RESEARCH ARTICLE

Estimating the Five-Year Survival of Cervical Cancer Patients Treated in Hospital Universiti Sains Malaysia

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Abstract

Objective: The objective of this study was to determine the five-year survival among patients with cervical cancer treated in Hospital Universiti Sains Malaysia. Methods: One hundred and twenty cervical cancer patients diagnosed between 1st July 1995 and 30th June 2007 were identified. Data were obtained from medical records. The survival probability was determined using the Kaplan-Meier method and the log-rank test was applied to compare the survival distribution between groups. Results: The overall five-year survival was 39.7% [95%CI (Confidence Interval): 30.7, 51.3] with a median survival time of 40.8 (95%CI: 34.0, 62.0) months. The log-rank test showed that there were survival differences between the groups for the following variables: stage at diagnosis (p=0.005); and primary treatment (p=0.0242). Patients who were diagnosed at the latest stage (III-IV) were found to have the lowest survival, 18.4% (95%CI: 6.75, 50.1), compared to stage I and II where the five-year survival was 54.7% (95%CI: 38.7, 77.2) and 40.8% (95%CI: 27.7, 60.3), respectively. The five-year survival was higher in patients who received surgery [52.6% (95%CI: 37.5, 73.6)] as a primary treatment compared to the non-surgical group [33.3% (95%CI: 22.9, 48.4)]. Conclusion: The five-year survival of cervical cancer patients in this study was low. The survival of those diagnosed at an advanced stage was low compared to early stages. In addition, those who underwent surgery had higher survival than those who had no surgery for primary treatment.

Keywords: Cervical cancer - five-year survival - median survival time - prognostic factor

Asian Pacific J Cancer Prev, **14 (2)**, 825-828

Introduction

Cervical cancer is the second most common cancer in developing countries, yet the tenth most common cancer in developed countries among women (Ferlay et al., 2010). Worldwide, the cancer incidence increased from 378,000 cases per year in 1980 to 454,000 cases per year in 2010 with the increase rate of 0.6% annually (Forouzanfar et al., 2011). In Malaysia, the cancer is the fifth most common cancer to occur, but ranked second among female-related cancers (Zainal and Nor, 2011). The age standardized incidence (ASR) for cancer of the cervix was 7.8 as per 100,000 populations. There were about 847 cases registered with National Cancer Registry Malaysia in 2007 (Zainal and Nor, 2011).

The five-year survival of cervical cancer in developed countries such as United State of America, Germany and Spain were higher than 60% (American Cancer Society, 2011). Flores-Luna et al. (2001) studied the survival of Mexican women who were diagnosed with cervical cancer and they found that the overall five-year survival was 66.6%. In Asian country like China (Xiang et al., 2011) and Thailand (Sumitsawan et al., 2011), the five-year survival exceeded 50%. Pomros et al. (2007) had done a study on cervical cancer patients treated with radiation therapy in Srinagarind Hospital, Thailand and found that the five-year survival was 62.5%. Meanwhile, the five-year survival in least developed countries such as Gambia and Uganda was remarkably low which was less than 25% (Sankaranarayanan et al., 2011).

Many studies reported the survival rate for cervical carcinoma based on stage of the disease. Generally, the overall five-year survival nearly approaches 100% for patients diagnosed at stage IA and drops remarkably to almost 20% for stage IVB (Kyrgiou and Shafi, 2010). In Korea, a study found that the relative five-year survival rate according to stage were 94.2%, 69.7%, 38.9% and 21.1% for stage I, II, II and IV respectively (Chung et al., 2006). Meanwhile, a study at Dr Cipto Mangunkusumo General Hospital, Indonesia, obtained lower five-year survival; for stage I was 50%, stage II was 40%, stage III was 20% and stage IV was 0% (Aziz, 2009).

Hospital Universiti Sains Malaysia (HUSM) is situated in Kubang Kerian, Kelantan and it is regarded as a referral

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centre for the East Coast region of Malaysia. Previously, there were studies conducted on survival of other types of cancer patients treated in HUSM such as on prostate cancer (Chemay et al., 2008), oral cancer (Razak et al., 2010), colorectal cancer (Ghazali et al., 2010) and bone cancer (Wahidah et al., 2012). This study was conducted mainly to determine the five-year survival among patients with cervical cancer treated at HUSM. To our knowledge, information on survival of cervical cancer patients in Malaysia is scarce. This study also provides a preliminary insight into possible factors that may affect the survival of cervical cancer patients by inspecting the Kaplan-Meier survival curve and the log-rank test.

Materials and Methods

Study design

Retrospective record review design was performed to achieve the study's objective. Patients' medical records were reviewed and information on socio-demographic background, clinical characteristics and survival status were collected. One hundred twenty cervical cancer patients, histopathologically and clinically diagnosed between 1st July 1995 and 30th June 2007 were identified. They must have received at least one treatment related to cervical cancer in HUSM. Patients were followed until 31st December 2008. At the end of the study, 66 (55%) deaths were identified whereas 54 (45%) were censored, which was consisted of 49 alive patients and 5 lost to follow up. Survival time was measured (in months) from the date of first diagnosis to death. Ethical clearance was obtained from Research and Ethics Committee of University Sains Malaysia (Reference number: USMKK/PPP/JEPeM [205.4 (2.4)]).

Patient characteristics

There are factors that may affect the survival of patients which are known as prognostic factors. Factors considered in the analysis of this study were stage at diagnosis, ethnicity, histologic type, lymph node involvement, age at diagnosis, and primary treatment received.

The stage of cancer followed the International Federation of Gynecology and Obstetrics (FIGO) system. The number of patients diagnosed at stage IV was smaller compared to other stages. Thus, it was decided to combine both groups, stage III and stage IV, which yielded to 31 (25.8 %) patients. This variable was classified into three groups namely; stage I, stage II and stage III-IV. For the histologic type, cases were divided into squamous cell carcinoma and adenocarcinoma. Whenever the cancer had metastasized to the lymph node either to pelvic, para-aortic or both, that patient was considered to have lymph node involvement. Patients were grouped according to their age namely; younger than 40, 40-49 years, 50-59 years, and 60 and older. Ethnicity was classified according to Malays and non-Malays. The type of primary treatment received was divided into either surgery or non-surgery (chemotherapy and/or radiotherapy).

Statistical analysis

One way to describe the distribution of survival times is by survival function, S(t). This function is defined as the probability that an individual survives longer than or equal to time t. The survival probability of patients with cervical cancer was estimated using the Kaplan-Meier (or product limit) method. The survivorship function or the Kaplan-Meier survival curve was used to estimate the 50th percentile (the median) of survival time and to compare survival distributions of two or more groups (Lee and Wang, 2003). The log-rank test was also used to compare the survival differences among the groups. Data was analysed by R software, version 2.14.2.

Results

Table 1 shows the characteristics of 120 patients diagnosed with cervical cancer and treated in HUSM. The mean age at diagnosis and its standard deviation was 49.73 years and 9.52 respectively. Majority of these patients were Malays [99 (82.5%)] and diagnosed at the age of 40 to 49 years [46 (38.3%)]. There were 35 (29.2%), 54 (45.0%) and 31 patients (25.8%) diagnosed in stage I, II, III-IV respectively. About a quarter of the patients were diagnosed with lymph node involvement. Meanwhile, the squamous cell carcinoma type constituted about 77.5% (93 patients) of all histologic types. Of 120 patients, there were 40 (33.3%) patients primarily treated with surgical treatment.

The overall five-year survival of 120 cervical cancer patients treated in HUSM was 39.7% (95%CI: 30.7, 51.3). The median survival time was 40.8 (95%CI: 34.0, 62.0) months. Figure 1 depicts the overall survival probability curve for cervical cancer patients in this study. The five-year survival according to each factor is tabulated in Table 2. The log-rank test results show that there were significant differences between the groups for the following variables namely; stage at diagnosis (p=0.005) and primary treatment (p=0.0242).

Patients who were diagnosed at the latest stage (III-IV) were found to have the lowest five-year survival compared

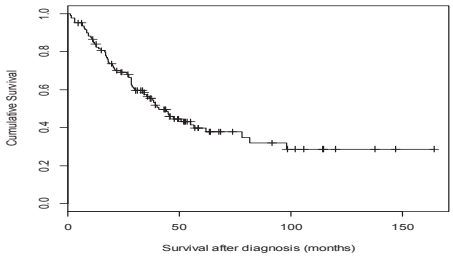

Figure 1. Kaplan-Meier Curve for Cervical Cancer Survival among Patients Treated in HUSM

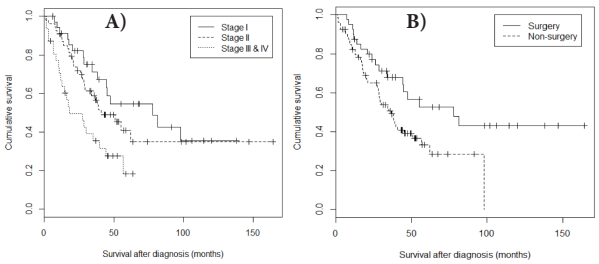

Figure 2. Kaplan-Meier Survival Curves. A) Stage at diagnosis and B) Primary treatment

Table 1. Characteristics of Cervical Cancer Patients Treated in HUSM (n=120)

Characteristic		N	%
Ethnicity	Non-Malay	21	17.5
	Malay	99	82.5
Lymph node involvement	Negative	89	74.2
	Positive	31	25.8
Histologic type	Squamous cell carcinoma	93	77.5
	Adenocarcinoma	27	22.5
Age at diagnosis	≤39	15	12.5
	40-49	46	38.3
	50-59	38	31.7
	≥ -60	21	17.5
Stage	I	35	29.2
	II	54	45
	III–IV	31	25.8
Primary Treatment	Surgery	40	33.3
	Non-surgery	80	66.7

Table 2. Five-year Survival According to Patients' Characteristics

Characteristic		5-year survival (%)	95% CI	X^2 (df)	p value[a]
Ethnicity	Non-Malay	33	12.7-86.0	0.2 (1)	0.631
	Malay	40.6	31.1-52.9		
Lymph node involvement					
Negative		36.6	26.6-50.4	0.1 (1)	0.762
Positive		52.3	37.0-74.0		
Histologic type					
Squamous cell carcinoma		41.2	30.9-54.8	1.4 (1)	0.244
Adenocarcinoma		35.2	19.9-62.3		
Age at diagnosis	≤39	29.6	13.1-66.8	3.3 (3)	0.345
	40-49	44.6	30.6-65.0		
	50-59	38.9	25.0-60.3		
	≥60	42.1	23.6-75.1		
Stage	I	54.7	38.7-77.2	10.8 (2)	0.005
	II	40.8	27.7-60.3		
	III–IV	18.4	6.75-50.1		
Primary Treatment	Surgery	52.6	37.5-73.6	5.1 (1)	0.0242
	Non-surgery	33.3	22.9-48.4		

[a]log-rank test

with stage I and stage II. Figure 2A illustrates the survival curves for stage at diagnosis. The survivorship function for stage III-IV lies below the other two groups (stage I and stage II) suggesting that this group had the least favorable survival experience. The five-year survival was higher for patients who were primarily treated with surgery. The estimated survivorship function for the surgery group lies above the non-surgery group (Figure 2B). Meanwhile, the five-year survival was the lowest for the following groups; non-Malays, negative lymph node involvement, adenocarcinoma type, or diagnosed at the age of ≤39 years. However, the survival differences were not statistically significant.

Discussion

Our study found that most cervical cancer patients in this study were diagnosed at stage II. Similarly, it was reported that higher percentage of cervical cancer patients registered at National Cancer Registry Malaysia in 2007 were diagnosed at stage II (Zainal Ariffin and Nor Saleha, 2011). Majority participants were Malays.

The overall five-year survival of 120 cervical cancer patients treated in HUSM was 39.7%. The result was similar to a study in Dharmais Cancer Hospital, Indonesia, where the overall five-year survival was 40.3% with median survival time of 1208 days (Sirait et al., 2003). Similarly, the five-year survival of cervical cancer patients in Manila, Philippines, was 34% (Laudico and Mapua, 2011). On the other hand, our finding was low compared to the overall five-year survival in other countries in Asia such as Hong Kong, the Republic of Korea and Singapore where the overall survival exceeded 65% (Sankaranarayanan et al., 2011). In a study in France, Brun et al. (2003) found that the five-year survival was 70%. The result was higher than our study's finding might be due to high percentage of younger patients was included in their study.

This study found that the five-year survival according to stage I, II and III-IV was 54.7%, 40.8% and 18.4% respectively. Our finding was similar to other studies (Chen et al., 1999; Sirait et al., 2003; Chung et al., 2006) where the survival decreased as the stage of the disease increased. Kumari et al. (2010) also found that stage at diagnosis significantly influenced the prognosis of cervical cancer patients. However, the five-year survival obtained according to stage was higher compared to our study. In fact, the survival of patients diagnosed at advanced stage, stage IVA was considerably high where the survival rate was 33%.

In our study, higher five-year survival was observed in patients treated with surgery compared to non-surgical treatment and the difference was statistically significant. Flores-Luna et al. (2001) found that patients who underwent surgical treatment had better survival (85.7%) than those who received radiotherapy (62.5%). Large proportion of individuals in surgery group was diagnosed at early stage. Therefore, longer survival time in this group was noted. Furthermore, the percentage of dying in surgical treatment group was lower than radiotherapy group.

The five-year survival of non-Malays was worse than Malay group but the difference was not significant. As noted by Zainal Ariffin and Nor Saleha (2011), non-Malays are more susceptible to cervical cancer than Malay women. In our study, there was no significant difference between the survivals of patients with or without lymph node involvement. In contrast, Yeh et al. (1999) reported a significant difference in five-year survival of patients with lymph node and those without lymph node involvement.

Our study discovered that there was no difference in five-year survival by age. This finding was similar to study by Garipagaoglu et al. (1999) and Flores-Luna et al. (2001). Garipagaoglu et al. (1999) claimed that the survival difference was not statistically significant due to a very small number of patients in younger age group (< 40 years). In contrast, Brun et al. (2003) reported opposite finding. It was identified that the percentage of younger patients was large in their study.

Patients with histologic type of squamous cell carcinoma were found to have better survival than those with adenocarcinoma although there was no statistical significance. Similarly, Shingleton et al. (1995) reported that the survival according to histologic type was not significant in their study. Galic et al. (2012) found that

tumor histology significantly affects the outcomes of women with cervical cancer where adenocarcinoma type had negative impacts on survival for both early and advanced stage of cancer.

In conclusion, the five-year survival of cervical cancer patients in this study was low. There are evidences that the prognosis of cervical cancer patients treated in HUSM were dependent on the stage at diagnosis and primary treatment received. The survival of patients who were diagnosed at advanced stage was lower compared to early stage. In addition, those who underwent surgery had higher survival than those who had no surgery for primary treatment.

Acknowledgements

We would like to thank the Ethic Community Groups of USM for giving an ethical clearance, the HUSM staff of record office for their help and all patients who were willing to participate in this study.

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