

Delays in Cervical Cancer Treatment Initiation and Associated Factors in a Hospital-Based Cohort in the Brazilian Western Amazon

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Atrasos no Início do Tratamento do Câncer Cervical e Fatores Associados em uma Coorte Hospitalar da Amazônia Ocidental Brasileira

Retrasos en el Inicio del Tratamiento del Cáncer Cervical y Factores Asociados en una Cohorte Hospitalaria de la Amazonía Occidental Brasileña

Liz Rodrigues de Souza¹; Maria Fernanda de Sousa Oliveira Borges²; Ilce Ferreira da Silva³

ABSTRACT

Introduction: Early diagnosis followed by timely treatment of cervical cancer are essential for better prognosis and survival. **Objective:** To estimate the prevalence of delay in cervical cancer treatment initiation and associated factors in women diagnosed and treated in Rio Branco-Acre between 2012 and 2017. **Method:** Cross-sectional study of a hospital cohort involved women with cervical cancer treated between 2012 and 2017 in Rio Branco, Acre. The time in days from diagnosis to the first treatment was categorized according to the Brazilian law. Student's t and Kruskal-Wallis tests analyzed continuous variables, while categorical variables were evaluated using X2-Pearson and Fisher tests, with a 5% significance level. Crude and adjusted prevalence ratios (OR) were estimated by Poisson regression with robust variance, with 95% CI. **Results:** The median time between diagnosis and first treatment was 39 days, ranging from 81 days for surgical treatment to 29 days for isolated radiotherapy. The prevalence of delay in treatment initiation was 34%, and the factors associated with the delay included being aged >40 years, waiting >30 days for specialist consultation, and first surgical treatment. The radiotherapy with/without brachytherapy treatment protocol and stages IIIB-IVA were inversely associated with delay. **Conclusion:** Delay in cervical cancer treatment initiation in Acre was shorter than in other regions of the country. Age >40 years, waiting >30 days for a specialist consultation were positively associated with delay, while advanced stages were inversely associated.

Key words: Uterine Cervical Neoplasms; Women's Health; Time-to-Treatment; Treatment Delay/statistics & numerical data.

RESUMO

Introdução: O diagnóstico precoce seguido de tratamento em tempo oportuno do câncer cervical são fundamentais para melhor prognóstico e sobrevida. **Objetivo:** Estimar a prevalência do atraso no início do tratamento do câncer cervical e os fatores associados em mulheres diagnosticadas e tratadas em Rio Branco-Acre entre 2012 e 2017. **Método:** Estudo transversal da coorte hospitalar de mulheres com câncer cervical tratadas entre 2012 e 2017 em Rio Branco, Acre. O tempo entre o diagnóstico e o primeiro tratamento foi categorizado conforme a legislação brasileira. Variáveis contínuas foram analisadas pelos testes t de Student e Kruskal-Wallis, enquanto variáveis categóricas foram avaliadas por X2-Pearson e Fisher, com significância de 5%. As razões de prevalência (PR) brutas e ajustadas foram calculadas por regressão de Poisson com variância robusta, com intervalo de confiança de 95%. **Resultados:** O tempo mediano entre o diagnóstico e o primeiro tratamento foi de 39 dias, variando de 81 dias para tratamento cirúrgico a 29 dias para radioterapia isolada. A prevalência de atraso no início do tratamento foi de 34%. Fatores associados ao atraso incluíram idade acima de 40 anos e tempo >30 dias para consulta com especialista e primeiro tratamento cirúrgico. O protocolo de tratamento radioterapia com e sem braquiterapia e estadiamentos IIIB-IVA foram inversamente relacionados ao atraso. **Conclusão:** O atraso no início do tratamento do câncer cervical no Acre foi menor do que em outras localidades do país. Idade >40 anos e esperar >30 dias por consulta com especialista foram fatores positivamente associados ao atraso, enquanto estadiamentos avançados foram inversamente associados.

Palavras-chave: Neoplasias do Colo do Útero; Saúde da Mulher; Tempo para o Tratamento; Atraso no tratamento/estatística & dados numéricos.

RESUMEN

Introducción: El diagnóstico temprano seguido de un tratamiento oportuno del cáncer cervical son fundamentales para un mejor pronóstico y supervivencia. **Objetivo:** Estimar la prevalencia del retraso en el inicio del tratamiento del cáncer cervical y los factores asociados en mujeres diagnosticadas y tratadas en Río Branco, Acre, entre 2012 y 2017. **Método:** Estudio transversal de la cohorte hospitalaria de mujeres con cáncer cervical tratadas en Río Branco, Acre, entre 2012 y 2017. Se categorizó el tiempo entre el diagnóstico y el primer tratamiento según la legislación brasileña. Las variables continuas fueron analizadas con pruebas t de Student y Kruskal-Wallis, y las categóricas con X2-Pearson y Fisher. Se calcularon razones de prevalencia (RP) brutas y ajustadas mediante regresión de Poisson con varianza robusta, con intervalos de confianza del 95%. **Resultados:** La mediana del tiempo mediano entre el diagnóstico y el primer tratamiento fue de 39 días, con variaciones entre 81 días para cirugía y 29 días para radioterapia aislada. La prevalencia del retraso fue del 34%. Factores asociados al retraso incluyeron edad >40 años, espera >30 días para consulta con especialista y tratamiento quirúrgico. La radioterapia con/sin braquiterapia y los estadios IIIB-IVA estuvieron inversamente relacionados con el retraso. **Conclusión:** El retraso en el inicio del tratamiento del cáncer cervical en Acre fue menor que en otras regiones del país. Edad >40 años, esperar >30 días para consulta con especialista y cirugía como primer tratamiento estuvieron asociados positivamente con el retraso, mientras que los estadios avanzados estuvieron inversamente asociados.

Palabras clave: Neoplasias del Cuello Uterino; Tiempo de Tratamiento; Salud de la Mujer; Retraso en el Tratamiento/estadística & datos numéricos.

^{1,2}Universidade Federal do Acre (UFAC), Programa de Pós-Graduação em Saúde Coletiva. Rio Branco (AC), Brasil. E-mails: lizrodriguesouza@gmail.com; maria.borges@ufac.br. Orcid iD: <https://orcid.org/0009-0009-0539-0558>; Orcid iD: <https://orcid.org/0000-0002-5536-6507>

³UFAC. Rio Branco (AC), Brasil. Fundação Oswaldo Cruz (Fiocruz), Escola Nacional de Saúde Pública Sérgio Arouca (Ensp). Rio de Janeiro (RJ), Brasil. E-mail: ilce23@hotmail.com. Orcid iD: <https://orcid.org/0000-0002-7134-3030>

Corresponding author: Ilce Ferreira da Silva. Ensp/Fiocruz. Rua Leopoldo Bulhões, 1480 – 8º andar, sala 821 – Manguinhos. Rio de Janeiro (RJ), Brasil. CEP 21041-210. E-mail: ilce23@hotmail.com



INTRODUCTION

Cervical cancer is considered a serious public health problem, accounting for approximately 660,000 new cases and 348,000 deaths in women worldwide in 2022¹. In Brazil, incidence rates vary by region, the highest incidence and mortality rates were registered in the North and Northeast regions^{2,3}. According to the Population-Based Cancer Registry (PBCR), incidence rates varied from 7.43 in Porto Alegre-RS (2013 to 2017) to 10.95 in Curitiba-PR (2014 to 2018) in the South region, while in the North region, the incidence varied from 28.98 in Amapá-AP (2016) to 38.25 in Manaus-AM (2012 to 2016)⁴. In 2020, cervical cancer was the most common cancer among women in the same region, accounting for 21% of all primary neoplasms⁴. In the state of Acre (Western Brazilian Amazon), the incidence of this neoplasm, the second most common, was 41.3/100,000 women between 2007 and 2009⁵.

Cervical cancer mortality can be influenced by sociodemographic, clinical-epidemiological factors, tumor characteristics (staging at diagnosis, histological type, tumor grade, among others), and treatment type⁶⁻⁸, besides structural and organizational aspects of access to diagnosis and waiting time between diagnosis and treatment initiation^{8,9}. Conservative surgical procedures are preferred for young patients in stages IA2 and IB1 to preserve ovaries and hormonal reproductive functions^{7,10,11} and adjuvant treatments vary based on risk, medical history, and cancer size¹⁰⁻¹². Advanced stages need more aggressive treatment.

The literature divides delays in treatment initiation into ‘healthcare-related delays’ and ‘patient-related delays’¹³⁻¹⁵. The first would be associated with difficulties or lack of access to health services, poor quality of services provided, long waiting periods for treatment initiation and long waiting lists, and the second, with low education, lack of resources for transportation and other sociodemographic factors, poor knowledge about the disease, seeking a second or third opinion, comorbidities, previous experiences, and family history^{13,16}.

Although some studies have not identified a significant association between delay in treatment initiation of cervical cancer and lower survival rates¹⁷⁻¹⁹, evidence indicates that a period over 60 days between the diagnosis and the treatment initiation could lead to a worse prognosis compared to women who were treated within 60 days after diagnosis²⁰⁻²². Furthermore, the lack of association may be related to non-standardized waiting time among the studies^{13,23}, the variation staging at diagnosis, small sample size, and different study bases (hospital *vs.* population)¹¹.

While international studies contribute to the understanding of care intervals – the time between

diagnosis and the first specialist consultation or treatment initiation – they often do not provide a standardized definition of what a “delay” is in oncological care. Although they offer valuable references for understanding time management and structuring care pathways, their findings are not directly comparable^{13,14,18,24}.

In contrast, Brazil has a legally established benchmark for oncological care: Law number 12,732/2012 ensures free cancer treatment through the National Health System (SUS) that should begin within 60 days of diagnosis²⁵. This legal clarity not only provides a normative standard for evaluating access to care but also enables the development of studies that consistently define what constitutes a treatment delay.

However, recent studies suggest that the interval between diagnosis and treatment initiation still varies according to the patient’s residence and type of tumor, often exceeding the mandated deadline^{21,25-28}. Among these studies, the prevalence of delays varied from 65.1% in Bahia to 92.8% in Rio de Janeiro^{28,29}. This variation may be due to differences in study bases (hospital *vs.* population), which may compromise the results due to sample size and representativeness³⁰. In addition, oncology service organization varies among states and regions, affecting the staging at diagnosis and the prevalence of delays^{21,29,31}.

Moreover, a population-based study revealed that over 70% of women diagnosed with cervical cancer in the North region initiated treatment more than 60 days after diagnosis. This high percentage remained stable until 2018 and only declined to 60% in 2020³². These findings reinforce the disparities in access to cancer care across regions and demonstrate the need for localized investigations to better understand structural and systemic barriers in different parts of the country.

Only one of these studies assessed the factors associated with the delay in cervical cancer treatment initiation²⁸, and none of them was conducted in the Western Brazilian Amazon. Therefore, this study aims to estimate the prevalence of the delay in cervical cancer treatment initiation and associated factors in women diagnosed and treated in Rio Branco-Acre, Western Brazilian Amazon, between 2012 and 2017.

METHOD

This is a cross-sectional study based on a cohort of women with cervical cancer treated from 2012 to 2017 in all hospital units authorized to provide oncological care in the city of Rio Branco, Acre.

Women diagnosed with cervical cancer treated between January 1, 2012, and December 31, 2017 at the High Complexity Oncology Unit (Unacon) – “*Hospital de Câncer de Acre*” – and at “*Hospital Santa Juliana*” were

eligible for this study. Unacon is the SUS reference state unit for oncological care in Acre and the only health facility providing radiotherapy treatment in the state. “Hospital Santa Juliana” is the reference private health network for gynecological surgeries.

Women eligible for the study were those diagnosed with primary cervical cancer according to the International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD 10)³³, codes C53, C53.0, C53.1, C53.8, and C53.9. Eligible women were identified from Unacon’s Cancer Hospital Registry databases and by evaluating the medical records of each woman who underwent gynecological surgery at “Hospital Santa Juliana”. The diagnosis was confirmed by their histopathological results.

Exclusion criteria were women whose treatment protocol was defined and implemented outside Rio Branco, who presented tumors other than epithelial, those who had neoplasms in a second primary site, pregnant women who waited until the end of pregnancy to start treatment, and those at stage IVB because the treatment was palliative and not curative. Thus, among the 480 women identified according to ICD C53 in the hospitals’ databases, 54 (11.25%) were excluded. Of the 426 patients included in the study, there were 23 losses (5.3%). Thus, the study population consisted of 403 women with cervical cancer (Figure 1).

Data were extracted from physical medical records by a trained nurse, with a standardized form developed for this purpose, with information covering socioeconomic and demographic data, clinical history, family history of cancer, tumor characteristics, treatment performed, diagnostic data, start and end data for each treatment implemented.

Treatment and staging were found in patient records, with the stage following the recommendations of the International Federation of Gynecology and Obstetrics (FIGO)¹⁰. Radiotherapy and chemotherapy procedures were performed at Unacon, based on the treatment plan established during the initial consultation with a specialist. In case of a defective radiation device, these patients were referred through the Out-of-Home Treatment (OHT) program for treatment at another institution, and returned to Unacon to continue subsequent treatments or post-treatment follow-up.

Since Unacon has no surgical center, patients in the early stage of diagnosis were referred for surgery outside of its facilities. The reference surgical center for oncological surgeries is SUS’ *Hospital de Clínicas do Acre* (also known as FUNDHACRE – *Fundação Hospital Estadual do Acre*) of which Unacon is part of the hospital complex. For surgeries performed at “Hospital Santa Juliana”, of the 448 women who underwent hysterectomy procedures between 2012 and 2017, only three were diagnosed with cervical cancer, and all three were being followed-up at Unacon.

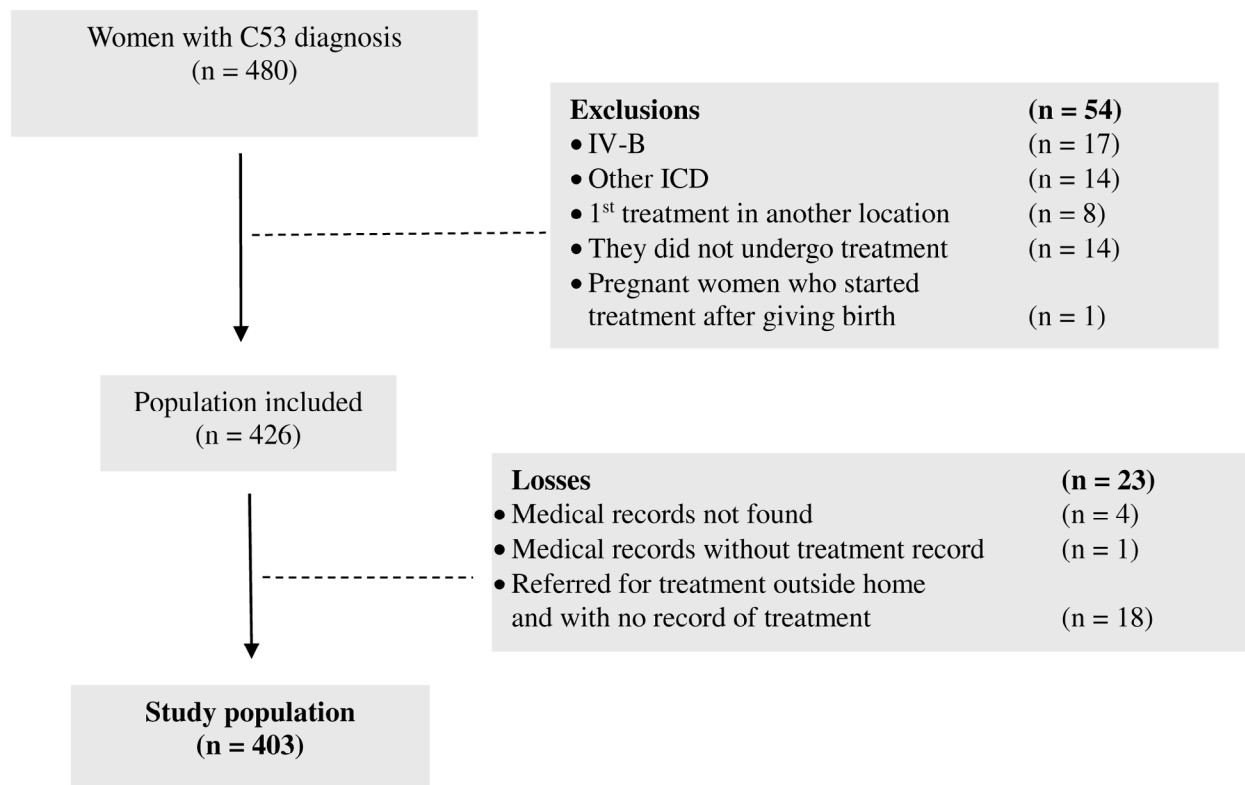


Figure 1. Eligibility flowchart of the study population in Rio Branco, Acre (2012 to 2017)



The dependent variable was defined as the waiting time (in days) between the date of diagnosis and the date of the first treatment, analyzed as a continuous variable and then categorized into ≤ 60 days and > 60 days, according to Law 12,732/2012²⁵.

A time-related variable was derived from three specific dates collected from medical records: the diagnosis date, defined as the date of histopathological confirmation; the specialist consultation date is the first appointment with an oncology specialist; and the treatment initiation date is the date of the first therapeutic procedure (surgery, radiotherapy, or chemoradiotherapy).

Based on these dates, two time intervals were calculated: the first (T1) refers to the number of days between diagnosis and the first specialist consultation, categorized as <30 days and ≥ 30 days; the second (T2) corresponds to the interval between diagnosis and treatment initiation, categorized as <60 days, 60–90 days, and >90 days, and analyzed both as a continuous and a categorical variable.

The independent variables included sociodemographic and economic characteristics (age at admission, residence, skin color, education level, and marital status), lifestyle habits (smoking and alcohol use), family history of cancer, clinical history/tumor characteristics (comorbidities, histological type, FIGO (International Federation of Gynecology and Obstetrics) stage¹⁰), treatment performed (surgery only; surgery + radiation; radiation only; chemoradiotherapy) and OHT, which refers to situations where women were referred to other SUS network units to carry out part of the treatment due to defects and maintenance in the radiation device.

Descriptive analyses were performed using frequency distributions of variables according to the type of treatment received. Percentage differences were assessed using Pearson's Chi-square test (χ^2) and Fisher's tests, considering a significance level of 5%. Waiting times (between diagnosis and first specialist consultation and diagnosis and treatment initiation) were analyzed both as continuous and categorical variables, assigning them the times of ≤ 30 , 31–60, >60 and ≤ 60 , 61–90, >90 days. The distribution of time intervals according to the first treatment and stage of diagnosis were analyzed using the Kruskal-Wallis and Mann-Whitney tests, both with a significance level of 5%. The prevalence of delay in treatment initiation was categorized for each variable according to the stage at diagnosis. Crude prevalence ratios (PR) were then estimated for all stages and stratified by stage, with 95% confidence intervals, using Poisson regression with robust variance^{34,35}. Multiple Poisson regression models were performed to estimate adjusted prevalence ratios for delay in treatment initiation

according to the independent variables and their respective 95%CI using the Wald test. Biological relevance and statistical significance in the crude analyses were used as inclusion criteria in the final model. The final model underwent residual analysis and assessment of model fit.

All analyses were performed using the SPSS³⁶ statistical package (version 20.0, SPSS, Chicago, IL).

The Ethics Committee of "Universidade Federal do Acre" approved the study, report number 6,409,404 on October 6th, 2023, in compliance with Directive 466/2012 of the National Health Council, CAAE (submission for ethical review) 74178923.1.0000.5010³⁷.

RESULTS

Of the 403 women included, 72% were aged 40 years or older and 54.3% lived outside Rio Branco. The majority self-identified as Brown (80.9%), had completed elementary school (40.5%), were married (47.8%) and had a history of smoking (62.5%). 94.3% were diagnosed with squamous cell carcinoma and 78.4% with late stage (IIB or higher) according to histological and staging characteristics. Of the women included in the study, 46.7% underwent some part of the radiation treatment outside their home through referral by "Hospital de Câncer do Acre" (Unacon) to another public institution due to problems with the radiation equipment. The first specialist consultation within a period of less than or equal to 30 days from the date of diagnosis was observed in 69.7% of the women. In relation to patients who underwent exclusive surgery, those who were treated with chemoradiation were at more advanced stage of the disease (96.3%) (Table 1).

The median time between diagnosis and the first specialist consultation was 18 days, 23 days for surgery (alone or combined with radiation) and 17 days for radiotherapy and chemoradiation. The stages at diagnosis varied between 22 days for IA1 and IIA2 and 17 days for IIIB and IVA while the majority of the women (66%) started treatment within the 60-day range. A median of 39 days was identified, with 81 days of time interval for surgical treatment, 29 days for treatment with radiation alone and 36 days for treatment with chemoradiation. According to the stages, it is possible to identify a median of 84 days for initial stages (IA1 to IIA2), and 39 and 28 days for more advanced stages (IIB-IIIA and IIIB-IVA, respectively) (Table 2).

The prevalence of delay in treatment initiation was less than 50% for all variables evaluated, considering all stages, except for the variables time between diagnosis and first consultation with a specialist, in which the prevalence was 65.6% for times greater than 30 days, first surgical

Table 1. Distribution of characteristics of a cohort of women diagnosed with cervical cancer and treated in Rio Branco, Acre (2012 to 2017)

Characteristics	Treatment Protocol					X ² Test <i>p-value</i>
	Total*	Exclusive surgery	Surgery + Radiation**	Exclusive radiation***	Chemoradiation	
	N (%)	N (%)	N (%)	N (%)	N (%)	
	403 (100)	48 (100)	29 (100)	139 (100)	187 (100)	
Age at admission						0.037 ^a
<40	113 (28.0)	14 (29.2)	11 (37.9)	27 (19.4)	61 (32.6)	
≥40	290 (72.0)	34 (70.8)	18 (62.1)	112 (80.6)	126 (67.4)	
Residence						0.384 ^a
Rio Branco	184 (45.7)	26 (54.2)	16 (55.2)	60 (43.2)	82 (43.9)	
Others	219 (54.3)	22 (45.8)	13 (44.8)	79 (56.8)	105 (56.1)	
Skin color						0.804 ^b
Brown	263 (80.9)	36 (83.7)	19 (86.4)	81 (78.6)	127 (80.9)	
Others	62 (19.1)	7 (16.3)	3 (13.6)	22 (21.4)	30 (19.1)	
Education						0.000 ^a
> High school	74 (23.8)	14 (37.8)	10 (50.0)	12 (11.2)	38 (25.9)	
Elementary school	126 (40.5)	13 (35.1)	6 (30.0)	41 (38.3)	66 (44.9)	
Illiterate	111 (35.7)	10 (27.0)	4 (20.0)	54 (50.5)	43 (29.3)	
Marital status						0.002 ^b
Married/stable union	183 (47.8)	29 (60.4)	16 (59.3)	46 (35.7)	92 (51.4)	
Widow	60 (15.7)	5 (10.4)	3 (11.1)	35 (27.1)	17 (9.5)	
Divorced/separated	28 (7.3)	1 (2.1)	1 (3.7)	11 (8.5)	15 (8.4)	
Single	112 (29.2)	13 (27.1)	7 (25.9)	37 (28.7)	55 (30.7)	
Comorbidities						0.000 ^a
No	209 (59.0)	19 (55.9)	19 (79.2)	48 (39.3)	123 (70.7)	
Yes	145 (41.0)	15 (44.1)	5 (20.8)	74 (60.7)	51 (29.3)	
Smoking history						0.020 ^a
No	132 (37.5)	12 (37.5)	12 (48.0)	33 (26.8)	75 (43.6)	
Yes	220 (62.5)	20 (62.5)	13 (52.0)	90 (73.2)	97 (56.4)	
Alcohol history						0.101 ^a
No	182 (53.4)	16 (51.6)	13 (52.0)	72 (62.6)	81 (47.6)	
Yes	159 (46.6)	15 (48.4)	12 (48.0)	43 (37.4)	89 (52.4)	
Histological type						0.140 ^b
Squamous cell carcinoma	380 (94.3)	44 (91.7)	25 (86.2)	131 (94.2)	180 (96.3)	
Adenocarcinoma	23 (5.7)	4 (8.3)	4 (13.8)	8 (5.8)	7 (3.7)	
Stage						0.000 ^b
IA1 – IIA2	87 (21.6)	48 (100)	13 (44.8)	19 (13.7)	7 (3.7)	
IIB – IIIA	75 (18.6)	0 (0.0)	4 (13.8)	25 (18.0)	46 (24.6)	
IIIB - IVA	241 (59.8)	0 (0.0)	12 (41.4)	95 (68.3)	134 (71.7)	
OHT						0.000 ^a
No	215 (53.3)	48 (100)	23 (79.3)	75 (54.0)	69 (36.9)	
Yes	188 (46.7)	0 (0.0)	6 (20.7)	64 (46.0)	118 (63.1)	
Time to first specialist consultation						0.403 ^a
< 30 days	281 (69.7)	31 (64.6)	17 (58.6)	101 (72.7)	132 (70.6)	
> 30 days	122 (30.3)	17 (35.4)	12 (41.4)	38 (27.3)	55 (29.4)	

*Totals may vary due to missing values; **Radiation with or without chemotherapy; ***Radiation with or without brachytherapy; ^aChi-square test; ^bFisher's exact test.



Table 2. Distribution of the time interval between women diagnosed with cervical cancer and treated in Rio Branco, Acre, according to the first treatment, stage at diagnosis and part of the treatment through OHT (2012 to 2017)

Estimate	Treatment protocol				Stage at diagnosis				OHT	
	Surgery**		Exclusive Radiotherapy***		Chemoradiation		X ² Test		X ² Test	
	Total* N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	IA1-IIA2 N (%)	IIB-III A N (%)	IIIB-IVA N (%)	Yes N (%)
Total	403 (100)	77 (100)	139 (100)	187 (100)	87 (100)	75 (100)	241 (100)	215 (100)	188 (100)	
Time between diagnosis and first specialist assessment										
Mean (SD)	33.3 (52.5)	47.1 (7.4)	33.0 (5.0)	27.9 (2.8)	0.050 ^b	43.9 (6.7)	30.2 (6.2)	30.5 (3.0)	0.056 ^b	27.4 (31.7)
Median	18	23	17	17		22	19	17		18
Min - Max	0 - 456	2 - 322	0 - 456	0 - 403		0 - 322	0 - 456	0 - 403		0 - 280
≤ 30	281 (69.7)	48 (62.3)	101 (72.7)	132 (70.6)	0.201 ^a	54 (62.1)	54 (72.0)	173 (71.8)	0.221 ^a	135 (71.8)
31-60	67 (16.6)	12 (15.6)	22 (15.8)	33 (17.6)		17 (19.5)	15 (20.0)	35 (14.5)		34 (18.1)
> 60	55 (13.6)	17 (22.1)	16 (11.5)	22 (11.8)		16 (18.4)	6 (8.0)	33 (13.7)		19 (10.1)
Time between diagnosis and first treatment initiation										
Mean (SD)	63.6 (87.6)	112.3(16.9)	53.6 (5.8)	51.0 (3.9)	0.000 ^b	119.6 (15.1)	57.8 (7.6)	45.3 (3.4)	0.000 ^b	67.5 (105.9)
Median	39	81	29	36		84	39	28		41
Min - Max	0 - 1087	0 - 1087	1 - 457	1 - 404		0 - 1087	0 - 457	0 - 404		0 - 384
≤ 60	266 (66.0)	32 (41.6)	103 (74.1)	131 (70.1)	0.000 ^a	33 (37.9)	53 (70.7)	180 (74.7)	0.000 ^a	124 (66.0)
61-90	58 (14.4)	11 (14.3)	19 (13.7)	28 (15.0)		14 (16.1)	11 (14.7)	33 (13.7)		29 (15.4)
> 90	79 (19.6)	34 (44.2)	17 (12.2)	28 (15.0)		40 (46.0)	11 (14.7)	28 (11.6)		35 (18.6)

*Totals may vary due to missing values; **Surgery only or combined with radiation (with or without chemotherapy); ***Radiation with or without brachytherapy. ^aChi-square test; ^bKruskal-Wallis test; ^cMann-Whitney test.



treatment, in which the prevalence was 58.4% and first radiation treatment, where the delay was greater in 57.7% of women who did not undergo radiotherapy treatment at first (Table 3).

Overall, age > 40 years (PR= 1.83; 95%CI: 1.25-2.69), smoking history (PR= 1.42; 95% CI: 1.02-1.98), alcohol use history (PR= 1.51; 95% CI: 1.12-2.03), time to first consultation >30 days (PR= 3.23; 95% CI: 2.48-4.21) and first surgical treatment (PR= 2.07; 95% CI: 1.60-2.67) were positively associated with delayed treatment initiation, while first radiotherapy treatment (PR= 0.49; 95% CI: 0.37-0.63) was negatively associated with delayed treatment initiation. Women at IA1 to IIA2 who underwent their first surgical treatment were positively associated with delays (PR= 1.87; 95% CI: 1.12-3.12), while the same group of women who underwent their first radiotherapy treatment were negatively associated with delay (PR= 0.53; 95% CI: 0.32-0.88). At more advanced stages (IIIB to IVA), women aged >40 years (PR= 2.61; 95%CI: 1.19-5.74), with a history of alcohol use (PR= 1.78; 95%CI: 1.34-2.80) and waiting time between diagnosis and first consultation >30 days (PR= 6.07; 95%CI: 3.78-9.75) were positively associated with delays in treatment initiation (Table 3). It should be noted that the stratification by stage in Table 3, although important for understanding specific patterns of delay, resulted in reduced sample sizes within each stratum, which may have compromised the precision of the estimates, as indicated by the wider 95% confidence intervals.

In Table 4, delays were independently associated with age >40 years (PR 1.75; 95%CI 1.26-2.42), time >30 days to first specialist consultation (PR 2.94; 95%CI 2.27-3.81), and stage IIIB-IVA (PR 0.51; 95%CI 0.35-0.76).

DISCUSSION

In Rio Branco, Acre, women with cervical cancer stages IA1 to IVA experienced a median time of 39 days between diagnosis and treatment initiation, with a 34% prevalence of delays (>60 days). These results comply with the 60-day range (law 12,732/2012) to initiate treatment. Factors positively associated with treatment delays included age >40 years and waiting >30 days for specialist consultation. Conversely, advanced stages IIIB-IVA were factors negatively associated with delays. The waiting times for treatment initiation observed in this study suggest that the oncology service in Rio Branco is more organized and better at complying with the legal deadlines for oncological treatment compared to other regions in Brazil. For instance, in Rio de Janeiro, the median waiting time is 114 days, with a delay prevalence (>60 days) of 92.8% for the first treatment²⁸. In another

study conducted in Paraná, the prevalence of delay was 62.2%³⁸. This result is surprising given the high incidence and mortality indicators in the North compared to the Southeast and South regions, respectively.

During the period studied, there were reports of defective radiotherapy equipment requiring skilled servicing. In such circumstances, patients were referred to other reference centers of the SUS network to continue treatment via OHT and returned to continue therapy and follow-up. Despite these inconveniences and the bureaucracy involved in the process, radiotherapy treatment proved to be a protective factor against delays in treatment initiation, with a crude prevalence ratio of 0.49 (95%IC 0.37-0.63). Although it did not reach statistical significance in the adjusted model, it remained a protective factor.

However, the scarcity of skilled equipment servicing in Acre often negatively influences this process. Patients wouldn't need to be referred if timely preventive and corrective equipment maintenance were available, in addition to reducing costs for the institution. Thus, women referred to OHT had a median of 41 days to treatment initiation, which was longer than the 35 days for those not referred, but still within the recommended 60-day timeframe.

Other results of this study, as the high percentage of advanced-stage diagnoses and the effect of surgery on treatment initiation delay, seem to corroborate findings from studies conducted in other regions of the country. In Rio Branco, the frequency of advanced staging at diagnosis (IIB-IVA) was considered high (78.4%) compared to Belém, PA (30.7%) in the North³⁹, Rio de Janeiro (67.7%) in the Southeast²⁸, Porto Alegre (77.3%) and Paraná (73.9) in the South regions^{26,38}. In this context, most women with advanced-stage cervical cancer (94.93%) received treatment with exclusive radiation or chemoradiation, with very low median waiting times of 29 and 36 days, respectively. In contrast, the median waiting time for surgical treatment was 81 days. This extended waiting time aligns with findings from a study conducted in Rio de Janeiro, where women who underwent surgery had a median time of 115 days between diagnosis and treatment initiation²⁸. Another study conducted in Paraná shows that 71% of women submitted to surgery as their first treatment experienced a delay of more than 60 days²⁶.

Although the mean prevalence of delays in treatment initiation was considered low in Rio Branco, these findings may raise concerns. The survival rate of women treated at early stages is higher than that of women treated at locally advanced and advanced stages^{17,19,40,41}. Delays in treatment initiation for early-stage patients who usually undergo surgery (62.1%) could negatively impact the survival of



Table 3. Prevalence of delay in treatment initiation* and prevalence ratio according to stage at diagnosis in a cohort of women diagnosed with cervical cancer and treated in Rio Branco, Acre, between 2012 and 2017

Characteristics	All stages			IA1 - IIA2			IIB - IIIA			IIIB - IVA		
	Prevalence	PR (95%CI)	p-value	Prevalence (%)	PR (95%CI)		Prevalence (%)	PR (95%CI)		Prevalence (%)	PR (95%CI)	
Age at admission	(%)			(%)			(%)			(%)		
< 40	21.2	1		47.8	1		20.7	1		11.5	1	
≥ 40	39.0	1.83 (1.25-2.69)	0.002	67.2	1.40 (0.72-2.72)		34.8	1.68 (0.65-4.29)		30.0	2.61 (1.19-5.74)	
Residence												
Rio Branco	36.4	1		53.5	1		34.3	1		30.2	1	
Others	32.0	0.87 (0.66-1.15)	0.347	70.5	1.31 (0.93-1.84)		25.0	0.72 (0.36-1.47)		21.5	0.71 (0.46-1.09)	
Skin color												
Brown	33.8	1		63.3	1		25.0	1		25.2	1	
Not Brown	38.7	1.14 (0.80-1.63)	0.459	63.6	1.00 (0.61-1.63)		60.0	2.40 (1.21-4.73)		26.8	1.06 (0.59-1.89)	
Education												
High school and college	31.1	1		54.2	1		15.4	1		21.6	1	
Illiterate and elementary school	36.3	1.16 (0.79-1.70)	0.423	64.4	1.19 (0.77-1.82)		36.6	2.37 (0.62-9.05)		27.8	1.28 (0.66-2.50)	
Comorbidities												
No	35.4	1		68.4	1		32.5	1		26.7	1	
Yes	36.6	1.03 (0.77-1.36)	0.825	59.4	0.86 (0.60-1.24)		33.3	1.02 (0.51-2.05)		29.1	1.08 (0.70-1.68)	
Smoking history												
No	26.5	1		52.0	1		25.9	1		18.8	1	
Yes	37.7	1.42 (1.02-1.98)	0.037	63.6	1.22 (0.79-1.89)		31.7	1.22 (0.56-2.66)		31.1	1.65 (0.98-2.79)	
Alcohol history												
No	27.5	1		58.6	1		26.5	1		20.2	1	
Yes	41.5	1.51 (1.12-2.03)	0.007	60.5	1.03 (0.69-1.53)		34.4	1.29 (0.62-2.71)		36.0	1.78 (1.13-2.80)	
Histological type												
Squamous cell carcinoma	33.9	1		63.3	1		29.6	1		25.2	1	
Adenocarcinoma	34.8	1.02 (0.57-1.82)	0.934	50.0	0.79 (0.38-1.61)		25.0	0.84 (0.14-4.79)		27.3	1.08 (0.40-2.91)	
Time to first specialist consultation												
≤ 30 days	20.3	1		55.6	1		16.7	1		10.4	1	
> 30 days	65.6	3.23 (2.48-4.21)	0.000	72.7	1.30 (0.95-1.79)		61.9	3.71 (1.87-7.36)		63.2	6.07 (3.78-9.75)	
1 st surgical treatment												
No	28.2	1		38.5	1		31.0	1		26.2	1	
Yes	58.4	2.07 (1.60-2.67)	0.000	72.1	1.87 (1.12-3.12)		-	-		8.3	0.31 (0.04-2.10)	
1 st treatment radiotherapy												
No	57.7	1		72.1	1		-	1		8.3	1	
Yes	28.3	0.49 (0.37-0.63)	0.000	38.5	0.53 (0.32-0.88)		31.4	-		26.2	3.14 (0.47-20.79)	

* <60 days or >60 days.



Table 4. Crude and adjusted prevalence ratios (PR) for delay in treatment initiation* in a cohort of women diagnosed with cervical cancer in Rio Branco, Acre, between 2012 and 2017

	Crude PR (95% CI)	Adjusted PR ^a (95% CI)
Age at admission		
≤40	1	1
>40	1.83 (1.25-2.69)	1.75 (1.26-2.42)
Time to first specialist consultation		
≤ 30 days	1	1
> 30 days	3.23 (2.48-4.21)	2.94 (2.27-3.81)
Treatment protocol		
Surgery**	1	1
Radiation Only or Chemoradiation	0.48 (0.37-0.62)	0.80 (0.54-1.19)
Stage		
IA1 – IIA2	1	1
IIB – IIIA	0.47 (0.32-0.69)	0.64 (0.40-1.03)
IIIB – IVA	0.40 (0.31-0.53)	0.51 (0.35-0.76)

*≤60 days or >60 days; **Surgery only or combined with radiation (with or without chemotherapy). ^aAdjusted by all other variables in the model.

this subgroup in Rio Branco. However, this result is similar to those observed in cities in more developed regions, as Rio de Janeiro (Southeast) and Paraná (South), where the prevalence of delays in treatment initiation among women undergoing surgery ranged from 79.4% to 71%, respectively^{26,28}.

These findings contrast with those of a population-based study³² which reported a higher prevalence of treatment delays in the North region, with over 70% of women initiating treatment in 60+ days after diagnosis. This high percentage remained stable from 2013 to 2018 and only declined to around 60% in 2020. Although that study provides important population-level insights, the estimates were based on aggregated data and might be overestimated due to repeated counts of procedures rather than individual patients. Moreover, all Northern states were grouped in the analysis, disregarding structural and organizational differences in health service provision across the region. By comparison, the present study employed primary data collection from medical records and histopathological reports, allowing more accurate and individualized estimates of treatment delays in Acre. These findings, based on patient-level trajectories, portray a more accurate picture of the situation in Rio Branco and underscore the value of localized studies for regional health planning.

In this context, compared to surgical treatment, it was observed that in Rio Branco, treatments with exclusive radiation and chemoradiation were protective factors against delays in treatment initiation, as opposed to a study conducted in Rio de Janeiro, where surgical treatment was shown to be a protective factor against delays in treatment initiation²⁸. This result can be

explained by the fact that, in the state of Acre, a single reference center accredited by SUS (Unacon) located in the capital, performs oncological treatment of cervical neoplasms using external radiation (teletherapy), internal radiation (brachytherapy), and chemotherapy.

In contrast, surgical treatments are performed outside Unacon based on referral and counter-referral systems. After surgical treatment, patients return to Unacon for post-treatment follow-up. In the study conducted in Rio de Janeiro, surgical treatments were performed at the institution where the patient was enrolled, while radiotherapy treatments rely on the regulatory system for referral. Consequently, the likelihood of delays in chemoradiation treatment initiation for patients in Rio de Janeiro was 1.84 times higher compared to those who underwent surgical treatment²⁸.

Therefore, Brazilian bureaucratic processes for regulating referrals, planning surgeries, availability of vacancies, and waiting lists for surgical procedures could partially explain the delays in surgical treatment initiation observed in Rio Branco. To reduce the waiting time to start treatment, oncology care centers need a structure that allows the performance of all treatments for patients with cervical cancer, avoiding the referral through regulatory systems. Additionally, evidence suggests a subjective influence of health professionals, who may prioritize patients with more severe signs and symptoms, as intense bleeding and pain, instead of those in the early stages of the disease^{10,12}.

A delay of more than 30 days between diagnosis and the first consultation with a specialist was independently associated with delayed treatment initiation. The



prevalence ratio for this delay was 3.23 (95% CI 2.48-4.21), compared to those who had their first specialist consultation within 30 days. This prolonged time between diagnosis and the first specialized care reflects the quality of the health services offered and provided in the health unit^{13-5,42}. On the other hand, delays may result from structural problems, as the geographical distance of the health unit where treatment is offered and the availability of transportation. Non-structural problems, as individual factors of the patient and the doctor, may also contribute^{8,16,42,43}.

The variable “time to first specialist consultation” was included to explore its association with delayed treatment initiation, despite sharing the same reference point (diagnosis date) as the outcome. While this temporal overlap limits the independence between the variables, the analysis was conducted cautiously and without the intention of establishing causality. This choice aimed to highlight potential delays in different stages of the care pathway and to identify systemic bottlenecks that may contribute to treatment delays.

Thus, in the present study, women aged 40 or older had a prevalence ratio of 1.83 for delays in treatment initiation, compared to those under 40, which indicates an 83% higher likelihood of experiencing delays. It is also worth highlighting that 62.5% of this cohort had a history of smoking, and 46.6% had a history of alcohol use. In crude analyses, both factors were associated with delays in treatment initiation, with prevalence ratios of 1.42 and 1.51, respectively.

To the best existing knowledge, this groundbreaking study is the first in the Western Brazilian Amazon to describe the waiting time in the therapeutic trajectory for women diagnosed with cervical cancer at stages IA1 and IVA. It stands out due to its meticulous data collection from all medical records of women diagnosed with cervical cancer and treated at hospitals in Rio Branco, Acre. The diagnosis and treatment data were confirmed through histopathological reports and medical records, ensuring the utmost accuracy and reliability of the findings.

In addition, the study evaluated the role of the OHT program in delays in treatment initiation, which is a very relevant factor for a state as isolated as Acre, further to the low percentage of patient and data losses, reducing the risk of selection bias and increasing its validity.

Finally, considering that the Unacon is the only oncology treatment center of SUS in the entire state of Acre that offers radiotherapy treatment and that “Hospital Santa Juliana” is the private reference hospital for gynecological surgeries in the city of Rio Branco, the population of women with cervical cancer in this study could approximately represent the entire state of Acre.

The study limitations are inherent to retrospective studies based on data collection from medical records. Among these, the lack of information about the reality of women at the time of treatment may have contributed to delays, as socioeconomic conditions, lack of knowledge of the clinical condition, or geographical limitations for health monitoring. Another limitation was the lack of information before diagnosis, as the screening history of these women, which is generally done in primary care. Even with the computerization of data in health institutions, including SUS, the systems are not interconnected, preventing access to basic information and previous follow-up of patients.

CONCLUSION

When evaluating the population, the time between diagnosis and treatment initiation showed a median of 39 days, which is within the law-mandated 60-day in Brazil. However, when stratifying these results by treatment protocols performed and by staging, surgical protocols and initial staging showed medians of 81 and 84 days respectively, outside the recommended period.

Despite the consensus regarding access and treatments in the North region, and the high incidence and mortality rates, Acre surprisingly presents good results of delays in cervical cancer treatment initiation when compared with studies carried out in the South and Southeast regions.

Older ages and the time between diagnosis and the first consultation with a specialist were positively associated with the likelihood of delay, while advanced stages were inversely associated with delay in treatment initiation. The implementation of interconnected information systems would facilitate the construction of the therapeutic pathway from screening to treatment for these women, contributing to wider analysis and new studies. Prospective studies should be conducted to identify and monitor delays related to patient's factors and investigate the effects of delays on treatment response and survival.

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CONTRIBUTIONS

Ilce Ferreira da Silva contributed to the conceptualization and design of the study, supervision, review and writing. Liz Rodrigues de Souza contributed to the analysis, data curation,

supervision and writing. Maria Fernanda de Sousa Oliveira Borges contributed to data curation, supervision and writing. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

DATA AVAILABILITY STATEMENT

Given ethical and confidentiality issues, data can be requested to the corresponding author with reasonable justification.

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