Lynch syndrome and decision-making for risk-reducing oophorectomy: considerations beyond cancer

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BACKGROUND

- Lynch syndrome (LS), the most common hereditary colorectal cancer syndrome, also causes an increased risk for ovarian cancer.
- Only risk-reducing bilateral salpingo-oophorectomy (BSO) is effective at reducing risk for ovarian cancer.
- However, younger age at surgical menopause is associated with increased all-cause mortality
- Relevant health impacts include:
  - Increased risk of cardiovascular disease, kidney disease, osteoporosis, dementia; impact on sexual health, relationships, body image
- The extent to which these factors play a role in decision-making for or against risk-reducing gynecologic surgery is poorly understood.

RESEARCH CONTEXT

GENE-SPECIFIC RISKS AND RECOMMENDATIONS

- General population risk of ovarian cancer: 1.1%
- LS risks and recommendations For BSO vary by gene
- Insufficient evidence to recommend BSO for PMS2 and MSH6

LS gene	Ovarian cancer risk	Recommendation for BSO
MLH1	4-20%	•BSO may reduce incidence of ovarian cancer •Decision for BSO should be individualized by LS gene, childbearing plans, family history, comorbidities
MSH2/ EPCAM	8-38%	•Same as MLH1
MSH6	1-13%	**•Insufficient evidence to recommend BSO** •Decision should be individualized •Timing should be individualized
PMS2	1.1-3%	•Insufficient evidence to recommend BSO •PMS2 carriers appear to be at no greater than average risk for ovarian cancer **•May reasonably elect not to have BSO** •Decision for BSO should be individualized

CARDIOVASCULAR DISEASE FACTS

- Cardiovascular disease is the No. 1 killer of women (1 in 3 deaths)
- Deaths due to cardiovascular disease have increased for women ages 35-44.
- Cardiovascular disease kills more women than all forms of cancer combined and yet only 44% of women recognize that cardiovascular disease is their greatest health threat.

CLINICAL PRACTICE IMPLICATIONS AND ETHICAL IMPORT

- Improved understanding of decision-making for/against risk-reducing BSO can improve counseling and patient education to ensure informed decision-making.
- The balance of risks and benefits of pre-menopausal oophorectomy for individuals with certain comorbidities, low-penetrance variants, and/or no family history of Lynch cancers may be different than for individuals with high-penetrance variants.

METHODS

- Semi-structured interviews with 20 women with Lynch syndrome.
  - 14 with low-penetrance variant; 6 with high penetrant variant
  - Ages 22-55
  - 10 with BSO; 10 without
- Open-ended questions about risk-reduction decisions for Lynch-related cancers.
- Targeted questions about role of other health factors in decision-making for BSO: cardiovascular disease, osteoporosis, dementia, menopause symptoms, sexual functioning, romantic relationships
- Interview data were analyzed using thematic analysis and content analysis.

RESULTS

Theme	Key findings	Exemplar quotes
Cancer risk-perception	•Perceived themselves as highly susceptible to a severe condition, regardless of LS variant •BSO understood as high reward and low-risk	• I think like a lot of the things that are recommended through Lynch syndrome for lowering risks or whatever, I just go with it, because like what's the worst that could happen. (P08, HP, age 25-30) •The risk versus benefit is not really there for me as far as not having it done. (P18, LP, age 40-45)
Embodiment and decision framing	•Many framed the decision as either getting cancer or removing unneeded body parts •Many used abstractions and body-distancing language to describe their ovaries	•[T]here really were no cons except for major surgery. The risks were getting cancer as life went on….[T]here really wasn't a con to it except for losing your body parts. (P09, LP, age 50-55) •I knew I wasn't having any more kids so if I don't need those parts anyways, just take them out. (P01, LP, 45-50) • [R]ight now I picture them kind of being these raisins that aren't doing anything for me at this point, and so go ahead and get rid of them. (P06, LP, age 50-55)
Physician recommendation	•Many participants described their physician's recommendation as a key aspect of their decision-making •Most described physician recommendations as strong, regardless of gene-specific risk	•Well, my initial visit, the doctor that I saw kind of said well if you were my wife, I'd recommend you get signed up for the surgery right now, so it was kind of a bit of a shock initially. (P05, LP, 40-45) •I went to my OB/GYN and he was like you're playing with fire. He was like you need to have this done. (P09, LP, age 50-55) •I think ovarian, there was less of a risk than uterus but you know through talking with the physician that was their recommendation with Lynch, why leave the ovaries and still have that increased risk of ovarian cancer when they could remove them and do hormone therapy for a couple of years. (P15, LP, age 45-50)
Temporality/ relationship to past and future	•Some described their decision in terms of looking to the future, e.g., wanting as much time as possible with their children •Other described looking to the past and making sense of the decision in terms of a family history of cancer •Several described the decision for/against BSO as interrupting their present family planning and/or forcing an alternative timeline on childbearing plans	•[W]e had just started the process of wanting to start trying for a second kid, and so just finding out that I had Lynch syndrome completely changed our plan, because first we were, well we need to make sure that I didn't have cancer before having any children, and then the second thing was 'What does this mean? Do we have a child naturally, or do we go for IVF and try to make sure that we have a child who does not have Lynch syndrome?' (P13, LP, age 30-33) •I always told myself from a very young age that if there was something I could do to try to prevent the cancer, I was going to do that, and then here I was debating on whether or not I wanted to do that, and so I just reminded myself, like you need to do what's best for your health, so that's what I did. (P14, HP, age 40-45) • •So that puts a timeline on, I need to the have kids that I want to have by the time I'm 32 if I want to carry my own children. (P03, HP, age 20-22)

LP: lower penetrance variants (PMS2, MSH6)
HP: higher penetrance variants (MLH1, MSH2)

Content Analysis: Factors other than cancer considered when deciding for/against BSO	
Health factors besides cancer	•Participants **did not** consider cardiovascular health or cognitive health/dementia in deciding for/against BSO •Some participants considered osteoporosis and mood health •A few considered sexual functioning/impact on romantic relationship •Most considered menopause symptoms
Other life factors	•Some raised other factors for not having surgery such as not wanting to disrupt exercise routine, needing to rely on others during recovery, recovering from other surgeries, bad experience from previous surgery, wanting the ability to bear children even if not planning on more children.

CONCLUSION

- **Patients were largely unfamiliar with the health impacts of surgical menopause that could shorten their lifespan.**
- Gene-specific risks and recommendations were not a factor, even for individuals with low-penetrance variants.
- Concerns about menopause, not feeling ready, and wanting more children were important factors against BSO.
- Doctor's recommendations, cancer risk-perception, and beliefs about ovaries having no function were the primary factors in decisions for BSO.

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