Original Research

Variables Associated With Resolution and Persistence of Ovarian Cysts

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OBJECTIVE: To estimate surveillance intervals of incident ovarian cysts, and describe variables associated with cyst resolution times.

METHODS: The UK-OCST (University of Kentucky Ovarian Cancer Screening Trial) was a prospective cohort that enrolled 47,762 individuals over 30 years, including 2,638 individuals with incident cysts. Cyst diameter and structure and patient age, body mass index, use of hormone therapy (HT), family history of ovarian cancer, and menopausal status were examined as variables associated with cyst resolution using *t* tests, χ^2 test, Kaplan Meier, and Cox multiple regression.

RESULTS: Of 2,638 individuals with incident cysts, 1,667 experienced resolution (63.2%) within 1.2 years, and 971 experienced persistence (36.8%). Within 1 year, unilocular and septated cysts had similar resolution rates (35.4% and 36.7%, respectively, $P>.05$), but time to resolution was shorter for unilocular cysts compared with septated cysts (mean 1.89 years vs 2.58 years, respectively, $P<.001$). Both unilocular and septated cysts smaller than 3 cm resolved faster than cysts larger than 6 cm ($P<.001$). Variables associated with percent resolution included being of younger age, premenopausal status (but not for synchronous bilateral cysts), and those reporting a family history of ovarian cancer ($P<.05$). Variables associated with a faster cyst resolution rate included being older than age 70 years and not using hormone therapy. Body mass index and family history were not associated with cyst resolution time.

CONCLUSION: Different surveillance times may be appropriate depending on cyst structure and size and patient age and HT use.

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Roughly 15–20% of individuals will develop an ovarian cyst during their lifetime.[1] A benign ovarian cyst or benign cystic ovarian mass is a solid or fluid-filled sac or pocket (cyst) within or on the surface of an ovary. Ovarian cysts can originate from hormonal changes that affect the ovary, especially ovarian follicles. It is important to distinguish a benign ovarian cyst from an ovarian malignancy.[2] Although, ovarian cysts are common and have a very low potential for malignancy,[3–8] the development of ovarian cysts can be distressing to patients.[9–13] Previous studies have reported that 85% of ovarian cysts will resolve in up to 5 years[4,8,14] but have not described how resolution time may vary with regard to patient characteristics and cyst morphology.

Transvaginal ultrasonography (TVUS), the preferred imaging modality for adnexal pathology, is widely available, affordable, safe, well-tolerated, and proven more useful than other imaging methods for evaluating ovarian cysts.[15–25] Findings on TVUS suggestive of benign pathology include a cyst appearance with smooth thin walls, lack of solid components and

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septations, and little internal blood flow.[4,26–29] For incidental ovarian cysts, the American College of Obstetricians and Gynecologists recommends repeat imaging without surgical intervention for simple cysts with a diameter up to 10 cm; however, there is no established duration for serial surveillance.[18,29,30] Surgical intervention is recommended when there is suspicion of malignancy. Characteristics that are highly suspicious of malignancy include increasing size, the inclusion of papillary or solid components, mass irregularity, presence of ascites, and high internal color Doppler flow.[1,18,31–35]

Expectations for cyst resolution are essential to help the practicing physician pivot between continuing surveillance and considering surgical management. The objective of this study is to identify factors associated with cyst resolution to assist health care professionals in determining the length of cyst surveillance.

METHODS

Individuals enrolled in the UK-OCST (University of Kentucky Ovarian Cancer Screening Trial) from November 1987 to March 2019 were evaluated. This prospective cohort trial was approved by the University of Kentucky IRB for Human Studies (IRB# 45030) and is registered at ClinicalTrials.gov: NCT04473833. Eligibility criteria included 1) asymptomatic postmenopausal individuals aged 50 years or older and 2) premenopausal individuals older than age 25 years but younger than age 50 years who had at least the same expected risk as postmenopausal individuals due to family history, personal *BRCA* status, Ashkenazi background, or Lynch syndrome. All study participants completed a questionnaire that included medical history, surgical history, menopausal status, hormone use, and family history of cancer, as previously published.[13] *Menopausal status* was defined as the self-reported absence of menses for 12 months. This definition, described by the National Institute of Aging, is suited for self-reporting.[36] Individuals with prevalent cysts, a known complex or solid ovarian mass or a personal history of ovarian cancer were excluded.

Transvaginal ultrasonography and color Doppler were performed using General Electric Voluson P5, P8 and P10 units with a 4–11-mHz vaginal probe on individuals with an empty bladder. When performing the TVUS examination, the transducer was gradually inserted while observing the ultrasound image on a monitor. The urinary bladder was used as a consistent landmark in the pelvis for assessing transducer orientation as the uterus and ovaries have much more variable positions. Three approaches comprehensively assessed the pelvis: probe movements from side-to-side for sagittal imaging, 90° rotations for semi-coronal images and angulation of the probe vertically. By changing the depth of probe insertion, different pelvic structures could be brought into the fields of view.[35–39] By sweeping the ultrasonographic cone across the sagittal plane from the midline to the lateral pelvic side walls, followed by turning the probe 90° into the coronal plane and extending the beam from cervix to the fundus,[35–39] a survey of the pelvis was made. The iliac vessels in the pelvic sidewall and the tubal vessels located posterior and parallel to the fallopian tubes served as landmarks for proving structure. By applying pressure to at least three regions of the abdominal surface, bowel repositioning was made possible to make visualizations more distinct.[35–39] Every image was reviewed by a physician and minimally by one of the authors.[35–38] The protocol of this study specified that ovarian measurements be obtained in three dimensions; the largest diameter was used for the work reported here.[35–38] Thus, each visualization was validated by the requirement that all three measurements were obtained.[35–38] A normal ovary is ovoid in shape and will have an echotexture with a central echogenic medulla.[39] Changes in echogenicity will involve hypoechogenic cystic fluid and hyperechogenic septations within cysts.[39] In general, normal ovarian size was considered to be less than 20 cm^3 for premenopausal women and less than 10 cm^3 for postmenopausal women. A total of 36 ultrasonographers performed the TVUS examinations over the course of the more than 31 years of the screening program operation. All participating ultrasonographers were ARDMS-certified and trained at the University of Kentucky according to the methodology described.

All screening data were entered into a networked database (MEDLOG Systems).[35–38] Individuals who had normal screen results were scheduled for their next screen in 12 months.[35–38] Only individuals with both ovaries visible and normal-appearing on their initial TVUS encounter were included in this study.[35–38] Individuals were eligible to enroll in the screening protocol if they underwent hysterectomy at least 12 months before their first ultrasound screen. If individuals underwent subsequent pelvic surgery, they were censored from the present analysis so that surgical interventions did not influence estimates of cyst resolution.[35–38] Cyst characteristics included maximum cyst diameter, cyst type (unilocular or septated), and cyst duration. Those who had bilateral cysts were further classified as to bilateral cysts that appeared at the same time (synchronous) and those bilateral cysts that appeared at different times (asynchronous).

Cyst survival was determined by Kaplan Meier curves for univariate analysis and Cox regression models for multivariate analysis with individuals with cysts nested within groupings. Chi-square and *t* tests were used for the tests of association among subgroups with Yates and Pearson *P*-values. For all analyses, a two-sided significance level of $P<.05$ was considered statistically significant.

RESULTS

A total of 47,762 individuals were screened for ovarian cancer and underwent 321,566 TVUS examinations over the more than 31 active years of the UKOCST (Fig. 1). There was an average of 6.7 screening encounters per person, with a mean follow-up of 7.9±0.04 years. A total of 1,334 cases were censored due to surgery. Surgery due to findings from screening accounted for 543 cases, and incidental surgeries unrelated to screening accounted for 791 cases. The average number of encounters before surgery for individuals censored due to surgery was 7.2±0.2. Of the 47,762 screened individuals, 7,251 (15.2%) had prevalent cysts and were excluded (Fig. 1). Of 40,511 individuals without cysts on initial examination, 37,873 (93.5%) never had cysts identified subsequently and 2,638 (6.5%) had new cysts identified and comprised the incident group (Fig. 1). A total of 1,667 (63.2%) individuals had incident cysts that resolved, of whom 630 (37.8%) were premenopausal and 1,037 (62.2%) were postmenopausal. Of 971 (36.8%) individuals with persistent incident cysts, 281 (28.9%) were premenopausal and 690 (71.1%) were postmenopausal (Fig. 1). Demographics of individuals with incident cysts are shown in Table 1. Body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) and cyst structure were not associated with cyst resolution or persistence.

As shown in Table 2, a higher proportion of premenopausal individuals had cyst resolution (69.2%) compared with postmenopausal individuals (60.0%). Resolution was similarly greater for premenopausal individuals with unilateral (76.4%), bilateral (66.1%), and asynchronous bilateral (68.7%) cysts than for postmenopausal individuals with unilateral (63.4%), bilateral (54.0%), and asynchronous bilateral (54.8%) cysts ($P<.05$), but not for synchronous bilateral cysts (Table 2). The resolution time of incident septated cysts was generally more rapid than the resolution time of incident unilocular cysts (Fig. 2). Septated cysts and unilocular cysts had a mean resolution of 1.89 years and 2.58 years, respectively ($P<.001$).

The median resolution time of all incident cysts was 14.4 months, and 63.2% resolved within 1 year. Individuals with cysts that resolved were younger (53.2±0.3 years) than individuals with persistent cysts (57.3±0.5 years) ($P<.05$). The fraction of unilocular (35.4%) and septated cysts (36.7%) that resolved within 1 year was similar; however, septated cysts resolved more quickly than unilocular cysts ($P<.05$, Table 3). Cyst mean diameters for unilocular cysts (n=2,465, 3.4±0.03 cm) were not significantly different from those for septated cysts (n=1,420, 3.8±0.03 cm). The time to cyst resolution was highly dependent on cyst size and was relatively similar for both unilocular (Fig. 3A) and septated incident cysts (Fig. 3B). These relationships were consistent when unilocular and septated cysts were grouped together (Fig. 3C). By size, the median resolution time was 1 year for small cysts of less than 3 cm in diameter, 1.58 years for cysts 3–6 cm in diameter, and 3.5 years for large cysts larger than 6 cm in diameter (Table 3).

Individuals using hormone therapy (HT) during the study had a higher proportion of cysts that persisted compared with those that resolved (59.2% [302/510] vs 40.8% [208/510]) ($P<.05$), and the median resolution time was longer (2 years) than nonusers (1.17 years) (Table 3). By age category, median time to resolution was 1 year for individuals older than age 70 years, 1.25 years for individuals aged 40–69 years, and 1.8 years for individuals younger than age 40 years ($P<.05$; Table 3). When segregated by decade, resolution times of both unilocular and septated cysts in individuals 40–69 year old (decades 40–49 vs 50–59 vs 60–69) were not significantly different.

Menopausal status, BMI, and family history of ovarian cancer were not associated with median cyst resolution time for either unilocular or septated cysts (Table 3). The mean diameter of cysts did not differ significantly over the range of BMIs (3.5–3.9 cm). A higher proportion of individuals with a family history of ovarian cancer experienced cyst resolution (64.3% [640/996] vs persistence 35.7% [356/996]); however, resolution times were not different based on family history of ovarian cancer ($P=.629$, Table 3).

In multivariate analysis, septated cysts were more likely to resolve than unilocular cysts (hazard ratio [HR] 1.46 [95% CI 1.35–1.59], $P<.05$) (Table 4). For every centimeter increase in cyst diameter, the hazard for resolution decreased by 21.0% (HR 0.79 [95% CI 0.76–0.83], $P<.05$) (Table 4). Individuals using HT were less likely to experience resolution compared with those who were not (HR 0.74 [95% CI 0.67–0.83], $P<.05$) (Table 4). For every 1-year increase in age, the HR for resolution increased by 1.8% (HR

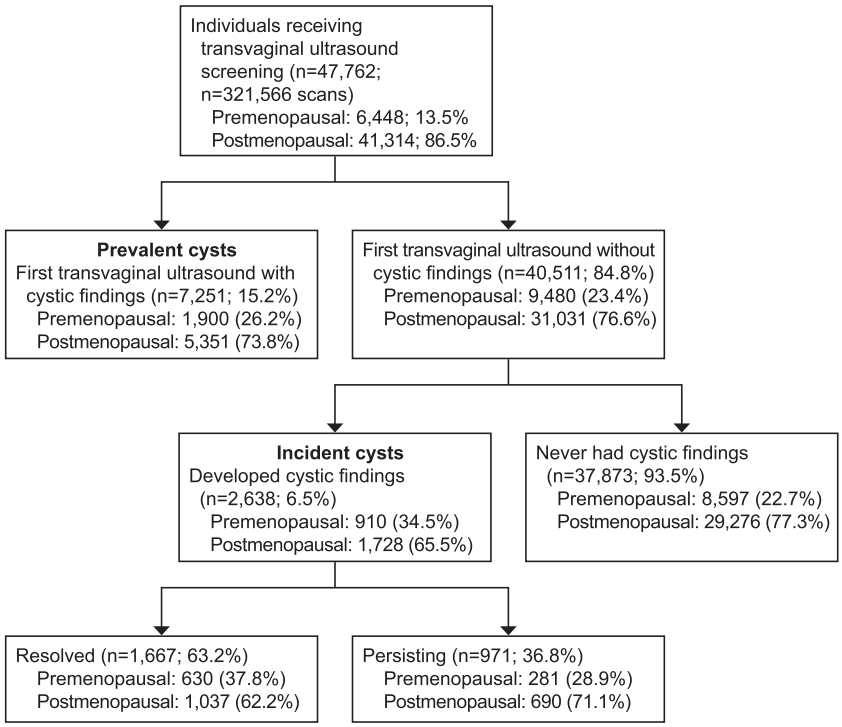

Fig. 1. Occurrence of cystic findings. A total of 47,762 individuals enrolled in the UK-OCST (University of Kentucky Ovarian Cancer Screening Trial) from November 1987 to March 2019 and were evaluated with transvaginal ultrasonography in 321,566 screening encounters. Individuals were noted to have either prevalent ovarian cysts or no ovarian cysts on initial examination. Individuals were monitored for the appearance of new cysts with subsequent transvaginal ultrasound examination. Those who had subsequent cysts were monitored for resolution or persistence. Percentages indicate percent composition of each group.

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Table 1. Demographics for Individuals With Incident Cysts

Factor*	Total (N=2,638)	Resolved Cysts (n=1,667)	Persistent Cysts (n=971)
HT use	510	303 (59.4)	202 (40.6)
Age (y)			
Younger than 40	243	132 (7.9)	111 (11.4)
40–69	2,014	1,369 (82.1)	645 (66.4)
Older than 70	381	166 (10.0)	215 (22.2)
Menopausal status			
Premenopausal	1,489	1,053 (63.2)	436 (44.9)
Postmenopausal	1,149	614 (36.8)	535 (55.1)
BMI (kg/m^2)†			
Lower than 18.5	61	22 (1.3)	39 (1.8)
18.5–24.9	1,698	738 (44.4)	960 (43.1)
25–29.9	1,205	518 (31.1)	687 (30.9)
30–34.9	572	237 (14.2)	335 (15.0)
35 or higher	357	152 (9.1)	205 (9.2)
Family history of ovarian cancer	996	640 (64.3)	356 (35.7)
Cyst structure†			
Unilocular	2,475	1,557 (64.2)	918 (64.3)
Septated	1,423	867 (35.8)	556 (37.7)
Cyst diameter (cm)			
Less than 3	1,326	905 (37.3)	421 (28.6)
3–6	2,416	1,468 (60.6)	948 (64.3)
Larger than 6	156	51 (2.1)	105 (7.1)

HT, hormone therapy; BMI, body mass index.
Data are n or n (%).
* Family history of ovarian cancer, cyst diameter, patient age, and BMI were analyzed as ordinal variables; cyst characteristics, HT use, menopausal status, and family history of ovarian cancer were analyzed as nominal variables.
† Not significantly different—$P<.05$ for resolved cysts vs persistent cysts by χ^2 test.

Table 2. Incident Cyst Resolution in Premenopausal and Postmenopausal Individuals*

Factor	n	Resolved
Individuals with incident cysts	2,638	1,667 (63.2±0.9)
Unilateral†	1,378	909 (66.0±1.3)
Bilateral‡	1,260	758 (60.2±1.4)
Asynchronous bilateral§	907	561 (61.9±1.6)
Synchronous bilateral‖	353	197 (55.8±2.6)
Premenopausal individuals with incident cysts	909	629 (69.2±1.5)¶
Unilateral†	271	207 (76.4±2.6)¶
Bilateral‡	638	422 (66.1±2.0)¶
Asynchronous bilateral§	460	316 (68.7±2.2)¶
Synchronous bilateral‖	178	106 (59.6±3.7)#
postmenopausal individuals with incident cysts	1,729	1,038 (60.0±1.2)¶
Unilateral†	1,107	702 (63.4±1.4)¶
Bilateral‡	622	336 (54.0±2.0)¶
Asynchronous bilateral§	447	245 (54.8±2.4)¶
Synchronous bilateral‖	175	91 (52.0±3.8)#

Data are n or n (%±SEM).
* *Menopause* was defined as the absence of menses for 12 months. Findings are subject to the surveillance intervals described here.
Individuals with cysts only on
† one side,
‡ both sides,
§ both sides but at different times,
‖ both sides at the same time. Individuals with multiple cyst findings were included, so all cyst findings exceed the total number of individuals in each group.Significantly different $P<.05$.
Not significantly different: $P>.05$ for premenopausal vs postmenopausal.

1.018 [95% CI 1.011–1.024], $P<.05$) (Table 4). Postmenopausal status was associated with a decreased likelihood of resolution (HR 0.67 [95% CI 0.58–0.77], $P<.05$) (Table 4). Neither BMI nor family history of ovarian cancer were found to be associated with cyst resolution in either univariate or multivariate analysis (Table 4).

DISCUSSION

In this prospective cohort study, we have identified characteristics associated with ovarian cyst resolution. Our results indicate that cysts smaller than 3 cm resolve significantly more quickly than cysts larger than 6 cm. Septated cysts resolve more quickly than unilocular cysts, even though septated cysts are often

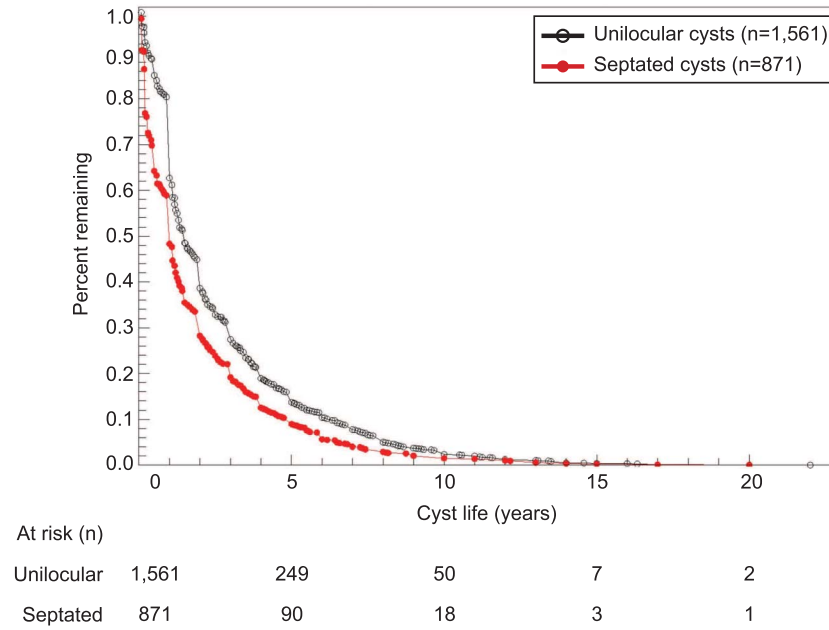

Fig. 2. Resolution of incident unilocular cysts and septated cysts. Ovarian cysts found on transvaginal ultrasonography were characterized by structure. The number of cysts remaining as a function of time after the appearance of the first cyst was converted to the percent of ovarian cysts remaining. Unilocular and septated cysts were monitored until resolution. Results were obtained using the Kaplan-Meier method. $P<.001$.
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Table 3. Analysis of Cyst Time to Resolution

	Univariate Analysis	
Factor*	Resolution Time (y)	*P*
Cyst structure		
Unilocular†	1.5 (2.33),1,557	<.05
Septated	1 (2.08), 867	
Cyst diameter (cm)		
Less than 3†	1 (1), 905	<.05
3–6	1.58 (3.09), 1,468	
Larger than 6	3.5 (4.17), 51	
HT use		
No†	1.17 (2.3), 1,986	<.05
Yes	2 (3), 438	
Age (y)		
Younger than 40†	1.8 (2.77), 228	<.05
40–69	1.25 (2.3), 2,007	
Older than 70	1 (1.5), 189	
Menopausal status		
Premenopausal†	1.5 (2.17), 1,679	.113
Postmenopausal	1.1 (2.42), 745	
BMI (kg/m^2)		
Lower than 18.5†	1.51 (2.05), 35	.953
18.5–24.9	1.15 (2.23), 1,104	
25–29.9	1.14 (2.48), 725	
30–34.9	0.98 (2.25), 476	
35 or higher	1.02 (2.5), 84	
Family history of ovarian cancer		
No†	1.2 (2.4), 1,420	.629
Yes	1.33 (2.25), 1,004	

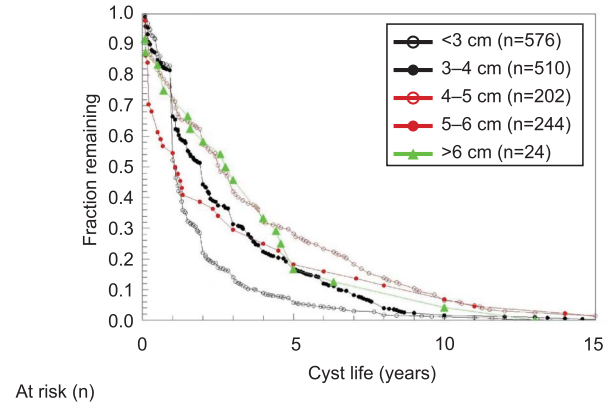
HT, hormone therapy; BMI, body mass index.
Data are median (interquartile range), n unless otherwise specified.
* Cyst diameter, patient age, and BMI were analyzed as ordinal variables; cyst characteristics, HT use, menopausal status, and family history of ovarian cancer were analyzed as nominal variables.
† Referent.

larger. Although younger age is associated with cyst resolution, the actual resolution takes significantly longer in younger individuals than in individuals older than age 70 years. Individuals using HT had slower resolution of their cysts than nonusers. Finally, there was no difference in time to cyst resolution based on BMI or family history of ovarian cancer.

The current recommendation from the American College of Obstetricians and Gynecologists is to repeat imaging without surgical intervention for cysts up to 10 cm, but the duration of follow-up has not been established.[18] We have described how cyst structure and size and patient HT use, age, menopausal status, BMI, and family history of ovarian cancer influence cyst resolution times to provide guidance for follow-up management. We can make an extrapolation of the findings reported here to estimate surveillance intervals. Our data are normally distributed with regard to resolution time, size, and BMI. Thus, the medians and means will be equal, and 99.7% of a normal distribution will be within 3 standard deviations. In a standardized normal distribution, the mean is 0 and the standard deviation is 1, so a multiplier greater than 3 should include virtually all of the distribution. By rounding the multiplier to 4, we can extrapolate that all of the distribution of resolving cysts can be covered. Consequently, for the 2-year median resolution of cysts in HT users (Table 3), 6–8 years of follow-up should predict the resolution of all cysts in all individuals using HT. In summary, with regard to length of surveillance, we are estimating that surveillance should continue for as long as three to four times the expected median resolution time. When there is a high suspicion of malignancy, surgical intervention certainly should be considered.[18]

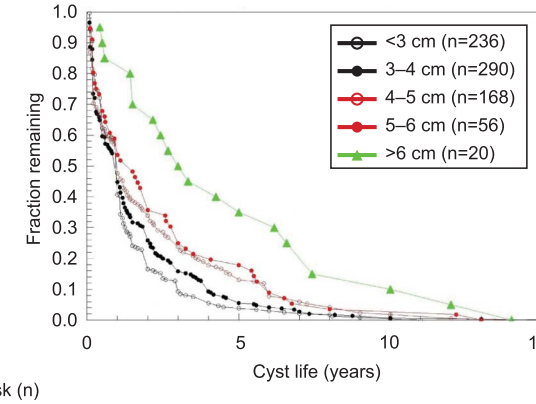
The UK-OCST has been active since 1987, allowing opportunities to both follow individuals and to accumulate a large number of participants. This work as a single-institution study, has the potential for selection bias; however, data were collected from six remote locations outside of the University of Kentucky so that participants were from all of Kentucky's 120 counties extending over a land mass of 40,407 square miles (involving 6.5% of Kentucky individuals eligible by the screening criterion of being at least age 50 years). These data from multiple populations across Kentucky allowed the inclusion of individuals from many different backgrounds, especially those from medically underserved areas and areas of poverty. In addition to high accessibility, screening was free, which allowed individuals from all socioeconomic backgrounds to participate in the trial and limited volunteer bias. Thus, statewide participation decreased a potential bias associated with a single-institution study and fostered social and economic diversity within the study population.

Limitations of the UK-OCST included fewer premenopausal individuals relative to postmenopausal individuals, because younger individuals are at a lower risk for developing ovarian cancer and, therefore, were not eligible for this screening trial unless they had increased predisposing risks equal to or higher than postmenopausal screening candidates. This could cause ascertainment bias as there were more participants in the postmenopausal group. However, this bias is minimized due to the large size of the premenopausal group, despite its size relative to the postmenopausal group. Certain realizations about the multivariate analysis reported on here are important. The Cox models fitted in Table 4 assume that a proportional hazards assumption is met by each risk



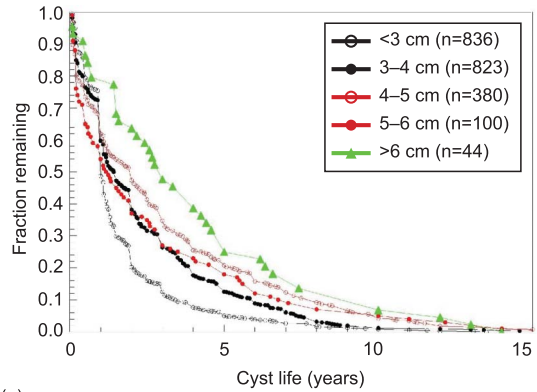
At risk (n)				
<3 cm	576	42	7	0
3–4 cm	510	98	12	3
4–5 cm	202	60	17	4
5–6 cm	44	10	5	2
>6 cm	24	6	3	0

A



At risk (n)				
<3 cm	236	10	2	0
3–4 cm	290	21	4	2
4–5 cm	168	25	10	0
5–6 cm	56	11	3	0
>6 cm	20	8	3	0

B



At risk (n)				
<3 cm	836	52	9	0
3–4 cm	823	119	16	5
4–5 cm	350	65	27	4
5–6 cm	100	21	8	2
>6 cm	44	14	6	0

C

Fig. 3. Resolution of unilocular cysts and septated cysts according to size. Ovarian cysts found on transvaginal ultrasonography were characterized by structure. Cysts remaining as a function of time after the appearance of the first cyst are expressed as the fraction of ovarian cysts remaining. Unilocular and septated cysts were monitored until resolution. Comparison of resolution time of unilocular **(A)**, septated **(B)**, and unilocular+septated **(C)** cysts based on diameter size (cm). Results were obtained using the Kaplan-Meier method.

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factor listed in column one of the table. However, only BMI met this assumption when it was assessed by the supremum test for proportional hazards. All the other risk factors did not meet this assumption in this well-known test. Further analysis showed that, for each risk factor, the assumption failed to be met whenever the time to cyst resolution was less than 2.3 years; for longer resolution times, the HRs listed in Table 4 were unchanged. In addition, it should be noted that the reported associations in this study are

Table 4. Univariate and Multivariate Analysis for All Factors to Assess Cyst Time to Resolution*

	Univariate Analysis			Multivariate Analysis		
Factor†,‡	HR	95% CI	*P*	HR	95% CI	*P*
Septated cyst	1.35	1.24–1.47	<.001	1.46	1.35–1.59	<.001
Cyst diameter	0.83	0.79–0.86	<.001	0.79	0.76–0.83	<.001
HT use	0.74	0.66–0.82	<.001	0.74	0.67–0.83	<.001
Age	1.006	1.002–1.010	<.002	1.018	1.011–1.024	<.001
Postmenopausal§	0.97	0.89–1.06	.56	0.67	0.58–0.77	<.001
Positive family history	1.02	0.94–1.11	.63	1.10	1.004–1.20	.04
BMI	1	0.99–1.01	.78	1	0.99–1.01	.83

HR, hazard ratio; HT, hormone therapy.
* Cox regression using SPSS for both univariate and multivariate analysis.
† Cyst diameter, patient age, and BMI were analyzed as continuous variables for both univariate and multivariate analysis; cyst structure, HT use, menopausal status, and family history of ovarian cancer were analyzed as nominal variables.
‡ N for each group is presented in Table 3. All of the factors listed were the variables retained in the final multivariate models.
§ *Menopause* was defined as the absence of menses for 12 months.

based on our series of patients with cysts serving as the denominators for reported proportions. This cohort may not represent a random sample of the U.S. population.

Although this study provides valuable information for the practicing clinician, there are still gaps in our understanding of ovarian cysts. Future research should be directed at understanding cyst structural progression. Additionally, a common dilemma among clinicians is when to refer a patient to a gynecologic oncologist for evaluation of an adnexal mass. Additional research and tools to stratify patients based on malignancy risk will help clinicians with their medical decision making.

REFERENCES

1. Farghaly SA. Current diagnosis and management of ovarian cysts. Clin Exp Obstet Gynecol 2014;41:609–12. doi: 10.12891/ceog20322014
2. Mobeen S, Apostol R. Ovarian cyst. StatPearls. Treasure Island (FL) ineligible companies; 2023. Accessed August 28, 2023 https://www.ncbi.nlm.nih.gov/books/NBK560541/
3. Bailey CL, Ueland FR, Land GL, DePriest PD, Gallion HH, Kryscio RJ, et al. The malignant potential of small cystic ovarian tumors in women over 50 years of age. Gynecol Oncol 1998;69:3–7. doi: 10.1006/gyno.1998.4965
4. Modesitt SC, Pavlik EJ, Ueland FR, DePriest PD, Kryscio RJ, van Nagell JR Jr. Risk of malignancy in unilocular ovarian cystic tumors less than 10 centimeters in diameter. Obstet Gynecol 2003;102:594–9. doi: 10.1016/s0029-7844(03)00670-7
5. Saunders BA, Podzielinski I, Ware RA, Goodrich S, DeSimone CP, Ueland FR, et al. Risk of malignancy in sonographically confirmed septated cystic ovarian tumors. Gynecol Oncol 2010;118:278–82. doi: 10.1016/j.ygyno.2010.05.013
6. van Nagell JR Jr., Miller RW. Evaluation and management of ultrasonographically detected ovarian tumors in asymptomatic women. Obstet Gynecol 2016;127:848–58. doi: 10.1097/AOG.0000000000001384
7. Suh-Burgmann E, Hung YY, Kinney W. Outcomes from ultrasound follow-up of small complex adnexal masses in women over 50. Am J Obstet Gynecol 2014;211:623.e1–7. doi: 10.1016/j.ajog.2014.07.044
8. Greenlee RT, Kessel B, Williams CR, Riley TL, Ragard LR, Hartge P, et al. Prevalence, incidence, and natural history of simple ovarian cysts among women >55 years old in a large cancer screening trial. Am J Obstet Gynecol 2010;202:373.e1–9. doi: 10.1016/j.ajog.2009.11.029
9. Wiggins AT, Pavlik EJ, Andrykowski MA. Psychological response to a false positive ovarian cancer screening test result: distinct distress trajectories and their associated characteristics. Diagnostics (Basel) 2019;9:128. doi: 10.3390/diagnostics9040128
10. Wiggins AT, Pavlik EJ, Andrykowski MA. Affective, cognitive and behavioral outcomes associated with a false positive ovarian cancer screening test result. J Behav Med 2017;40:803–13. doi: 10.1007/s10865-017-9851-1
11. Andrykowski MA, Pavlik EJ. Response to an abnormal ovarian cancer-screening test result: test of the social cognitive processing and cognitive social health information processing models. Psychol Health 2011;26:383–97. doi: 10.1080/08870440903437034
12. Lykins EL, Pavlik EL, Andrykowski MA. Validity of self-reports of return for routine repeat screening in an ovarian cancer screening program. Cancer Epidemiol Biomarkers Prev 2007;16:490–3. doi: 10.1158/1055-9965.EPI-06-0433
13. Andrykowski MA, Zhang M, Pavlik EJ, Kryscio RJ. Factors associated with return for routine annual screening in an ovarian cancer screening program. Gynecol Oncol 2007;104:695–701. doi: 10.1016/j.ygyno.2006.10.044
14. Alcázar JL, Castillo G, Jurado M, García GL. Is expectant management of sonographically benign adnexal cysts an option in selected asymptomatic premenopausal women? Hum Reprod 2005;20:3231–4. doi: 10.1093/humrep/dei206
15. Harris RD, Javitt MC, Glanc P, Brown DL, Dubinsky T, Harisinghani MG, et al. ACR appropriateness Criteria® clinically suspected adnexal mass. Ultrasound Q 2013;29:79–86. doi: 10.1097/RUQ.0b013e3182814d9b
16. Kaijser J, Bourne T, Valentin L, Sayasneh A, Van Holsbeke C, Vergote I, et al. Improving strategies for diagnosing ovarian cancer: a summary of the International Ovarian Tumor Anal-

ysis (IOTA) studies. Ultrasound Obstet Gynecol 2013;41:9–20. doi: 10.1002/uog.12323

17. Ormsby EL, Pavlik EJ, van Nagell JR. Ultrasound follow up of an adnexal mass has the potential to save lives. Am J Obstet Gynecol 2015;213:657–61. doi: 10.1016/j.ajog.2015.06.041
18. Evaluation and management of adnexal masses. Practice Bulletin No. 174. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;128:e210–26. doi: 10.1097/AOG.0000000000001768
19. Pavlik EJ, Saunders BA, Doran S, McHugh KW, Ueland FR, Desimone CP, et al. The search for meaning-Symptoms and transvaginal sonography screening for ovarian cancer: predicting malignancy. Cancer 2009;115:3689–98. doi: 10.1002/cncr.24407
20. Ueland FR, Depriest PD, Desimone CP, Pavlik EJ, Lele SM, Kryscio RJ, et al. The accuracy of examination under anesthesia and transvaginal sonography in evaluating ovarian size. Gynecol Oncol 2005;99:400–3. doi: 10.1016/j.ygyno.2005.06.030
21. Padilla LA, Radosevich DM, Milad MP. Accuracy of the pelvic examination in detecting adnexal masses. Obstet Gynecol 2000;96:593–8. doi: 10.1016/s0029-7844(00)00970-4
22. Jacobs I, Bridges J, Reynolds C, Stabile I, Kemsley P, Grudzinskas J, et al. Multimodal approach to screening for ovarian cancer. Lancet 1988;331:268–71. doi: 10.1016/s0140-6736(88)90351-0
23. van Nagell JR Jr., DePriest PD, Ueland FR, DeSimone CP, Cooper AL, McDonald JM, et al. Ovarian cancer screening with annual transvaginal sonography: findings of 25,000 women screened. Cancer 2007;109:1887–96. doi: 10.1002/cncr.22594
24. Sato S, Yokoyama Y, Sakamoto T, Futagami M, Saito Y. Usefulness of mass screening for ovarian carcinoma using transvaginal ultrasonography. Cancer 2000;89:582–8. doi: 10.1002/1097-0142(20000801)89:3<582::aid-cncr13>3.0.co;2-#
25. van Nagell JR Jr., Miller RW, DeSimone CP, Ueland FR, Podzielinski I, Goodrich ST, et al. Long-term survival of women with epithelial ovarian cancer detected by ultrasonographic screening. Obstet Gynecol 2011;118:1212–21. doi: 10.1097/AOG.0b013e318238d030
26. Sokalska A, Timmerman D, Testa AC, Van Holsbeke C, Lissoni AA, Leone FP, et al. Diagnostic accuracy of transvaginal ultrasound examination for assigning a specific diagnosis to adnexal masses. Ultrasound Obstet Gynecol 2009;34:462–70. doi: 10.1002/uog.6444
27. Castillo G, Alcazar JL, Jurado M. Natural history of sonographically detected simple unilocular adnexal cysts in asymptomatic postmenopausal women. Gynecol Oncol 2004;92:965–9. doi: 10.1016/j.ygyno.2003.11.029
28. Ekerhovd E, Wienerroith H, Staudach A, Granberg S. Preoperative assessment of unilocular adnexal cysts by transvaginal ultrasonography: a comparison between ultrasonographic morphologic imaging and histopathologic diagnosis. Am J Obstet Gynecol 2001;184:48–54. doi: 10.1067/mob.2001.108330
29. Guraslan H, Dogan K. Management of unilocular or multilocular cysts more than 5 centimeters in postmenopausal women. Eur J Obstet Gynecol Reprod Biol 2016;203:40–3. doi: 10.1016/j.ejogrb.2016.05.028
30. Pavlik EJ, Ueland FR, Miller RW, Ubellacker JM, DeSimone CP, Elder J, et al. Frequency and disposition of ovarian abnormalities followed with serial transvaginal ultrasonography. Obstet Gynecol 2013;122:210–7. doi: 10.1097/AOG.0b013e318298def5
31. Brun JL, Fritel X, Aubard Y, Borghese B, Bourdel N, Chabbert-Buffet N, et al. Management of presumed benign ovarian tumors: updated French guidelines. Eur J Obstet Gynecol Reprod Biol 2014;183:52–8. doi: 10.1016/j.ejogrb.2014.10.012
32. McDonald JM, Doran S, DeSimone CP, Ueland FR, DePriest PD, Ware RA, et al. Predicting risk of malignancy in adnexal masses. Obstet Gynecol 2010;115:687–94. doi: 10.1097/AOG.0b013e3181d44053
33. Oyelese Y, Kueck AS, Barter JF, Zalud I. Asymptomatic postmenopausal simple ovarian cyst. Obstet Gynecol Surv 2002;57:803–9. doi: 10.1097/00006254-200212000-00004
34. Brown DL, Doubilet PM, Miller FH, Frates MC, Laing FC, DiSalvo DN, et al. Benign and malignant ovarian masses: selection of the most discriminating gray-scale and Doppler sonographic features. Radiology 1998;208:103–10. doi: 10.1148/radiology.208.1.9646799
35. Barroilhet L, Vitonis A, Shipp T, Muto M, Benacerraf B. Sonographic predictors of ovarian malignancy. J Clin Ultrasound 2013;41:269–74. doi: 10.1002/jcu.22014
36. Pavlik EJ, Brekke E, Gorski J, Baldwin-Branch L, Miller R, DeSimone CP, et al. Ultrasonographic visualization of the ovaries to detect ovarian cancer according to age, menopausal status and body type. Diagnostics (Basel) 2022;12:128. doi: 10.3390/diagnostics12010128
37. Higgins RV, van Nagell JR Jr., Woods CH, Thompson EA, Kryscio RJ. Interobserver variation in ovarian measurements using transvaginal sonography. Gynecol Oncol 1990;39:69–71. doi: 10.1016/0090-8258(90)90401-6
38. Pavlik EJ, Fancher H, Dietrich CS, van Nagell JR Jr. Subsequent ultrasonographic non-visualization of the ovaries is hastened in women with only one ovary visualized initially. Healthcare (Basel) 2022;10:433. doi: 10.3390/healthcare10030433
39. Lyons EA, Gratton D, Harrington C. Transvaginal sonography of normal pelvic anatomy. Radiol Clin North Am 1992;30:663–75.

Authors' Data Sharing Statement

Will individual participant data be available (including data dictionaries)? *No.*

What data in particular will be shared? *Data that are institutionally approved.*

What other documents will be available? *None available.*

When will data be available (start and end dates)? *Not applicable.*

By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)? *Not applicable.*

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