Ovarian Cancer Prevention and Screening

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Question 1:
You mentioned several different strategies to mainstream genetic screening for ovarian cancer with the most accepted being testing at time of diagnosis. What strategy would you like to see adopted?

Response from Menon, Karpinskyj, and Gentry-Maharaj:
We would like to see mainstream testing for BRCA gene mutations at the point of ovarian cancer diagnosis become the standard of care in countries where it is cost-effective. However, it is important that the testing is carried out in specialized laboratories and in association with family cancer and clinical genetics services, so that patients and their families can be appropriately counselled and managed by a multidisciplinary team if a mutation is discovered.

In specialized centers, such genetic testing has been broadened to include a multigene panel (RAD51C, RAD51D, BRIP1, EPCAM, MLH1, MSH2, MSH6, and TP53). As this currently poses challenges in interpreting and managing results, it is best that this extended panel testing is undertaken by specialized clinical genetics centers and limited to patients who test negative for BRCA mutations but have additional risk based on family cancer history.

Question 2:
As the number of women having genetic testing increases, along with the ever-evolving information regarding genetic testing, it can be difficult to stay up to date on recommendations. What is the role of the general gynecologist in counseling women on screening and prevention? Should all at-risk women all be referred to a cancer management center?

Response from Menon, Karpinskyj, and Gentry-Maharaj:
At this point it is essential that general gynecologists are able to provide patients with an overview of risk factors, genetic testing, and available preventative/screening approaches. Most importantly, they should be
aware of the national and local guidelines for referral to a family cancer and clinical genetics service and should identify a local clinic where they could refer unaffected patients who are at risk (currently this is largely based on family history). In unaffected women, confirmation of risk, counseling, genetic testing, and finalization of a tailored risk management plan is best carried out in the specialized multidisciplinary clinic. In some situations, the general gynecologist (as opposed to a gynecologic oncologist) may wish to work along with the family cancer multidisciplinary team to implement the agreed risk management (prevention and screening) plan in their high-risk patients. In the latter case, it is important that there is good communication between both teams so that any updates to recommendations are passed on to both the gynecologist and the patient.

Question 3:

With increasing use of long-acting reversible contraceptives (LARC) by young women, do you feel there is a role for an oral contraceptive pill (OCP) in addition to LARC purely for chemoprophylaxis? Would you only recommend this in the high-risk population?

Response from Menon, Karpinskyj, and Gentry-Maharaj:

In the general population, an OCP is not advised solely for ovarian cancer chemoprophylaxis. The risk reduction associated with OCP use is something women need to consider when they are choosing their contraception. Of note, LARC, due to its high continuation rates, has the highest contraceptive efficacy.

In women at high risk, our opinion is that women with BRCA mutations should consider taking OCPs to reduce their ovarian cancer risk. There is currently no recommendation to do so. To our knowledge, there are no data demonstrating outcomes of combined use of LARC with OCPs. While LARCs are breast-safe options in perimenopausal women, the risks of combining two hormonal contraceptives in tandem are not well-established.

Question 4:

With the rapid adoption of opportunistic salpingectomy, do you have concerns about premature menopause in these women? Do you think younger women should be counseled differently regarding salpingectomy, for example, at the time of surgical sterilization?

Response from Menon, Karpinskyj, and Gentry-Maharaj:

The long-term effects on ovarian function of women undergoing salpingectomy is unknown. Current evidence, based on short-term follow-up suggests that it does not affect ovarian reserve and function.2 Therefore, it is our view that this must be made clear to young women, especially those undergoing surgical sterilization, so that they are fully informed. My preference would be for a register of such patients so that we can monitor effectiveness alongside any long-term issues.

Question 5:

Ovarian conservation does have known health benefits. Is there a risk group that you feel might benefit from risk-reducing salpingectomy alone without delayed oophorectomy? Would there be a role for this in women at low or moderate risk?

Response from Menon, Karpinskyj, and Gentry-Maharaj:

In young women at high risk, there is a definite role and the potential benefits and harms are being assessed in the context of multiple studies. In women at low risk, it is important to explore and discuss risk-reducing salpingectomy during intra-abdominal procedures where this might be safely carried out. However, presently there is no evidence to suggest that primary risk-reducing salpingectomy in patients at low or moderate risk is cost-effective.
**Question 6:**

Most of the research on screening has been done in either high-risk women or the general population. What are your screening recommendations for women at low or moderate risk for development of ovarian cancer?

**Response from Menon, Karpinskyj, and Gentry-Maharaj:**

*Our trial, the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS), excluded high-risk women, defined as those with a 10% or greater lifetime risk of ovarian cancer based on family history. The women included were mainly low risk (2% lifetime risk) or intermediate risk (3–9% lifetime risk). Currently there is insufficient evidence to recommend screening in either of these populations. We found a significant stage shift with multimodal screening in UKCTOCS in this population, but we have to await the mortality results on extended follow-up in 2019 for a definitive answer to this question.*

*It is important to note that our modelling suggests that in the intermediate risk group of women with a risk over 5%, postmenopausal risk reducing surgery is cost-effective.*

**Question 7:**

Which future screening strategies do you think will be most promising and why?

**Response from Menon, Karpinskyj, and Gentry-Maharaj:**

*User-friendly risk prediction quantitative tools that incorporate both genetic and epidemiological risk factors such as CanRisk (see [http://cge.medschl.cam.ac.uk/canrisk/](http://cge.medschl.cam.ac.uk/canrisk/)) would allow us to accurately triage women into risk groups where the risks and benefits of screening differ. Also, screening using panels comprised of serial CA125 and highly specific second-line circulating tumor DNA tests either using blood or vaginal–endocervical samples.*

**References**