GYNECOLOGY

The impact of opportunistic salpingectomy on ovarian cancer mortality and healthcare costs: a call for universal insurance coverage

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BACKGROUND: Opportunistic salpingectomy at the time of hysterectomy or as an alternative to bilateral tubal ligation may reduce the incidence of ovarian cancer, because it has been demonstrated that most serous ovarian cancers begin in the fallopian tubes. However, salpingectomy at the time of sterilization is not always financially covered by third-party payers, and this represents a barrier to adoption. Routine salpingectomy has become more common but is not always practiced at the time of hysterectomy.

OBJECTIVE: This study aimed to determine the impact of opportunistic salpingectomy as an alternative tubal ligation and routine salpingectomy at the time of hysterectomy on ovarian cancer mortality and overall cost.

STUDY DESIGN: An 8-state Markov state transition model was constructed, including hysterectomy, tubal ligation, and ovarian cancer. Transition probabilities were informed by previously reported population data and include age-adjusted rates of elective sterilization and hysterectomy. This model was used to predict ovarian cancer incidence and the cost effectiveness of opportunistic salpingectomy. Testing of this model suggested that it accurately predicted overall life expectancy and closely predicted the rate of hysterectomy in the population. The model may underestimate the rate of tubal sterilization, making it conservative with respect to the benefits of salpingectomy.

RESULTS: The recursive Markov model was run from ages 20 to 85 years in 1-year intervals with a half step correction and included age-adjusted rates of tubal ligation, hysterectomy (with and without oophorectomy), and ovarian cancer. The model predicts that opportunistic salpingectomy at the time of tubal ligation will reduce ovarian cancer mortality by 8.13%. Opportunistic salpingectomy at the time of hysterectomy will reduce ovarian cancer mortality by 6.34% for a combined decrease of 14.5%. Both strategies are cost effective when considering only the cost of the opportunistic salpingectomy. The excess cost of opportunistic salpingectomy at the time of tubal ligation was $433.91 with an incremental cost-effective ratio of $6401 per life-year and $5469 per quality-adjusted life year gained when adjusting for ovarian cancer with a utility of 0.64. The incremental cost-effective ratio for opportunistic salpingectomy during hysterectomy at a cost of $124.70 was $2006 per life-year and $1667 per quality-adjusted life year. When considering the impact of ovarian cancer prevention with respect to the cost of ovarian cancer treatment, opportunistic salpingectomy may produce a substantial healthcare savings. Utilizing a 3% discount rate, it is estimated that the total savings for universal salpingectomy could be as high as $445 million annually in the United States. A sensitivity analysis around the benefit of opportunistic salpingectomy suggests that this procedure will be cost effective even if salpingectomy provides only a modest reduction in the risk of ovarian cancer.

CONCLUSION: It is estimated that universal opportunistic salpingectomy may prevent 1854 deaths per year from ovarian cancer and may reduce healthcare costs. Given these data, universal opportunistic salpingectomy should be considered at the time of tubal ligation and hysterectomy and covered by third-party payers.

Key words: cost-effective analysis, ovarian cancer, ovarian cancer mortality, salpingectomy

Introduction

Epithelial ovarian cancer is the leading cause of death from gynecologic malignancies.[1] Extensive efforts have been directed toward screening for this disease. The results of a large trial using ultrasound and tumor markers have shown a shift toward earlier stage at the time of diagnosis.[2] Unfortunately, the calculated effect of these screening programs conducted yearly starting at the age of 50 years showed only a modest 6% reduction in the mortality from ovarian cancer and is not considered cost effective.[3]

Because most cases of epithelial ovarian cancer develop in the fallopian tube, prevention may be possible by electively removing the fallopian tubes at the time of hysterectomy or tubal ligation.[4,5] Data from the Nordic tumor registry suggest that removal of the fallopian tubes results in a 65% reduction in subsequent risk of ovarian cancer, which is greater than the reduction conferred by either tubal ligation or hysterectomy without salpingo-oophorectomy.[6] Salpingectomy is technically straightforward as a means of tubal sterilization or during hysterectomy and does not significantly decrease ovarian function.[7] Because hysterectomy for benign disease and tubal ligation are common procedures, opportunistic salpingectomy has been suggested as a cost-effect method of preventing epithelial ovarian cancer.[8]

Salpingectomy is increasingly performed at the time of hysterectomy and sterilization, but it is not uniformly covered by third-party insurance carriers. Unfortunately, the lack of insurance coverage may not only increase future rates of ovarian cancer but may also increase overall health costs owing to the development of ovarian cancer. The actual impact of salpingectomy on

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AJOG at a Glance

Why was this study conducted?

This study aimed to determine whether salpingectomy is a cost-effective cancer prevention strategy.

Key findings

Modeling predicts opportunistic salpingectomy at the time of tubal ligation, and hysterectomy will reduce ovarian cancer mortality by 14.5%. Performing opportunistic salpingectomy is cost effective both at the time of tubal ligation and at the time of hysterectomy. It is estimated that there will be a substantial cost savings from the prevention of ovarian cancer in the future.

What does this add to what is known?

This study suggests that salpingectomy may significantly decrease ovarian cancer mortality and should be financially covered by all payers as modeling demonstrates overall cost savings.

the prevention of ovarian cancer will not be known for some time. However, given the known rates of hysterectomy, tubal ligation, and ovarian cancer, we sought to construct a model to evaluate the cost effectiveness of opportunistic salpingectomy and its impact on the incidence of ovarian cancer, including the cost of preventing ovarian cancer.

Materials and Methods

A recursive Markov model was created using TreeAge Pro 2011 (TreeAge Software, LLC, Williamstown, MA) to simulate the risk of ovarian cancer and ovarian cancer mortality vs all other causes of mortality in all women from ages 20 to 85 years to calculate lifetime costs associated with salpingectomy and ovarian cancer. This range was selected, because almost all events of interest would be included in this range. Because there were no human subjects involved this study, this study was exempt from institutional review board oversight. Notably, 8 transition states were included in the model: healthy, healthy with a hysterectomy, healthy with a hysterectomy and bilateral salpingectomy, healthy with a hysterectomy and bilateral salpingo-oophorectomy, development of ovarian cancer, death from ovarian cancer, and death from other causes. The model tested 2 strategies. In the standard arm, transition probabilities for the development of ovarian cancer were used considering tubal ligation was used for permanent sterilization and salpingectomy was not performed at the time of hysterectomy for benign disease. In the salpingectomy arm, transition probabilities were calculated based on the assumption that salpingectomy would be performed in lieu of tubal ligation and at the time of hysterectomy for benign disease. The model was constructed using guidelines from the Consolidated Health Economic Evaluation Reporting Standards. All-cause mortality was calculated from the United States Social Security Actuarial Life table.[9] Age-related incidence of ovarian cancer was taken from the Surveillance, Epidemiology, and End Result database.[10] To model ovarian cancer mortality, it was estimated that the annual mortality after developing ovarian cancer would be 13% per year for 10 years. Moreover, 5-year survival rates for ovarian cancer were calculated to correspond to those published by the American Cancer Society at 49%.[11] For 10-year survivors, the mortality rate would return to actuarial, giving a long-term survival for all women diagnosed as having ovarian cancer of 25%.

Each cycle in the model corresponded to 1 year. A half step correction was added to the end of the cycle for the Markov state rewards. Each year, the population was subjected to the age-specific rate of tubal ligation, hysterectomy, or hysterectomy with salpingo-oophorectomy as shown in Table 1. For each procedure, there was an estimated future reduction in ovarian cancer based on the data from the Nordic tumor registry as noted in Table 2. For all other states, transition probabilities for death were calculated from the social security life tables minus the risk of death from ovarian cancer.

The overall yearly rate of hysterectomy by age has been reported from the National Hospital Discharge Survey and used to calculate the transition from healthy to healthy with a hysterectomy.[12] This data set was chosen as the actual rates by age were given and required for the model. These data were collected before the widespread use of outpatient hysterectomy and would be conservative with respect to the benefit of salpingectomy if the rates are lower than the current rates of hysterectomy. The rate varied by age and estimates are shown in Table 1. Oophorectomy rates were taken from the New York State Department of Health, Statewide Planning and Research Cooperative System, because these data contained the best source of age-related rates of oophorectomy.[13] It was assumed that all hysterectomies for ovarian cancer included a bilateral oophorectomy and these were subtracted from the rate of hysterectomy and bilateral salpingo-oophorectomy rates for benign disease. Previous estimates of age-specific tubal ligation rates were used to determine the timing of the tubal ligation or salpingectomy.[14] It is assumed that if a hysterectomy was performed after tubal ligation or salpingectomy, the rate of ovarian cancer was not estimated to change unless a bilateral salpingo-oophorectomy was performed because salpingectomy has been shown to be more protective for ovarian cancer than a hysterectomy alone.[6]

The estimates for protection from ovarian cancer are derived from the Nordic tumor registry. The annual rate of ovarian cancer was decreased in women after a hysterectomy, tubal ligation, salpingectomy, or hysterectomy and bilateral salpingo-oophorectomy based on the rates in Table 2.[6] Although the data are limited to the Scandinavian population, this database

TABLE 1
Estimates used in the model as absolute risk per year per person

Age, y	Hysterectomy rate[12]	Percentage of hysterectomies with oophorectomy[13]	BTL rate[13]	Ovarian cancer[10]
15–24	0.0002	0.217	0.0126	0.00008
25–29	0.0025	0.217	0.0188	0.00012
30–34	0.0058	0.217	0.186	0.00014
35–39	0.0061	0.217	0.0124	0.00016
40–44	0.0125	0.426	0.0028	0.00018
45–49	0.012	0.426	0.0028	0.0002
50–54	0.0067	0.259	0	0.00027
55–59	0.003	0.317	0	0.00035
60–64	0.003	0.499	0	0.00046
65–69	0.003	0.499	0	0.00052
70–74	0.003	0.499	0	0.00056
>75	0.003	0.499	0	0.00055

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is the most extensive data derived estimate of ovarian cancer protection resulting from the removal of the fallopian tubes, bilateral tubal ligation, and hysterectomy. Costs were estimated from the point of view of overall healthcare expenditures and not societal costs, because the purpose of this model was to demonstrate that coverage of this procedure was cost effective from a third-party payer's perspective. The excess cost of salpingectomy was calculated based on the difference in the 2020 Medicare reimbursement for Current Procedural Terminology (CPT) code 58600 for bilateral tubal ligation ($372.28) and the code 58700 for bilateral salpingectomy ($806.19).[15] For the excess cost of salpingectomy at the time of hysterectomy, the difference between CPT code 58570 for total laparoscopic hysterectomy and CPT code 58571 for laparoscopic hysterectomy and bilateral salpingo-oophorectomy was $806.19 and $930.89, respectively. This yielded a cost of opportunistic salpingectomy at tubal ligation of $433.91 and salpingectomy at the time of hysterectomy of $124.70. A health utility of 0.64 was assigned to the cohort that developed ovarian cancer based on previous work.[8] The cost of ovarian cancer was estimated to be $65,882 for the first year with an annual associated cost of $4975 and a final year of life cost estimate of $64,101.[8] A discount rate of 3% was used to be conservative with respect to future costs saved by the procedure. Because all surgeries are opportunistic and there is likely to be no significant difference in morbidity or mortality when removing the tubes, the only factors that were considered were the difference in the cost of the procedure, the reduction of the risk of ovarian cancer after any surgery, and the cost savings associated with the prevention of ovarian cancer.

Results

The Markov model was run from ages 20 to 85 years because it is unlikely that tubal ligation or hysterectomy would be performed before the age of 20 years. The model was tested in several respects. The model accurately predicted that the median overall life expectancy would be 78.6 years, which is identical to the current median life expectancy reported in other recent studies.[16] To see whether statewide and inpatient databases accurately predicted the national rate of tubal and hysterectomy by the age of 44 years, the model was run to the age of 44 years to calculate rates of salpingectomy and hysterectomy. The model predicted rate of hysterectomy was 11.1% compared with an actual rate of 10.6% by the age of 44 years in the United States.[16] The model slightly underpredicted the rate of tubal sterilization at 22.1% compared with the reported rate of 29.8%. Thus, this model seems to be conservative with respect to the prediction of the benefits of universal opportunistic salpingectomy.

The model was then run from ages 20 to 85 years to determine the cost effectiveness of opportunistic salpingectomy and the risk of death from ovarian cancer. The rate of ovarian cancer mortality predicted in the model without any salpingectomy is 1.2%. The model predicts that the mortality from ovarian cancer would be reduced by 8.13% if salpingectomy were performed instead of tubal ligation during sterilization procedures. Opportunistic salpingectomy at the time of hysterectomy will reduce ovarian cancer mortality by 6.34% for a combined decrease in ovarian cancer incidence and mortality of 14.5%. This would potentially save 1854 lives per year from ovarian cancer. Both strategies are cost effective when considering the cost of opportunistic salpingectomy alone. If the excess cost of opportunistic salpingectomy at the time of tubal ligation

TABLE 2
Relative risk of ovarian cancer reduction by procedure taken from the Nordic tumor registry

Procedure	Relative risk of ovarian cancer[6]	95% CI
Tubal ligation	0.67	0.70–0.88
Hysterectomy	0.79	0.70–0.88
Bilateral salpingectomy	0.35	0.17–0.73
Hysterectomy with bilateral salpingo-oophorectomy	0.06	0.03–0.12

CI, confidence interval.

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were $433.91, this would create an incremental cost-effective ratio (ICER) of $6401 per life-year (LY) and $5469 per quality-adjusted life year (QALY) when adjusting for ovarian cancer with a utility of 0.64 accounting only for the excess cost of the salpingectomy alone. The ICER for opportunistic salpingectomy during hysterectomy at a cost of $124.70 was $2006 per LY and $1667 per QALY. However, when accounting for the cost of treating ovarian cancer, opportunistic salpingectomy created a significant healthcare cost savings. It is estimated that the per capita lifetime undiscounted savings for opportunistic salpingectomy at both tubal ligation and hysterectomy would be $185.97 or approximately $392 million per year in the United States assuming a female population of 166 million and an average life span of 78.6 years. The savings from ovarian cancer are realized later than the costs for preventative surgery. Therefore, a 3% discount rate was used, and it was noted a healthcare savings would still be realized.

A sensitivity analysis was performed to determine the cost effectiveness across a range of values for the protective effect of bilateral salpingectomy for ovarian cancer. The reported relative risk of developing ovarian cancer after salpingectomy in the Nordic tumor registry data was 0.35, and the confidence interval ranged from 0.17 to 0.73. When this range was tested in a sensitivity analysis of the effectiveness of salpingectomy, the model predicted these procedures would be cost effective over the majority of this range. Opportunistic salpingectomy at the time of tubal ligation remained cost saving up to a relative risk of salpingectomy for ovarian cancer below 0.23. Salpingectomy at the time of hysterectomy was cost saving below a relative risk of ovarian cancer of 0.67. Both of these procedures combined were cost effective at an ICER of <$50,000 per LY when the projected relative risk of developing ovarian cancer after salpingectomy was below 0.67, which would be the same protective effect of a tubal ligation.

The values for the cost of ovarian cancer care are from published data before the introduction of several new drugs in the treatment of ovarian cancer. Recent approvals of maintenance therapy options for ovarian cancer were not taken into consideration with these costs.[16] The current cost of poly-ADP ribose polymerase (PARP) inhibitor maintenance for 3 years could increase the total cost of care by up to $495,133 or about $99,026 per year if spread over 5 years.[17] In the PRIMA study, high-risk patients received an average of 14 months of PARP inhibitor which would cost an estimated $164,122 total or $32,824 per year.[18] The Platine, Avastin, and olaparib in first line regimen would be more expensive, which included both bevacizumab for an average of 11 months and PARP inhibitor for an average of 17.3 months, for a total cost of approximately $302,159 or $60,432 per year over 5 years.[17,19,20] If the yearly maintenance cost of ovarian cancer care is increased by $32,824, the total savings with a 3% annual discount is approximately $245 million in the United States. If the maintenance cost is $60,432 per year, the discounted savings would be $445 million per year in the United States with a 3% discount for future costs.

Comment

Principal findings

This analysis demonstrates the utility of prophylactic salpingectomy during hysterectomy or tubal sterilization. This Markov model evaluated the effect of opportunistic salpingectomy on the development of ovarian cancer using actual age-specific rates of hysterectomy and bilateral salpingo-oophorectomy, incorporating the cost savings associated with ovarian cancer prevention into a cost-effective model. Age-specific rates of surgery and ovarian cancer incidence were incorporated into the model to produce a better "real world" scenario and produce a more accurate estimate of the costs and cost savings associated with opportunistic salpingectomy. The protection afforded by tubal ligation and hysterectomy was also built into the model to avoid overestimating the benefit from opportunistic salpingectomy over tubal ligation alone. With these modifications, the model predicts that opportunistic salpingectomy at the time of hysterectomy and tubal ligation will be cost effective when considering only the cost of the procedure under a wide range of assumptions. More importantly, this model predicts that opportunistic salpingectomy will reduce the mortality in ovarian cancer by 14.5% and would be cost saving when considering the reduction in costs owing to the prevention of ovarian cancer.

Results

This model confirms previous work suggesting the cost effectiveness of opportunistic salpingectomy. However, this is a better "real world" estimate of the benefit of this procedure on the development of ovarian cancer because it takes into account the age-adjusted rates of tubal ligation and hysterectomy. The model estimates the lifetime risk of death from ovarian cancer to be 1.2% or 1 in 83. If salpingectomy reduced the death rate by 14.5%, this would suggest that 1 life would be saved from ovarian cancer for every 572

procedures. Although this is a small benefit per procedure, the morbidity of the procedure is low, the acceptance rate high, and the excess cost of these procedures is low with an ICER that is cost effective.[17,18] The overall ICER for both procedures combined is $4865 for LY saved and $4120 per QALY saved. These numbers are lower than previous models, in which the ICER ranged from $27,000 to $31,432.[8,19] Our results predicted by this Markov model are likely to be more accurate owing to the ability of the Markov model to give realistic estimates of the age at which the surgery was performed. In this study, overall health savings have been demonstrated by incorporating the cost savings of preventing ovarian cancer in a Markov model.

Clinical implications

Salpingectomy has been found to be acceptable to the vast majority of women both at the time of tubal ligation and hysterectomy.[20] Opportunistic salpingectomy is increasingly being practiced, particularly at the time of elective tubal sterilization where it was reported that the rate increased from 0.4% to 35.5% over a 6-year period.[21] However, this trend lags behind when performed at the time of cesarean delivery where an increase of only from 0.1% to 9.2% was observed during the same time period despite the fact that cost-effective modeling has shown that salpingectomy is cost effective at the time of cesarean delivery based on data from a randomized trial.[22] The protection from ovarian cancer from salpingectomy is substantial, and this procedure does not seem to have a significant impact on ovarian function.[23] At the time of abdominal or laparoscopic hysterectomy, there is probably little increase in morbidity from salpingectomy. Salpingectomy can be done quickly with a median time of only 16 minutes.[24] Even at the time of vaginal hysterectomy, removal of the tubes can be accomplished the majority of the time.[25] The sensitivity analysis suggests that this procedure is cost saving across the entire range of effectiveness reported.

Tubal sterilization is the most common form of birth control and is the primary method of birth control practiced in 18.6% of women at the age of 15 to 49 years.[26] It is estimated that at the age of 44 years, the tubal sterilization rate is 29.8%.[27] Given that the model predicts a tubal sterilization rate of only 22.1% at the age of 44 years, the model is likely conservative with respect to the benefit of this procedure.

It does not seem that salpingectomy carries more morbidity than a bilateral tubal ligation. A cohort study including 49,275 women conducted in Canada demonstrated no increased risk of physician visits for surgical infection, surgical complication, ordering a laboratory test, or ordering imaging in the 2 weeks after discharge for women who underwent salpingectomy.[28] Opportunistic salpingectomy at the time of planned tubal ligation may even have a bigger impact on the reduction of ovarian cancer mortality than at the time of hysterectomy, but there are some potential drawbacks. The cost of salpingectomy at the time of tubal ligation is more than 3 times the excess cost than at the time of hysterectomy. In addition, removal of the entire fallopian tube does not allow for the option of future tubal reanastomosis. Regret after tubal ligation was 4.3% in women at the age of 20 to 24 years and 2.4% in women in the 30- to 34-year age group.[29] Issues with tubal regret merit consideration when counseling young women before bilateral salpingectomy. However, in vitro fertilization could still provide women with an option for conception after salpingectomy.

Research implications

Reliable population-based data on the protective effect of salpingectomy are only available from the Nordic countries, and it is unclear whether the same protective effects will be seen in all populations. Long-term prospective data inclusive of diverse populations will be required for validation across a diverse population.

Strengths and limitations

The strength of this model is the ability to account for the age-specific rate of hysterectomy, tubal ligation, bilateral salpingo-oophorectomy, and ovarian cancer to create a more realistic estimate of outcomes. The model also accounted for the reduction of ovarian cancer associated with tubal ligation and hysterectomy, including the difference between these 2 types of surgery. However, the model did not account for future bilateral salpingo-oophorectomy after hysterectomy, because a reliable estimate of these data was not available. The future costs of surgery for retained tubes and adnexa were also not considered but this is unlikely to have a significant impact on the outcomes of the model.

Conclusions

Opportunistic salpingectomy is associated with a low morbidity but may significantly decrease mortality from ovarian cancer. Even without considering the cost of ovarian cancer, opportunistic salpingectomy is cost effective compared with other health interventions. This model suggests that opportunistic salpingectomy at the time of tubal sterilization or hysterectomy could provide a significant overall healthcare savings that the model predicts will exceed 1 billion dollars annually in the United States alone. Opportunistic salpingectomy should be offered to patients as a method of tubal sterilization and at the time of hysterectomy, and it should be financially covered by all third-party payers, because it confers an overall savings of both lives and healthcare dollars. ■

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