Ovarian cancer screening with the Risk of Ovarian Cancer Algorithm (ROCA): Good, bad, or just expensive?

R. Wendel Naumann *, Jubilee Brown
Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC, United States

HIGHLIGHTS
• The UKCTOCS trial demonstrated an increase in detection of stage I ovarian cancer.
• Modeling shows screening can reduce mortality by only 6%–9% and is not cost-effective.
• The criticism of ovarian cancer screening by the FDA is justified.

ARTICLE INFO
Article history:
Received 1 January 2018
Received in revised form 21 January 2018
Accepted 23 January 2018
Available online xxxx

ABSTRACT

Objectives. To measure the effectiveness of ovarian cancer screening using the Risk of Ovarian Cancer Algorithm (ROCA).

Methods. A Markov model was constructed based on the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). This model was used to predict the outcome of ovarian cancer screening with ROCA.

Results. The model predicted the ovarian cancer mortality from age 50 to age 85 to be 0.954% with a decrease in life expectancy of 0.178 years (yrs) per person. Using data from the UKCTOCS the model predicted a similar reduction in mortality (11% vs. 10%), and similar curves for ovarian cancer mortality. Screening at age 50 for 20 yrs reduced ovarian cancer mortality from 0.953% to 0.898%, an absolute decrease of 6%, yielding an increase in life expectancy of 0.0101 yrs, preventing 55 deaths per 100,000 screened at a cost of $585,946 per life-yr. Screening for 30 yrs reduced mortality from 0.954% to 0.872%, an absolute decrease of 9%, preventing 82 deaths at a cost of $763,970 per life-yr.

Conclusion. The ROCA test can improve the detection of early ovarian cancer but is not practical for screening in an average-risk population. We predict the ROCA test will reduce overall ovarian cancer mortality by 6% to 9% but at a substantial cost. For ROCA to be practical, the cost would need to be reduced ten-fold and would have only a marginal impact on mortality from ovarian cancer. This model supports the FDA’s criticism of the ROCA test.

Ovarian cancer screening may reduce mortality from ovarian cancer but is not cost effective.

© 2018 Elsevier Inc. All rights reserved.

1. Introduction

Ovarian cancer is the leading cause of death from gynecologic malignancy [1]. While treatment of early ovarian cancer results in an excellent prognosis, the majority of women present with advanced disease. Prior screening programs have not been able to reduce the mortality from ovarian cancer [2]. The recent hypothesis that most high grade serous ovarian carcinomas arise from the fallopian tube may explain why peritoneal spread often occurs before ovarian cancer can be detected by ultrasound or tumor marker elevation [3]. However, a minority of patients present with stage I disease, and screening could increase the detection of these patients or potentially detect patients with advanced disease at a point where surgery might be more efficacious.

Unfortunately, screening is fraught with difficulties. Isolated measurement of CA-125 is problematic as the value is often normal in early stage cancers and can be elevated in the absence of cancer [4]. The Risk of Ovarian Cancer Algorithm (ROCA) multimodal screening algorithm is a proprietary test that was developed and tested in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) in order to evaluate the rate of change of CA-125 over time rather than a single absolute value [5]. This trial demonstrated a shift toward earlier stage cancers in the group screened with the ROCA test. Despite the ability of this test to improve early detection of ovarian cancer, the FDA
recommended against testing in the United States due to concern that this test would give a false sense of security in preventing mortality from ovarian cancer [6].

To examine the effect of screening, we constructed a model to test the effect of the ROCA algorithm in preventing death from ovarian cancer as it would be used in screening post-menopausal women at an average risk of ovarian cancer. This model was used to simulate real-world conditions outside of the UKCTOCS trial and examine the effectiveness of screening with respect to the number of deaths prevented as well as the cost per year of life saved.

2. Materials and methods

A recursive Markov model was created using TreeAge Pro 2011 (TreeAge Software, Williamstown, MA) to simulate the risk of death from ovarian cancer versus all other causes of mortality from age 50 to age 85. In this model, transition states include healthy, death from other causes, development of ovarian cancer (stage I, II, IIIa, IIIb-IV) and death from ovarian cancer after development of this disease. The model simulates 5-year mortality from ovarian cancer based on the stage at diagnosis. All cause mortality was calculated from the US Social Security Actuarial Life table [7]. Age-related incidence of ovarian cancer was taken from the SEER database [8]. Five-year survival rates were calculated to correspond to those published by the American Cancer Society [9]. To simulate screening, the distribution of ovarian cancer stages was altered based on data from the UKCTOCS trial for women who did and did not undergo screening. For stage I ovarian cancer it is assumed that there is a 2% annual mortality for 5 years. After 5 years, the mortality in this group returns to actuarial. This corresponds to a 90% 5-year survival and cure. For other stages, the 5-year survival was set at 70% for Stage II, 59% for Stage IIIa, and 39% for stage IIIb-IV ovarian cancer. For stages II-IV disease, the risk of death from ovarian cancer was assumed to occur at a constant rate and continue indefinitely past the 5-year mark. The assumptions regarding stage distribution and mortality per stage are listed in Table 1.

The model was constructed to determine the effects of altering the stage at diagnosis for screening for any given number of years. The starting age and number of screening cycles could be altered in a manner similar to the way in might be used in clinical practice. Once screening was discontinued, it was assumed the stage distribution of ovarian cancer would return to that of the unscreened population. A half-cycle correction was added for all Markov nodes. The cost of the ROCA test was set at $295 annually, as this was the price set by the company immediately prior to discontinuation in the United States. This is approximately 50% more than the 150£ price in the United Kingdom. It is felt that the cost of the screening test accounted for the majority of the cost of screening. Therefore, the cost of repeat testing, ultrasound, or the cost of treatment was not considered as part of this model. The model was tested by using the data the stage shift from the UKCTOCS trial and was then used to evaluate different screening strategies.

3. Results

The model was confirmed by entering the data from the UKCTOCS trial, starting at an age of 61 years for initiation of screening with 9 screening events, and 14 total years of follow-up. Under these conditions, the predicted cumulative mortality due to ovarian cancer was 0.34% in the control group and a 0.31% in the screened group. This is almost identical to what was observed in the actual UKCTOCS trial (0.34% and 0.32%), thereby validating the model as accurate based on published data regarding observed outcomes. Similarly, the reduction in mortality predicted by the model was 10%, compared to the observed 11% in the UKCTOCS trial. Survival curves were generated from the model using the same mean age, number of screens, and follow-up as were used in the UKCTOCS trial. These curves begin to separate at 7 years similar to the survival curves in the UKCTOCS trial (Fig. 1). The model was then tested to reflect clinical practice using the most common scenarios anticipated in routine use to measure the effect of ROCA screening on the average-risk population under normal screening conditions. The model was tested for women who initially underwent ROCA testing at the age of 50 for either 20 or 30 years of annual screening. Screening for 20 years starting at age 50 predicted a reduction in ovarian cancer mortality from 0.954% to 0.898%, an absolute decrease of 6%. This corresponds to an increase in life expectancy of 0.0101 years per patient screened, and the prevention of 55 deaths from ovarian cancer per 100,000 women screened. With the cost of each screening test set at $295, the cost per life year gained was $585,946 under these assumptions.

When the parameters of ROCA testing were altered to screen for 30 years starting at age 50, the model predicted a reduction in ovarian cancer mortality from 0.954% to 0.872%, an absolute decrease of 9%. This corresponds to an increase in life expectancy of 0.0116 years per patient screened, and the prevention of 82 deaths from ovarian cancer per 100,000 women screened. With the cost of each screening test set at $295, the cost per life year gained for the population is $763,970. Predicted cumulative mortality from ovarian cancer with and without screening is shown in Fig. 2.

A sensitivity analysis was performed around the ability of screening to detect stage I cancers. In the screened group, 25% of women presented with stage I cancers. If one considers this a binomial distribution, the estimated 95th percentile distribution for the true incidence of stage I cancers would be between 20% and 30% [10]. The percentage of advanced cancers was adjusted to account for the increase or decrease in stage I cancers detected. Testing the model under these assumptions generated a cost of $406,236 to $1,050,796 per life year saved for 20 years of screening and $530,544 to $1,364,177 per life year saved for 30 years of screening.

Table 1

<table>
<thead>
<tr>
<th>Stage</th>
<th>Stage distribution</th>
<th>Annual mortality</th>
<th>5-Yr survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unscreened</td>
<td>Screened</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>15.88%</td>
<td>25.42%</td>
<td>2%</td>
</tr>
<tr>
<td>II</td>
<td>8.03%</td>
<td>10.70%</td>
<td>7%</td>
</tr>
<tr>
<td>IIIa</td>
<td>2.02%</td>
<td>3.68%</td>
<td>10%</td>
</tr>
<tr>
<td>IIIb-IV</td>
<td>74.00%</td>
<td>60.20%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Please cite this article as: R.W. Naumann, J. Brown, Ovarian cancer screening with the Risk of Ovarian Cancer Algorithm (ROCA): Good, bad, or just expensive?, Gynecol Oncol (2018), https://doi.org/10.1016/j.ygyno.2018.01.029
دریافت فوری
متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات