Cervical carcinoma: survival rate and prognostic factors in women in the state of Mato Grosso*

Carcinoma do colo do útero: taxa de sobrevida e fatores prognósticos em mulheres no Estado de Mato Grosso

Carcinoma de cuello de útero: tasa de sobrevida y factores pronósticos en mujeres en el Estado de Mato Grosso

Janete Tomiyoshi Nakagawa[1], Mariano Martínez Espinosa[2], Márcia Barbieri[3], Janine Schirmer[4]

ABSTRACT

Objectives: To analyze the survival rate of women undergoing treatment for cervical cancer in the state of Mato Grosso and identify the prognostic factors that most influenced the survival time. **Methods:** A cohort study, conducted by analysis of medical records, among others. The population included 55 women who experienced this type of carcinoma and had clinical follow-up between 2002 and 2007. **Results:** The overall survival rate was 66.7%. The prognostic factors that influenced survival rate were: age, presence of symptoms suggestive of cervical cancer, and late stage of disease at diagnosis. **Conclusion:** Although the overall survival rate was similar to the rates of developed countries, it was lower in women with unfavorable social conditions.
Descriptors: Survival rate; Uterine cervical neoplasms; Multivariate analysis; Prognosis

RESUMO

Objetivos: Analisar a taxa de sobrevida de mulheres submetidas ao tratamento de câncer do colo do útero no Estado de Mato Grosso e identificar os fatores prognósticos que mais influenciaram no tempo de sobrevida. **Métodos:** Estudo tipo coorte, realizado por meio da análise dos prontuários clínicos, e dados do Sistema de Informação do Colo do Útero, Sistema de Informação sobre Mortalidade, Sistema de Informação Autorização de Procedimentos Alta Complexidade. A população correspondeu a 55 mulheres que apresentaram esse tipo de carcinoma e tiveram seguimento clínico entre 2002 e 2007. **Resultados:** A taxa de sobrevida global foi de 66,7%. Os fatores prognósticos que influenciaram na taxa de sobrevida foram: idade, presença de sintomatologia sugestiva de câncer cervical e estágio tardio da doença no momento do diagnóstico. **Conclusão**: Apesar da taxa de sobrevida global encontrada assemelhar-se às taxas de países desenvolvidos, foi menor em mulheres com condições sociais desfavoráveis.
Descritores: Taxa de sobrevida; Neoplasias do colo do útero; Análise multivariada; Prognóstico

RESUMEN

Objetivos: Analizar la tasa de sobrevida de mujeres sometidas al tratamiento de cáncer de cuello de útero en el Estado de Mato Grosso e identificar los factores pronósticos que más influyeron en el tiempo de sobrevida. **Métodos:** Estudio de tipo cohorte, realizado por medio del análisis de las historias clínicas, entre otros. La población correspondió a 55 mujeres que presentaron ese tipo de carcinoma y tuvieron seguimiento clínico entre 2002 y 2007. **Resultados:** La tasa de sobrevida global fue del 66,7%. Los fatores pronósticos que influyeron en la tasa de sobrevida fueron: edad, presencia de sintomatología sugestiva de cáncer cervical y estadío tardío de la enfermedad en el momento del diagnóstico. **Conclusión**: A pesar de que la tasa de sobrevida global encontrada se asemeje a las tasas de países desarrollados, fue menor en mujeres con condiciones sociales desfavorables.
Descriptores: Tasa de supervivencia; Neoplasias del cuello uterino; Análisis mutivariante; Prognostico

INTRODUCTION

Cervical cancer or carcinoma is the most frequent type of neoplasia in women living in less developed areas, especially in the Northern region of Brazil, including part of Northern Mato Grosso. It is the second most frequent type of cancer in the female population of this state and the second cause of mortality from neoplasia, with an age-adjusted rate of 7.74/100,000 women in 2007[1].

Since 1998, in view of the high rate of mortality from cervical cancer, reduction in this disease has been one of the priorities of the Mato Grosso State Health Policy, with the implementation of the *Programa Nacional de Controle do Câncer do Colo do Útero* (PNCCU – National Cervical Cancer Control Program). In 2002, due to the priority given to this problem, there was a second phase of intensification of the program, when 92,000 women were screened in the entire state, thus resulting in 1,109 altered types of cytology that range from primary lesions to in situ and invasive carcinomas.

Aiming to analyze the results obtained from the PNCCU in the state of Mato Grosso, a study on the analysis of survival of invasive cervical carcinoma cases identified in 2002 and submitted to treatment and clinical follow-up between 2002 and 2007 was conducted, based on the following question: what is the impact of the PNCCU on the state of Mato Grosso?

It should be emphasized that studies on survival are an important indicator of cancer follow-up and control. They are frequently used to evaluate the efficacy of treatment, the availability and accessibility of available resources and they are useful in the assessment of health program results. In addition, studies of this nature enable the identification of the factors that mainly influence the survival rate of cancer cases.

Based on studies conducted in several countries, different survival rates have been recorded in cervical carcinoma cases. In the United States, more recent studies have identified a survival rate of 70.1%[2]. In Australia, France and England, the rates found were 72%, 67% and 60%, respectively, whereas the lowest rates were found in India (40%) and the Philippines (29%)[3]. These data show that there is a relevant difference in survival rate between developed and developing countries[2]. Several factors are associated with this difference, among which is early detection. This is because, according to studies conducted, there is a smaller proportion of in situ carcinoma in developing countries, indicating that the disease has only been detected in an advanced stage in these countries.

Studies conducted in Brazil found different survival rates, according to the treatment performed. The rate of women who had received chemotherapy was 62.6%[4]; that of those who underwent brachytherapy, 65.3%[5]; and that of those who underwent pelvic exenteration after primary radiotherapy treatment, 64.3%[6]. Probably, these differences are more closely associated with the extent of the disease, which determines the type of treatment. For this reason, a higher level of invasion is considered to be one of the most important indicators of prognosis.

Socio-demographic conditions have also caused a variation in survival rates. In particular, age has had a considerable influence on survival rates in cancer cases in general[7].

In view of this situation, the present study aimed to analyze the survival rate of women who underwent cervical cancer treatment in the state of Mato Grosso and to identify the prognostic factors that most influenced this rate among women who had invasive carcinoma in 2002 and who underwent treatment in the state of Mato Grosso, between 2002 and 2007.

METHODS

,A retrospective cohort study was conducted with a sample of 55 women who were present in secondary/tertiary care services, which are state referral cancer centers located in the city of Cuiabá, state of Mato Grosso. These women had a confirmed diagnosis of invasive cervical carcinoma in the second stage of intensification of the PNCCU and they underwent clinical follow-up between 2002 and 2007.

The inclusion criteria were women with a diagnosis of invasive cervical carcinoma, living in the Mato Grosso in 2002 and including a clinical follow-up in the Mato Grosso State Referral Services. On the other hand, the exclusion criteria were in situ carcinoma cases or women who, although having undergone treatment in Mato Grosso, went to other states, especially in Northern Brazil.

Data were collected in 2008 from clinical medical records and from the Cervix Information System, Mortality Information System, and Highly Complex Procedure Authorization Information System.

The dependent variable was death from cervical cancer and the independent socio-demographic variables were: age, ethnicity and occupation. Age was categorized into two age groups: less than 50 years and 50 years or more. Ethnicity was categorized into white and non-white, while occupation was divided into paid work and unpaid work.

Clinical variables were as follows: presence or not of symptoms suggestive of the disease, length of time between the diagnosis and treatment, and lastly the extent of the disease.

Presence of disease manifestation was dichotomized

into present of absent. The length of time between the diagnosis and beginning of the treatment was divided as follows: one month or less, between one and three months, and more than three months. The extent of the disease at the moment of diagnosis was analyzed and categorized into stages 1 through 4, according to the classification of the International Federation of Gynecology and Obstetrics[2]. Lastly, the presence of metastasis or not was analyzed. The Kaplan-Meier estimator was used to estimate the probability of survival[8-10]: firstly, in a global way, i.e. without stratification; secondly, with the stratification of the covariables determined in the study. The Logrank test was used to analyze the several curves, aiming to obtain the proportionality of risk.

With the purpose of estimating the effect of covariables on participants' survival, the Cox model was adjusted and, based on the significance of risks in relation to times defined by exponential parameters, the covariables that entered the multivariate model were selected[8].

In the initial multivariate analysis, all variables were included in the model and subsequently removed and replaced one by one, according to a statistical significance level of 0.05 established for the coefficients and based on the results of Wald tests and verisimilitude ratio among the adjusted models. In addition, all possible interactions among variables were tested. The variables that remained in the final model were those that had a statistical and epidemiological significance, after being controlled for the remaining ones in the Cox model. The assumption of proportionality required by the Cox model was tested with the graphic model and the time-dependent covariable test.

Survival time was calculated in months and it ranged from the date of surgery/beginning of treatment to the occurrence of death/last consultation, considering the last day of 2007 or the moment when the 60 months were completed, as the date when the study ended. Cases of death from cervical cancer that occurred during the period of study were considered to be "failures". On the other hand, cases that involved survival until the end of the study were categorized as "censored". Each case had their follow-up time included in the make-up of the risk group. With regard to the cases of loss of follow-up, the date of the last follow-up noted down in the medical records as that when the case was censored was taken into consideration.

The EPI INFO software program, version 3.5, was used for data collection, including double data entry. The SPSS 15.0 and EPI INFO software programs, version 3.5, were used in the descriptive and inferential statistical analyses.

The present research project was approved by the *Universidade Federal de São Paulo* Research Ethics Committee, under register number 0961/07 of July 6th 2007 and by the *Hospital Universitário Júlio Muller* Research Ethics Committee of the *Universidade Federal de Mato Grosso*, under register number 297/2006 of December 13th 2006, guaranteeing the anonymity of women who participated in this study.

RESULTS

The follow-up time varied between two and 60 months, the mean time was 47 months and the median time was 60 months.

At the end of the follow-up, the following results were observed in the 55 women who had invasive carcinoma:

- 36 women (65.5%) were alive and observed for 60 months. These cases were considered as censored;

- 18 cases (32.7%) were considered as failures, whose primary cause of death was cervical cancer;

- one case (1.8%) of death occurred due to a different cause and was thus considered as censored.

The overall survival rate, i.e. the rate without stratification in 60 months, estimated by the Kaplan-Meier method, was 66.7%. The mean survival time was 23.5 months, and the median survival time was 18.5 months. There were no follow-up losses.

Data in Table 1 show the number and proportion of women who had carcinoma, the number and proportion of cases that resulted in death, the survival rate and its respective p-value, obtained with the stratified Logrank curve (Mantel-Cox), according to clinical and socio-demographic variables.

Overall survival rate in 60 months was 63.6% among women aged less than 50 years and 71.4% among those aged 50 years or more, with a p-value = 0.524. The relative risk (RR) of death from cervical neoplasia in women aged more than 50 years was 1.12, with a p-value = 0.83.

The survival rate of white women was 75.9% and that of non-white ones was 56%, with p = 0.183. The RR of death among non-white women was 3.41, when compared to white ones. This result was found to be statistically significant (p = 0.028).

Women with a paid job had a survival rate of 70%, while those without paid jobs (housewives) had a lower survival rate of 65.9%.

With regard to clinical variables, women with complaints/symptoms suggestive of the disease had a worse diagnosis with a survival rate of 53.1%, while those without complaints had a survival rate of 86.4%, thus revealing a statistically significant difference (p = 0.012). Among these, there were a higher number of women who arrived at the health services with clinical

Table 1 - Stratified univariate analysis of survival, according to socio-demographic and clinical variables. State of Mato Grosso, Brazil, 2002-2007

n=55

Variables	Number of cases	(%)*	Number of deaths	(%)**	Survival in 60 months (%)***	P-value ****
Age group						
< 50 years	33	60.0	12	66.7	63.6	0.524
>50 years	22	40.0	6	33.3	71.4	
Ethnicity						
White	30	54.5	7	28.9	75.9	0.183
Non-white	25	45.5	11	61.1	56.0	
Occupation						
Paid	11	20.0	3	16.7	70.0	0.731
Unpaid	44	80.0	15	83.3	65.9	
Complaint						
Without symptoms	23	41.8	3	16.7	86.4	0.012
Suggestive symptoms	32	58.2	15	83.3	53.1	
Beginning of treatment						
1 month or less	17	31.0	6	33.3	62.5	
1 to 3 months	31	56.3	11	61.1	64.5	0.563
More than 3 months	7	12.7	1	5.6	85.7	
Extent of the disease						
Stage 1	8	14.5	-	-	100.0	
Stage 2	12	21.8	-	-	100.0	0.000
Stage 3	21	38.2	8	44.5	61.9	
Stage 4	14	25.5	10	55.5	28.6	
Metastasis						
No	41	74.5	8	44.5	80.0	0.000
Yes	14	25.5	10	55.5	28.6	

*total number of cases = 55; ** total number of deaths = 18; ***Kaplan-Meier method; **** Logrank (Mantel-Cox)

Table 2. Multivariate analysis between risk of death and prognostic factors of women with invasive carcinoma, relative risk (RR) between categories and their respective statistical significance levels (p-value). State of Mato Grosso, Brazil, 2002-2007.

n=55

Variables	Coefficient	Standard-error of coeficient	Wald test (W_i)	P-value	RR*	95%CI
Age group						
< 50 years	0.118	0.558	0.044	0.833	1.0	
> 50 years					1.125	0.37-3.36
Ethnicity						
White	1.227	0.559	4.816	0.028	1.0	
Non-white					3.41	1.14-10.2
Occupation						
Paid	0.571	0.692	0.681	0.409	1.0	
Unpaid					1.77	0.45-6.87
Complaint						
Without symptoms	1.020	0.652	2.447	0.118	1.0	
Suggestive symptoms					2.77	0.773-9.95
Metastasis						
No	1.953	0.585	11.147	0.010	1.0	
Yes					7.05	2.24-22.20

Total number of cases = 55; total number of deaths = 18; * Cox model

symptoms of the disease, showing that they often sought care only when the disease was manifesting itself.

The survival rate was 62.5% among women who began their treatment more quickly, i.e. in less than one month between the diagnosis and the beginning of this treatment. In contrast, women who began their treatment after one to three months had a survival rate of 64.5%

and those who began it after more than three months had a rate of 85.7%, with a p-value of 0.563.

With regard to the extent of the disease, the survival rate was 28.6%, unfavorable for women who had metastasis. When there was no metastasis, this rate was 80%.

Deaths occurred among women who were in stages

Table 3. Final multivariate analysis model between risk of death and prognostic factors of women with invasive carcinoma, with a relative risk (RR) of death, their respective 95%CI and statistical significance levels (p-value). State of Mato Grosso, Brazil, 2002-2007.

Variables	Coefficient	Standard-error of coefficient	Wald test (W_i)	p-value	RR*	95%CI
Metastasis	2.036	0.511	15.875	0.00	7.65	2.81-20.85
Ethnicity	1.102	0.510	4.657	0.03	3.00	1.10-8.18
		Log likelihood = -59.838524		p-value < 0.001		

3 and 4. These data are in agreement with the literature, whose prognosis of the disease is extremely favorable when detected early. Data in Table 2 show the prognostic factors that mainly influenced the risk of death from cervical cancer in the state.

Based on the results of the multivariate analysis, the factors that mostly influenced the survival time of women in the state of Mato Grosso were the disease in an advanced stage and ethnicity, as observed in Table 3. The RR in women who had the disease in an advanced stage was 7.65 times higher than those who did not have the disease in such stage, with p <0.001. The RR of death was three times higher in non-white women, compared to white women, with p < 0.05. The final model was statistically significant, with a p-value < 0.05, as shown in Table 3.

DISCUSSION

The overall survival rate in 60 months found in the present study was 66.7%, being close to the rates of developed countries, which vary between 51% and 66%[11]. Although similar, this study showed a shorter survival time among women living under unfavorable social conditions, a profile that more closely resembles that of developing countries where social inequalities predominate, determined by differences in access to early diagnosis and effective treatment[3].

Among the factors that were more closely associated with the survival rate, the extent of the disease and treatment provided stand out. The survival rate of the disease in stages 3 and 4 was 61.9% and 28.6%, respectively, while this rate was 100% in stages 1 and 2, as shown in Table 1. A Brazilian cohort study with a sample of 278 women with cervical cancer identified a survival rate in five years in stage 1 of 93.5%, while the rate in stage 4 was 35.5%[12]. When treated at an early stage, the disease can be completely cured and potentially raise the overall survival rate.

With the advent of radiotherapy in the 1920s, there was a significant increase in survival rates in the majority of developed countries[2]. However, after radiotherapy, there was not a significant improvement in the survival rate with the appearance of new therapies. In Denmark, for example, the survival rate in five years was 61.3%, between 1958 and 1962, and 63.9%, between 1983 and

1987. In the United States, the survival rate was 69.1%, in 1974-76, and 71.3%, in 1992-99. In Europe, the USA and Japan, there was not an improvement in survival[2].

In contrast, in many developing countries such as Singapore, there has been an improvement in the survival rate from 46%, between 1968 and 1972, to 63%, between 1988 and 1992[2], probably when the benefits of treatment technologies reached these countries. It is expected that diagnostic and treatment technologies, widely disseminated in developed countries, will soon be extended to populations with limited therapeutic resources.

However, the effectiveness of treatment is restricted when the disease is in an advanced stage, even in countries with advanced diagnostic and treatment technologies, as the survival rates have not been higher than 70% to 75%. Thus, it is believed that the disease needs to be stopped in its early stages so it can be fought. This can be achieved by adopting low-cost, early diagnosis and prevention measures, so that this can be a resource accessible to impoverished populations and so that women's education and self-care can be emphasized.

The present study revealed that women who began their treatment more quickly had a lower survival rate, as shown in Table 1. This result, although contradictory, reveals that women cared for during a shorter period of time were those under the most severe conditions, thus becoming a priority in the service.

Age is another factor that influences the survival rate. A study based on a sample of 1,815,584 adult patients with cancer, diagnosed between 1990 and 1994 and followed until 1998 in 22 European countries, identified survival rates in 60 months of 73% among women aged between 15 and 44 years. This rate was reduced to less than half (38%) among women aged more than 75 years, showing that there is a decreasing trend towards survival with age[7]. According to the International Agency for Research on Cancer, this fact may be associated with biological factors (growth tumor) or it could be the result of a higher prevalence of coexisting diseases, such as hypertension and cardiovascular diseases in elderly individuals, in addition to a lower probability of receiving proper treatment, thus affecting the diagnosis[2].

In the present study, the survival rate in women aged less than 50 years was lower (63.6%) than that of those

aged 50 years or more (71.4%). In addition, there were a higher number of women aged less than 50 years among those with invasive carcinoma (33 women – 60.0%) than those aged 50 years or more (22 women – 40.0%), as shown in Table 1.

The data indicate that a very significant proportion of cases of carcinoma and death occurred in women aged less than 50 years in the state. These deaths were considered premature and this can be attributed to early exposure to risk factors, lack of access to health resources, and lack of primary and secondary prevention and appropriate treatment. This is because, as observed in this study, many women sought health services only in the advanced stages of the disease, when symptoms were always present and the chance of cure was small.

Due to ethnic differences, distinct survival rates were observed in countries where social differences determine health conditions, such as the United States. In this country, the survival rate among white women was 71% and of black women was 57%, according to data from the Surveillance Epidemiology and End Results from 1986 to 1993.

In the present study, the survival rate found in white women was 75.9% and that of non-white ones was 56%. This result could be indicating that the adequate access to effective diagnostic means and types of treatment were key to improve the survival of white women and that such access was probably lower among non-white women.

In fact, the lack of access to preventive tests among black women was observed in the data from the *Pesquisa Nacional por Amostra de Domicílios* of 2006 (2006 National Household Sample Survey). This is because, among women aged 25 years or more, who had never had a cytology test performed, the proportion of white women was 17%, while that of black ones was 25%[13]. There are other factors associated with this, which do not benefit the black population (comprised of black and mixed individuals), because they are the ones with the lowest level of education and highest illiteracy rates, compared to other ethnic groups[13]. In addition, they are the ones with the lowest life expectancy, and who are most dependent on the public health system, receive most social benefits and, consequently, are most affected by inequalities of access to health services, contributing to the negative outcome of the disease.

Moreover, data in Table 1 show that women without paid jobs (housewives) have a lower survival rate than those with paid jobs/activities. These data also reveal that the fact of a woman being a housewife may be directly or indirectly associated with other unfavorable social conditions, such as low level of education, their condition of submission, low economic condition, lack of information about health and racial prejudice. These are some of the factors that segregate women in their homes, excluding them from the job market. The RR of death in the present study was 1.77 among housewives, when compared to non-housewives. A study conducted in the state of Ceará found that one of the main factors stopping preventive tests from being performed is associated with the socio-cultural context[14].

The survival rate of women who had symptoms at the moment of the first clinical consultation was lower (53.1%) than that of others who did not have any symptoms (86.4%). In addition, the proportion of women with suggestive symptoms/complaints was higher among those with carcinoma (58%). This finding emphasizes the fact that women sought health services only when they had symptoms/complaints, whose cases were diagnosed as having the disease in advanced stages. Disease prevention measures and the use of methods to identify this disease are well-recommended resources to prevent it from being detected solely according to the clinical manifestation.

The presence of metastasis at the moment of diagnosis was the factor most closely associated with lower survival time, as observed in Table 2. At the end of the study, the factors that mainly determined women's survival rate were as follows: having the disease in advanced stages and belonging to the non-white ethnic group, as shown in Table 3. This enables researchers to conclude that a set of unfavorable social factors determined by the condition of belonging to the non-white ethnic group could be hindering early access to health services, thus causing the diagnosis to be only established in the advanced stages of the disease. It should be emphasized that the present study had some limitations. As this study analyzed a rare event, one of these limitations is the fact that the population size was considered to be small, despite the entire population with the disease being included. This limitation did not enable generalizations and it restricted statistical analyses, as it reduced the significance level (p-value).

CONCLUSIONS

It could be concluded that, although the overall survival rate found was similar to the rates of developed countries, this rate was not equally distributed in the female population of the state of Mato Grosso. The survival rate of women of this state living under adverse social conditions is lower, when compared to the overall rate found in the present study. This revealed the unfavorable epidemiological profile of the poorest population groups of Mato Grosso, very similar to the profile of developing countries.

In this sense, the importance of maintaining political strategies similar to what is recommended by the

PNCCU was analyzed, so that certain population groups with limited access continue to be included and so that equality and easy access is guaranteed to the entire population using the *Sistema Único de Saúde* (Unified Health System). The importance of developing similar studies in other states where the PNCCU was implemented should also be emphasized, aiming to make

a general assessment of the National Cancer Policy.

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