

Factors affecting visualization of postmenopausal ovaries: descriptive study from the multicenter United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS)

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ABSTRACT

Objective Transvaginal sonography (TVS) is core to any ovarian cancer screening strategy. General-population screening involves older postmenopausal women in whom ovarian visualization is difficult because of decreasing ovarian size and lack of follicular activity. We report on factors affecting the visualization of postmenopausal ovaries in the multicenter United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS).

Methods The UKCTOCS is a randomized controlled trial of 202 638 postmenopausal women with 50 639 women in the ultrasound scan arm. TVS is the primary screening modality in the ultrasound scan arm. Age, education, ethnicity, body mass index (BMI), previous pelvic surgery, lifestyle and reproductive factors, and a personal/family history of cancer were assessed for their effects on ovarian visualization at the initial TVS.

Results Between 11 June 2001 and 18 August 2007, 43 867 women underwent TVS. The median age and BMI of the women were 60.6 (interquartile range (IQR), 9.9) years and 25.7 (IQR, 5.8), respectively. The right ovary was visualized in 29 297 (66.8%) and the left ovary was visualized in 28 726 (65.5%). Visualization of ovaries decreased with previous hysterectomy (odds ratio (OR) = 0.534; 95% CI, 0.504–0.567), previous tubal ligation (OR = 0.895; 95% CI, 0.852–0.940), increasing age (OR = 0.953; 95% CI, 0.950–0.956), unilateral

oophorectomy (OR = 0.224; 95% CI, 0.186–0.269) and being overweight (OR = 0.918; 95% CI, 0.876–0.962) or obese (OR = 0.715; 95% CI, 0.677–0.755). Increased visualization was observed with a history of infertility (OR = 1.134; 95% CI, 1.005–1.279) and increasing age (in years) at menopause (OR = 1.005; 95% CI, 1.001–1.009).

Conclusions Several factors affect the visualization of postmenopausal ovaries. Their impact needs to be taken into consideration when developing quality assurance for ovarian ultrasound scanning or comparing study results as their prevalence may differ between populations. Copyright © 2013 ISUOG. Published by John Wiley & Sons Ltd.

INTRODUCTION

Transvaginal sonography (TVS) is core to any ovarian cancer screening strategy. Its efficacy both as a first- and a second-line test is being evaluated in the multicenter United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS)¹ and in several other ovarian cancer screening trials worldwide^{2–4}. Visualization of ovaries underpins the identification of abnormal ovarian morphology. However, ovarian visualization can be difficult in general-population screening that involves older postmenopausal women with decreasing ovarian size and

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lack of follicular activity. The Kentucky Ovarian Cancer Screening group, in their report on efficacy of TVS screening in asymptomatic women at a single center, showed that it was possible to visualize the ovaries in 79.2% of the 57 214 scans performed in 14 469 women (including premenopausal women with a family history of ovarian cancer) enrolled on the trial between 1987 and 1999². A more recent study, of 515 asymptomatic postmenopausal women, has also reported similar visualization rates: 86.3% for the right ovary and 78% for the left ovary⁵. Of these 515 women, 481 attended for a repeat TVS 12 months later⁶. The right ovary was seen in 85.8% and the left ovary in 77.7% of women. For both scans, the right ovary was seen in 80% and the left ovary was seen in 68%. More variable visualization rates, of between 57% and 71%, have been reported in different subgroups from the ovarian screening arm of the Prostate Lung Colorectal and Ovarian Cancer (PLCO) study^{7,8}. Although there is some description of the baseline characteristics of the study populations, in none was the effect of confounding factors, such as hysterectomy, assessed on ovarian visualization. As TVS is likely to remain part of any ovarian cancer screening strategy, this is essential if we are to compare study results or develop quality assessment measures to assess sonographers. We report on factors impacting the visualization of ovaries in women undergoing TVS in the ultrasound scan arm of the UKCTOCS.

METHODS

The UKCTOCS is a randomized controlled trial of ovarian cancer screening of 202 638 postmenopausal women participants in the general population. The participants are allocated to a control group (no screening), a multimodal group (annual screening with CA 125 as a primary test and TVS as a secondary test) or an ultrasound scan group (annual screening with TVS) in a 2:1:1 ratio. Women were recruited through 13 trial centers located in National Health Service (NHS) Hospitals in England, Wales and Northern Ireland. Written consent was obtained from all participants. Women were included in the trial if they were postmenopausal (defined as >12 months amenorrhoea following a natural or surgical menopause or >12 months of hormone replacement therapy commenced for menopausal symptoms) and were ≥ 50 and 70–74 years of age. They were excluded if they had a history of bilateral oophorectomy, active malignancy (women with a past history of malignancy were eligible if they had no documented persistent or recurrent disease), increased risk of ovarian cancer because of familial predisposition or a previous history of ovarian cancer. Following confirmation of eligibility, 50 639 women were randomized to the ultrasound scan arm. At recruitment, women completed a baseline questionnaire, which included age, lifestyle factors, and reproductive, medical and family histories (Table 1). Women were sent a postal questionnaire 3.5 years after randomization in which information on education, smoking and alcohol use was obtained. Details of recruitment and design are described elsewhere^{1,9}.

A detailed ultrasound scan protocol¹ addressed all issues with regard to scanning, including technique, classification of morphological findings, further management algorithms and collection and storage of the ultrasound data. The majority of the scans (carried out from 2001 to 2007) were performed using the Kretz SA2000 (Kretztechnik AG, Zipf, Austria) ultrasound machine. For the main trial, annual scans were performed by Type 1 sonographers who were certified sonographers, trained midwives or doctors in the NHS trained in gynecological scanning. If the results of the annual scan were abnormal then women had a repeat scan, which was performed by Type 2 sonographers who were senior sonographers (mostly superintendent level), experienced certified gynecologists or radiologists. Where women found TVS unacceptable, transabdominal sonography (TAS) was performed.

At the annual screen visit, the sonographer initially ascertained whether the woman had previously undergone a hysterectomy or a unilateral oophorectomy. The first step on scanning was to decide if the ovaries were: (a) seen; (b) not seen, but a good view of the iliac vessels was obtained; and (c) not seen, with a poor view of the iliac vessels secondary to bowel, fibroids or other pelvic structures. Definitions of morphology and algorithms for the classification of scans and further management are detailed elsewhere¹. All data obtained from scans were entered on the central Web-based trial-management system⁹.

In this study, women in the ultrasound scan arm of the UKCTOCS who underwent TVS at the first annual screen were included. Those who only had transabdominal scans were excluded.

The UKCTOCS study was approved by the UK North West Multicentre Research Ethics Committees (North West MREC 00/8/34). It is registered as an International Standard Randomized Controlled Trial (no. ISRCTN22488978).

Statistical analysis

Frequency distributions of baseline characteristics of the population were derived. Visualization was defined as ovaries 'seen' and the rates were calculated based on all included scans. Visualization rates of the right and the left ovary were calculated separately. As they were proportionally similar, all further analyses were confined to visualization rates of the right ovary. All recorded factors (age, body mass index (BMI), hormone replacement therapy (HRT) use, previous hysterectomy, unilateral oophorectomy with intact uterus (LONH), presence of fibroids, years from menopause, previous contraceptive pill use, miscarriages, parity, infertility history, tubal ligation, ever smoker, alcohol use, educational qualification, personal history of breast cancer and ethnicity) were evaluated for their effect on visualization of ovaries. Logistic regression with backward stepwise elimination (probability of removal = 0.05) was used to determine which of the abovementioned variables were independently significant

Table 1 Baseline characteristics of women attending first-year transvaginal scan

Characteristic	Total (n = 43 867)	Visualization of RO (n = 29 297)
Age (years)		
50–54 years	7983 (18.2)	5932 (74.3)
55–59 years	12 335 (28.1)	8750 (70.9)
60–64 years	10 416 (23.7)	6995 (67.2)
65–69 years	8313 (19.0)	4984 (60.0)
70–74 years	4820 (11.0)	2636 (54.7)
Years from LMP		
< 5 years	10 277 (23.4)	7741 (75.3)
5 to < 10 years	9030 (20.6)	6411 (71.0)
10 to < 15 years	8462 (19.3)	5801 (68.6)
≥ 15 years	16 098 (36.7)	9344 (58.0)
BMI group		
Underweight (BMI 15 to <20 kg/m ²)	516 (1.2)	330 (64.0)
Normal (BMI 20 to < 25 kg/m ²)	18 054 (41.2)	12 598 (69.8)
Overweight (BMI 25 to < 30 kg/m ²)	16 010 (36.5)	10 685 (66.7)
Obese (BMI ≥ 30 kg/m ²)	9083 (20.7)	5560 (61.2)
Data errors/missing information	204 (0.5)	124 (60.8)
Ethnicity		
White	42 328 (96.5)	28 209 (66.6)
Black	615 (1.4)	428 (69.6)
Asian	374 (0.9)	280 (74.9)
Other	339 (0.8)	247 (72.9)
Missing information	211 (0.5)	133 (63.0)
History of breast cancer		
Personal	1614 (3.7)	1031 (63.9)
In sister	1910 (4.4)	1258 (65.9)
In mother	2601 (5.9)	1798 (69.1)
In sister and mother	199 (0.5)	134 (67.3)
None in first-degree relative	37 820 (86.2)	25 253 (66.8)
History of infertility		
Yes, nulliparous	290 (0.7)	198 (68.3)
Yes, parous	1032 (2.4)	758 (73.4)
No	42 418 (96.7)	28 250 (66.6)
Missing information	127 (0.3)	91 (71.7)
History of miscarriage		
Yes	13 546 (30.9)	9041 (66.7)
Missing information	582 (1.3)	373 (64.4)
Parity		
Nulliparous	4572 (10.5)	3073 (67.2)
1	5227 (12.3)	3594 (68.8)
2	18 823 (43.5)	12 746 (67.7)
3	9922 (22.5)	6591 (66.4)
> 3	5207 (11)	3214 (61.7)
Missing information	116 (0.3)	79 (68.1)
OCP use	26 888 (63)	18 469 (68.7)
HRT use	8356 (19.4)	5685 (68.0)
Previous hysterectomy	8201 (18.7)	4420 (53.9)
Previous contralateral oophorectomy (LO)		
Yes	704 (1.6)	537 (76.3)
No	43 163 (98.4)	28 760 (66.6)
Excluding those with previous hysterectomy	246 (0.6)	201 (81.7)
Previous sterilization	9552 (21.8)	6189 (64.8)
Ever smoker		
Yes	15 007 (34.2)	10 203 (68.0)
Missing information	2820 (6.4)	1624 (57.6)
Alcohol use		
Yes	25 884 (59)	17 667 (68.3)
Missing information	10 156 (23.2)	6485 (63.9)

Table 1 Continued

Characteristic	Total (n = 43 867)	Visualization of RO (n = 29 297)
Level of education		
None of the options given	3672 (8.4)	2511 (68.4)
Secondary education	1125 (2.6)	794 (70.6)
Clerical/administrative	8429 (19.2)	5663 (67.2)
Higher secondary education	3157 (7.2)	2083 (66.0)
Nursing/teaching	6885 (15.7)	4869 (70.7)
College/university degree	10 146 (23.1)	6705 (66.1)
Missing information	10 453 (23.8)	6672 (63.8)

Data are given as *n* (%). BMI, body mass index; HRT, hormone replacement therapy; LMP, last menstrual period; LO, left ovary; OCP, oral contraceptive pill; RO, right ovary.

in predicting ovarian visualization rates. All analyses were undertaken using Stata 12 (StataCorp LP, College Station, TX, USA).

RESULTS

Between 11 June 2001 and 18 August 2007, 48 230 women in the ultrasound scan arm had an initial scan performed by 109 sonographers. Of these women, 43 867 had a TVS (42 401 had a TVS only and 1466 had both a TVS and a TAS) and were included in the analysis. Women who underwent a TAS only (*n* = 4363) were excluded. The median age of the 43 867 women was 60.6 (IQR, 9.9). The majority of women were white, one in five was obese, 18.7% had previously had a hysterectomy and 1.6% had undergone a unilateral oophorectomy (Table 1).

The right ovary (RO) was visualized in 29 297 (66.8%) scans and the left ovary (LO) in 28 726 (65.5%) (Table 2). As the visualization of the RO and LO was proportionally similar, further analyses were limited to the RO. In women in whom the RO was visualized, the median age at the scan was 59.9 (IQR, 9.5) years. Visualization of the RO declined with increasing age (Figure 1a; Table 1) and being overweight or obese (Figure 1b; Table 1).

In total, 40 801 women had complete data with regard to factors assessed and were included in the model. In 27 717 of these women, the right ovary was visualized. From the logistic regression model, age at scan, raised BMI, previous hysterectomy, previous tubal ligation and LONH were identified as significant predictors at the 5% level, with fibroids, history of infertility and age

Table 2 Overall visualization of ovaries in 43 867 women undergoing transvaginal sonography

Visualization	Right ovary	Left ovary
Seen	29 297 (66.8)	28 726 (65.5)
Not seen		
Good view	11 905 (27.1)	12 428 (28.3)
Poor view	1942 (4.4)	2009 (4.6)
Previous oophorectomy	723 (1.6)	704 (1.6)

Values are given as *n* (%).

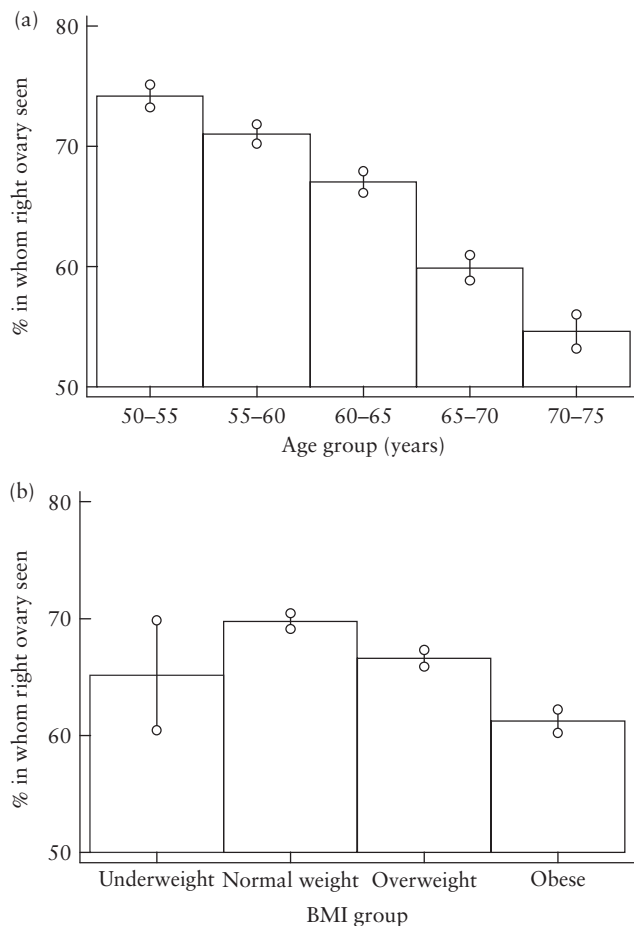


Figure 1 Visualization of right ovary on transvaginal scan in different age groups (a) and in different body mass index (BMI) groups (b). Bars represent means, and 95% confidence limits are shown.

at menopause only of marginal significance. Previous hysterectomy (OR = 0.534; 95% CI, 0.504–0.567), increasing age (OR = 0.953; 95% CI, 0.950–0.956), previous tubal ligation (OR = 0.895; CI, 0.852–0.940), LONH (OR = 0.224; 95% CI, 0.186–0.269) and being overweight (OR = 0.918; 95% CI, 0.876–0.962) or obese (OR = 0.715; 95% CI, 0.677–0.755) were associated with decreased visualization (Table 3). Increased visualization was associated with a history of infertility (OR = 1.134; 95% CI, 1.005–1.279), increasing age at menopause (OR = 1.005; 95% CI, 1.001–1.009) and the presence of fibroids (OR = 1.075; 95% CI, 1.013–1.140). There was a non-significant trend toward increased visualization in women of Black (OR = 1.226; 95% CI, 0.965–1.557) or Asian (OR = 1.178; 95% CI, 0.986–1.407) origin. History of contraceptive pill use or miscarriage, parity, smoking and alcohol use, educational qualification, and a personal history of breast cancer had no additional impact on visualization of ovaries.

DISCUSSION

This is the largest study describing factors affecting ovarian visualization on TVS in postmenopausal women.

Our results show a 47% decrease in ovarian visualization in women who have previously undergone hysterectomy and a 5% decrease with each increasing year of age. A 78% decrease in visualization is noted in women who have an intact uterus but unilateral oophorectomy, an 11% decrease in those who have had tubal ligation, a 9% decrease in overweight women and a 29% decrease in obese women. A history of infertility has a 14% increase in visualization of the ovary. There is also a non-significant increase in visualization of ovaries, of 22% and 17%, respectively, in women of Black and Asian origin.

The strengths of our study are the large sample size, involving participants from the general population, a multicenter design and performance of scans by over 100 sonographers, all of which increases the external validity of the findings. The two other major factors that can affect visualization are skill/experience of the individual sonographer and the overall quality of the team. While there are no studies comparing visualization rates with experience of sonographers, Timmerman *et al.* have shown that operator experience is a significant factor in accurately identifying malignant from benign lesions on ultrasound scans¹⁰. In an image review study of 300 women (166 premenopausal and 134 postmenopausal), an accuracy of 92% was achieved by the two most-experienced operators, while accuracy dropped to 82–87% for the less-experienced operators. Similarly, there was very good interobserver agreement between the two most-experienced operators but this varied with the less-experienced operators. It is also likely that organization and leadership of the team, together with training, support and monitoring of the sonographers, adds to the quality of scanning at any individual center. We are currently undertaking work which compares scanning between sonographers and trial centers and describes in detail the quantitative methods for quality assessment of TVS in postmenopausal women, adjusted for the non-subjective factors identified and quantified here to impact on ovarian visualization.

Our findings of decreased ovarian visualization with previous hysterectomy confirm the report from the PLCO trial that women with previous hysterectomy were less likely (47%) to have their ovaries seen in comparison with women who had no previous gynecological surgery of their ovaries (61%)⁸. The most likely reason for this is the loss of anatomical landmarks with the absence of the uterus, making it harder to identify the ovary. Changes in the relative position of the ovaries and in the position and size of the uterus, and the presence of fibroids, bowel in the pelvis and adhesions secondary to surgery could also impact on visualization. Except for the presence of fibroids, information on the other factors was not routinely recorded so we are unable to comment on their effect. Unlike previous reports, the presence of fibroids did not decrease visualization (although the evidence was not strong, being only just significant at the 5% level) but this could be a result of the fact that these would be atrophic in this postmenopausal cohort and were likely to have been of smaller size and asymptomatic in the past.

Table 3 Factors affecting visualization of right ovary on transvaginal scan

Factor	Odds ratio	Standard error	P	95% CI
Previous hysterectomy (yes)	0.534	0.016	< 0.0001	0.504–0.567
Previous tubal ligation (yes)	0.895	0.022	< 0.0001	0.852–0.940
Age at scan (years)	0.953	0.001	< 0.0001	0.950–0.956
Age at last menstrual period (years)	1.005	0.001	0.006	1.001–1.009
History of infertility (yes)	1.134	0.069	0.040	1.005–1.279
Unilateral (left) oophorectomy with intact uterus (yes)	0.224	0.020	< 0.0001	0.186–0.269
Presence of fibroids (yes)	1.075	0.032	0.016	1.013–1.140
Ethnicity*				
White (reference)				
Black	1.226	0.149	0.095	0.965–1.557
Asian	1.178	0.106	0.071	0.986–1.407
Other	1.216	0.154	0.121	0.949–1.559
BMI group†				
Normal (BMI 20 to < 25 kg/m ²) (reference)				
Underweight (BMI 15 to < 20 kg/m ²)	0.834	0.091	0.099	0.673–1.034
Overweight (BMI 25 < 30 kg/m ²)	0.918	0.021	< 0.0001	0.876–0.962
Obese (BMI ≥ 30 kg/m ²)	0.715	0.019	< 0.0001	0.677–0.755

*Overall *P* for ethnicity = 0.0404. †Overall *P* for BMI group < 0.0005. BMI, body mass index.

We noted that unilateral oophorectomy in the absence of hysterectomy was also associated with a significant (78%) decrease in visualization of the remaining ovary. Previous data also suggest that women who have had unilateral oophorectomy with hysterectomy have an accelerated decline in the function of the remaining ovary and an earlier menopause than do women who have had a hysterectomy alone during the premenopausal period¹¹. This should lead to a reduction in the size of the remaining ovary and reduced visualization. In the PLCO study, visualization of the ovary contralateral to the side of oophorectomy was also decreased (42%) when compared with women who had no previous gynecological surgery (61%)⁸. No difference in visualization of ovaries was observed between women who had previously undergone gynecological surgery (61%) and those who underwent sterilization (60%). However, in our study, an 11% decrease in visualization was noted in those who had undergone tubal ligation. It is difficult to speculate why this may be the case as the latter is a minor procedure; however, it is known to be associated with iatrogenic hydrosalpinx¹² and it is possible that this may have obscured the view of the ovary.

The visualization of ovaries was reduced in women with increasing age (a 5% decrease in the OR with each year), whereas increasing age at menopause improved visualization (although this was only marginally significant). Ovaries were visualized in 71% of 55- to 59-year-old women compared with 55% of women 70–74 years of age (Table 1). This is similar to the PLCO study, which reported decreased visualization in older women and increased rates in those who attained menopause in later years (after 55 years of age)⁸. There was a significant decrease in visualization of ovaries with BMI > 30. Increased fat leads to poor penetration of sound waves beyond the focal point, leading to poor views on ultrasound scans¹³. In TVS this is reduced as the transducer is closer to the pelvic structures, making

them easier to visualize. However, transducer movement may be restricted secondary to thigh and vulval obesity, especially in morbidly obese women.

Unlike other factors, information on smoking and alcohol use were obtained from the follow-up questionnaire completed 3 to 4 years following the first scan. Although unlikely, these habits may have changed from the time when the first scan was performed to when the data were actually collected. Other limitations include a small proportion (3.3%) of women who underwent both TVS and TAS and in whom it was not possible to determine whether the ovaries were visualized on TAS or TVS as this was not separately documented. In addition, the proportion of Black (1.4%), Asian (0.9%) and other ethnic-minority (0.8%) women in the study was small. This might have led to the lack of significant difference in visualization rates of ovaries.

In conclusion, several factors affect visualization of ovaries on TVS, with previous hysterectomy, previous LONH, tubal ligation, BMI and age having the largest impacts. Adjustments for these factors are necessary when developing quality assurance for ovarian ultrasound scanning or comparing results between studies as their prevalence may differ between populations.

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DISCLOSURES

Ian Jacobs has consultancy arrangements with Becton Dickinson, who have an interest in tumor markers and ovarian cancer. They have provided consulting fees, funds for research and staff but none directly related to this study. Usha Menon has a financial interest through UCL Business and Abcodia Ltd in the third-party exploitation of clinical trials biobanks, which have been developed through the research at UCL. No other financial disclosures.

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