
Gek-Hsiang Lim,1 BSc (Hons), Chia-Siong Wong,1 MBBS, MMed (Public Health), Khuan-Yew Chow,2 MBch (NUI), MMed (Public Health), FAMS, Vineta Bhalla,3 MBBS, MMed, Kee-Seng Chia,1,4 MSc (OM), MD, FAMS

Introduction

With increasing health awareness and the greater extent of healthcare provision over the years, the life expectancy of Singaporeans has increased from 75.3 in 1990 to 78.4 in 2001.1 This suggests that cancer patients are surviving longer than before, due to an increasing number of delayed cancer deaths. Hence, this may also indicate that the remaining life expectancy at the average age of cancer occurrence has increased. Although there have been reports about cancer survival in Singapore, they mainly referred to the prognosis of cancer patients with respect to a shorter period of 5-year follow-up.2 It is not clear how well cancer patients survive beyond 5 years. However, extensive information regarding cancer cases can be obtained from the Singapore Cancer Registry, which has been functioning for almost 40 years. It provides a comprehensive database for studying the cancer survival as a function of an increased length of follow-up. Hence with an increase in the remaining life expectancy of cancer patients as well as the length of cancer registration, it becomes increasingly important and relevant to use longer-term survival estimates for comparison and evaluation of cancer prevention programmes.

Longer-term survival estimates have rarely been reported by most cancer registries. One reason could be due to the methodology used to construct the estimates. The most common form of reporting by cancer registries were relative survival ratios obtained by cohort analysis.3 However, this measure may not be reflective of the current development of cancer progress since it requires follow-up information on patients diagnosed a long time ago. For example, a 10-
year relative survival estimate obtained from cohort analysis requires patients diagnosed 10 years ago and followed-up over time.

However in recent years, construction of relative survival estimates using period analysis was introduced. Unlike the cohort approach, the period approach is able to accommodate recent changes in temporal trends as the dataset is restricted to the most recently diagnosed patients through left truncation and right censoring of observations for a particular time period as shown in Figure 1. Several cancer registries in Western countries such as the United States, Germany, Sweden and Finland have reported longer-term cancer survival statistics using this approach. In this paper, we described the 10-year cumulative relative survival ratios of Singapore cancer patients using the period approach.

Materials and Methods

Study Cohort

The data used in this analysis was provided by the Singapore Cancer Registry. The registry, established in January 1968, collects basic epidemiological and clinical data of all incident cancer cases diagnosed in Singapore. The Registry ensures comprehensive cancer notifications by examining all pathology reports of cancer from public and private laboratories, hospital records and death certificates issued in Singapore. The coverage and quality of the data in the Singapore Cancer Registry is high, with only 3.2% of all notifications obtained from death certificates only (DCO). This is illustrated through breast cancer where the percentage of DCO dropped from 3.0% between 1968 and 1972 to 0.2% between 1998 and 2002.

Our dataset comprised a total of 142,252 patients (Singapore Citizens and Permanent Residents) diagnosed with a single invasive primary cancer between 1968 and 2002. Censoring due to second and subsequent primary cancers may be associated with death, and hence is informative. Thus individuals with more than 1 primary cancer had been excluded from the analysis, rather than censoring them at the time when the second primary cancer was diagnosed. In addition, DCO cases were excluded. Passive follow-up was done by matching with the death registry between 1 January 1968 and 31 December 2005. Patients who were not in the death register could either still be alive or lost to follow-up. The 1997 electoral register (the latest register available) was used to confirm the vital status of the unmatched subjects diagnosed prior to 1997. Patients diagnosed between 1 January 1968 and 31 December 1997, and who were not in the death or electoral register (6697, 4.7%), were excluded from the analysis. Patients who were not in the death register but in the 1997 Electoral Register, were censored at 31 December 1997 (19,598, 13.8%). Another 22,327 (15.7%) patients who were diagnosed between 1997 and 2002 were not found in the death register. The vital status of these subjects could not be confirmed. In order to avoid biasing the results toward a higher survival, median survival of those recently diagnosed and have died was assigned to them according to sex, stage, primary site and period of diagnosis.

Statistical Analysis

Relative survival was used to describe the survival experience of the patients in this population-based study. Relative survival is the ratio of the observed survival of the patients to the expected survival of a comparable group in the general population, usually in terms of sex, age and period. The latter is assumed to be free of the disease of interest. In addition, relative survival assumes independent competing risks.

The Singapore cancer patient population was matched to the general population by sex, attained age and year of diagnosis. The expected survival was estimated from the Singapore general population which described the annual probabilities of deaths from all causes. The probabilities are listed in single years of age from 0 to 99 years old for each calendar year. This means that for a 50-year-old from the general population, the probability of survival up to 10 years is partitioned to one person-year of a 51-year-old, 52-year-old, and up to a 59-year-old. The expected survival is taken from the life table corresponding to the attained calendar year. Expected survival rates were calculated using the Ederer II method.

Cumulative relative survival ratios were used as a summary measure to describe the survival experience of cancer patients. They were computed using the life table approach where the length of interval was fixed at 1 year. Greenwood’s method was used to calculate the standard errors of the relative survival ratios. The relative survival package (STRS Version 1.0.1) was used on a STATA version 8.2 platform.

The relative survival ratios were age-standardised for comparison with the data from the 9 cancer registries from the United States (US), Surveillance, Epidemiology, and End Results (SEER) Program using the World Standard Cancer Population. The same inclusion and exclusion criteria were applied to the SEER data so that it would consist of patients diagnosed with a single primary invasive cancer, similar to the Singapore study population. Relative survival estimates were calculated for all cancers, stratified by sex, with further sub-analyses performed on the different stages of individual cancers. In the Singapore data, clinical stage of the disease was determined by whether there was lymph node involvement, regional spread or distant metastasis. Using this information, cancer stage was re-
Cancer Survival in Singapore—Gek-Hsiang Lim et al

Fig. 1. Illustrations of the period and cohort approaches.
The numbers in each cell indicate the year of follow-up since diagnosis.

Fig. 2. Ten-year age-standardised relative survival ratios (%) for the 10 most frequent cancers occurring in males and females, 1998-2002.

Fig. 3. Trends in 10-year age-standardised relative survival (%) of selected cancers by stage.

categorised into localised, regional, metastatic and unknown. For the analysis of SEER data, the summary stage scheme was selected from among several choices of staging systems because it was the most similar to the staging classification employed in Singapore.

Results
Of the 142,552 patients in our study, 52.6% were males and 47.4% females. Among males, 28.2% of incident cancers were classified as localised, 24.4% regional, 16.1% metastatic and 31.3% unknown. Among the females, 31.5% were localised, 25.6% regional, 12.9% metastatic and 30.0% unknown. Within this period, the overall 10-year relative survival ratios for all cancer sites were 30.5% in males and 44.2% in females.

The age-standardised 10-year relative survival ratios for all cancer sites were 30.5% in males and 44.2% in females.
the 10 most frequent cancers in Singapore in the period between 1998 and 2002 are shown in Figure 2. The relative survival ratios varied widely among the different cancers, from $5.2\%$ (lung) to $59.5\%$ (bladder) in males and $7.2\%$ (lung) to $64.7\%$ (uterus) in females. Similar relative survival ratios between the males and females were seen in several cancers, such as the lung, colon-rectum and stomach cancers. We found consistently higher rates in females than in males for nasopharyngeal carcinoma and lymphoma.

The trend in 10-year age-standardised relative survival ratios for selected cancer sites is listed in Table 1. Overall, females had better cancer survival rates than males. Over calendar time, we found a general improvement in cancer survival in both sexes. However, the magnitude of improvement was not uniform with some cancers showing greater increase in the relative survival ratios than others. For example, during the period of our study, the 10-year relative survival ratio for cancer of the female breast jumped from $38.4\%$ to $64.2\%$, and that for cancer of the
prostate from 16.5% to 45.2%. On the other hand, for cancers of the lung, liver and pancreas, the 10-year relative survival ratio remained below 10.0% in both males and females.

The overall survival patterns by stage for the most frequent cancers among males and females in Singapore between 1998 and 2002 are shown in Figure 3. Over the years, cancers in the colon-rectum and breast had shown remarkable improvement in survival for both localised and regional stages. For breast cancer in the localised stage, the relative survival estimate steadily increased from 45.3% between 1978 and 1982 to 81.9% between 1998 and 2002. Similarly for breast cancer in the regional stage, the survival estimate increased from 26.0% to 44.3%. Although the survival for colon-rectum cancer saw a decline in the last 5-year period of analysis, the improvement over the years had been high, especially in the localised stage. In cancers with poor prognosis such as lung and liver, there did not seem to be any improvement in long-term survival except for localised cancers in recent years.

The 10-year age-standardised relative survival estimates for some selected cancer sites in the US and Singapore are shown in Table 2. Among the localised cancers, patients with colorectal, lung, breast and cervical cancers had better survival rates in the US. Large differences in survival were seen among colorectal and lung cancer patients with regional spread of their cancers. Except for cancer of the cervix, those with metastatic disease had similar survival in both populations.

### Discussion

Overall, there was improvement in longer-term survival among cancer patients diagnosed between 1968 and 2002 in Singapore although it varied widely for different cancers. A positive trend in relative survival was observed for localised cancers but little change was observed for metastatic tumours. Compared to the US, the survival of colorectal, lung and breast cancers were poorer in Singapore, especially among those with localised or regional disease.

Singapore is a small island state of 704.0km² with a population of 4,483,900 in 2006 consisting of 75.2% Chinese, 13.6% Malays, 8.8% Indians and 2.4% Others. Healthcare services in Singapore have improved dramatically over the last 35 years. The number of doctors increased 5-fold and the number of beds jumped from 7,771 to 11,798 from 1968 to 2000.

### Table 2. Comparisons of 10-year Age-standardised Relative Survival Ratios (%) Between Singapore and US† in 1998 to 2002 for Selected Cancers

<table>
<thead>
<tr>
<th></th>
<th>Colon-rectum</th>
<th>Stomach</th>
<th>Lung</th>
<th>Breast</th>
<th>Cervix</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>Singapore</td>
<td>71.7</td>
<td>60.8</td>
<td>45.9</td>
<td>46.2</td>
<td>18.5</td>
</tr>
<tr>
<td>(61.9-81.6)</td>
<td>(54.7-67.0)</td>
<td>(37.0-54.8)</td>
<td>(38.1-54.2)</td>
<td>(13.9-23.1)</td>
<td>(19.2-33.9)</td>
</tr>
<tr>
<td>US</td>
<td>89.6</td>
<td>82.1</td>
<td>50.0</td>
<td>50.1</td>
<td>34.6</td>
</tr>
<tr>
<td>(86.5-92.8)</td>
<td>(80.0-84.1)</td>
<td>(44.3-56.7)</td>
<td>(44.5-55.7)</td>
<td>(32.1-37.2)</td>
<td>(39.9-44.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Colon-rectum</th>
<th>Stomach</th>
<th>Lung</th>
<th>Breast</th>
<th>Cervix</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>Singapore</td>
<td>23.6</td>
<td>24.5</td>
<td>11.1</td>
<td>10.0</td>
<td>2.4</td>
</tr>
<tr>
<td>(18.8-28.3)</td>
<td>(19.5-29.4)</td>
<td>(6.9-15.2)</td>
<td>(5.5-14.4)</td>
<td>(1.2-3.5)</td>
<td>(0.2-2.8)</td>
</tr>
<tr>
<td>US</td>
<td>61.2</td>
<td>61.2</td>
<td>15.6</td>
<td>17.0</td>
<td>10.3</td>
</tr>
<tr>
<td>(58.2-64.1)</td>
<td>(59.1-63.3)</td>
<td>(12.6-18.7)</td>
<td>(13.3-20.7)</td>
<td>(9.3-11.3)</td>
<td>(11.3-13.6)</td>
</tr>
<tr>
<td>(c) Metastatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon-rectum</td>
<td>3.5(1.9-5.0)</td>
<td>2.8(1.0-4.5)</td>
<td>1.8(0.2-8.0)</td>
<td>–</td>
<td>0.3(0.1-1.3)</td>
</tr>
<tr>
<td>Stomach</td>
<td>7.5(6.3-8.7)</td>
<td>1.8(0.9-3.3)</td>
<td>2.0(0.9-3.8)</td>
<td>–</td>
<td>0.8(0.5-1.0)</td>
</tr>
<tr>
<td>Lung</td>
<td>Breast</td>
<td>Cervix</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singapore</td>
<td>5.4(4.3-6.5)</td>
<td>7.5(6.3-8.7)</td>
<td>1.8(0.9-3.3)</td>
<td>2.0(0.9-3.8)</td>
<td>0.8(0.5-1.0)</td>
</tr>
<tr>
<td>US</td>
<td>5.4(4.3-6.5)</td>
<td>7.5(6.3-8.7)</td>
<td>1.8(0.9-3.3)</td>
<td>2.0(0.9-3.8)</td>
<td>0.8(0.5-1.0)</td>
</tr>
</tbody>
</table>

† Estimates for the US are obtained from the SEER 9 registries with diagnosis years from 1973 to 1999, and followed through 2000. Based on November 2002 submission.

All estimates are age standardised according to the World Standard Cancer Population.

– means that the relative survival estimates are not computed due to small numbers (<10) and the unavailability of the age-specific estimates.
were established in the 1970s to provide subsidised and accessible healthcare services to the public.21 To date, there are 18 polyclinics offering primary healthcare services in the country. The outpatient consultation fee is about S$8 at the polyclinics, which is affordable for every Singaporean. This is in addition to the private medical clinics conveniently situated within the neighbourhood of each housing estate. There are 7 public hospitals and 6 specialty centres in Singapore. Out of the 7 hospitals, 5 of them provide a multi-disciplinary acute inpatient and specialist out-patient services, together with a 24-hour emergency department. The 6 specialty centres offer healthcare services for cancer, cardiac, eye, skin, neuroscience and dental care. Access to healthcare is made even more possible by the introduction of Medisave in April 1984. It is a medical savings scheme introduced nationwide, with the aim of helping Singapore residents save a portion of their monthly income so that they can meet future personal or immediate relative’s medical expenditure.22

Treatment facilities for cancer had been enhanced through the establishment of a comprehensive national oncology centre in 1997 and oncology units in the public restructured hospitals. In addition, private organisations and charities, for example, the Singapore Cancer Society, had contributed actively to cancer control in Singapore and to enhance cancer awareness that complemented government-led initiatives in cancer education. Currently, national breast and cervical cancer screening programmes are available in the country. Although Papanicolaou smear screening for cervical cancer had been available opportunistically since 1964, the national Cervical Screen Singapore programme was launched in 2004.23 Breast Screen Singapore (BSS), the first population-based nationwide mammographic breast-screening programme in Asia, was launched in 2002.

Reflecting this improvement, the crude mortality rates from all causes among Singapore residents decreased from 5.2 per 1000 in 1970 to 4.4 per 1000 in 2001.24 Therefore, it is not surprising to find improvement in longer-term cancer survival over this period.

The major limitation in this study was the inability to determine the vital status of 22,327 (14.2%) patients diagnosed between 1997 and 2002. By assigning the median survival of those who were diagnosed during the same period but have died, we artificially lowered the relative survival and underestimated any temporal improvement in cancer cure. If these patients were considered to be alive until the end of the study period, 1998 to 2002, 10-year relative survival estimates for male colorectal cancer patients would have been increased from 41.2% to 47.6%; male lung cancer patients from 5.2% to 8.3% and female breast cancer patients from 64.2% to 67.3%.

Apart from improvement in diagnosis and treatment, trends in relative survival are influenced by lead-time bias while improvement in stage-specific survival may be exaggerated by stage migration.12,25 Lead-time bias is a consequence of earlier diagnosis of the cancer. Earlier detection through increased awareness and improved diagnostic tools or screening can lead to an increased observed survival time even when the patient’s life has not been prolonged.

Stage migration is often the result of technological advancement bringing about the early detection of a tumour at its metastatic stage. In the earlier years, the patient would have been clinically classified as having localised cancer or cancer with regional spread. With improved technology, the patient is now diagnosed as having metastatic disease. Although this re-categorisation of patients would not affect the survival rates of the entire group of patients, it would enhance the survival rates at each stage. This phenomenon was illustrated by Feinstein et al when they studied 2 different cohorts of patients diagnosed with lung cancer between 1953 and 1964 and in 1977, with respect to the diagnostic tools and techniques at the 2 different time periods.26

In spite of the limitations and possible artefacts in this analysis, the improvement in overall relative survival was not unexpected. Other countries had reported improvements in cancer survival over the last few decades27, 28 and earlier publications had documented the improvement in 5-year cancer survival rates in Singapore between 1968 and 1992.2,29,30 The improvement of cancer survival in Singapore could be attributed largely to the steady development of healthcare services that had accompanied the rapid economic growth in the country over the last 40 years. There was increased access to healthcare services, enhancements in healthcare technology and improvements in the quality of healthcare in Singapore.

When compared with the US, there might be differences in the criteria used to stage cancers. However, overall survival rates are better in the US as many newer innovative treatment modalities and diagnostic procedures are developed, evaluated and implemented in academic medical centres in the US. It often takes several years before they become available to other populations overseas.

However, we noted a uniform lack of progress in lung, liver and prostate cancers in Singapore. This gives strong support for the idea that primary prevention may be the only realistic approach for improved cancer control. Substantial improvement was observed in the relative survival of prostate cancer between 1978 and 1992, which is a period during which no treatment with a curative intent was available. This seems to indicate that increased diagnostic activity, which entails detection of non-lethal disease,
played a role in Singapore, as it did in other countries including Sweden.31,32

Conclusion

There had been sustained improvement of cancer survival in Singapore that was related to the development of better healthcare services, including preventive and curative services targeted specifically at cancer control. Not only do the survival patterns and time trends of different cancers reflect greater access to healthcare services, they highlight the importance of early detection and increased use of systemic adjuvant therapy for improved survival. Cancers that had shown the most substantial improvement in survival are those in which tests for early detection and effective systemic therapy were available.

While several cancers had experienced marked improvement in cancer survival, this degree of survival improvement was not shared across all cancers of different sites. Some common cancers still had poor cancer survival, which served as a motivation to continue building upon our preventive strategies for cancer control. These findings serve as a platform to assess the efficacy of healthcare strategies implemented and to explore new directions for cancer control in Singapore.

REFERENCES