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Ovarian cancer prevention, screening and early detection: Report from the 11th Biennial Ovarian Cancer Research Symposium

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Abstract

Objective: The aim of this study is to provide a summary report on recent research advances in ovarian cancer prevention, screening, and early detection that were presented at the 11th Biennial Ovarian Cancer Research Symposium in Seattle, Wash.

Methods: At the symposium, researchers from around the world participated in the poster, invited oral presentation and keynote presentation, and discussed the latest advances in the areas of cancer prevention, screening, and early detection.

Results: In the Scientific Session for Prevention, Screening, and Early Detection, Usha Menon, PhD (University of College London), presented exploratory studies from the ongoing UK Collaborative Trial of Ovarian Cancer Screening trial. Karen Lu, MD, presented her studies on BRCA testing and salpingectomies as prevention strategies. Eight speakers were selected from the abstracts for short oral presentations, and the topic ranges from Ovarian Cancer Early Detection Program by Saul Rivkin, MD, to the ultra-deep sequencing of somatic mutations in TP53 in normal and cancer patients by Rosana Risques, PhD. Fourteen additional poster presentations, ranging from the potential role of cancer stem cells in recurrence to retrotransposons in ovarian cancer development, round up the session.

Conclusions: Although progress is being made in the areas of prevention, screening, and early detection, these advances have not yet translated into tangible clinical benefits for patients with ovarian cancer. A wide array of research topics presented in the session provides a glimmer of hope that better understanding of genetic risk factors, refining screening strategies, and developing new methods for early detection will eventually lead to improved outcome for patients with ovarian cancer.

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Keywords

Ovarian cancer; Meeting report; Prevention; Screening; Early detection

INTRODUCTION

Ovarian cancer is the fifth leading cause of cancer deaths among women in the developed world,[1] and approximately 1 in 54 women will develop ovarian cancer in her lifetime.[2] The 5-year survival among women diagnosed with ovarian cancer is 46.2%. This is mostly due to the late stage at which ovarian cancer is diagnosed: over 70% of women are diagnosed with advanced disease (stages III and IV).[3] There is currently no approved screening test for ovarian cancer or are there early detection modalities. In addition, most established risk factors for ovarian cancer (eg, first-degree family history, lack of parity, lack of use of oral contraceptive pills) are not modifiable on a population level. Thus, there remains a great need for developing new strategies for prevention, screening, and early detection. At the 2016 Ovarian Cancer Research Symposium, sponsored by the Rivkin Center for Ovarian Cancer and the American Association for Cancer Research, cutting edge research on these topics was presented, and the proceedings from the 2016 Ovarian Cancer Research Symposium are recently published in the journal Clinical Cancer Research.[4] Hereinafter, we summarize the research presentations and discuss the implications for improving ovarian cancer prevention and survival.

SCREENING AND EARLY DETECTION

Unfortunately, screening modalities currently available for the early detection of ovarian cancer are not sufficiently sensitive enough to detect ovarian cancer patients at early stages or improve the outcome of patients with ovarian cancer.[5,6] Therefore, the US Preventative Services Task Force currently discourages general population-based ovarian cancer screening because of the high potential for unnecessary interventions.[7] The European Group on Tumor Markers also does not recommend CA-125 as a routine screening test in asymptomatic women.[8] These reports highlight the urgent need to develop better screening modalities for early detection of ovarian cancer. These critical issues were addressed by Dr. Usha Menon in her recent keynote presentation. Dr. Menon is one of the principal investigators on the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) trial, which evaluated whether serial screening, either via CA-125 levels or transvaginal ultrasound, performed better than a 1-time evaluation.[9] Although the UKCTOCS trial showed no significant mortality benefit for either of the screening arms, Dr. Menon discussed some of the findings of the trial. For example, she noted that there was a “stage shift” in diagnosis for patients in the CA-125 screening arm, such that women diagnosed in that arm were diagnosed with lower stage disease than the women in the other trial arms. She also discussed the statistical analysis, particularly its sensitivity to the case definition (ie, whether primary peritoneal cancers were included as cases), and the observation that there seemed to be a benefit of screening after 7 years of follow-up, even though the trial was not originally planned for 7 years of screening. These results, although intriguing,

unfortunately did not yield an overall mortality benefit. However, continued follow-up of women in the UKCTOCS trial is ongoing.

Additional presentations in this session focused on markers besides CA-125, which could serve as either early detection markers or as markers of cancer recurrence. Dr. Katherine LaVigne presented data on HE4, suggesting that HE4 levels could supplement CA-125 as a marker for recurrence: in women whose CA-125 levels were not elevated at recurrence, HE-4 levels were elevated. This suggests that measuring multiple markers may be a more sensitive test for recurrence among ovarian cancer patients. Two additional presenters focused on identifying circulating tumor cells (CTCs), which could be used as prognostic markers among ovarian cancer patients. Dr. Eva Obermayr presented preliminary results using a microfluidic device to detect CTCs. Compared with RT-qPCR and immunofluorescent staining, this technology could detect CTCs in 78% of blood samples taken at the time of diagnosis and 80% of samples taken at cancer recurrence. Thus, this device has great promise in moving forward the field of CTC detection for use as a prognostic marker.

Dr. Rosana Risques presented on duplex sequencing to detect TP53 mutations, which is mutated in almost all high-grade serous carcinomas,[10,11] in the peritoneal fluid samples of patients with high-grade serous ovarian cancer or patients with benign pathologies. Dr. Risques reported the detection of somatic mutation in nearly all ovarian cancer and control samples. She also found that the mutation burden, calculated as mutant TP53 molecules per nucleotides sequenced, was useful for separating cancer samples from normal samples. Intriguingly, Dr. Risques reported that low-level TP53 mutations can be detected in control patients without ovarian cancer and that background mutations increased with age in control samples. This is concerning because these background mutations in normal cells may increase the background noise and lower the ability to detect cancer-specific mutation signal. A better understanding of background mutation patterns and rates relative to cancer-specific mutation rates is needed before mutation detection could be used to detect and screen for high-grade serous ovarian cancer.

Dr. Saul Rivkin presented on a project enrolling women at the Swedish Medical Center of Fred Hutchinson Cancer Research Center in Seattle for annual CA-125 testing ovarian ultrasounds. Over 6 years, 534 women were enrolled, during which 5 women were diagnosed with ovarian cancer. This program also offered genetic counseling for women in the program, and the screening study is ongoing.

PREVENTION

Because screening and early detection have thus far not yielded a clinically approved strategy, prevention is another key area of research. This session’s second invited speaker, Dr. Karen Lu, presented on her work on BRCA testing and salpingectomies as prevention strategies focusing on 3 areas: (1) universal BRCA testing, (2) cascade testing of relatives of patients, and (3) salpingectomy as a risk-reducing strategy in high-risk women. Dr. Lu’s shared results from a strategy developed at MD Anderson Cancer Center, in which they tested all high-grade non-mucinous tumors. Her data suggest that if all women were tested

for BRCA, there could be a 53% drop in ovarian cancer.12 We additionally heard a presentation from Dr. Carol Hanchette, who applied her training in geographic information systems to understand the geographical distributions of ovarian cancers in the United States. In examining these distributions, they noticed that there were overlaps in the distribution of ovarian cancer cases with areas that traditionally had higher numbers of pulp and paper mills. Using geospatial analysis, there was a suggested association between pulp and paper mills and ovarian cancer risk, although the data are ecologic. More careful studies that can adjust for individual-level confounders are needed to validate this novel finding. Dr. Elizabeth Poole, one of the coauthors on this review, presented data from the Nurses' Health Studies on a potential association between medication use and ovarian cancer prognosis. Although no association was observed for use of any of the medications she examined (aspirin, non-aspirin NSAIDs, acetaminophen, A-blocker medications) before diagnosis, there was a striking decreased risk of dying among women who used aspirin after diagnosis. These results are intriguing, but there were no data on cytoreductive surgeries, chemotherapeutic regimens, or recurrences. Thus, additional work is needed to confirm these findings.

METHYLATION PROFILING

Dr. Clara Bodelon presented data from the Polish Ovarian Cancer Study and the Surveillance, Epidemiology, and End Results Residual Tissue Repository, in which paraffin-embedded tumor tissues were profiled for global methylation. Her work identified 4 clusters into which tumors could be grouped; these clusters seemed to recapitulate histologic differences. Given that methylation signature can be disease and tissue specific, follow-up studies may lead to molecular signatures that are useful for prevention or screening of ovarian cancer.

CONCLUSIONS

Early detection is effective in improving the outcome of patients with cancer and has the potential to save lives. Unfortunately, current early detection modalities are not sufficiently sensitive or specific enough to detect high-grade serous ovarian cancer at early stages. Thus, additional efforts to identify novel markers for early detection as well as to improve prevention and detection of cancer recurrence are key to reducing deaths due to ovarian cancer. The "Detection and Prevention of Ovarian Cancer" session at the 11th Biennial Ovarian Cancer Research Symposium featured presentations on a wide variety of efforts to improve screening, early detection, prevention, recurrence, and ovarian cancer survival. This wide-ranging array of research has great potential to benefit women at risk of ovarian cancer and women who have been diagnosed with this deadly disease.

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