THE SOCIETY OF GYNECOLOGIC ONCOLOGY OF CANADA | LA SOCIÉTÉ DE GYNÉCO-ONCOLOGIE DU CANADA

January 8, 2016

THE SOCIETY OF GYNECOLOGIC ONCOLOGY OF CANADA (GOC)
OPINION STATEMENT REGARDING
THE UK COLLABORATIVE TRIAL OF OVARIAN CANCER SCREENING (UKCTOCS) RESULTS

GOC Recommendation:
Based on the results of the two large randomised phase three trials, the recent UKCTOCS[1] trial (December 2015) and the previously published PLCO[2] trial (2011), GOC does not recommend screening for "ovarian" cancer at this time.

Summary of UKCTOCS study:

- no statistical difference in number of women who succumbed to "ovarian" cancer between the control and study patients
- a small trend towards better survival in the later years of the study which needs to be followed longer
- increased interventions in the screened women with resulting morbidity
- routine screening cannot be recommended at this time

The purpose of "ovarian cancer screening" is to detect cancers on the ovaries before they cause symptoms. The hypothesis is that the overall survival of the women with these cancers will be better if detected at the stage before symptoms occur. Up until now, no reliable study has been able to show this outcome for what is commonly called "ovarian" cancer, which represents different types of cancers involving the ovaries (each with its own natural history).

The UKCTOCS trial involves 202,638 women and was initiated in Great Britain 15 years ago to evaluate whether screening for "ovarian" cancer can save lives. This important trial randomized women between the ages of 50 and 74 to either standard gynecologic follow-up, yearly transvaginal ultrasound to detect abnormalities, or yearly multimodal screening (MMS) with serial serum CA125 interpreted using the risk of ovarian cancer algorithm (ROCA).This algorithm uses the slope of CA125 changes to trigger further investigations and ultimately surgery. After 345,570 multimodal screenings and 327,775 annual ultrasound screening episodes for a total follow-up of 2.19 million women-years, the number of women who succumbed to ovarian cancer was not statistically different between any of the groups, despite the fact that a higher proportion of women (40%) were diagnosed with lower volume disease in the MMS screened group, compared to the non-screened group (26%). The difference in disease burden between the screened versus non-screened group needs to be interpreted with caution, as borderline and non-epithelial cancers, that are usually diagnosed at an early stage and which are associated with a better prognosis were found in 16 to 20% of screened patients, compared to only 9.5% in the non-screened cohort. In the screened women, over 40% of the cancers occurred between screening episodes (interval cancers). Further analysis indicated that if 641 women were screened using CA125 on an annual basis for 14 years, one life might be saved, but uncertainty

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remains upon the validity of the findings in view of the statistical considerations. Even if the finding is real, this benefit needs to be balanced against the complications resulting from the unnecessary surgery performed because both elevated CA125 and abnormal ultrasound findings are frequently not related to cancer. In the UKCTOCS study, for each ovarian cancer detected by screening, two additional women in the MMS group and ten additional women in the ultrasound group had false-positive surgery, and 3.1-3.5% of women undergoing surgery had major complications. These data are similar to what was described in the PLCO study published in 2011, however in the PLCO study, no difference in survival was found between the screening and the control group. It is hypothesized that this difference might be due to the improved sensitivity provided by the MMS-ROCA protocol. While these results may be seen as encouraging, the decrease in mortality associated with screening might just reflect a prolongation of time with disease and apparent delayed mortality due to earlier diagnosis (lead time bias). On the other hand, the fact that the mortality hazard rate in the no-screening group seems to increase, whereas it levels off in the two screened groups, is encouraging. Longer follow-up is needed to determine the true impact on mortality (whether screening indeed saves lives), the benefit ratio for the women, and the cost effectiveness of multi-modality ovarian cancer screening.

[1] Jacobs IJ, Menon U, Ryan A, Gentry-Maharaj A, Burnell M, Kalsi JK, Amso NN, Apostolidou S, Benjamin E, Cruickshank D, Crump DN, Davies SK, Dawnay A, Dobbs S, Fletcher G, Ford J, Godfrey K, Gunu R, Habib M, Hallett R, Herod J, Jenkins H, Karpinskyj C, Leeson S, Lewis SJ, Liston WR, Lopes A, Mould T, Murdoch J, Oram D, Rabideau DJ, Reynolds K, Scott I, Seif MW, Sharma A, Singh N, Taylor J, Warburton F, Widschwendter M, Williamson K, Woolas R, Fallowfield L, McGuire AJ, Campbell S, Parmar M, Skates SJ. Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (**UKCTOCS**): a randomised controlled trial. Lancet. 2015 Dec 16. pii: S0140-6736(15)01224-6. doi: 10.1016/S0140-6736(15)01224-6. [Epub ahead of print]

[2] Buys SS, Partridge E, Black A, et al. Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening randomized controlled trial. JAMA 2011;305: 2295–303.