RESEARCH COMMUNICATION

Survival Analysis of Malaysian Women with Breast Cancer: Results from The University of Malaya Medical Centre

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Abstract

Background: Breast cancer is the commonest cancer amongst Malaysian women but local survival data are scarce. The present study was therefore conducted to assess overall survival and prognostic factors in Malaysian breast cancer patients. Methods: The research sample was a prospective cohort of 413 patients diagnosed with breast cancer in the University of Malaya Medical Centre between 1993 to 1997. Survival data were obtained from the National Registry of Birth and Deaths in December 2000. The clinico-pathological variables studied were age, ethnic group, stage, tumour size, lymph node status, oestrogen receptor status and grade. The data was analysed utilizing Splus statistical software. The important prognostic factors were identified by fitting the Cox's proportional hazard model to the data set. Survival probabilities were estimated using the Kaplan-Meier method and differences were compared by the log-rank test. Results: The overall 5-year survival was 59.1%. The Cox's proportional hazard model identified stage, lymph node status, size and grade as factors that correlated with prognosis. Age was not a significant prognostic factor. The Cox regression model by stepwise selection showed stage, nodal status and grade of tumour to be independent prognostic factors, whereas ethnicity, age and ER status were not. Interpretation: The overall survival in our centre was low. Recognizing factors that affect prognosis of breast cancer patients in Malaysia may improve delivery of health care to at-risk groups by strategizing interventions as survival depends on early detection and effective treatment.

Key Words: Breast cancer - Malaysia - survival - prognostic factors

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Introduction

The National Cancer Registry was the first effort in obtaining accurate data for cancer in Malaysia. The data was obtained from Peninsular Malaysia or West Malaysia which comprise of 9 of the 13 states in Malaysia. In 2003, breast cancer was found to be the commonest cancer among Malaysian women comprising 31% of cancers affecting women (Lim and Halimah, 2004). The age standardized incidence rate was 46 per 100,000 women almost half that of the USA, but about double of India and Indonesia. The rates were similar to Thailand and Singapore. There is no national screening programme and screening with mammogram is opportunistic in nature.

Malaysia is a multi-ethnic country with three main ethnic groups, i.e. Malays, Chinese and Indians. There is difficulty in getting accurate data in developing countries as medically certified deaths are few, in Malaysia only about half of deaths are medically certified. Thus specific mortality due to breast cancer is under-reported. Hospital based registries may give an indication of mortality rates in Malaysia. University Malaya Medical Centre is a 957 bedded teaching hospital and tertiary referral center. The Breast Services led by a general surgeon commenced in 1993. Oncology services by trained oncologists were present only in 1997 and in-house radiotherapy services in 1998. Surgeons were administering chemotherapy to patients before that. This practice is still seen in most parts of the country to ensure patients actually receive adjuvant chemotherapy. Currently, multidisciplinary care of patients like diagnostic services, surgery, chemotherapy and radiotherapy are offered in this center. This paper aims to highlight the survival rate of Malaysian breast cancer patients in hope by knowing the pattern of survival and related prognostic factors, planning of public health and cancer treatment services can be done for this country.

Subjects and Methods

The study sample was a prospective cohort of 413 patients diagnosed with breast cancer in the University of Malaya Medical Centre between 1993 to 1997. Survival status was obtained from the National Registry of Birth and Deaths in December 2000. Demographic data like age and ethnic group and prognostic indicators like stage, tumour size, tumour grade, estrogen status were studied. The data was analysed utilizing S plus statistical software. The important prognostic factors were identified by fitting

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the Cox's proportional hazard model on the data set. The survival probabilities were estimated using the Kaplan-Meier method and differences in survival effect were compared by the log-rank test.

Overall survival rates were calculated using the Kaplan Meier method. Disease free survival was not available due to the unavailability of recurrence data. Relative survival was also unavailable due to lack of data on specific cause of death. The survival time of a patient is referred to the number of months from the day an individual was diagnosed until the date the individual dies or was last known to be alive.

Malaysia is a multiracial country, with three main ethnic communities; Malay, Chinese and Indian. The other races were not included in this study as their number was very few (3 patients). The stage of cancer was according to the American Joint Committee on Cancer System. The estrogens receptor (ER) status was determined by using immuno-histochemistry on post-operative specimens. Histological tumour grade was classified using the Scarff-Bloom- Richardson system. Tumour size were determined in centimetres (cm) from histopathological examination. Clinical size was obtained for cases that were not operated upon as in metastatic disease or inoperable disease.

The data were analysed using the statistical software Splus 2000. Survival estimates were determined by the Kaplan-Meier method and differences in survival were compared by the log-rank test. The influence of the prognostic factors was investigated using the Cox's proportional hazards models from which the corresponding hazard ratio and the associated 95% confidence intervals were obtained.

Table 1. Clinico-pathological Characteristics of the Study Subjects (Total 413)

		No. of patients	(%)
Ethnic group	Malay	85	(21)
	Chinese	261	(63)
	Indian	67	(16)
Age	≤ 40	77	(19)
	41-59	241	(58)
	≥ 60	95	(23)
Age at diagnosis	Mean	51 years old	
	Median	49 years old	
	Minimum	25 years old	
	Maximum	90 years old	
Stage at diagnosis	I	71	(17)
	II	205	(50)
	III	69	(17)
	IV	68	(16)
Tumor size	Mean	5.48 cm	
	Median	4.00 cm	
Lymph node status	0	162	(39)
	1-3	95	(23)
	≥4	75	(18)
	Not available	81	(20)
Grade*	1 and 2	160	(39)
	3	77	(19)
	Not available	176	(43)
Estrogen receptor	Positive	69	(17)
	Negative	79	(19)
	Not available	265	(64)
Primary therapy	Surgery	333	(81)
Mastectomy and axillary dissection		268	(65)
Lumpectomy and axillary dissection		65	(16)
	Chemotherapy	58	(14)
	Tamoxifen	20	(5)
	Supportive care	2	(>1)

*Bloom-Richardson histological grade

Results

After exclusion of carcinoma in-situ, sarcomas, incomplete data and those that defaulted treatment, 413 patients were included in the study. The clinico-pathological variables are tabulated in Table 1. The overall 5-year survival of patients with breast cancer in the University of Malaya Medical Centre was 59.1% (CI 0.545 -0.642). Based on the Kaplan-Meier plot the median survival was 86 months. Median follow-up was 56 months (SD 28.99)

The log-rank test identified ethnic group (Figure 1) to correlate with prognosis. We found a disparity of the 5-year survival between the three major ethnic groups in this study with more Chinese women surviving 63.5% in 5 years compared to Indian 57.4% and the Malay ethnic group which recorded the lowest 5-year survival of 47.5%. Age was not a significant prognostic factor when compared between three age groupings (Figure 2). However, we found that women aged 40 years and below showed a significant poorer survival compared to women 41 to 59 years of age (p= 0.026). Survival of women 60 years and above was significantly poorer to women in the 41 to 59 age group (p= 0.0426). Patients aged 41-59 had a 5-year survival of 64% compared to 50.5 % in the 60 years and above group.

Pathological characteristics that were found to correlate with survival were clinical stage (Figure 3), size of tumour (Figure 4), lymph node (LN) status (Figure 5) and grade of tumour (Figure 6). Estrogen receptor(ER)

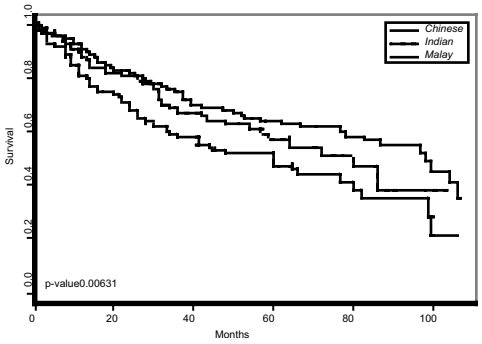

Figure 1. Survival Based on Ethnic Group

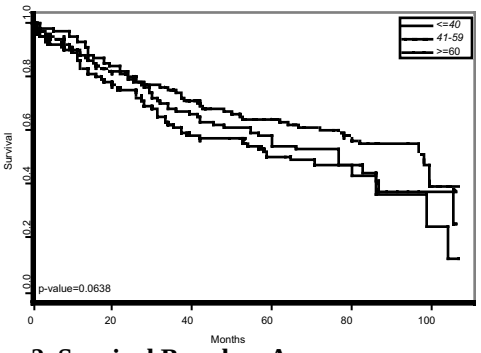

Figure 2. Survival Based on Age

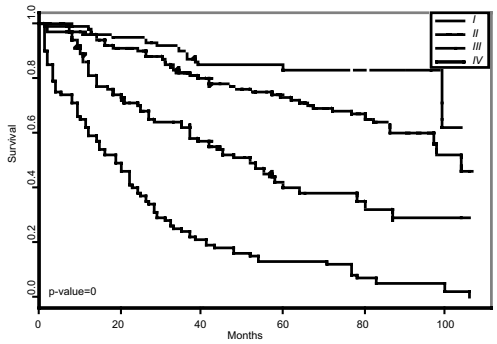

Figure 3. Survival Based on Clinical Stage

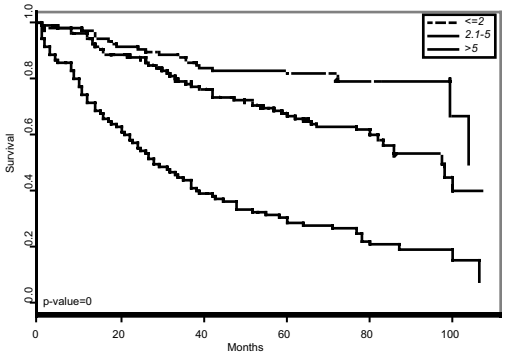

Figure 4. Survival Based On Size Of Tumour

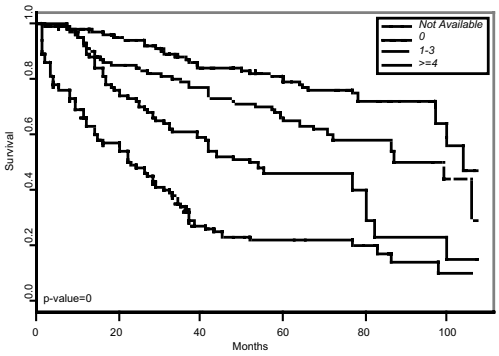

Figure 5. Survival Based of Lymph Node Status

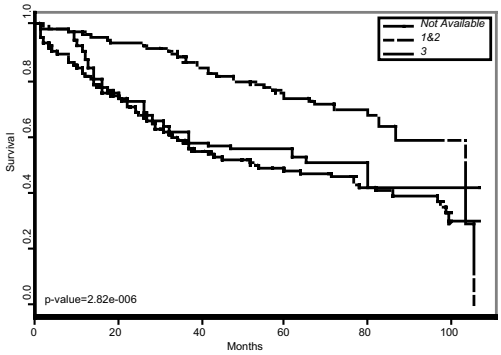

Figure 6. Survival Based on Tumour Grade

status did not correlate with survival (p=0.215). The 5-year survival probability for all variables is tabulated in Table 2.

The Cox regression model by stepwise selection found that Stage, lymph node status and grade of tumour were important prognostic factors(p=0.028). Ethnic group, age and ER status were not significant prognostic factors. The hazard ratio of patients with Stage IV disease patients dying were 2.5 times more than stage I. Having four or more involved lymph nodes puts the patient at risk of

Table 2. 5-Year Survival Probabilities with Various Clinico-pathological Variables

		Surv.Prob	95%CI
Race	Chinese	0.635	0.578-0.697
	Indian	0.574	0.466-0.708
	Malay	0.475	0.378-0.596
Stage	stage1	0.826	0.741-0.921
	stage2	0.728	0.668-0.793
	stage3	0.398	0.294-0.539
	stage4	0.132	0.072-0.243
Age	≤ 40	0.548	0.446-0.675
(years)	41-59	0.640	0.582-0.705
	≥ 60	0.505	0.412-0.619
Size	≤2	0.818	0.745-0.898
(cm)	>2-5	0.671	0.605-0.744
	>5	0.293	0.222-0.386
LN status	N.A	0.221	0.146-0.336
	0	0.797	0.736-0.863
	1-3	0.651	0.559-0.757
	≥ 4	0.462	0.359-0.595
Grade	N.A	0.479	0.410-0.560
	1&2	0.734	0.666-0.810
	3	0.554	0.453-0.678
ER	N.A	0.605	0.549-0.668
	Positive	0.621	0.511-0.755
	Negative	0.504	0.397-0.638

mortality 1.3 times more than being node negative. Grade 3 had a hazard ratio of 1.2 as compared to grade 1.

Discussion

UMMC is a tertiary centre located in urban Kuala Lumpur the former capital of Malaysia. 63% of the women seen in this study were Chinese and this is in concordance with the National Cancer registry report in 2003, where Chinese and Indian Malaysian women had the highest incidence of breast cancer (Lim and Halimah, 2004). The Malay patients were 21% and Indians 16% respectively. According to the 2005 BHGI Resource Stratification (Anderson, 2006), Malaysia has a spectrum of basic to enhanced level of resource for early detection and access to care as well as treatment. Basic to maximal resources in diagnosis, pathology, treatment and allocation of resources are available to most Malaysians. The health care systems and public policy ranged from basic to enhanced depending on location i.e. rural or urban areas and practice i.e. private or public health services.

Laws in Malaysia require that all deaths are registered but it is not compulsory that they are medically certified. A study on 2,000 deaths certification from the vital registration system of the Statistic Department, Malaysia where random selection of cases were done for the year 2000 showed that certifications of deaths by medical professional and lay people were 49.2% and 50.8% respectively. Lay diagnosis constituted those made by police and village headmen. With adjustment of underreporting of deaths, the estimated life expectancy at birth for the Malaysian male and female were 69.4 years and 74.5 years. Two thirds of the burden of premature deaths in Malaysia resulted from non-communicable diseases. Breast cancer was found to be the 7th leading

cause of years of life lost (YLL) for females in 2001 (Yusoff and Institute for Public Health 2005).

In 1997 cancer was the third principal cause of death in hospital, making about 10.1% of deaths in hospital and breast cancer mortality rates have risen since 1985. (Narimahet al., 1999) In Hospital Kuala Lumpur (HKL) between 1998 to 2001 the average size of the tumour was 5.4 cm in diameter, during the same time, the average tumour size in UMMC was 4.2 cm (Hisham and Yip, 2004).

Survival of breast cancer in developed nations, approached 80%. The SEER 5-year survival rates in United States for 1990 was 89% in the European series 79%(Sant et al., 2004). The 5-year survival in less developed nations range between 59.6% in the mid 1990s in Riyadh Saudi Arabia (Ravichandran et al., 2005), 68.8% in Bahrain in the 1980s to 1990s (Fakhro et al., 1999) to 79% in Tianjin China in the 1980s (Hao et al., 2002) and 84.1% in Asan Medical Centre in Korea (Son, 2006). Cancer mortality and incidence in developing countries already accounted for over 60% and about half of the global total, respectively (Shibuya et al., 2002) The 5-year relative survival for women younger than 75 years with breast carcinoma was 43-63% in developing countries, as compared with 65% in 1967- 1973, 76% in 1974-1986, and 82% (in 1986-1991) in the US. It seems likely that the survival differences are due to both late stage of disease at presentation well as the availability and quality of adjuvant treatment (Sankaranarayanan et al., 1996).

The relative survival rate was not available in our study. As the survival rate is not disease specific, there could be underestimation of the survival rate in our centre. It was also seen the survival rates for women 60 years and above were lower, this could be attributed to non-breast cancer causes, thus underestimating breast cancer survival. The mortality status of all patients in this study was accurate as reporting of death in Malaysia is mandatory; however disease specific mortality data cannot be ascertained in this study. The omission of stage 0 cancer may also contribute to underestimation of survival. There were only 22 stage 0 patients which made only 4.6 % of cases in UMMC.

In our study the significant prognostic factors were clinical stage, ethnicity, size of tumour, lymph node status and grade of tumour . Independent prognostic factors were stage, lymph node status and grade of tumour . These factors were also found to be significant in other studies. Lymph node status and clinical stage seems to be the most important factor in a study in Indonesia This result was in line with other studies that lymph node status, tumor size and stage were significant prognostic factors for overall survival (Aryandono et al., 2006).

In this study the survival by stage of disease were lower to other studies in the same period. For stage 1, the 5-year survival was 82.6% in comparison to 97% (Lim et al., 2001) and 95.3% (Son, 2006). For stage II, III and IV were 72.8% , 39.8% and 13.2% respectively. The survival rates for Lim et al 2001 were 83%, 56% and 17% and for Son 86%, 65% and 29.3% respectively. The disparity could be due to inaccuracy of staging at diagnosis where investigations like CT scan for early breast cancer were deferred to be cost effective, therefore this may have downstaged our patients, thus underestimating the survival for stage 1 and 2 disease. Also the use of anthracycline based chemotherapy begun in UMMC only in 1996. The compliance and quality of the adjuvant treatment with relation to delay in cycle due to neutropenia and the inaccessible to prophylactic growth colony stimulating factors were beyond the scope of this paper that would require further study. Accessibility of second, third and fourth line chemotherapy for high risk patients was not readily available due to the cost incurred to the individual patient and lack of insurance coverage. In this study the hazard ratio of dying for stage IV patients was 2.510 as compared to stage I disease.

Ethnicity was found to be a significant prognostic factor, but not an independent prognostic factor, therefore the low survival could be due to other factors that were found to be independent prognostic factors like stage, nodal status and grade of tumour. The disparity in survival was seen between the three major ethnic groups in Malaysia in UMMC, the reason could be due to the differing stage at diagnosis where Malay women present with more advance disease. 40% of Malays presented with stage III (13%) and stage IV (27%) in comparison to the Chinese 30% and Indians 31% respectively. In all ethnic groups most women were diagnosed with stage II disease, Chinese (48%), Indian (58%) and Malay women (49%). Stage 1 cancer were diagnosed in 21% of Chinese women as compared to Indian women 10% and Malay women 11%. This could be due to differing health behaviour and practices (Ariff and Beng, 2006). In the Asia pacific region, Singapore has similarities as we share a similar history in terms of population migration therefore the ethnic groups present in Malaysia and Singapore are similar. A study by Tan et al showed a similar pattern among Singaporean breast cancer patients where Malay ethnicity was associated with a more advanced stage at diagnosis (Tan et al. 2005). There are other studies on racial disparities among other ethnicities, like the black and white American breast cancer patients where black Americans were found to survive less and the reasons were attributed not only to delay in diagnosis and treatment (Gorin et al., 2006), but also to adverse co-morbidities like diabetes and hypertension (Tammegi et al., 2005). In UMMC we found that the Malay women were diagnosed at a later stage and at an earlier age where presumable there are less co-morbidities, further study is needed to ascertain this pattern. Suggestions of use of traditional medicine between the ethnic groups may explain this phenomenon, where in a comparative study of two sub-population of patients, in a predominant Malay rural centre the reported rates of traditional medicine use was 40% as compared to 20% in urban centre with more Chinese patients (Taib, 2007). Factoring causes for this disparity, further information should be studied to ascertain on whether there is delay in diagnosis in terms of access to health care among the different races, or is it the delay due to health seeking behaviour where certain groups of women delay seeking treatment. There are studies that show that clinician delays of up to 36 months was not

found to worsen prognostic factors or survival rates in breast cancer patients, but this is more relevant in the screening population (Hardin et al., 2006).

As seen in Asian countries the mean age of our study population was 51 years with a median of 49 years. The youngest patient was 25 years and the oldest was 90 years. 77% of our women presented below the age of 60. 19% were 40 years and younger. 58% were between 41 to 59 years. The patients in this series show earlier onset of disease as seen in other parts of the Asia pacific region as seen in Singapore and Korea. (Lim et al., 2001; Son, 2006). In our study we found that women 40 years and younger had a 50% 5-year survival as compared to those 41 to 59 years had a 5-year survival of 64% and 60 years and older had survival of 50.5%. In our study we found that younger women (40 years younger) usually present with larger tumours, mean size of 5.76 cm(SD 5.53) as compared to 5.45 cm(SD 4.93 cm) for women 41-59 years and 5.34 cm (SD 4.69) for those 60 years and above, however this difference was not statistically significant($p= 0.6406$). The larger size tumour in the younger women may be due to delay in seeking treatment, as this group of women may have more body image issues, this would require further study to confirm this. Young age has been correlated as a negative prognostic factor. In Indonesia women <40 years were found to have poorer prognosis than women >60 years due to more aggressive phenotype, larger tumour size and more lymph node involvement (Aryandono et al., 2006; El Saghir et al., 2006), also showed that young age at presentation conferred a worse prognosis despite being more hormone sensitive and having more anthracylcine based chemotherapy and hormonal therapy (El Saghir et al., 2006). Khanfir et al 2006 noted that the 5-year survival rates for < 35 years was 57%, no different from those 36- 50 years (Khanfir et al., 2006).

The older age group in this study showed a poorer prognosis compared to the 41-59 age group. Studies show that older age groups did not confer a poorer prognosis (Livi et al., 2006). This could be related to increased co-morbidities and less aggressive treatment amongst the elderly in our centre. In this study, only 22.1% of women 60 years and older received adjuvant chemotherapy, as compared to 59.7% in the 40 years and below and 47.7% in the 41-59 years age group. The stage distribution also showed that older women present with later stage disease, women 60 and above 41.05% presented with stage 3 and 4 as compared to 31.6% for women 41-59 years. However, it was not statistically significant ($p=0.3574$). Sant et al found that older women in Europe presented with later stage than in the US therefore having poorer survival than US women. This could be due to health behaviour of older women or the availability of screening for this age group (Sant et al., 2004). In Malaysia older patients acceptance of disease as a natural aging process and therefore not needing treatment is reflected on the non-medically certified cause of death where 44.4% of deaths in non-medically certified were caused by "old age and "unknown causes" (Yusoff, 2005). It is not uncommon for women above 55 years of age who defers surgery and adjuvant chemotherapy as they feel that they were too old. This phenomenon is also reflected in the retirement age in Malaysia where in the public sector in Malaysia where the age of retirement is 56 years old. Many studies addresses the issues of treatment in the elderly, Rosenkranz et al in 2006 showed that elderly patients 80 years or older were safely treated with surgery and radiation in accordance with accepted recommendations for their stage of cancer. However, chemotherapy brought about significant complications in this group of elderly patients.(Rosenkranz et al., 2006) Other studies that showed that age was not a prognostic indicator found almost a similar pattern in that women older than 50 survived the least compared to <40 and 40 to 49 age group (Ravichandran et al., 2005)

Nodal status remains a major prognostic in breast cancer. In our study population it also follows the pattern seen in previous study with stratification of 4 and more lymph nodes correlated with a poorer prognosis. The 5-year survival was only 22.1% in women who had no available data, as these women were not operated due to metastatic disease, hence the poorer survival. Node negative tumour had 79.7% survival compared to 46.2%. in node positive patients. The Hazard ratio for mortality of 4 or more lymph nodes was 1.346 compared to node negative patients.

In our study 64% of the patients did not have ER status reported. In the UMMC Estrogen Receptor immunochemistry was only routinely done in 1996. In many parts of the country, especially in private practice we still see histopathological reports without ER status today, due to the added cost of this test. The contraction of the data, could be the reason why hormone sensitivity was not found to be a significant prognostic factor in this study. Further cohort of patients will be studied to see whether this factor is found to be a prognostic factor. Estrogen receptor was also not found to be significant prognostic factor in Indonesia. Estrogen receptor was not found to improve prognosis. This was reported to be due to the advance stage at presentation (Aryandono et al., 2006).

Limitations of this study were the unavailability of data on disease free survival as well as relative survival. The data is mainly from the pre-oncology era in UMMC where trained oncologist were not available, surgeons were administering chemotherapy on their own, even at this time, this practice exists in parts of the country where there is no resident oncologist. This cohort of patients was from more than 10 years ago, this would be useful to compare with a more recent cohort after oncology services were available. Contraction of database where routine testing of grade and ER status were not done and also removal of incomplete data from patients who default also limits this study. Other studies on survival were difficult to compare mainly due to differing time periods and differing variables especially age groupings.

Nations with limited resources will have to meet the challenge of the increasing incidence of cancer expected in the next few decades, health authorities in developing countries should be aware of the importance of investing in a range of cancer control activities, including primary prevention and early detection programs as well as treatment. (Sankaranarayanan, Swaminathan et al. 1996)

. In this study the prognostic finding that were relevant in the past in developed nations where stage of tumour, lymph node involvement and size remain major prognostic factors. This study confirms the same in a population of Malaysian women. Therefore these findings should be sufficient to steer the directions of public health intervention in Malaysia towards the establishment of a screening program, be it mammographic or using clinical breast examination to allow early detection and therefore improving survival. The screening program must be planned research to ascertain acceptance and effectiveness before being carried out in a large scale. This is clearly seen in other studies that acceptance of a screening method may be lower than expected, such as the study on clinical breast examination in the Phillipines (Pisani et al., 2006).

In conclusion, overall survival in our centre was low for the cohort of patient from 1993 to 1997. Significant prognostic factors found in this study were ethnicity, stage, size of tumour, nodal status and grade. Cox regression analysis found stage, nodal status and size to be independent prognostic factors in UMMC. Identifying high risk groups i.e. high incidence in Chinese ethnicity, and groups that have higher risk of mortality like Malay ethnicity, younger and older age groups may allow strategic planning in overcoming associated problems like compliance and prescription of more efficacious adjuvant agents in these subgroups of patients.

References

Anderson B (2006). Breast cancer in limited resource countries: an overview of the Breast Health Global Initiative 2005 Guidelines.

Ariff K, Beng K (2006). Health beliefs in a rural family practice: A Malaysian perspective. *Aust J Rural Health*. **14**, 2-8.

Aryandono T, Harijadi, et al (2006). Breast cancer in young women: prognostic factors and clinicopathological features. *Asian Pac J Cancer Prev*, **7**, 451-4.

El Saghir N, Seoud M, et al (2006). Effects of young age at presentation on survival in breast cancer. *BMC Cancer*, **6**, 194.

Fakhro A, Fateha B, et al (1999). Breast cancer: patient characteristics and survival analysis at Salmaniya Medical Complex, Bahrain. *East Mediterr Health J*, **5**, 430-9.

Gorin SS, Heck JE, et al (2006). Delays in breast cancer diagnosis and treatment by racial/ethnic group. *Arch Intern Med*, **166**, 2244-52.

Hao X-S, Chen K-X, et al. (2002). Analysis of female breast cancer descriptive epidemiology in Tianjin, China. *Asian Pacific J Cancer Prev*, **3**, 143-8.

Hardin C, Pommier S, et al (2006). The relationships among clinician delay of diagnosis of breast cancer and tumor size, nodal status, and stage. *Am J Surg*,**192**, 506-8.

Hisham A, Yip C (2004). Overview of breast cancer in Malaysian women: a problem with late diagnosis. *Asian J Surg*, **27**, 130-3.

Khanfir A, Frikha M, et al. (2006). Breast cancer in young women in the south of Tunisia. *Cancer Radiother*, **10**, 565-71.

Lim G, Halimah Y (2004). Second Report of the National Cancer Registry. Cancer Incidence in Malaysia 2003. National Cancer Registry. Kuala Lumpur, Ministry of Health Malaysia.

Lim S, Wong J, et al (2001). Clinical features and survival analysis of 848 Asian women with invasive breast cancer: results from a single institution in Singapore. *Breast Cancer Res Treat*, **69**, 281.

Livi L, Paiar F, et al (2006). Breast cancer in the elderly: treatment of 1500 patients. *Breast J*, **12**, 353-9.

Narimah ARH, Tahir A, Maimunah AH (1999). Breast Examination, National Health and Morbidity Survey 1996 MOH Public Health Institute, Malaysia 20.

Pisani P, Parkin D, et al (2006). Outcome of screening by clinical examination of the breast in a trial in the Philippines. *Int J Cancer*, **118**, 149-54.

Ravichandran, K., N. Al Hamdan, et al. (2005). Population based survival of female breast cancer cases in Riyadh Region, Saudi Arabia. *Asian Pacific J Cancer Prev*, **6**, 72-76.

Rosenkranz K, Bedrosian I, et al (2006). Breast cancer in the very elderly: treatment patterns and complications in a tertiary cancer center. *Am J Surg*, **192**, 541-4.

Sankaranarayanan R, Swaminathan R, et al (1996). Global variations in cancer survival. *Cancer*, **78**, 2461-4.

Sant M, Allemani C, et al (2004). Breast carcinoma survival in Europe and the United States. Comparative Study. *Cancer*, **100**, 715-22.

Shibuya K, Mathers CD, et al (2002). Global and regional estimates of cancer mortality and incidence by site: II. results for the global burden of disease 2000. *BMC Cancer*, **2**, 37.

Son BHK (2006). Changing patterns in the clinical characteristics of Korean patients with breast cancer during the last 15 years. *Arch Surg*, **141**, 155-60.

Taib NA, Yip CH, Mohamed I, Ng CJ, Farizah H (2007). Breast cancer in Malaysia: are our women getting the right message? 10 year-experience in a single institution in Malaysia. *Asian Pac J Cancer Prev*, **8**, 141-5.

Tammegi C, Narenz D, et al (2005). Comorbidity and survival disparities among black and white patients wth breast cancer. *JAMA*, **294**, 1765-73.

Tan EY, Wong HB, et al (2005). Locally advanced and metastatic breast cancer in a tertiary hospital. *Ann Acad Med Singapore*, **34**, 595-601.

Yusoff AFN (2005). Malaysian burden of disease and injury study. I. o. H. Institute for Public Health, Malaysia.Forum 9. Mumbai, India.