RESEARCH ARTICLE

Comparison of Survival Rates between Chinese and Thai Patients with Breast Cancer

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Abstract

Background: The burden and severity of a cancer can be reflected by patterns of survival. Breast cancer prognosis between two countries with a different socioeconomic status and cultural beliefs may exhibit wide variation. This study aimed to describe survival in patients with breast cancer in China and Thailand in relation to demographic and clinical prognostic information. Materials and Methods: We compared the survival of 1,504 Chinese women in Yunnan province and 929 Thai women in Songkhla with breast cancer from 2006 to 2010. Descriptive prognostic comparisons between the Chinese and Thai women were performed by relative survival analysis. A Cox regression model was used to calculate the hazard ratios of death, taking into account the age, disease stage, period of diagnosis and country. Results: The overall 5-year survival proportion for patients diagnosed with breast cancer for Yunnan province (0.72) appeared slightly better than Songkhla (0.70) without statistical significance. Thai women diagnosed with distant and regional breast cancer had poorer survival than Chinese women. Disease stage was the most important determinant of survival from the results of Cox regression model. Conclusions: Breast cancer patients in Kunming had slightly greater five-year survival rate than patients in Songkhla. Both Chinese and Thai women need improvement in prognosis, which could conceivably be attained through increased public education and awareness regarding early detection and compliance to treatment protocols.

Keywords: Breast cancer - survival - stage - prognosis - comparison - Thailand - China

Introduction

The global rise in breast cancer incidence rates is observed to be about 0.5% annually since 1990. In contrast, Chinese cancer registries report rapid increasing annual incidence rates of 3-4% even in the absence of population-based breast cancer screening (Parkin et al., 2005). In GLOBOCAN 2012, the estimated rate of increase in ASR being 2.5% per year seems to be slowing down (Ferlay et al., 2013). Breast cancer was estimated to cause almost 459,000 female death in 2008 and around 522,000 in 2012 worldwide with an age-standardized rate of 13.9 deaths per 100,000 and the 2012, the rate is expected to decline to 12.9 (Ferlay et al., 2010; 2013), thus in contrast, a longer survival time. Despite the decreasing mortality rate of breast cancer, it remains the leading cause of cancer-related mortality amongst females internationally, and accounts for almost 14% of all cancer deaths. Breast cancer mortality among Chinese women has been decreasing a lot but, in contrast, the incidence has doubled during the past 30 years (Parkin et al., 2005;

Zhao et al., 2010). In Thailand, the incidence of breast cancer has been rapidly increasing throughout the country and the largest proportion is observed in the central region (Sriplung et al., 2006). The phenomenon of rapid increase in breast cancer incidence can be observed in other Asian countries (Shin et al., 2010; Teo and Soo, 2013).

In conjunction with the incidence rates, survival is another important measure of chronic disease burden. Survival is considered as a key index of the overall effectiveness of health services in the management of patients with cancer. Differences in survival have prompted or guided cancer control strategies. A cancer registry usually uses relative survival to describe survival probability of cancer patients in a population. The benefit of using relative survival is comparability of survival across populations with different age structure and background probability of death. Usually in countries where the cause of death is not accurately registered, the use of relative survival in population-based cancer registries is unavoidable. Indicators of trends in incidence, survival, and mortality are all required for cancer control. However,

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statistical reports of breast cancer incidence, pathological characteristics, and survival data are still inadequately reported in many Asian countries. Representative data on the breast cancer profile of Chinese women and its time trend over years are relatively rare. The findings from survival analysis will provide information critical for guiding cancer prevention and control research and service provision.

Relative survival (RS) is typically used in the analysis of cancer registry data (Gamel and Vogel, 2001). It is adopted to measure and represent the survival probability of cancer and defined as the ratio of the proportion of observed survivors in a cohort of cancer patients to the proportion of expected survivors in case they were in general population. The advantage of relative survival is that it requires no information on cause of death, thus, problems of unavailability and inaccuracy of death certificates can be overcome. The observed survival consider all cause of death are events. The expected survival is estimated from national population life tables stratified by age, sex, and calendar time.

Thailand is a country with over 20 years history of population-based cancer registration. It is just to the south of Kunming. However, the social and economic situations as well as health system are different, thus, it is a good country to be compared with. Songkhla is a province in the southern region of Thailand where native population is rather heterogeneous. The majority of the people are Buddhist and around 25% are Muslim (National Statistical Office, 2012). Chinese has long colonized in the cities of Songkhla and Hat Yai.

In this study we aimed to compare the survival rates of patients with breast cancer in Yunnan to represent Chinese women and in Songkhla representing Thai women to see if some socio-demographic factors might play some roles in clinical prognosis for breast cancer. The population-based cancer registry of Songkhla was used while the data from Yunnan was extracted from hospital-based medical records since there was no available population-based cancer registry covering Yunnan population.

Materials and Methods

This was a retrospective study based on data collected from two sources, one in Yunnan, China and another from population-based cancer registry of Songkhla, Thailand. In Yunnan, the data were collected from the two largest hospitals in Kunming providing treatment for breast cancer patients. The database covered 1504 women who were diagnosed with breast cancer between January 1st, 2006 and December 31st, 2010. All medical records of patients diagnosed with breast cancer retrieved from existing database of those two hospitals. Follow-up time was until December 31, 2011 by matching the list of diagnosed cases with the death register of Yunnan province by their name, family names, residential area, sex, birth date. The cause of death was registered as the International Classification of Diseases and Causes of Death ICD 10 codes.

The cancer registry system in Songkhla province has been in operation since 1989. Cancer cases residing in the province are registered into the population-based registry. Up till the end of 2010, the registry did regular follow-up of patients by 3 methods: 1) passive follow up by patient revisit to the hospitals they were treated; 2) checking against the death registry of the Ministry of Interior, and if possible; 3) contacting local health personnel who took care of the patients. Usually, cancer treating hospitals had their own system of routine follow up for patients under their responsibility. To compare with the data from Kunming, female breast cancer cases diagnosed from January 1st, 2006 to December 31st, 2010 were drawn. The study has been approved by ethical committees at the two hospitals in Yunnan and also that of Faculty of Medicine, Prince of Songkla University.

Stage information in hospital-based data in the two settings was available in TNM staging system: tumor stage, lymph node stage and metastatic spread. This information was reclassified to the summary staging (Shambaugh et al., 1993). The summary stage of disease describes the extent or spread of the cancer at the time of diagnosis. A cancer's stage is based on the primary tumor's size and whether it has spread to other areas of the body. A different system of summary staging (*in situ*, local, regional, and distant) is used for descriptive and statistical analysis of tumor registry data. In situ lesion was excluded from this study since it was considered as a premalignant lesion, not an invasive cancer.

A local tumor is defined as an invasive malignant cancer confined entirely to the organ of origin. A regional lesion is a malignant cancer that: 1) has extended beyond the limits of the organ of origin directly into surrounding organs or tissues; 2) involves regional lymph nodes by way of lymphatic system; 3) has both regional extension and involvement of regional lymph nodes. Distant tumor is a malignant cancer that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis to distant organ, tissue, or via the lymph nodes (Young et al., 2001).

In Yunnan, the date of death was confirmed directly by the death registry. Information on patients' age and date at diagnosis, gender and pathological results was obtained from the hospital records. Songkhla cancer registry routinely collected follow-up data by hospital service system. Death was confirmed by hospital records and the national death registry. Other medical data were available in cancer registry database.

Statistical analysis

Descriptive prognostic comparisons between China and Thailand women were performed by relative survival analysis. In calculating survival, cumulative 5-year survival rates were calculated starting from the date of diagnosis. Survival time was determined from cancer diagnosis to the end of follow-up, with vital status of alive or dead. Cases whose vital status was unknown at 5 years after diagnosis were assumed to be alive as of the last known date of living. Expected survival rates were calculated using the cohort survival table based on WHO life tables of the Chinese and Thai populations (Lopez et al., 2014) and afterwards using the survival probability in the general population similar to the patients in sex,

birth-year and age.

Since all breast cancer patients in this report were female, only age and summary distribution of demographic data in the two populations were to be compared. Median age at diagnosis and percentage of patients with age at diagnosis below or equal 50 and above 50 years were shown. All the tests were set at significance level of 95%. All statistical analysis was performed using R software version 3.0.2 (R Core Team, 2013). RS probability was computed by a function in CRStat package for R (Sriplung, 2013). Log-rank test for relative survival was performed using log-rank function in Hmisc package (Harrell, 2013). Within the same population, a Cox regression model was used to calculate the hazards ratio of death, taking into account the age, disease stage, and period of diagnosis.

Results

Characteristics of the patients with breast cancer are present in Table 1. The median and range of age at diagnosis in Yunnan and Songkhla women was 47 (range: 20-84) and 51 (range: 16-86) years, respectively. Chinese women diagnosed with breast cancer earlier in life than the Thai women 3 years younger on average (Table 1). Distribution of summary stage differs in both settings. Since breast cancer patients in Yunnan in this study were hospital-based cases, the unknown stages were much less than population-based setting in Songkhla province where data were collected from various independent source even community hospitals and death certificates. However, among those with known stage, a significant proportion of Kunming (Yunnan) patients were in local and regional stages.

The overall 5-year RS for patients with breast cancer diagnosed from 2006 to 2010 appeared better for Yunnan (0.72) than Songkhla women (0.70) (Table 2 and Figure 1). There was no difference in the relative survival between the two populations.

The RS probability for patients diagnosed with breast cancer at different stage in the two areas was different from that of the overall relative survival. The disease was analyzed by summary stage to avoid dependency of the overall RS on stage distribution of breast cancer in the two different populations. In both populations, RS probability among localized disease was similar. Thai women diagnosed with regional and distant stages of breast cancer had significantly poorer survival than Chinese women (Table 2 and Figure 2) with log-rank p value <0.01. Table 2 gives the relative survival probability values of breast cancer patients in Yunnan and Songkhla together with their 95% confidence intervals in terms of overall RS and RS by summary stage, while Figure 2 compares the RS in the two populations by summary stage in graphic format which clearly demonstrates the difference in the RS in regional and distant summary stages.

It is clear from Table 3 that disease stage was the most important determinant of survival while patients' age at diagnosis was not. Those with regional disease
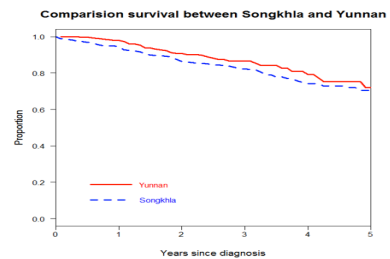

Figure 1. Comparison of Relative 5 Year Survival between Yunnan and Songkhla

Table 2. Relative Survival (RS) Probability for Breast Cancer in Yunnan and Songkhla

RS probability		Yunnan		Songkhla	
		survival prob.	95% CI	survival prob.	95% CI
Overall RS	1 year	0.98	0.96-0.98	0.94	0.92-0.95
	3 year	0.87	0.85-0.89	0.82	0.79-0.84
	5 year	0.72	0.70-0.74	0.70	0.67-0.73
RS, summary stage					
Local	1 year	0.97	0.96-0.98	0.99	0.98-1.00
	3 year	0.97	0.96-0.98	0.98	0.97-0.99
	5 year	0.97	0.96-0.98	0.98	0.97-0.99
Regional	1 year	0.98	0.96-0.98	0.97	0.96-0.99
	3 year	0.91	0.89-0.92	0.84	0.81-0.86
	5 year	0.85	0.83-0.87	0.73	0.70-0.76
Distant	1 year	0.90	0.88-0.91	0.64	0.61-0.67
	3 year	0.66	0.64-0.68	0.42	0.39-0.45
	5 year	0.33	0.31-0.35	0.14	0.12-0.16
Unknown	1 year	0.92	0.91-0.93	0.93	0.91-0.95
	3 year	0.77	0.75-0.79	0.80	0.77-0.83
	5 year	0.77	0.75-0.79	0.71	0.68-0.74

Table 1. Age and Summary Stage Distribution of Breast Cancer Patients in Yunnan and Songkhla

Characteristics		Yunnan N=1504	Songkhla N=929	p value (chi-square)
Age at diagnosis (Years)	≤50 years (%)	910 (60.5)	463 (49.8)	<0.001
	>50 years (%)	594 (39.5)	466 (50.2)	
Summary stage	Local (%)	217 (14.4)	137 (14.7)	0.048*
	Regional (%)	1126 (74.9)	536 (57.7)	
	Distant (%)	118 (7.8)	67 (7.2)	
	Unknown (%)	43 (2.9)	189 (20.3)	

*Excluding unknown stage

Table 3. Factors Affecting Survival by Cox Regression of Breast Cancer Patients in Yunnan and Songkhla

		Yunnan province			Songkhla province		
		adj. HR (95%CI)	p (Wald)	p (LR)	adj. HR (95%CI)	p (Wald)	p (LR)
Summary stage	Local	Ref.		0.001	Ref.		<0.001
	Regional	2.30 (0.53, 10.04)	0.268		5.38 (1.97, 14.72)	0.001	
	Distant	13.74 (3.09, 60.99)	<0.001		31.14 (11.13, 87.11)	<0.001	
	Unknown	6.45 (0.87, 47.64)	0.068		9.75 (3.49, 27.22)	<0.001	
Age group (years)	≤50	Ref.		0.119	Ref.		0.219
	(50,60]	1.37 (0.72, 2.60)	0.34		1.15 (0.8, 1.65)	0.456	
	(60,70]	3.58 (1.59, 8.04)	0.002		1.27 (0.76, 2.14)	0.36	
	>70	1.20 (0.16, 8.91)	0.86		1.71 (1.04, 2.8)	0.034	

*p (Wald)=p value from Wald's test; p (LR)=p value from likelihood ratio test
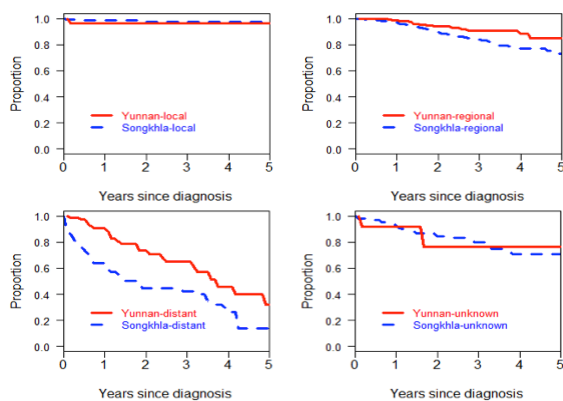
Figure 2. Comparison of Relative Survival by Stage between Yunnan and Songkhla

had poorer prognosis than those with local disease and those with distant metastasis had the poorest survival in both populations.

Discussion

The overall RS of population of Songkhla was slightly lower than that of Yunnan. While those with localized disease had the same survival probability, Thai women in Songkhla with regional cancer had significantly poorer prognosis and the difference in relative survival between the two populations was more pronounced among women with metastatic disease. A study of Muangpaisan et al using Songkhla cancer registry data showed a poor survival among Muslims and those who lived in remote areas with difficulty in health care accessibility (Muangpaisan and Sriplung, 2000). This issue is the difference among the two populations in Songkhla and Kunming where hospital-based patients in Kunming setting mostly lived in urban or suburban areas while patients in Songkhla included all cases both living in urban and rural areas. The issue of Islamic belief on disease treatment and encountering the end of life is one of the differences among the two populations. As mentioned by some studies that Muslims tended to accept 'good death' and interpretation 'good death' as the 'will of God' was different from other religion believers (Tayeb et al., 2010) could be another reason for poorer survival in Songkhla than Kunming population, especially in advanced stage.

In comparison to women with breast cancer in Malaysia reported by Abdullah et al. (2013), 1, 3, and 5 year survival rates in Songkhla and Kunming women in 2006-2010 cohort were all better than all three ethnic groups in Malaysia: Malay, Chinese, and Indian, in 2000-2005 cohort. However, there are two important issues to be mentioned in comparison of the two papers. The survival rates calculated by the Malaysian report were observed survival rates not adjusted for baseline survival probability of the population while we reported relative survival values. It is well known that relative survival is, to some extent, better than observed survival because of the adjustment (Gamel and Vogel, 2001). The second point is the time period of comparison, the survival reported by Abdullah was from 2000-2005 cohort while in our study the patients were from 2006-2010 cohort. We observed a

better survival in 2006-2010 cohort than the cohort in the first half of the decade (unpublished data). It is possible that in comparison of the same time period using relative survival, the survival rates in Songkhla (Thailand), Malaysia, and Kunming (Southern China) might not be much different.

Breast cancer survival rates vary greatly worldwide, ranging from over 80% in North America and Western Europe, around 70% in Eastern Europe (Allemani et al., 2013), 90% in Hong Kong, 60% in Qidong, China, and 44% in Uganda (Sankaranarayanan et al., 2011). Survival of breast cancer in Songkhla in the period of 1990-1999 published in the book 'Cancer Survival in Africa, Asia, the Caribbean and Central America' was approximately 62.7% in middle-income countries and less than 40% in low-income countries. The low survival rates in less-developed countries are mainly due to late diagnosis of the majority of cases. In this study, the 5-year relative survival between Yunnan and Songkhla province was similar though the survival rate in Songkhla was slightly lower. The rates of 72% and 70% in Yunnan and Songkhla were as high as that of Eastern European countries.

Relative survival of those with unknown stage being within the range of probability of localized and advanced stages suggested an unbiased reporting of stage in both Kunming and Songkhla. Even the percentage of unknown stage was higher in Songkhla than in Kunming situations, such the difference would not alter our conclusion when the bias in stage distribution was unlikely.

In conclusions, breast cancer patients in Kunming had greater five-year survival rates than patients in Songkhla, especially in advanced stage disease. These findings support the need for early detection of breast cancer which can improve overall survival by providing public education to increase awareness of the women and as well as education of heath care providers.

Acknowledgements

References

Abdullah NA, Mahiyuddin WRW, Muhammad NA, et al (2013). Survival rate of breast cancer patients in Malaysia: a population-based study. *Asian Pac J Cancer Prev*, **14**, 4591-4.

Allemani C, Sant M, Weir HK, et al (2013). Breast cancer survival in the US and Europe: a CONCORD high-resolution study. *Int J Cancer*, **132**, 1170-81.

Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer,* **127**, 2893-917.

Ferlay J, Soerjomataram I, Ervik M, et al (2013). GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; Available

from: http://globocan.iarc.fr, accessed on 9 January 2013.

Gamel JW, Vogel RL (2001). Non-parametric comparison of relative versus cause-specific survival in Surveillance, Epidemiology and End Results (SEER) programme breast cancer patients. *Stat Methods Med Res*, **10**, 339-52.

Harrell Jr FE (2013). HMisc package for R version 3.13.0. Available from http://cran.r-project.org/web/packages/Hmisc/index.html.

Lopez AD, Salomon J, Ahmad O, et al (2014). Life Tables for 191 Countries: Data, Methods and Results. GPE Discussion Paper Series: No. 9. World Health Organization. Available from: http://www.who.int/healthinfo/paper09.pdf.

Muangpaisan T, Sriplung H (2000). Social and geographic predictors of cancer survival: a role for a population-based cancer registry in cancer control. *Asian Pac J Cancer Prev*, **1**, 319-23.

National Statistical Office (2012). 2010 Population and Housing Census of Songkhla. National Statistical Office. 2012. Available from: http://service.nso.go.th/nso/nso_center/project/search_center/province-th.htm.

Parkin DM, Bray F, Ferlay J, et al. (2005). Global cancer statistics, 2002. *CA Cancer J Clin*, **55**, 74-108.

R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.

Sankaranarayanan R, Swaminathan R, Lucas E (2011). Cancer survival in Africa, Asia, the Caribbean and Central America (SurvCan). IARC Scientific Publications volume 162, ISBN 978-92-832-2162-3, Lyon, International Agency for Research on Cancer, 2011.

Shambaugh EM, Weiss MA, Ries LAG, et al (1993). Cancer Statistics Branch Surveillance Program: SEER: Comparative Staging Guide for Cancer version Division of Cancer Prevention and Control, National Cancer Institute; Bethesda, MD; 1993. Division of Cancer Prevention and Control, National Cancer Institute; Bethesda, MD; 1993.

Shin HR, Joubert C, Boniol M, et al (2010). Recent trends and patterns in breast cancer incidence among Eastern and Southeastern Asian women. *Cancer Causes Control*, **21**, 1777-85.

Sriplung H (2013). CRStat package for R version 3.0.0.1. Available at: http://r-ice-project.org/grains/CRStat.html.

Sriplung H, Wiangnon S, Sontipong S, et al (2006). Cancer incidence trends in Thailand, 1989-2000. *Asian Pac J Cancer Prev*, **7**, 239-44.

Tayeb MA, Al-Zamel E, Fareed MM, et al (2010). A "good death": perspectives of Muslim patients and health care providers. *Ann Saudi Med*, **30**, 215-21.

Teo MC, Soo KC (2013). Cancer trends and incidences in Singapore. *Jpn J Clin Oncol*, **43**, 219-24.

Young JJ Jr, Roffers SD, Ries LAG, et al (2001). SEER Summary Staging Manual-2000:Codes and Coding Instructions. National Cancer Institute, NIH Pub. No. 01-4969, Bethesda, MD.

Zhao P, Dai M, Chen W, et al. (2010). Cancer trends in China. *Jpn J Clin Oncol*, **40**, 281-5.