

Survival of Cervical Cancer Patients in Brunei Darussalam: 2002-2017

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Research Article

Keywords: Cervical cancer, Survival rate, Survival duration, Brunei Darussalam, Cancer Registry

Posted Date: January 27th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-148839/v1>

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Abstract

BACKGROUND: Cervical cancer is the fourth leading cause of cancer deaths among Bruneian women. This study aims to investigate the survival rate of cervical cancer patients in Brunei Darussalam between 2002 and 2017, to compare survival of cervical cancer patients between two periods: 2002-2009 and 2010-2017 and to identify prognostic factors of cervical cancer.

METHODS: A retrospective cohort study on cervical cancer patients registered in Brunei Darussalam Cancer Registry between 2002 and 2017. De-identified data from the registry was extracted and survival analysis was performed using Kaplan-Meier estimator, log-rank test and multiple Cox regression analysis.

RESULTS: The 1-, 3- and 5-year survival rates of cervical cancer patients in Brunei Darussalam were 88.2%, 78.9% and 74.1% respectively from 2002-2017. The 5-year survival rate for 2002-2009 and 2010-2017 were 77.5% and 72.1% respectively. The risk of mortality was significantly higher in 2010-2017 compared to 2002-2009 after adjusting for other variables (Adjusted HR=1.57; 95% CI: 1.06, 2.31; $p=0.025$). Cervical cancer patients ≥ 60 years (Adjusted HR=1.85; 95% CI: 1.11, 3.09; $p=0.019$), and patients with distant cancer (Adjusted HR=49.47; 95% CI: 6.64, 368.52; $p<0.001$) had the highest risk of mortality.

CONCLUSION: The 5-year survival rate of cervical cancer patients in Brunei Darussalam was 74.1%, which ranks relatively high globally. However, increased mortality among elderly patients, and patients diagnosed with cervical cancers at the later stages, calls for raising awareness, early detection, and management.

Introduction

Cervical cancer is the fourth most prevalent female cancer worldwide ^[1]. Among ASEAN member states, Brunei Darussalam ranked third highest in terms of the age-standardized incidence rate (ASR) of cervical cancer ^[2], where the ASR has been estimated to increase from 16.8 (per 100,000 women) in 2012 to 20.6 in 2018 ^[3] (the global average ASR of cervical cancer was 13.1 ^[4]). Cervical cancer is the fourth leading cause of cancer deaths followed by mortality from breast, lung, and rectum and anus cancer among Bruneian women in 2017 ^[5].

Cervical cancer is caused by human papillomavirus (HPV) infection where the most common types detected in about 70% of all cervical cancer cases are HPV 16 and 18 (high-risk subtypes) ^[6]. The National Cervical Cancer Prevention and Control Programme was introduced in November 2009, with subsequent establishment of the National Pap Test Registry in 2011. Married Bruneian women between the ages of 20 and 65 years receive mail invitation to attend routine cervical cancer screening every 3 years through the registry. The primary screening test used in Brunei Darussalam is Papanicolaou (Pap) test/cytology ^[6]. Another cervical cancer preventive strategy is the implementation of the national HPV immunization programme in January 2012, (with either a bivalent or quadrivalent vaccine that protects

against high-risk HPV subtypes: type 16 and 18 or type 6, 11, 16 & 18 respectively) directed at female school students from Year 7/10–12 years old, with coverage at 91.9% in 2015 [7].

Survival studies provide important indicators on healthcare performance in terms of diagnosis and treatment of a particular disease. Understanding the survival rate of cervical cancer patients is crucial to determine the effectiveness of existing national preventive strategies and management plans. Additionally, elucidating the associated prognostic factors may also enable targeted interventions to increase awareness on the risk factors and the benefits of early detection.

This study aims to investigate the survival rate of cervical cancer patients in Brunei Darussalam between 2002 and 2017, to compare survival rate between two periods: 2002-2009 vs 2010-2017, as well as to identify associated prognostic factors of cervical cancer.

Methods

Study Design, Population, and Sample

This is a retrospective cohort study involving 457 patients diagnosed with cervical cancer from 1st January 2002 to 31st December 2017 (inclusive). The study included all eligible cervical cancer patients who are registered in the Brunei Darussalam Cancer Registry (BDCR) without sampling. The BDCR registers all cancer patients in Brunei Darussalam. Since the BDCR was established in 2002, only data from January 2002 to December 2017 were included in this study.

Data Collection

De-identified data of the study population was obtained from the Ministry of Health Brunei Darussalam. The password-protected data was provided in Microsoft Excel format, omitting any personal information to ensure patients' confidentiality and anonymity. Variables collected and analysed include demographic details (such as date of birth, age, and ethnicity), and clinical details (the date of diagnosis, stage at diagnosis, histology of tumor at diagnosis, ICD-10-CM code, and date of death). Stage at diagnosis (based on Surveillance, Epidemiology, and End Results (SEER) staging) was classified as in situ, local, regional, distant or unknown.

Statistical Analysis

The Excel data sheet was read by the statistical software, R version 4.0.2 and RStudio version 1.3.1056. Kaplan-Meier method was used to estimate the survival rates of cervical cancer patients at 1-, 3-, and 5-year for different age groups, cancer staging and ethnicities, where relevant survival curves were plotted. Log-rank test was used to compare the survival rates of cervical cancer patients. Multiple Cox proportional hazard regression model was used to compare the survival of cervical cancer patients

between two periods controlling for other significant variables. Using the stepwise automatic variable selection procedure of multiple Cox model, we tested variables namely two periods, age, ethnicity, SEER staging, and histology. Ethnicity and histology were not included by the procedure. In addition, as these two variables did not change or affect the hazard ratio (HR) of two periods, they were omitted from the model. Model assumptions, possible interactions and multicollinearity were validated before establishing the final model. We considered statistical significance if the p-value was less than 0.05.

Results

Demographics and Clinical Characteristics

This study included all 457 cervical cancer patients registered in BDCR from January 2002 to December 2017. Out of the 457 patients, 73.7% (n=337) patients were still alive at the end of this study (Table 1). Majority of the patients are Malays (75.1%, n=343), with age ranging between 40 to 59 years old (52.7%, n=241), have squamous cell carcinoma at diagnosis (54.0%, n=247), and are being diagnosed at the regional stage (48.6%, n=222). There is a considerable increase (39.3%) in the number of cervical cancer patients from 191 in 2002-2009 to 266 in 2010-2017. There is also a significant shift in age distribution ($p < 0.001$) between the two periods with a 2.46 fold increase in proportion of younger patients (<40 years) being diagnosed from 21.5% (n=41) in 2002-2009 to 38.0% (n=101) in 2010-2017. The youngest patient diagnosed was 25 and 22 years old in 2002-2009 and 2010-2017 respectively (data not shown). There is also a significant difference in the incidence rate of cervical cancer between ethnic groups ($p = 0.011$) between the two study periods. The proportion of Malay patients increased from 73.3% (n=140) to 76.3% (n=203) whereas the proportion of Chinese patients decreased from 20.9% (n=40) to 12.4% (n=33). Distribution by cancer (SEER) staging also exhibited significant changes between the two study periods ($p < 0.001$): in situ cases increased 14.5-fold, from 1.0% (n=2) to 10.9% (n=29), with minor changes in other staging categories (localized, regional and distant).

Table 1
Demographic and clinical characteristics of 457 cervical cancer patients

Characteristic	Overall		2002-2009 (<i>n</i> =191)		2010-2017 (<i>n</i> =266)		<i>p</i> value ^a
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Age in years							
<40	142	(31.1)	41	(21.5)	101	(38.0)	<0.001
40-59	241	(52.7)	111	(58.1)	130	(48.9)	
≥60	74	(16.2)	39	(20.4)	35	(13.2)	
Ethnicity							
Malay	343	(75.1)	140	(73.3)	203	(76.3)	0.011
Chinese	73	(16.0)	40	(20.9)	33	(12.4)	
Others	41	(9.0)	11	(5.8)	30	(11.3)	
SEER stage							
<i>In situ</i>	31	(6.8)	2	(1.0)	29	(10.9)	<0.001
Localised	158	(34.6)	74	(38.7)	84	(31.6)	
Regional	222	(48.6)	99	(51.8)	123	(46.2)	
Distant	46	(10.0)	16	(8.4)	30	(11.3)	
Histology							
Squamous CC	247	(54.0)	108	(56.5)	139	(52.3)	0.160
Adenocarcinoma	74	(16.2)	35	(18.3)	39	(14.7)	
Others	136	(29.8)	48	(25.1)	88	(33.1)	
Living Status							
Alive	337	(73.7)	140	(73.3)	197	(74.1)	0.940
Deceased	120	(26.3)	51	(26.7)	69	(25.9)	

^a Chi-square test (comparison between two study periods); *cell carcinoma (CC)

Survival Rate and Survival Duration of Cervical Cancer Patients

Kaplan-Meier survival analyses reveal that the overall 1-, 3- and 5-year survival rates were 88.2%, 78.9% and 74.1% respectively from 2002-2017 (Table 2). Kaplan-Meier curve (Figure 1) shows that more than half of the patients survive for 17 years after diagnosis (or till the end of this study), therefore the overall median survival time (MST) was not estimated. When comparing the two study periods, Kaplan-Meier survival curves of cervical cancer patients indicate that the 5-year survival rates of cervical cancer patients were 77.5% and 72.1% for 2002-2009 and 2010-2017 respectively (Figure 2).

Table 2
Comparison of survival by periods and other characteristics

Characteristic	Survival Rate			χ^2 (df)	p value ^a
	1-year	3-year	5-year		
Overall	88.2%	78.9%	74.1%		
Two periods					
2002-09	91.1%	83.2%	77.5%	2.80 (1)	0.090
2010-17	86.1%	75.8%	72.1%		
Age in years					
<40	88.7%	80.4%	77.2%	29.80 (2)	<0.001
40-59	91.7%	83.9%	79.2%		
≥60	75.7%	60.0%	51.7%		
Ethnicity					
Malay	86.0%	75.6%	71.6%	2.70 (2)	0.300
Chinese	94.5%	88.7%	83.1%		
Others	95.1%	89.4%	79.7%		
SEER stage					
<i>In situ</i>	100.0%	100.0%	96.3%	121.00 (3)	<0.001
Localised	97.5%	93.4%	87.7%		
Regional	85.1%	76.0%	71.3%		
Distant	63.0%	28.4%	24.9%		
Histology					
Squamous CC*	87.9%	78.6%	76.5%	0.30 (2)	0.900
Adenocarcinoma	95.9%	83.2%	65.8%		
Others	84.6%	77.5%	75.1%		
^a Log-rank test (comparing survival); *cell carcinoma (CC)					

Comparison of Survival Rate and Survival Duration by Age Groups

There is a significant difference in survival rate among the different age groups ($p < 0.001$) (Table 2), with significantly lower survival in the ≥ 60 years (5-year survival: 51.7%). The 5-year survival rate is highest in the age group 40-59 years (79.2%). This is followed by 77.2% in the < 40 years group. MST for the age group ≥ 60 years was 5.17 years whereas this cannot be estimated for < 40 years and 40-59 years as more than half of the patients were still alive at the end of this study (Figure 3).

Comparison of Survival Rate and Survival Duration by SEER Staging

Survival rate of cervical cancer patients was significantly according to cancer stage (SEER staging) ($p < 0.001$) (Table 2). The 5-year survival rate for patients who present with in situ cervical cancer is highest at 96.3% followed by 87.7%, 71.3% and 24.9% for localized, regional and distant SEER stages respectively. Patients with distant SEER stage had a MST of 1.31 years (Table 2 and Supplementary Figure 1 (S1)). Patients diagnosed at in situ, local and regional cancer stages do not have a MST as more than 50% of the patients were still alive at the end of this study.

Comparison of Survival Rate and Survival Duration by Ethnicity

There is no significant difference in survival rate between ethnicities ($p = 0.300$) (Table 2). The 5-year survival rate for Chinese is highest at 83.1% followed by 79.7% for "Others" (non-Malays and non-Chinese), with the lowest 5-year survival rate noted in the Malays at 71.6% (Table 2 and Supplementary Figure 2 (S2)).

Comparison of Survival Rate and Survival Duration by Cancer Histology

Cancer histology has no impact on the survival rate of cervical cancer patients ($p = 0.900$) (Table 2). The 5-year survival rate for patients diagnosed with squamous cell carcinoma was highest at 76.5%, followed by "Others" (75.1%) and adenocarcinoma (65.8%) (Table 2 and Supplementary Figure 3 (S3)).

Comparison of Survival between Two Periods Controlling for other Variables using Multiple Cox Regression

Although the overall 5-year survival rate of cervical cancer patients was quite high (74.1% in 2002-2017), multiple Cox regression showed that the mortality risk was 57% higher in 2010-2017 (Adjusted(Adj.) HR=1.57; 95% CI: 1.06, 2.31; p=0.025) compared to 2002-2009 (Table 3). Age group (≥ 60 years) (Adj. HR=1.85; 95% CI: 1.11, 3.09, p=0.019) and advanced SEER staging (regional stage (Adj. HR=12.42; 95% CI: 1.70, 90.59; p=0.013); distant stage (Adj. HR=49.47; 95% CI: 6.64, 368.52; p<0.001)) were associated with increased risk of mortality. In the multiple Cox model, both ethnicity and histology were not associated with mortality risk (p>0.05).

Table 3
Comparing survival between two periods controlling for other variables using multiple Cox regression

Characteristic	Simple Cox Model			Multiple Cox Model		
	C.HR ^a	(95% CI)	p-value	Adj. HR ^b	(95% CI)	p-value ^c
Two periods						
2002-09	1.00			1.00		
2010-17	1.38	(0.95, 2.01)	0.091	1.57	(1.06, 2.31)	0.025
Age in years						
<40	1.00			1.00		
40-59	0.98	(0.63, 1.54)	0.947	0.75	(0.47, 1.20)	0.230
≥60	2.76	(1.71, 4.45)	<0.001	1.85	(1.11, 3.09)	0.019
Ethnicity						
Malay	1.00					
Chinese	0.68	(0.40, 1.16)	0.160			
Others	0.69	(0.34, 1.43)	0.321			
SEER stage						
<i>In situ</i>	1.00			1.00		
Localised	3.77	(0.50, 28.19)	0.196	4.12	(0.55, 31.08)	0.169
Regional	11.11	(1.54, 80.09)	0.017	12.42	(1.70, 90.59)	0.013
Distant	45.45	(6.20, 333.13)	<0.001	49.47	(6.64, 368.52)	<0.001
Histology						
Squamous CC*	1.00					
Adenocarcinoma	1.14	(0.71, 1.83)	0.597			
Others	1.01	(0.67, 1.54)	0.955			
^a Crude Hazard Ratio; ^b Adjusted Hazard Ratio; ^c Wald test; *cell carcinoma (CC)						

Relationship between SEER staging and other variables (age and ethnicity)

As age and ethnicity had significantly different distributions between the two periods (2002-2009 and 2010-2017) (Table 1), the relationship between SEER staging and these two variables were also evaluated (Table 4). There is a significant association between age and SEER staging where patients ≥ 60 years had the highest proportions of advanced cancer stages (regional: 60.8% and distant: 16.2%) ($p < 0.001$) compared to other age groups (Table 4). There is no association between ethnicity and SEER staging ($p > 0.05$) (Table 4).

Table 4

Relationship between SEER staging and two sociodemographic variables (age and ethnicity)

Characteristics	<i>In Situ</i> (<i>n</i> =31)		Localised (<i>n</i> =158)		Regional (<i>n</i> =222)		Distant (<i>n</i> =46)		<i>p</i> -value ^a
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Age in year									
<40 (<i>n</i> =142)	17	(12.0)	66	(46.5)	51	(35.9)	8	(5.6)	<0.001
40-59 (<i>n</i> =241)	12	(5.0)	77	(32.0)	126	(52.3)	26	(10.8)	
≥ 60 (<i>n</i> =74)	2	(2.7)	15	(20.3)	45	(60.8)	12	(16.2)	
Ethnicity									
Malay (<i>n</i> =343)	26	(7.6)	118	(34.4)	162	(47.2)	37	(10.8)	0.611
Chinese (<i>n</i> =73)	3	(4.1)	29	(39.7)	36	(49.3)	5	(6.8)	
Others (<i>n</i> =41)	2	(4.9)	11	(26.8)	24	(58.5)	4	(9.8)	
^a Chi-square test									

Discussion

Our study shows that the overall national 5-year survival rate in Brunei is 74.1% from 2002-2017. This indicates that survival of cervical cancer patients in Brunei is at par with survival in high-resource nations (in 2010-2014, the highest 5-year survival in women with cervical cancer in Europe was in Iceland (80%), Norway (73%) and Switzerland (71%) [8]). Meanwhile, the highest 5-year survival rates among Organisation for Economic Co-operation and Development (OECD) countries have previously been reported in Korea (76.8%), Norway (71.4%) and Israel (71.4%), with the average from 19 OECD countries

(OECD19) at 66% for the period 2006-2011 [9]. The high 5-year survival rate of cervical cancer patients in Brunei may be accounted for by the two-pronged preventive approach including Pap cytology screening and HPV prophylactic vaccine, as well as a universal healthcare system, with highly accessible diagnosis and treatment facilities which are available at no cost to all citizens. The heterogeneity in the 5-year survival rates of cervical cancer patients globally may be due to inequality or inequity to healthcare access and resources. A global estimation of the incidence and mortality of cervical cancer in 2018 showed that cervical cancer was the main cause of cancer-related death in women in Eastern, Western, Middle, and Southern Africa, correlating with a lack of preventive approaches including screening and HPV immunisation vaccine, or inadequate healthcare in these regions [4]. Therefore, cautious consideration should be made when comparing the survival rate of cervical cancer patients between countries due to variation in healthcare infrastructure, study design, study time frames, statistical analysis, population size, sociodemographic features, cultural and/or social factors.

There is a 39.2% increase in the number of cervical cancer patients diagnosed in 2010-2017 compared to 2002-2009. There is also a shift in the demographics of patients with cervical cancer in Brunei where the proportion of younger patients (<40 years) as well as *in situ* and distant stage diagnoses increased in the later period (2010-2017). Although more patients are being diagnosed at an early (*in situ*) stage, it has been shown that there is a 57% significantly higher risk of mortality in the later (2010-2017) period ($p<0.05$) suggesting that recently-diagnosed patients have poorer survival outcomes. However, this may not reflect clinical reality due to several reasons. Implementation of the Bru-HIMS system (since September 2012) may have led to improved surveillance in recording of vital statistics including cervical cancer patients' death certification (i.e. The lack of surveillance infrastructure and harmonised coding system may not have captured all cervical-cancer related deaths pre-Bru-HIMS, leading to an overestimation of patients' survival in the earlier period (2002-2009)). The increased risk of mortality in 2010-2017 may also be attributed to other factors (such as the presence of co-morbidities including diabetes and obesity) that are not included and/or analysed in this study. Therefore, prognostic factors behind the increased mortality in 2010-2017 remain to be determined. Increased uptake of Pap smear cytology upon implementation of the national screening programme in 2011 may also account for the increasing incidence in 2010-2017, increased proportion of younger patients (<40 years) diagnosed (38% in 2010-2017 compared with 21.5% in 2002-2009) as well as the increase (14.5-fold) in *in situ* cases (10.9% in 2010-2017 compared with 1.0% in 2002-2009). As cancers have a long latency period [10], increased distant stage cases may be due to improved surveillance and or management following the introduction of the national screening programme in 2011. An analysis of national data (1982–2006) has revealed increasing rates of cervical cancer in young women between 20 to 29-year-olds across most regions in England from 1996 onwards, whereas incidence rates in women aged 30–39 years have mainly stabilised [11]. HPV infection solely is not sufficient (although necessary) to promote cervical cancer, and other factors affect the risk of HPV infections progressing to cervical intraepithelial neoplasia (CIN). As HPV is sexually transmitted, aspects of sexual behaviour and multiple reproductive factors influence the risk of CIN and invasive cancer (including number of sexual partners, age at first intercourse, early age at first full-term pregnancy, smoking and passive smoking [12] and increasing duration of oral

contraceptive use (reviewed in ^[11]). The association between these risk factors and the increasing proportion of cervical cancer diagnosis in women <40 years in our study remains to be determined. Evaluating cervical screening intervals between age groups and lifestyle/social factors is essential to facilitate informed decisions pertaining to changes in recommendations for screening guidelines and vaccination against HPV infections ^[13]. In 2022, the inaugural birth cohorts of women offered HPV vaccination as girls (under the national vaccination programme in 2012) will enter cervical screening. These women are better safeguarded against cervical cancer and could therefore receive recommendations for less intensive screening ^[14]. Therefore, it is timely for an update of the screening guidelines in terms of the initiation and interval of screening for HPV-vaccinated women.

Currently, screening for cervical cancer in Brunei Darussalam is based on Pap cytology. HPV testing and Pap smear cytology (co-testing) could potentially result in earlier identification of women at high risk of cervical cancer, especially those with adenocarcinoma ^[15]. While there is no published data on the coverage rate of cervical cancer screening in Brunei Darussalam, WHO has proposed a global target of screening coverage (at ages 35 years and 45 years) of at least 70% by 2030 in order to achieve cervical cancer elimination ^[16]. National organised screening and treatment programmes in many countries has contributed to significant reduction of the incidence and mortality of cervical cancer over the past 30 years and regular screening has been estimated to prevent up to 83% of cervical cancer deaths ^[17]. Early detection and treatment of pre-cancerous lesions remain the optimal option for millions of women already infected with cancer-causing HPV as the HPV prophylactic vaccine is ineffective if infection is already present ^[18]. Public health initiatives to uncover the screening coverage rate and if necessary, propel culturally-appropriate education and raise knowledge regarding the benefits of early diagnosis, improving perceptions or attitudes towards screening, as well as implementing self-sampling HPV test ^[19] and patient-friendly care may be beneficial to reduce barriers or improve screening compliance and reduce risks of mortality and incidence of cervical cancer.

Majority of the women in this study (52.7%) were diagnosed between the age group 40-59 years, which is concordant with findings from other studies ^{[20][21]}. A significantly lower survival as well as a higher mortality risk for age group ≥ 60 years was observed compared with the other two younger age groups (<40 and 40-59 years) ($p < 0.001$). Differences in treatment regime has been reported where elderly patients are less likely to receive treatment or not receive treatment at all, compared to the younger age groups as they may not tolerate the aggressiveness of the standard treatment regime and also because they are perceived to have reduced life years compared to younger patients ^[22]. It remains to be determined whether differences in treatment among the different age groups influence survival rates of cervical cancer patients in Brunei. The poor prognosis in patients ≥ 60 years may also be attributed to the presence of comorbidities. Therefore adaptation of comorbidity management strategies for elderly adults with cancer is necessary to optimize care ^[23].

SEER staging was used to categorize cervical cancer patients in this study and is comparable to FIGO (International Federation of Gynaecology and Obstetrics) staging where *in situ*, localized, regionalized

and distant SEER stages corresponds to FIGO stage 0, FIGO stage I, FIGO stage II-IV respectively [24]. This study shows that advanced SEER staging is significantly associated with poor 1-,3- and 5-year survival rates ($p<0.001$), consistent with previous reports [17,20]; underscoring the importance of early diagnosis.

The difference in survival experience among the different ethnicities (Malay, Chinese, Others) was not significant ($p=0.300$). However, there was a slight difference in 5-year survival rate where Chinese patients (82.7%) have a slightly higher survival rate compared to Malay patients (71.6%). A study reported a significant difference in survival between different ethnic groups (Malays, Chinese and Indians). The lowered survival in the Malays was attributed to their unconventional way of seeking good health, with the belief that traditional medicine is more effective than modern medication. The Malays also tend to present to the clinic at later stages of cancer with large tumors, which may account for the lower survival rate compared with other ethnicities [25].

In this study, the predominant histology at diagnosis is squamous cell carcinoma (54.0%) compared to 68% and 83% by two other studies [20,26]. Meanwhile, 16.2% of patients in this study presented with adenocarcinoma. Although there is no significant difference ($p=0.091$) in terms of cancer histology and survival rate, the risk of death for cervical cancer patients with adenocarcinoma was 53% higher than patients with squamous cell carcinoma indicating that patients with adenocarcinoma have worse prognosis than those with squamous cell carcinoma in this study. This finding is similar to another study where the relative risk of death was 60% higher for patients with adenocarcinomas than for patients with squamous cell carcinoma [27]. As adenocarcinoma is associated with a poorer prognosis and a greater probability of distant recurrence compared with squamous cell carcinoma, novel or alternative therapeutic strategies for adenocarcinoma patients may be required [28].

Some study limitations include the low population size of this study (457 patients), relative to other studies (a reflection of the small population of Brunei (459,500)). Ethnic ambiguity in medical records may also affect our results. In addition, since Brunei does not currently offer HPV-testing, the distribution of HPV subtypes in our population and the efficacy of the national HPV vaccination programme remains to be evaluated. Future studies on potential prognostic variables (such as presence of comorbidities, cervical screening uptake rate, HPV subtypes, sites of metastasis or treatment received), social history (socioeconomic status, education level, and age at first sexual intercourse) and family health history may better inform predictors of cervical cancer in Brunei, to enable targeted intervention. Current European Guidelines recommend organized population-based screening with primary HPV testing [29]. National health policy makers may wish to review the recommendations for cervical cancer screening as relevant data emerges, in terms of implementing HPV testing concurrently with Pap smear cytology, as well as the flexibility of service options including provision of HPV self-sampling kits to identify high-risk virus subtypes, with close follow-up and monitoring of high-risk patients. Assessing the effectiveness of the national HPV vaccination and screening in Brunei Darussalam will also allow for evaluation of policy and strategy to reduce cervical cancer burden.

Conclusions

To conclude, the 5-year survival rate was 74.1% for cervical cancer patients from 2002-2017 in Brunei Darussalam, which is in the upper range globally (compared to the OECD19 average at 66%) [9]. This study also showed a difference in survival rate between the two periods where patients diagnosed between 2010-2017 have a lower 5-year survival rate compared to those diagnosed between 2002-2009. There was a significant difference in terms of survival rate of cervical cancer patients among different age groups, and SEER stages.

List Of Abbreviations

Adj. Adjusted

ASR Age-Standardized Incidence Rate

BDCR Brunei Darussalam Cancer Registry

Bru-HIMS Brunei Darussalam Healthcare Information and Management System

CIN Cervical Intraepithelial Neoplasia

FIGO The International Federation of Gynecology and Obstetrics

HPV Human Papillomavirus

ICD-10-CM International Classification of Diseases, Tenth Revision, Clinical Modification

MST Median Survival Time

OECD Organisation for Economic Co-operation and Development

Pap Papanicolaou

SEER Surveillance, Epidemiology, and End Results

Declarations

Ethics approval

Ethics approval was obtained from the joint PAPRSB Institute of Health Sciences Research and Ethics Committee and Medical and Health Research and Ethics Committee, Ministry of Health, Brunei Darussalam (UBD/PAPRSBIHSREC/2018/121) before the study commenced. Informed consent from patients has been waived by the joint PAPRSB Institute of Health Sciences Research and Ethics Committee and Medical and Health Research and Ethics Committee. Administrative approval was

obtained from the Director General Medical and Health Services at Ministry of Health, Brunei Darussalam. Study methods were carried out in accordance with relevant guidelines and regulations to ensure patients' confidentiality and anonymity.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study is available from the corresponding author on reasonable request.

Competing interests

All authors have no conflict of interest to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

L.N. and S.K.O. designed the research; L.N., H.A.R. and N.A.R. analysed the data; N.A.R. and S.H.F.L. wrote the paper and all authors critically revised the manuscript for important intellectual content.

Acknowledgements

Not applicable

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Figures

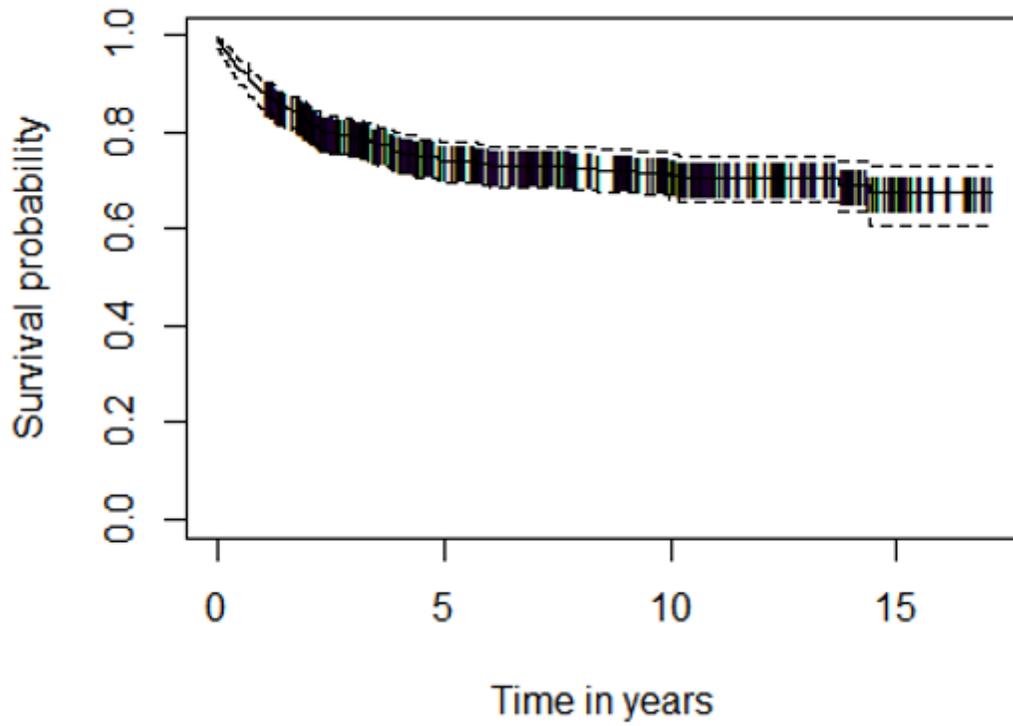


Figure 1

Kaplan-Meier Survival Curve of Cervical Cancer Patients (2002-2017)

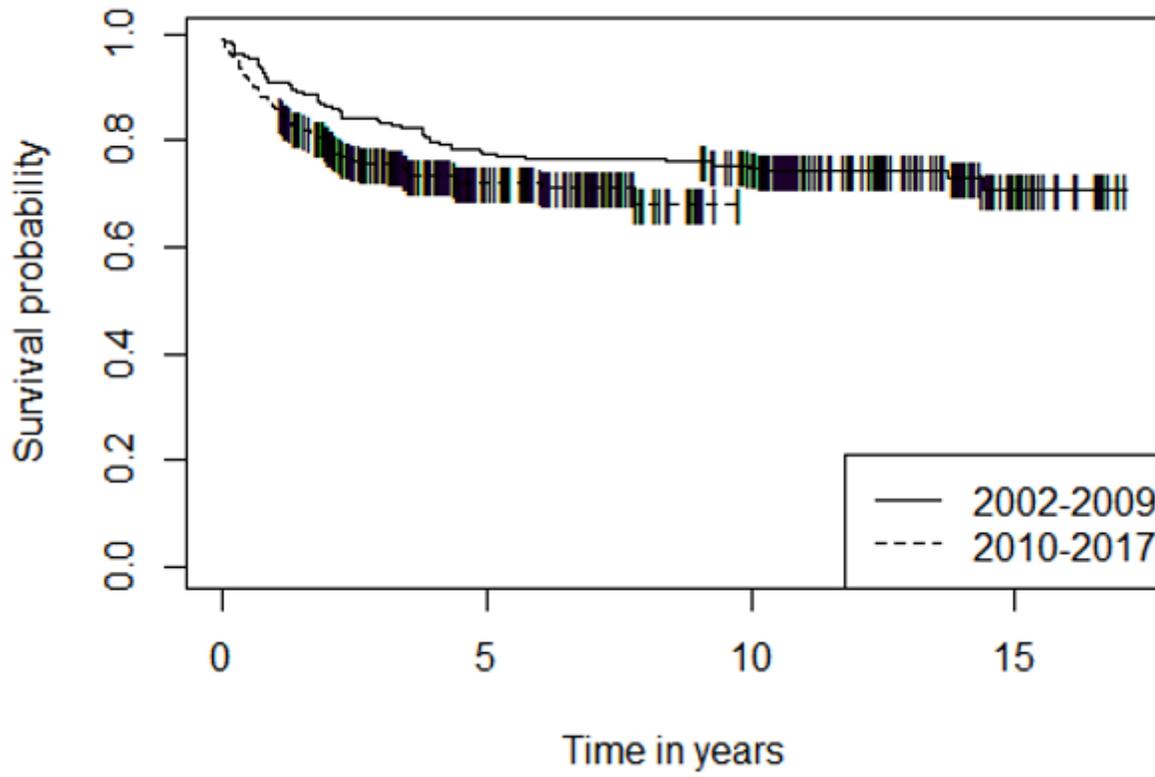


Figure 2

Kaplan-Meier Survival Curve of Cervical Cancer Patients (comparing two study periods)

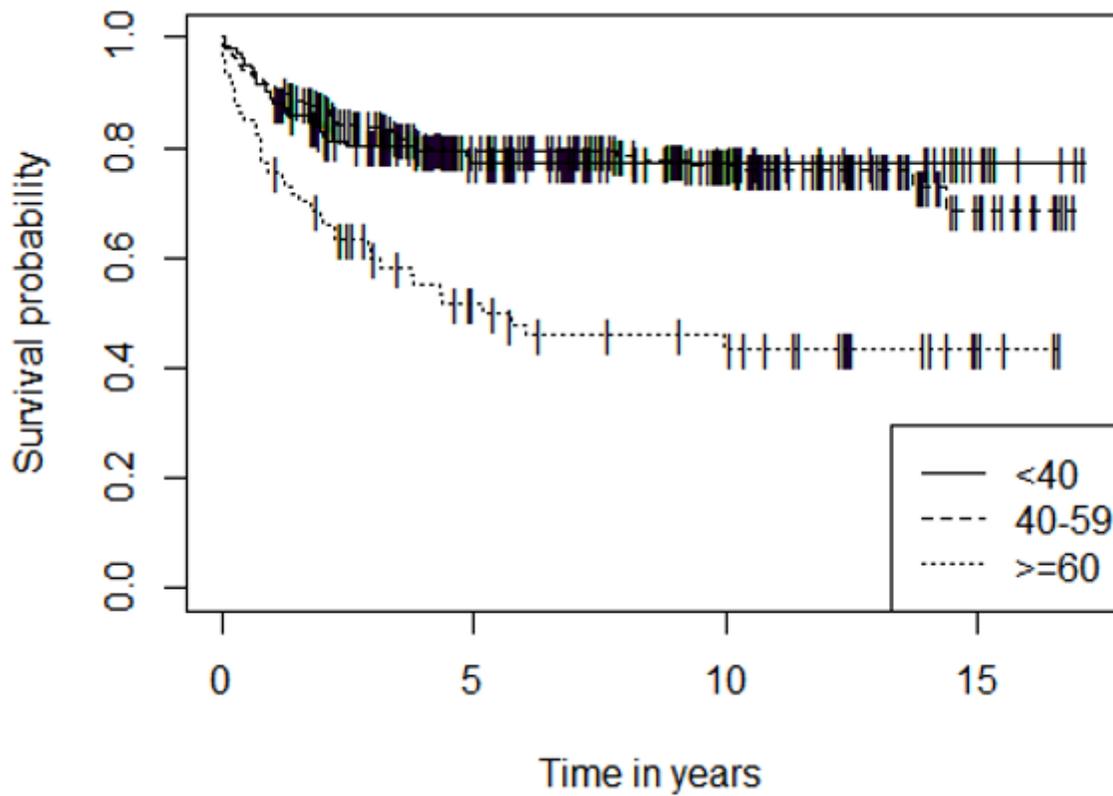


Figure 3

Kaplan-Meier Survival Curve of Cervical Cancer Patients by Age Groups

Supplementary Files

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