort to describe the specific characteristics of POCs. In addition, during the course of this study, there have been many changes in the way medical history is taken, in the nature of the auxiliary tests, and the documentation collected.

In addition, the study is limited by a lack of comparison group of women with POC who did not undergo surgery, so it is difficult to draw clear conclusions about the characteristics that would allow for conservative follow-up. However, despite its limitations, the study presents the largest series of patients with POC from a single tertiary care center.

**CONCLUSIONS**

The study emphasizes the importance of being aware of POCs, especially when clinical suspicion of torsion is raised, to improve the management of these cases. Surgical intervention may be considered, especially in adolescent population who are most prone to torsion.

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**Capsule**

**Preparing antiviral defenses**

Antiviral drugs are an important tool in the battle against COVID-19. Both remdesivir and molnupiravir, which target the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase, were first developed against other RNA viruses. This finding highlights the importance of broad-spectrum antivirals that can be rapidly deployed against related emerging pathogens. **Sourimant et al.** used respiratory syncytial virus (RSV) as a primary

indication in identifying further drugs that target the polymerase enzyme of RNA viruses. The authors explored derivatives of molnupiravir and identified 4' fluorouridine (EIDD-2749) as an inhibitor of the polymerase of RSV and SARS-CoV-2. This drug can be delivered orally and was effective against RSV in mice and SARS-CoV-2 in ferrets.

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