Cancer screening and life expectancy of Canadian patients with kidney failure

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Abstract

Background. Patients with end-stage renal disease (ESRD) have at least the same prevalence of breast and cervical cancer but a reduced life expectancy compared with the general population. Whereas cancer screening has been found to be effective in the general population, competing risks in ESRD patients may obviate any screening benefit in this population. The purpose of this study was to determine if patients with ESRD benefit, in terms of life expectancy, by screening for breast and cervical cancer.

Methods. The ESRD mortality data from the Canadian Organ Replacement Registry was combined with North American statistics for breast and cervical cancer mortality, incidence, and screening efficacy for 40-, 60-, and 70-year-old women. A validated method of calculating life expectancy, the declining exponential approximation of life expectancy (DEALE), was used to estimate the average life expectancy with and without screening. The benefit of screening is then the estimated difference in the life expectancy with and without mammography or PAP smears.

Results. Without screening, the maximum reduction in life expectancy would be 12 days for 60-year-old women with breast cancer. The maximum calculated benefit from screening was an increase in life expectancy of only 3 days with PAP smears for 60-year-old women.

Conclusions. Breast and cervical cancer screening, in women with ESRD, is not associated with as large a gain in life expectancy as for women of the general population. This conclusion does not necessarily apply to the individual woman with multiple risk factors for breast or cervical cancer and few comorbidities.

Keywords: breast neoplasms; cancer screening; cervix neoplasms; life expectancy; renal failure

Introduction

It has been consistently described that patients on dialysis have a reduced overall life expectancy compared with the general population. For all patients starting dialysis, in the USA, the mean life expectancy is approximately 5 years with a further reduction to only 2.5 years if the elderly population is considered separately [1]. The majority of deaths are secondary to cardiovascular diseases and infections [2], with only a very small proportion due to cancer [2,3]. Currently, there are no cancer screening guidelines that pertain specifically to the end-stage renal disease (ESRD) population. However, applying the standard screening recommendations for the general population to this group of patients is unlikely to result in an equivalent gain in life expectancy. In previous studies, using American mortality data, the gain in life expectancy from cancer screening in ESRD patients has failed to demonstrate a substantial survival benefit [1,4,5]. For example, Chertow et al. [1] have shown that cancer screening results in only a 0.02% reduction in mortality in dialysis patients; a similar reduction, which could be seen by improving the adequacy of dialysis.

The objective of this study was to determine the gain in life expectancy with cancer screening, for patients on dialysis in Canada. Although the mortality from cancer is similar in Canada and the USA, the mortality rate of the Canadian dialysis population is less than the USA dialysis population [6]. We focused on breast and cervical cancer screening, as there are widely accepted screening programmes for these, currently in effect in Canada.

Subjects and methods

A literature search of MEDLINE (1966 to latest update), CANCERLIT (1983 to latest update), and EMBASE published reports was performed to obtain data on incidence, screening efficacy and annual mortality of breast and cervical cancer. The key words, breast neoplasms, cervical...
neoplasms, mass screening, incidence, sensitivity and specificity were used for the search. The results were restricted to human and English language. Data on the mortality rate for the ESRD population was obtained from the Canadian Organ Replacement Register (CORR), which is a national information system on organ failure and transplantation [7]. The 5-year survival for the above cancers was taken from Global Cancer Statistics, using North American data [8]. Values for cancer incidence and screening efficacy were obtained from observational studies [9,10]. All data were entered into an Excel spreadsheet program with separate columns for 40-, 60- and 70-year-old women. The input data used in the calculations are summarized in Table 1.

The declining exponential approximation of life expectancy (DEALE) method was utilized to estimate life expectancy. This method is based on the assumption that survival follows a simple declining exponential function [11,12]. Assuming that the annual mortality for a population is relatively constant, in the absence of disease, life expectancy can be computed by taking the reciprocal of the age- and sex-specific annual mortality rate. If there are other disease-specific mortalities in existence, the overall mortality rate is calculated as the sum of the individual rates. Overall survival is then the reciprocal of this sum. Using this approach, the reciprocal of the age- and sex-adjusted life expectancy for ESRD patients were taken to arrive at the mortality rate for this population. To calculate the effect of cancer-specific mortality on life expectancy of an ESRD patient, the annual mortality rate for breast and cervical cancer was first multiplied by the cancer incidence. This was then added to the ESRD mortality and the reciprocal of the sum was taken. This method has been validated previously [11].

The influence of cancer screening on overall life expectancy was computed by first multiplying the complement of the efficacy of screening [i.e. (1 − efficacy of screening)] with cancer incidence and mortality and then taking the reciprocal of the above value plus ESRD mortality.

Of note, to convert the 5-year survival data into annual mortality rates, a logarithmic equation was used as follows: annual mortality = −1/t ln(S) where t is the number of years and S is the 5-year survival probability.

For example:

(i) Life expectancy for breast cancer (BC) without screening = 1/[ESRD mortality + (BC incidence × BC mortality)].

(ii) Life expectancy for BC with screening = 1/[ESRD mortality + (BC incidence × (1 − efficacy of screening) × BC mortality)].

The gain in life expectancy with screening is then simply calculated as the difference between (ii) and (i).

In order to determine the maximum possible gain in life expectancy with screening, the calculations were repeated using the upper limit of efficacy of screening that has been reported in the literature.

Results

According to CORR data, the average life expectancy in the ESRD is 13.2 years in 40-year-old women, 11.8 years in 60-year-old women and 6.8 years in the 70-year age group. The calculated reduction in life expectancy without screening and the gain in life expectancy, as a result of screening are shown in Tables 2 and 3 respectively. The maximum reduction in life expectancy without screening was 11.63 days in a 60-year-old woman with breast cancer. This number is even lower at 5.63 days in the same age group for cervical cancer. In the 40-year-old age group no screening results in 6.05 and 1.5 days loss of life expectancy in breast and cervical cancer, respectively. The same calculations for the 70-year-old category resulted in 4.44 days for breast cancer and 2.12 days for cervical cancer.

With screening, the largest gain in life expectancy is again in the 60-year-old age group at 2.09 days for breast cancer, and 3.24 days for cervical cancer. Comparable calculations for the 40-year age group are 1.09 days for breast and 0.86 days for cervical cancer. Finally, in 70-year-old women the numbers were 0.80 days for breast cancer and 1.22 days for cervical cancer.

The results of life expectancy with reported maximum screening efficacies for breast and cervical cancer are summarized in Table 4. The results are largely unchanged, from those calculated using the reported average values for screening efficacy. Specifically, the value increases to 3.72 days for breast cancer and 5.07 days for cervical cancer, in the 60-year-old age category. The values for breast and cervical cancer in

<table>
<thead>
<tr>
<th>Table 1. Baseline assumptions</th>
<th>Breast cancer</th>
<th>Cervical cancer</th>
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</thead>
<tbody>
<tr>
<td>10 year incidence</td>
<td></td>
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<tr>
<td>40 year</td>
<td>1.5%</td>
<td>0.19%</td>
</tr>
<tr>
<td>60 year</td>
<td>3.6%</td>
<td>0.90%</td>
</tr>
<tr>
<td>70 year</td>
<td>4.2%</td>
<td>1.0%</td>
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Screening efficacy

<table>
<thead>
<tr>
<th>Confidence interval</th>
<th>Baseline scenario</th>
<th>5-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4–32%</td>
<td>25–90%</td>
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<tr>
<td></td>
<td>18%</td>
<td>57.5%</td>
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<tr>
<td></td>
<td>73%</td>
<td>54%</td>
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Baseline scenario is the midpoint of screening efficacy.

| Table 2. Reduction in life expectancy without screening (days) |
|---------------|-----------------|-----------------|
| Age (years)   | Breast cancer   | Cervical cancer |
| 40            | 6.05            | 1.50            |
| 60            | 11.63           | 5.63            |
| 70            | 4.44            | 2.12            |

| Table 3. Gain in life expectancy with screening (days) |
|---------------|-----------------|-----------------|
| Age (years)   | Breast cancer   | Cervical cancer |
| 40            | 1.09            | 0.86            |
| 60            | 2.09            | 3.24            |
| 70            | 0.80            | 1.22            |

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the 40-year-old women were 1.94 and 1.35 days, and for 70-year-old women, 1.42 and 1.91 days, respectively.

In a large international study, it was noted that cervical cancer might have a higher prevalence in the ESRD population [14]. The incidence of observed cervical cancer to expected was 2.5 times more than the general population in USA. Hence, life expectancy measurements were evaluated again, incorporating this higher incidence into the calculations. Calculation of life expectancy using the potentially higher incidence of cervical cancer in ESRD patients, resulted in a maximum of 14.05 days gain in life expectancy of 60-year-old women (range for all age groups 3.73–14.05).

### Discussion

Based on the results of our study, routine screening for breast and cervical cancer in the Canadian ESRD population, is unlikely to be associated with much gain in life expectancy. Even if the efficacy of screening by mammography or PAP smears were 100%, the maximum gain in life expectancy using this model would still be less than 2 weeks. Such a difference would generally be considered small [15]. Moreover, even if the risk of cervical cancer is higher in this population [13], the gain in life expectancy remains small. These results highlight the important effect of co-morbidities on the life expectancy of patients with ESRD, compared with the general population. The outcome of this study is consistent with the previously reported American studies in spite of the lower mortality rates that are experienced by Canadian dialysis patients [1,4,5].

The above noted gain in life expectancy is not surprising considering that the gain in life expectancy by screening for women of the general population can be measured in months. According to Wright and Weinstein [15], mammography results in a gain of 0.8 months in life expectancy with biannual mammography for 10 years, starting at age 50. PAP smears every 3 years from 20 to 75 are associated with 3.2 months gain in life expectancy [15]. However, a more recent analysis by investigators associated with the Cochrane collaboration found no mortality benefit to screening mammography [16].

In addition to the issue of life expectancy, it is also prudent to remember that screening itself is not a benign process. It can cause undue harm and stress if it is done without considering the rational behind screening [17]. Screening is most efficacious when the burden of suffering from the disease is significant and the test has a low probability of false positive and false negative results. In addition, the test (and the confirmatory tests in the event of a positive result) should not pose harm to the patient [17,18]. Finally, there should be a viable treatment option for the condition being screened. Forty-nine per cent of women screened with mammography from the general population will experience at least one false positive mammogram during 10 screening rounds and 19% will undergo biopsy [18]. In addition, screening also leads to more aggressive treatment, increasing the number of mastectomies by 20% [19]. Even in the general population, serious questions are being raised as to the utility of screening mammography as clinicians struggle to determine the most appropriate management of individuals who are by definition asymptomatic [16,19,20].

Considering the inherent rate of false positive results in any screening procedure, the risk of subsequent intervention for false positives, the psychological and monetary cost, the argument can be made that screening of all women on dialysis for breast and cervical cancer is not warranted. However, it is important to recognize that the results obtained in this study are average results for the ESRD population and do not apply to the individual patient with multiple cancer risk factors. This issue also applies to the use of screening in the general population. One cannot ignore the significant benefit to a patient who is discovered to have breast or cervical neoplasm at an early stage, as a result of screening, and could potentially receive curative therapy. Therefore, the results of this study certainly do not invalidate the role of screening in the dialysis population. The decision to screen for breast or cervical cancer needs to be made on an individual basis such that the potential for maximal benefit and minimal harm will be realized.

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