Salpingectomy in Ovarian Ca Prevention on Trial

BY SUSAN LONDON
EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE SOCIETY OF OBSTETRICIANS AND GYNECOLOGISTS OF CANADA VANCOUVER, B.C. — A clin- ical trial is needed to assess the risk-benefit profile of salpingec- tomy for ovarian cancer preven- tion, said Dr. Barry Rosen.

A recent, serendipitous dis- covery, resulting from pathology examination of tissues removed during prophylactic salpingo- oophorectomy in patients with BRCA mutations, was that serious “ovarian” cancers actually arise from the fimbrae of the fallopian tube.

“We didn’t know it when we started doing [the surgery],” Dr. Rosen explained. “We sort of all of a sudden started to identify cancers, and most of them were in the tube. … All of a sudden, these findings were opening our eyes to understand that ovarian carcinoma do come from the tube.”

In the wake of this new information, the Society of Gynecologic Oncology of Canada (GOC) issued two key recommen- dations, according to Dr. Rosen, professor of OB-GYN and head of gynecologic oncology at the University of Toronto.

First, the GOC recommends that physicians discuss the risk-benefit profile of salpingectomy with women who are already having a hysterectomy or seeking irreversible contraception. “We don’t come out and say ‘Do it,’” he noted. “But we are coming out to say that it makes sense, and you should discuss it, and in that discussion, if it makes sense, that you should go ahead and proceed to do it.”

Second, the GOC recom- mends that, given the lack of evi- dence, a national study of ovar- ian cancer prevention through salpingectomy be a priority of the society. “We want to collect the evidence to support this, and we want to be sure that the evi- dence supports it before we really jump in and say everybody should be doing this,” Dr. Rosen said.

“I don’t think there’s any question that salp- ingectomy makes sense. Serous carcino- ma is the worst (ovari- an) cancer, it’s the most common cancer, [and] it causes more deaths than any,” he commented. “So if you can prevent this cancer, you are prob- ably going to have the biggest im- pact on ovarian cancer that we have today. Bigger than screening, for sure — we know [screen- ing] doesn’t work. But bigger than any treatment and any of the fancy treatments that are coming out that are really very expensive treatments.”

Adding salpingectomy to other, planned surgeries could po- tentially provide preventive ben- efit to tens of thousands of women annually in Canada alone. For starters, roughly 47,000 Canadian women under- go hysterectomy nationally each year. Removal of the ovaries and tubes at the same time is fairly standard for those who are post- menopausal. “But it’s the pre- go pelvic surgery as a result. There are many “other situa- tions where urologists or gener- al surgeons are doing surgery, so I don’t think we have to limit this discussion to gynecologists,” commented Dr. Rosen. “We need to expand it to all disciplines that may operate in the pelvis, be- cause a surgeon can take out the tubes as well as we can.”

When asked by an attendee whether it might perhaps be better to recommend simpler distal salpingectomy instead of total salpingectomy, he expressed reservations.

“While the belief is that most of these cancers arise in the fim- briated end, there are some that do arise further up the tube.” Additionally, “we have to be care- ful if we put in the word ‘distal.’ We also have to define what dis- tal is. So it’s trickier than you think.”

Dr. Rosen offered a few notes of caution from his own per- spective. “Salpingectomy at open hysterectomy is different than at laparoscopic hysterectomy or laparoscopic salpingectomy,” he said. “It’s pret- ty simple if you have an open case to be able to put your fa- vorite clamp across the tube and remove it; laparoscopically, [for some it may be] a little bit more difficult. … When doing the pro- cedure, you need to treat this as a surgical procedure, and not just think, ‘Oh yeah, we’ll just take you out, and find yourself in some trouble with bleeding or an injury of some sort.”

Also, the medical profession must decide what level of com- plications is acceptable. “I don’t know the answer to that, but we need to know what the compli- cation rate is, and we do know that there will be complications,” Dr. Rosen said.

Finally, the new recommenda- tions are currently based on a hy- pothesis, not on evidence. “There are other situations in our histo- ry in medicine where physicians really believed something very strongly and proceeded with lim- ited information,” he noted, cit- ing by way of example the use of diethylstilbestrol in the 1940s and 1950s to prevent miscarriage, and its subsequent linkage to cancer. “We need to be sure that we get the evidence. I believe that we need to evaluate this in some form of clinical trial.”

Should salpingectomy prove to be effective and adequately safe for preventing ovarian can- cer, it would constitute a major turning point in a disease that still has a poor prognosis, he said.

“To be sure, treatments have improved steadily over the past 23 years, prolonging life and im- proving its quality. We can con- tinue to expect improvements, but I think they are going to be gradual and they are going to be small,” he said.

Efforts to detect the cancer early through screening have thus far not panned out. Three large screening studies were ini- tiated in 1985-2001, one each in the United Kingdom, Japan, and the United States.

Results from the last – the PLCO (Prostate, Lung, Colorec- tal, and Ovarian) trial, which test- ed screening with cancer antigen 125 (CA 125) and transvaginal ul- trasound – were recently report- ed (JAMA 2011;305:2295-303). They showed that 20 surgeries had to be performed to detect one cancer, and the rate of ma- jor complications was 20% among patients who underwent surgery. And at the end of the day, there was no reduction in ovarian cancer mortality.

Results of the U.K. study, which is using a different, serial multimodality approach to screening, are expected in the 2014 timeframe.

Prevention efforts up to this point have been limited to birth control pills and to BRCA testing with prophylactic surgery for car- riers, but this group makes up only about a tenth of all patients with ovarian cancer, he noted. Dr. Rosen said he had no relevant financial disclosures.

BRCA2 Gene Mutation Tied to Better Survival in Ovarian Ca

BY SHARON WORCESTER
FROM THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ORLANDO – Ovarian cancer patients with BRCA1 or BRCA2 gene mutations have better survival than do those with neither mutation, and those with the BRCA2 mutation have better survival than do those with the BRCA1 mutation, according to the findings of a large, mul- ticenter study.

The findings confirm the results of sev- eral prior smaller studies showing a survival advantage in mutation carriers vs. nonmutation carriers, and they provide the first direct evidence that BRCA1 and BRCA2 mutations have different effects on survival, according to Dr. Rosen.

She and her colleagues studied 3,531 women with invasive epithelial ovarian cancer who were enrolled in one of 24 studies in the United States, Europe, Israel, and Asia, and for whom survival data were avail- able. Included were 1,178 women with BRCA1,367 with BRCA2, and 1,986 who were BRCA-negative. The 5-year survival was 36% in those with no mutation, 46% of those with the BRCA1 mutation, and 61% in those with the BRCA2 mutation, after ad- justment for stage, grade, histology, and age at diagnosis.

Data Source: A large, multicenter study investi- gating the impact of germline BRCA1 and BRCA2 mutations in 3,531 women with invasive epithelial ovarian cancer.

Disclosures: Ms. Bolton said she had no relevant financial disclosures.

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