Do Female Cancer Patients Display Better Survival Rates Compared with Males? Analysis of the Korean National Registry Data, 2005–2009

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Abstract

Background: Sex differences have been reported in the prognosis of certain cancers. In this study, we investigated whether Korean females display better survival rates compared with male patients for solid tumor sites.

Methods: We analyzed data from the Korean National Cancer Incidence Database from 599,288 adult patients diagnosed with solid cancers between 2005 and 2009. Patients were followed until December 2010. We applied a relative excess risk (RER) model adjusting for year of follow-up, age at diagnosis, and stage at diagnosis.

Results: For all solid cancer sites combined, women displayed an 11% lower risk of death compared to men (RER 0.89; 95% CI 0.88–0.90) after adjusting for year of follow-up, age, stage, and case mix. Women showed significantly lower RERs for the following sites: head/neck, esophagus, small intestine, liver, nasal cavities, lung, bone/cartilages, melanoma of skin, soft tissue, brain and CNS, and thyroid. In contrast, women displayed a poorer prognosis than men for colorectal, laryngeal, kidney and bladder cancer. However, the survival gaps between men and women narrowed by increase in age; female patients over 75 years of age displayed a 3% higher RER of death compared with males in this age group.

Conclusions: Female cancer patients display an improved survival for the majority of solid tumor sites, even after adjustment for age and stage. Age at diagnosis was the major contributor to the women’s survival advantage.

Introduction

Sex is known to be an important factor in pathogenesis, diagnosis and treatment of cancers, and it has been an independent prognostic factor for several cancer sites.

There have been some studies that showed better cancer survival rates in women for lung [1,2,3,4], CNS lymphoma [5], melanoma [6,7,8], and renal cell carcinoma [9]. Conversely, it has been reported that male patients with colorectal [4] and bladder cancer display a better prognosis over females [4,10,11]. When all cancer sites are combined, the survival rates for women are thought to be more favorable when compared with those of male patients [7,8]. However, most studies have been conducted in western countries, and there were only few Asian data.

Women have a longer life expectancy in most countries [12,13], and are more likely to be diagnosed with cancer at older age than men. If their asymptomatic cancers through cancer screening tended to be diagnosed more frequently in women, they could show better survival rates than men. Neither biological nor cultural factors clearly explain the survival advantage of women.

The purpose of this study was to investigate sex differences in survival among solid cancer patients after adjusting for age and stage of disease in a population-based setting using the Korean National Cancer Incidence Data for patients diagnosed from 2005 to 2009.

Methods

Study Population

Details of the history, objectives, and activity of the KCCR have been documented [14]. Brieﬂy, the Korean Ministry of Health and Welfare initiated a nationwide, hospital-based cancer registry, the Korea Central Cancer Registry (KCCR), in 1980. The KCCR expanded cancer registration to cover the entire population under the population-based regional cancer registry program, and additional medical-record surveys have been conducted since 2003. The national cancer incidence reports for cancer patients
diagnosed since 1999 have been published since 2005. The KCCR
data from 1999 to 2002 have been published as Cancer Incidence
in Five Continents [15], which reflects the completeness of the
incidence data.

The current analysis included patients with solid cancers
diagnosed between 2005 and 2009. We excluded non-melanoma
skin cancer, and sex-specific sites, such as ovary, cervix, corpus,
other gynecological sites, prostate, testis, and other male genital
systems. Additional exclusion for breast cancer was done, as breast
cancer is predominantly found in females and the sexes are known
to differ with regard to biologically-based behaviors. The analysis
was restricted to patients older than 20 years of age, since many
features of childhood cancers differ from those of adult cancers.
We included the first primary cancer only, and we excluded death
certificate only cases.

Overall, a total of 599,288 adult patients with solid cancer were
analyzed. Patients were followed until December 2010. The
duration of survival for each case was calculated as the difference
between date of initial diagnosis and date of death, loss to follow-
up, or date of follow-up termination, whichever came first.

Definitions and Statistical Analysis

The KCCR routinely collects data related to cancer, including
information about demographic characteristics, location of the
primary tumor, morphology, and stage at diagnosis.

The primary cancer was classified according to the Interna-
tional Classification of Diseases for Oncology, 3rd edition [16] and
converted to the classification system used by the Interna-
tional Classification of Diseases, 10th edition [17]. Age at diagnosis
was classified into four groups: 20–49, 50–64, 65–74, and 75 years
or older. Stage at diagnosis was classified into four groups developed
by Surveillance Epidemiology and End Results (SEER) [18]:
localized, regional, distant, and unknown.

We applied a relative excess risk (RER) model to explain the sex
difference between male and female [19,20]. At first, we calculated
relative survival rates, and these relative survival rates are then
modeled using a generalized linear model with a Poisson error
structure based on grouped data [19]. The hazard function, \( \lambda(t,x) \) for a patients with characteristics \( x \) at time \( t \) is estimated as the sum of the
known baseline hazard, \( \lambda^*(t,x) \), and the excess hazard due to
a diagnosis of cancer, \( \nu(t,x) \). That is,

\[
\lambda(t,x) = \lambda^*(t,x) + \nu(t,x)
\]

The model is written as

\[
\lambda(t,x) = \lambda^*(t,x) + \exp (X \beta)
\]

We included follow-up time in all models and restricted the
analysis to the first 5 years of follow-up, as it is typically
inappropriate to adopt proportional hazard assumptions for
longer follow-up periods. To model the simultaneous effects of
age and stage on patient survival, we applied a RER model
adjusting for year of follow-up, age at diagnosis, and stage at
diagnosis. All RERs given by the respective RER model were for
women compared with men as the reference group. Models for
each site were built separately.

To assess the effect of stage and age, we used a reduced model
that excluded these covariates (Model 1). Model 2 estimated the
RER adjusted for age, Model 3 estimated the RER adjusted for
stage, and Model 4 considered both effects; 95% confidence
intervals (95% CI) were also estimated. The regression analysis
was performed on all ages combined and on four age groups. All
analyses were conducted using SAS version 9.2.

Results

Table 1 shows the characteristics of the study population and the
stage distribution by cancer site. We analyzed a total of
599,288 solid cancer sites; 41.9% of these were in women. Most
cancer types were more frequent in men, except for bladder and
thyroid cancer. When we looked at 5-year relative survival,
survival rates in women were higher than in men for 13 out of 20
cancer sites. For stomach, colorectal, liver, gallbladder, larynx,
kidney, and bladder cancers, men’s survivals were better than
women.

The median age of male cases was older than that of female
cases for all solid cancer sites combined (63 vs. 59 years). However,
female cases were older than males for the majority of cancer sites.
This discrepancy is due to the case mix. The median age of those
with thyroid cancer was the lowest among the 20 cancer sites and
accounted for 35% of all solid cancers in females (87,933 cases
among 251,264 female cancers). When thyroid cancer was
excluded, male patients were, on average, 2 years younger than
female patients (64 vs. 66 years, data not shown).

Distinct differences were observed in the stage distribution
between men and women: those of regional origin accounted for
28.1% in men and 32.3% in women. For stomach, colorectal,
liver, and kidney cancers, no differences in the stage distribution
were observed between men and women. For head/neck,
esophageal, small intestine, nasal cavity, bone/cartilage, melano-
ma of skin and thyroid cancers, women displayed a more favorable
stage distribution than men.

Table 2 shows the RER analysis for 20 cancer sites. Four
models are shown for the all-age analysis: Model 1 with follow-
up years; Model 2 with follow-up year and stage; Model 3 with follow-
up year and age; and Model 4 with follow-up year, age, and stage.

According to analyses including participants of all ages, Model 1
showed that women displayed a significantly lower RER of death
than did men for 10 out of 20 sites (head/neck, esophagus, small
intestine, lung, melanoma of skin, soft tissue, brain/CNS, thyroid,
all others, and all solid cancers), and men displayed a significantly
lower RER than did women for 6 out of 20 sites (stomach, colon/
rectum, gallbladder, larynx, kidney, and bladder). In Model 2, women
displayed a significantly lower RER of death than did men
for 9 out of 20 sites (head/neck, small intestine, lung, melanoma of
skin, soft tissue, brain/CNS, thyroid, all others, and all solid
cancers), and men displayed a significantly lower did than women
for 7 out of 20 sites (stomach, colon/rectum, liver, gallbladder,
pancreas, kidney, and bladder). In Model 3, women displayed a
significantly lower RER of death than did men for 14 out of 20
sites (head/neck, esophagus, small intestine, lung, melanoma of
skin, soft tissue, brain/CNS, thyroid, all others, and all solid
cancers), and men displayed a significantly lower did than women
for 7 out of 20 sites (stomach, colon/rectum, liver, gallbladder,
pancreas, kidney, and bladder). In Model 4, women displayed a
significantly lower RER of death than did men for 14 out of 20
sites (head/neck, esophagus, small intestine, lung, nasal cavity,
bone/cartilage, melanoma of skin, soft tissue, brain/CNS, thyroid,
al others, and all solid cancers), and men displayed a significantly
lower RER than did women for only 2 out of 20 sites (colon/rectum and bladder). When we adjusted for follow-up
years, age, and stage, the female advantage was almost identical to
that in Model 3, with exception of larynx and kidney cancers,
which favored male patients. All four models indicated an
advantage for men in only two cancer sites (colon/rectum, and
bladder).

When the analysis was performed by age group, women
displayed a significantly lower RER than did men in most cancer
sites, except for bladder (20–64 years) and colorectal (65–74 years)
cancers, in the analysis for age groups younger than 75 years.
When the analysis was restricted to older patients (older than 75 years), women displayed a lower RER than men only for head/neck, nasal cavity, and lung cancers. Conversely, men displayed a survival advantage over women for 8 out of 20 cancer sites.

### Table 1. Characteristics and stage distribution of the study population of Korean adults, 2005–2009.

| ICD–10 | Cancer site     | Sex    | N (% ) | 5 yr Relative survival | Age | Stage distribution (%) |
|--------|-----------------|--------|--------|------------------------|-----|------------------------|
|        |                 |        |        |                        |     | Localized | Regional | Distant | Unknown |
|        |                 |        |        |                        |     | Median    | Mean     |         |         |
| C32    | Larynx          | Male   | 4,631 (93.5) | 71.6 | 65 | 64.4 | 55.3 | 20.6 | 5.1 | 19.1 |
|        |                 | Female | 320 (6.5) | 65.9 | 69.5 | 66.7 | 47.2 | 27.2 | 4.4 | 21.3 |
| C15    | Esophagus       | Male   | 8,378 (92.0) | 26.7 | 66 | 65.9 | 29.4 | 34.3 | 18.1 | 18.2 |
|        |                 | Female | 733 (8.1) | 36.6 | 71 | 68.7 | 34.2 | 28.7 | 13.4 | 23.7 |
| C67    | Bladder         | Male   | 11,527 (80.5) | 77.6 | 67 | 65.9 | 65.2 | 12.4 | 3.4 | 19.1 |
|        |                 | Female | 2,798 (19.5) | 69.2 | 71 | 69.1 | 60.6 | 12.8 | 4.8 | 21.8 |
| C64–C66, C68 | Kidney    | Male   | 10,817 (80.5) | 74.4 | 59 | 58.8 | 59.0 | 13.9 | 13.7 | 13.4 |
|        |                 | Female | 2,798 (19.5) | 70.8 | 63 | 61.5 | 59.4 | 12.8 | 12.3 | 15.5 |
| C22    | Liver           | Male   | 52,945 (75.4) | 25.1 | 59 | 59.0 | 42.4 | 21.7 | 12.8 | 23.1 |
|        |                 | Female | 17,236 (24.6) | 24.9 | 66 | 64.8 | 42.2 | 19.3 | 13.3 | 25.1 |
| C00–C14 | Head and Neck | Male   | 7,613 (73.6) | 54.0 | 60 | 59.2 | 28.1 | 44.1 | 9.1 | 18.6 |
|        |                 | Female | 2,733 (26.4) | 70.5 | 58 | 57.5 | 42.3 | 32.6 | 6.8 | 18.3 |
| C33–C34 | Lung, bronchus, and trachea | Male | 57,031 (72.5) | 17.0 | 68 | 67.2 | 17.6 | 26.6 | 37.1 | 18.7 |
|        |                 | Female | 21,658 (27.5) | 23.8 | 69 | 67.4 | 19.3 | 20.4 | 41.1 | 19.2 |
| C16    | Stomach         | Male   | 86,908 (67.0) | 65.9 | 63 | 61.7 | 48.4 | 26.2 | 12.2 | 13.2 |
|        |                 | Female | 42,898 (33.1) | 64.0 | 64 | 61.8 | 47.4 | 25.8 | 12.1 | 14.6 |
| C30–C31 | Nasal cavities | Male   | 739 (62.7) | 50.6 | 60 | 59.2 | 32.9 | 37.2 | 7.3 | 22.6 |
|        |                 | Female | 439 (37.3) | 55.5 | 66 | 63.4 | 38.5 | 26.4 | 11.4 | 23.7 |
| C18–C21 | Colon and rectum | Male | 58,338 (59.1) | 73.1 | 63 | 62.0 | 34.4 | 38.9 | 13.9 | 12.8 |
|        |                 | Female | 40,343 (40.9) | 68.6 | 65 | 63.8 | 31.5 | 39.9 | 15.0 | 13.6 |
| C17    | Small intestine | Male   | 1,272 (57.6) | 48.1 | 62 | 60.4 | 36.4 | 25.6 | 21.0 | 17.0 |
|        |                 | Female | 936 (42.4) | 58.4 | 65 | 63.1 | 40.7 | 21.6 | 16.5 | 21.3 |
| C47+C49 | Soft tissue    | Male   | 1,686 (56.6) | 60.2 | 55 | 54.3 | 52.9 | 7.7 | 12.4 | 27.1 |
|        |                 | Female | 1,294 (43.4) | 68.0 | 55 | 55.2 | 51.9 | 9.5 | 10.7 | 27.8 |
| C25    | Pancreas        | Male   | 10,038 (55.4) | 7.9 | 66 | 64.8 | 10.0 | 28.0 | 44.1 | 17.9 |
|        |                 | Female | 8,099 (44.7) | 8.0 | 71 | 69.1 | 11.4 | 29.0 | 39.3 | 20.4 |
| C40–C41 | Bone and cartilages | Male | 739 (53.8) | 62.7 | 48 | 48.1 | 42.8 | 11.1 | 12.0 | 34.1 |
|        |                 | Female | 636 (46.3) | 65.2 | 52 | 52.2 | 44.7 | 8.8 | 12.3 | 34.3 |
| C70–C72 | Brain and CNS  | Male   | 3,270 (52.8) | 37.4 | 52 | 52.5 | 62.0 | 3.6 | 2.3 | 32.1 |
|        |                 | Female | 2,923 (47.2) | 41.6 | 56 | 55.4 | 60.1 | 2.9 | 2.6 | 34.4 |
| C43    | Melanoma of skin| Male   | 901 (50.0) | 47.1 | 62 | 59.6 | 43.5 | 17.2 | 16.1 | 23.2 |
|        |                 | Female | 902 (50.0) | 62.5 | 63 | 61.2 | 49.7 | 16.7 | 10.2 | 23.4 |
| C23–C24 | Gallbladder and biliary tract | Male | 9,295 (49.4) | 27.0 | 67 | 66.6 | 23.7 | 37.1 | 19.7 | 19.5 |
|        |                 | Female | 9,541 (50.7) | 25.2 | 71 | 69.6 | 23.0 | 33.0 | 23.2 | 20.8 |
| C73    | Thyroid         | Male   | 15,786 (15.2) | 99.3 | 46 | 47.2 | 36.6 | 48.9 | 1.9 | 12.7 |
|        |                 | Female | 87,933 (84.8) | 99.8 | 47 | 47.3 | 43.9 | 42.7 | 0.9 | 12.6 |
|        | All other solid cancers | Male | 6,110 (55.9) | 31.2 | 65 | 62.5 | 14.8 | 9.2 | 18.3 | 57.8 |
|        |                 | Female | 4,816 (44.1) | 31.5 | 68 | 64.8 | 12.4 | 7.3 | 20.9 | 59.4 |
| C00–C80, except All solid cancers | Male | 348,024 (58.1) | 49.9 | 63 | 61.8 | 37.3 | 28.1 | 17.1 | 17.5 |
| C44 and C50–C63 | | | | | | | | | |
|        |                 | Female | 251,264 (41.9) | 66.6 | 59 | 58.3 | 38.5 | 32.3 | 12.5 | 16.7 |

doi:10.1371/journal.pone.0052457.t001

(Table 3). When the analysis was restricted to older patients (older than 75 years), women displayed a lower RER than did men only for head/neck, nasal cavity, and lung cancers. Conversely, men displayed a survival advantage over women for 8 out of 20 cancer sites.
Discussion

To our knowledge, this is the first study among an Asian population to use a population-based registry to investigate sex differences in cancer survival. We applied a RER model that adjusted for age and stage distribution using the KCRR database. We found that women displayed better survival rates for the majority of cancer sites; the exceptions were colorectal, laryngeal, kidney and bladder cancers. However, the female survival advantage diminished with age, with men displaying a survival advantage over women in patients aged 75 years or older.

For all the cancer sites combined, the excess mortality for females was 0.89 after adjusting for follow-up years, age, stage, and case mix. This difference was larger than those of a previous European study (4% lower RER) [8]. However, this big difference could be explained by case-mix with thyroid cancer which showed very high overall survival rate. Thyroid cancer accounted for 35% of all solid cancers in Korean females, female patients had a significant 46% lower RER than males. The observed sex differences in survival may be explained by tumor characteristics, such as distribution of morphologies [21], and difference in risk factors such as hormones [2], infections [22,23], and chromosomal changes [24]. Differences in risk factor, particularly smoking, also constitute important factors. Smoking is known to be associated with a higher risk of death in cancer, and the smoking rate in Korean adults is 67.6% for males and 3.0% for females [25].

Previous studies [26,27] have suggested that men are characterized by more co-morbid conditions at the point of cancer diagnosis than are women, and pre-existing chronic conditions may contribute to sex differences in survival rates.

We observed lower survival rates for women in cases of colorectal, laryngeal, bladder, and kidney cancer. For bladder cancer, we observed a RER of 1.24 for females following the adjustment for follow-up years, age, and stage. Recent analyses indicated poorer survival rates for women in the USA [28] and Europe [7,8]. The disparity between sexes may represent differential levels of exposure to tobacco in addition to differences in the effects of genetic, anatomical, hormonal, and environmental factors [10]. For laryngeal cancer, our results are consistent with those of previous studies [4,8]. We observed significant disadvantage for females (RER 1.03, 95% CI 1.01–1.19) of laryngeal cancer in Korea. For USA and Europe, females had a higher RER over males, but showed statistically non-significant results.

We observed a higher RER 1.08 (95% CI 1.04–1.11) for females of colorectal cancer after adjusting for follow-up years, age, and stage. Previous data on colorectal cancer are controversial and show both higher [7] and lower RERs of death in female patients [8,29].

In contrast to previous reports, we observed a higher RER 1.10 (95% CI 1.02–1.19) for females of kidney cancer in Korea. In the majority of previous studies, women displayed better survival rates [4,8,9,30,31,32]. In one study investigating sex differences in

Table 2. Relative excess risk (RER) for solid cancer sites among Korean adults, 2005–2009.

| ICD–10 | Cancer site | RER for women |
|--------|-------------|---------------|
|        |             | Model 1α RER (95% CI) | Model 2β RER (95% CI) | Model 3γ RER (95% CI) | Model 4δ RER (95% CI) |
| C2    | Larynx      | 1.36 (1.08–1.71) | 1.26 (0.99–1.59) | 1.14 (0.90–1.45) | 1.03 (1.01–1.09) |
| C15   | Esophagus    | 0.87 (0.79–0.96) | 0.90 (0.81–1.00) | 0.80 (0.72–0.89) | 0.83 (0.75–0.92) |
| C67   | Bladder      | 1.57 (1.42–1.73) | 1.47 (1.33–1.62) | 1.34 (1.22–1.48) | 1.24 (1.12–1.37) |
| C64–C66, C68 | Kidney   | 1.15 (1.07–1.24) | 1.21 (1.13–1.31) | 1.00 (0.93–1.08) | 1.10 (1.02–1.19) |
| C22   | Liver        | 1.02 (1.00–1.05) | 1.03 (1.01–1.05) | 0.94 (0.92–0.96) | 0.95 (0.93–0.97) |
| C00–C14 | Head and neck | 0.58 (0.53–0.63) | 0.64 (0.58–0.70) | 0.56 (0.51–0.62) | 0.63 (0.57–0.68) |
| C33–C34 | Lung, bronchus, and trachea | 0.77 (0.76–0.79) | 0.74 (0.73–0.76) | 0.76 (0.75–0.78) | 0.73 (0.72–0.75) |
| C16   | Stomach      | 1.09 (1.07–1.12) | 1.07 (1.05–1.09) | 0.99 (0.97–1.01) | 1.00 (0.98–1.03) |
| C30–C31 | Nasal cavities | 0.85 (0.70–1.04) | 0.84 (0.69–1.03) | 0.74 (0.60–0.91) | 0.73 (0.59–0.90) |
| C18–C21 | Colon and rectum | 1.25 (1.21–1.28) | 1.18 (1.15–1.22) | 1.12 (1.08–1.15) | 1.08 (1.04–1.11) |
| C17   | Small intestine | 0.76 (0.66–0.87) | 0.80 (0.69–0.92) | 0.65 (0.56–0.75) | 0.70 (0.60–0.80) |
| C47–C49 | Soft tissue | 0.79 (0.69–0.92) | 0.84 (0.72–0.97) | 0.76 (0.66–0.88) | 0.78 (0.68–0.91) |
| C25   | Pancreas      | 1.01 (0.98–1.05) | 1.03 (1.001–1.07) | 0.95 (0.92–0.98) | 0.97 (0.94–1.00) |
| C40–C41 | Bone and cartilages | 0.93 (0.76–1.14) | 0.94 (0.77–1.15) | 0.78 (0.63–0.95) | 0.78 (0.64–0.95) |
| C70–C72 | Brain and CNS | 0.89 (0.83–0.95) | 0.89 (0.83–0.95) | 0.79 (0.77–0.85) | 0.79 (0.74–0.85) |
| C43   | Melanoma of skin | 0.65 (0.55–0.78) | 0.74 (0.62–0.88) | 0.64 (0.54–0.76) | 0.73 (0.61–0.87) |
| C23–C24 | Gallbladder and biliary tract | 1.11 (1.07–1.15) | 1.07 (1.22–1.19) | 1.03 (0.99–1.07) | 1.00 (0.96–1.03) |
| C7   | Thyroid       | 0.39 (0.35–0.51) | 0.56 (0.45–0.69) | 0.53 (0.41–0.70) | 0.54 (0.44–0.67) |
| All other solid cancers | 0.94 (0.90–0.99) | 0.88 (0.84–0.93) | 0.88 (0.84–0.93) | 0.83 (0.79–0.87) |
| C00–C30, except C44 and C50–C63 | All solid cancers | 0.92 (0.88–0.97) | 0.96 (0.95–0.97) | 0.91 (0.90–0.92) | 0.89 (0.88–0.90) |

αadjusted for year of follow up;  
βadjusted for year of follow up and stage;  
γadjusted for year of follow up and age;  
δadjusted for year of follow up, age, and stage;  
*adjusted for year of follow up, age, and case mix.  
doi:10.1371/journal.pone.0052457.t002
kidney cancer, Woldrich et al [32] displayed a male prevalence of 62% among kidney cancer patients. Women displayed a better stage distribution and a higher incidence of stage I tumors (54%) compared with men. In Korea, male patients were dominant (81% of kidney cancer patients), and women cancer patients were, on average, 4 years older than males (63 vs. 59 years). However, no sex differences in stage distribution were reported. The survival rates of kidney cancer patients were reported to be superior in females (64.4% in males and 69.7% in females diagnosed between 1996 and 2000), but these findings have been contradicted by other systems, reports indicate that the SEER stages provide effective adjustments for stage at diagnosis [34]. However, the proportion of unknown staged cases reported in Korea was relatively high, rendering the data difficult to interpret and a direct comparison of RERs after adjusting for stage distribution difficult.

To assess the effect of stage and age on the RER separately, we used reduced models that excluded age (model 2) or stage (model 3) covariate. For most cancer sites, the RERs for females in model 2 were much higher than those of model 4. Therefore, the age covariate seemed to play a role in the lower RERs of women. For liver cancer, we saw the reverse results, i.e., the male advantage in model 2 turned into a female advantage in model 4. When we assessed the effect of the stage covariate, some cancer sites had higher RERs in model 3 than model 4, including colorectal, gallbladder, laryngeal, lung, and bladder cancers. These cancer sites showed that stage distribution in men was more favorable than in women.

We have found that age at diagnosis was the major contributor to the women’s survival advantage. The RERs for women increased with age; female patients displayed a 3% higher RER of death compared with men older than 75 years for all solid cancer combined. Women’s advantage was most marked in 50–64 years, and reduced drastically in older than 75 years in most cancer sites. This female disadvantage with older age group was reported in recent European [7,8] studies. Micheli et al [8] suggested that age at diagnosis might be a proxy for biological factors that changed more markedly in women than men as they got older.

We have some limitations in our study. First, we did not have information about histologic grade, co-morbidities, or risk factors including smoking. Thus, we adjusted only for age and stage, which may affect certain cancers. However, differences in the prevalence of smoking in women and men may have influenced the survival differences observed. Second, validation of the stage information is critical for a comparison of survival rates. Many registries routinely collect stage at-diagnosis data using the SEER summary due to the ease of data collection using medical records. Although the SEER stages are not as detailed as the stages defined by other systems, reports indicate that the SEER stages provide effective adjustments for stage at diagnosis [34]. However, the proportion of unknown staged cases reported in Korea was relatively high, rendering the data difficult to interpret and a direct comparison of RERs after adjusting for stage distribution difficult.

In conclusion, our analysis demonstrates that female cancer patients possess a lower mortality risk than do males after adjusting for year of follow up, age at diagnosis, and case mix. However, data are insufficient to draw firm conclusions.
for follow up, age, stage, and case mix. Age at diagnosis was the main determinant of the female advantage with regard to cancer death. This was most evident in young and middle-aged patients, but it reversed in patients older than 75 years. Future studies should therefore focus on the etiological factors responsible for the systematically lower mortality risk among women.

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Author Contributions

Conceived and designed the experiments: KWJ. Performed the experiments: KWJ. Analyzed the data: KWJ. Contributed reagents/materials/analysis tools: KWJ SP AS HJK CMO JKJ YJW. Wrote the paper: KWJ.