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# Factors contributing to delays in initiation of front-line cervical cancer therapy: disparities in a diverse south Florida population

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## **HIGHLIGHTS**

- ⇒ Treatment initiation of newly diagnosed cervical cancer is affected by multiple factors.
- ⇒ Insurance type contributed to delay in treatment initiation regardless of treatment modality.
- ⇒ Hispanic White and Spanish speaking patients had a lower risk of treatment delay in this predominantly minority population.

#### **ABSTRACT**

**Objective** Delay in initiating cervical cancer treatment may impact outcomes. In a cohort of patients initially treated by surgery, chemoradiation, chemotherapy, or in a clinical trial, we aim to define factors contributing to prolonged time to treatment initiation.

**Methods** Data from patients initiating treatment for cervical cancer at a single institution was abstracted. Time to treatment initiation was defined as the interval from the date of cancer diagnosis to the date of treatment initiation. Poisson regression model was used for analysis.

**Results** Of 274 patients studied, the median time to treatment initiation was 60 days (range 0-551). The median times to initiate surgery (54 days, range 3-96) and chemoradiation (58 days, range 4-187) were not significantly different (relative risk (RR) 1.01, 95% Cl 0.98 to 1.04, p=0.54). The shortest median initiation time was for chemotherapy (47 days: RR 1.13, 95% Cl 1.08 to 1.19. p<0.0001) and the longest was for clinical trial (62 days; RR 1.18, 95% CI 1.12 to 1.24, p<0.0001). Charity care (RR 1.09, 95% CI 1.05 to 1.14, p<0.0001), Medicare or Medicaid (RR 1.10, 95% Cl 1.06 to 1.14, p<0.0001), and self-pay (RR 1.38, 95% Cl 1.32 to 1.45, p<0.0001) delayed treatment initiation more than private insurance. Hispanic White women (RR 0.69, 95% CI 0.66 to 0.73, p<0.0001) had a shorter treatment initiation time compared with non-Hispanic White patients, while Afro-Caribbean/Afro-Latina women (RR 0.86, 95% Cl 0.81 to 0.90, p<0.0001) and African-American patients (RR 1.13, 95% Cl 1.07 to 1.19, p<0.0001) had longer initiation times. Spanish speaking patients did not have a prolonged treatment initiation (RR 0.68, 95% CI 0.66 to 0.71, p<0.0001), though Haitian-Creole speaking patients did (RR 1.07, 95% Cl 1.01 to 1.13, p<0.002). Diagnosis at an outside institution delayed treatment initiation time (RR 1.24, 95% CI 1.18 to 1.30, p<0.0001) compared with diagnosis at the cancer center. **Conclusion** Factors associated with prolonged time to treatment initiation include treatment modality, insurance status, language spoken, and institution of diagnosis. By closely examining each of these factors, barriers

#### WHAT IS ALREADY KNOWN IN THIS TOPIC

⇒ A national study on factors affecting time to treatment initiation in cervical cancer patients receiving primary radiation therapy demonstrated significantly longer times for non-Hispanic Black and Hispanic women. This study examines time to initiate treatment within our institution as it compares to national trends to identify modifiable factors associated with longer initiation times in cervical cancer.

## WHAT THIS STUDY ADDS

⇒ Our study shows factors associated with prolonged time to treatment initiation include treatment modality, insurance status, language, and institution of diagnosis. Our study identified Spanish-only speakers as having a lower risk of treatment delay, likely reflecting the unique ethnic and linguistic composition locally.

# HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings demonstrate the benefits to patient care when appropriate resources for navigating language barriers are in place. The impact of physician and staff demographics, cultural training, and language proficiency on time to treatment initiation may be observed in other areas of large minority populations.

to treatment can be identified and modified to shorten treatment initiation time.

# INTRODUCTION

As the fourth most common cancer among women worldwide, with 604127 new diagnoses and over 300000 deaths in 2020, the impact of cervical cancer is devastating. The incidence is approximately three times higher and mortality seven times higher in



low income countries, highlighting disparities in prevention, early detection, and access to treatment. Although the incidence and mortality are lower in the USA, racial and regional disparities persist in the country. Mortality rates were reported at 2.0 per 100 000 non-Hispanic White women versus 3.4 and 2.6 per 100 000 non-Hispanic Black and Hispanic women, respectively. While the overall 5-year relative survival rate of cervical cancer is 66%, it varies significantly from 78% for non-Hispanic White women younger than 50 years old, to 46% for non-Hispanic Black women 50 years or older. Among cervical cancer survivors, health-related quality of life metrics are poorer among Hispanic and non-Hispanic Black women compared with non-Hispanic White women. Understanding and addressing these disparities are important priorities in gynecologic oncology.

Generally, early-stage cervical cancer is treated by surgery, locally advanced disease by chemoradiation with brachytherapy. and distant metastatic disease with upfront systemic chemotherapy with bevacizumab. The rate of guideline-based care has proven to be significantly lower in Hispanic and non-Hispanic Black women.<sup>6</sup> Time to treatment initiation of front-line therapy has been lengthening for many cancers in recent years.<sup>7-9</sup> This trend may reflect the more widespread use of advanced imaging modalities including magnetic resonance imaging (MRI) or positron emission tomography/computed tomography (PET/CT) scan before treatment initiation. 10 The National Comprehensive Cancer Network recommends such imaging for women diagnosed with cervical cancer. 11 National trends have shown that delays in care disproportionately affect Hispanic and non-Hispanic Black patients, and have been linked to worse outcomes as well as increased patient anxiety and decreased satisfaction with care. 10 12-16

A National Cancer Database (NCDB) study on factors affecting time to initiate treatment in over 14900 cervical cancer patients receiving radiation therapy or chemoradiation demonstrated significantly longer times for non-Hispanic Black and Hispanic women. <sup>10</sup> Our clinical service provides care to a diverse patient population at a county safety net hospital and a National Cancer Institute designated cancer center. The primary purpose of this study was to examine time to initiation of treatment within our institution in order to identify modifiable factors associated with longer initiation times in cervical cancer. Secondarily, we sought to determine whether delays in initiation of treatment influenced progression-free and overall survival.

#### **METHODS**

Institutional review board approval was obtained (IRB #20120351). Using an institutional tumor registry, we identified patients treated for cervical cancer diagnosed from December 2012 to December 2017. Patients receiving all of their frontline therapy at our two institutions were included, and were excluded if they did not. The variables extracted included age, diagnosing institution, treating institution, race/ethnicity, language, insurance, pretreatment workup performed (including examination under anesthesia, PET scan, CT scan of the abdomen/pelvis, and MRI of the pelvis), first treatment modality, International Federation of Gynecology and Obstetrics (FIGO) stage at diagnosis, date, and status at last contact. Treatment response, date of recurrence, subsequent treatments, and

date of death were also included. Race and ethnicity were categorized to capture the nuanced differences that may reflect biases within ethnicities. The categories were self-reported by patients and abstracted from the medical records. Insurance types included private, Medicare, Medicaid, charity care provided by the safety net hospital, and self-pay. To qualify for charity care, patients needed to prove county residency and have a maximum total household income of 300% of the Federal Poverty Guidelines. These requirements remained constant during the study period. Study data were collected and managed using research electronic data capture at the University of Miami. 17 18

Statistical analysis was performed using Statistical Analysis Software version 9.4 (Cary, NC). Time to treatment was calculated as the interval from the date of cancer diagnosis to the first date of first treatment received for newly diagnosed patients. In order to accurately determine the time from diagnosis to the initiation of any treatment, the first treatment modality was defined as the treatment received on the first day of treatment. A Poisson regression model was used to assess association between treatment initiation time and patient characteristics in univariable and multivariable analyses. Outliers and missing data points were excluded. For the most common treatment modalities, surgery and chemoradiation therapy, a subgroup analysis was performed to assess specific factors associated with prolonged initiation time. Cox proportional hazards models were then used to examine the effects of treatment initiation time on progression-free and overall survival.

As the time frame of our study encompassed patients staged using both the 2009 and 2018 staging criteria, patients were restaged using the FIGO 2018 criteria, and the stages were grouped according to the standard of care treatment for each stage. This allowed for sufficient numbers for analysis and accounted for staging criteria differences before and after 2018. Three staging groups were defined: group 1 (IA1, 1A2, IB1, IB2); group 2 (IB3, IIA1, IIA2, IIB, IIIA, IIIB, IVA); and group 3 (IVB). Significant variables on univariable analysis were included for multivariable analysis. All tests were two sided, and significance was set at p<0.05.

# **RESULTS**

A total of 274 patients met the inclusion criteria. Demographic data are summarized in Table 1. Median age at diagnosis was 49 years (range 24–82). Seventy-four patients (27%) were diagnosed at an outside institution and referred for treatment. The majority of patients were treated at the safety net hospital compared with the cancer center (61.3% vs 38.7%). Most patients were Hispanic White (166, 60.6%), followed by Afro-Caribbean/Afro-Latina (42, 15.3%), African American (34, 12.4%), and non-Hispanic White (29, 10.6%). The majority (92.7%) of the patients' primary language was Spanish or English (51.1% Spanish and 41.6% English). Ninetynine patients (36.1%) had either Medicare or Medicaid, 82 (29.9%) had private insurance, 64 (23.4%) had charity care insurance, and 29 patients (10.6%) were self-pay at diagnosis. Overall, the recurrence rate observed in our cohort was 35.4%.

Preoperative workup included PET/CT in 191 (69.7%) patients, pelvic MRI in 84 (30.7%) patients, and exam under anesthesia with or without cystoscopy and proctoscopy in 113 (41.2%) patients. Most patients were treated for local disease, with 105 (38.3%) receiving chemoradiation and

Variable	n=274	%
Median age, years (range)	49 (24–82)	
Diagnosis institution	,	
SNH	139	50.7
NCI CC	61	22.3
OSH	74	27
Treating institution		
SNH	168	61.3
NCI CC	106	38.7
Race/ethnicity		
Non-Hispanic White	29	10.6
Hispanic White	166	60.6
African American	34	12.4
Afro-Caribbean/Afro-Latina	42	15.3
Other	3	1.1
Language		
English	114	41.6
Spanish	140	51.1
Haitian Creole	18	6.6
Other/unknown	2	0.8
Insurance status		
Private	82	29.9
Medicare/Medicaid	99	36.1
County charity care	64	23.4
Self-pay	29	10.6
Stage*		
Group 1: IA1–IB2	116	42.3
Group 2: IB3–IVA	141	51.5
Group 3: IVB	16	5.8
Pre-treatment PET		
Yes	191	69.7
No	83	30.3
Pre-treatment MRI pelvis		
Yes	84	30.7
No	190	69.3
Pre-treatment EUA		
Yes	113	41.2
No	161	58.8
First treatment received*	101	00.0
Surgery	105	38.3
Chemoradiation	110	40.1
Systemic chemotherapy	29	10.6
Clinical trial	24	8.8
Recurrence	<b>4</b> T	0.0
Yes	97	35.4
No	177	64.6
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Table 1 Continued		
Variable	n=274	%
Moore		
0	246	89.8
1	28	10.2

Moore criteria: performance status, pelvic disease, African-American ancestry, disease-free interval <1 year, and prior platinum exposure were assigned a score and tabulated as a total. Risk was assigned: low risk (0-1 factor), mid-risk (2-3 factors), & high risk (4 or 5 factors).

\*Missing data points were excluded from analysis.
EUA, exam under anesthesia; MRI, magnetic resonance imaging; NCI CC, National Cancer Institute designated cancer center; OSH, outside institution; PET, positron emission tomography; SNH, safety net hospital.

105 (38.3%) receiving surgery as their initial therapy. The overall median treatment initiation time was 60 days and the mean was 71 days (range 0–551). The median times to initiate surgery (54 days, range 3–96) and chemoradiation (58 days, range 4–187) were not significantly different (relative risk (RR) 1.01, 95% Cl 0.98 to 1.04, p=0.54). Table 2 shows the univariable analysis of the variables' effects on time, and multivariable analysis results are shown in Table 3. Diagnosis at an outside facility showed an increased median time to initiate treatment compared with the cancer center (median 53 vs 47 days; relative risk (RR) 1.24, 95% Cl 1.18 to 1.30, p<0.0001). Stratified by treating institution, being treated at the cancer center was associated with a shorter initiation time compared with being treated at the safety net hospital (median 49 vs 62 days; RR 1.25, 95% Cl 1.21 to 1.29, p<0.0001), though this effect was not seen on multivariable analysis.

The racial cohort with the longest median time to treatment of 63 days was the combined Afro-Latina/Afro-Caribbean group. Spanish-only speakers had a decreased risk of prolonged treatment time (49.5 days; RR 0.68, 95% Cl 0.66 to 0.71, p<0.001). All insurance types were inferior to private insurance, with self-pay patients having the most prolonged initiation time of 68 days (RR 1.59, 95% Cl 1.49 to 1.69, p<0.0001) in multivariable analysis. The longest median time to treatment stratified by stage was for stage IVB at 59 days. In multivariable analysis, pre-treatment PET/CT (RR 1.05, 95% Cl 1.01 to 1.09, p<0.0001), MRI (RR 1.13, 95% Cl 1.09 to 1.17, p<0.0001), and exam under anesthesia (RR 1.09, 95% Cl 1.05 to 1.12, p<0.0001) were associated with treatment delays, with the median times being 56, 56, and 57.5 days, respectively.

Compared with chemoradiation, treatment initiation was longest for those starting a clinical trial, median of 62 days (RR 1.18, 95% Cl 1.12 to 1.24, p<0.0001), and shortest, 47 days, for those initiating chemotherapy (RR 1.13, 95% Cl 1.08 to 1.19, p<0.0001). However, initiating treatment with surgery was not significantly longer (median of 54 vs 58 days; RR 1.01, 95% Cl 0.98 to 1.04, p=0.54). Multivariable analysis demonstrated no significant difference in treatment initiation times between the two most common modalities for upfront therapies of surgery and chemoradiation. Specific factors which prolonged initiation times in patients receiving either upfront chemoradiation or surgery was assessed by performing a subgroup analysis of each of these cohorts. Multivariable analysis results are shown in Table 4. While patients undergoing surgery had a longer time to treatment at the safety net hospital compared with

**Table 2** Univariable analysis showing relative risk for prolonged time to treatment initiation, with median number of days to treatment for each cohort

Variable	Cohort	Median TTI (days)	Mean TTI (days)	RR (95% CI)	P value
Age at diagnosis (years)	≤50	52	63	Ref	_
	>50	60	71.2	1.13 (1.10 to 1.16)	< 0.0001
Diagnosis institution	NCI CC	47	52.6	Ref	_
	SNH	62	73.6	1.40 (1.35 to 1.46)	< 0.0001
	OSH	53	65.1	1.24 (1.18 to 1.30)	<0.0001
Treating institution	NCI CC	49	57.8	Ref	-
	SNH	62	72.1	1.25 (1.21 to 1.29)	<0.0001
Race/ethnicity	Non-Hispanic White	56	83	Ref	-
	Hispanic White	54	57.6	0.69 (0.66 to 0.73)	<0.0001
	African American	60	93.7	1.13 (1.07 to 1.19)	<0.0001
	Afro-Caribbean/Afro-Latin	63	71	0.86 (0.81 to 0.90)	<0.0001
Language	English	57	78.5	Ref	_
	Spanish	49.5	53.8	0.68 (0.66 to 0.71)	<0.0001
	Haitian Creole	77.5	83.9	1.07 (1.01 to 1.13)	0.002
	Other	116	116	1.48 (1.23 to 1.77)	<0.0001
Insurance status	Private	50	60.7	Ref	_
	Medicare/Medicaid	56	66.9	1.10 (1.06 to 1.14)	<0.0001
	County charity care	56	66.3	1.09 (1.05 to 1.14)	<0.0001
	Self-pay	68	83.8	1.38 (1.32 to 1.45)	<0.0001
Stage group	Group1: IA1-IB2	55.5	68.5	Ref	_
	Group 2: IB3-IVA	55	63.7	0.93 (0.90 to 0.96)	<0.0001
	Group3: IVB	59	82.2	1.20 (1.13 to 1.27)	<0.0001
Pre-treatment PET	No	47	60.4	Ref	-
	Yes	56	69.2	1.15 (1.11 to 1.18)	<0.0001
Pre-treatment MRI pelvis	No	54	64.5	Ref	-
	Yes	56	71.4	1.11 (1.07 to 1.14)	<0.0001
Pre-treatment EUA	No	53.5	63.1	Ref	-
	Yes	57.5	71.5	1.13 (1.10 to 1.17)	<0.0001
First treatment received	Chemoradiation	58	64.4	Ref	-
	Surgery	54	65.1	1.01 (0.98 to 1.04)	0.537
	Systemic chemotherapy	47	72.8	1.13 (1.08 to 1.19)	<0.0001
	Clinical trial	62	76	1.18 (1.12 to 1.24)	<0.0001

EUA, exam under anesthesia; MRI, magnetic resonance imaging; NCI CC, National Cancer Institute designated cancer center; OSH, outside institution; PET, positron emission tomography; Ref, reference; SNH, safety net hospital; TTI, time to treatment initiation.

the cancer center (RR 1.25, 95% Cl 1.21 to 1.29, p<0.0001), patients receiving chemoradiation at the safety net hospital had decreased time to treatment (RR 0.72, 95% Cl 0.65 to 0.79, p<0.0001).

There were significant differences in starting treatment between patients receiving chemoradiation based on their insurance status. Medicare/Medicaid increased delay in initiation. Medicare/Medicaid patients had a median initiation time of 56 days versus 50 days for privately insured patients (RR 1.64, 95% Cl 1.50 to 1.80, p<0.0001); self-pay patients, with a median time of 68 days, had an RR of 2.94 (95% Cl 2.65 to 3.26, p<0.0001), the largest RR magnitude of any risk factor examined. No difference in progression-free survival (hazard ratio (HR) 1, 95% Cl 0.996 to 1.004, p=0.96) or overall survival (HR 1, 95% Cl 0.995 to 1.005, p=0.93) with increasing time to treatment was detected. Separating the cohorts by treatment

received did not affect this outcome, as survival remained nonsignificantly altered by prolonged times to initiate surgery, chemotherapy, or chemoradiation.

## **DISCUSSION**

#### **Summary of Main Results**

In this study, patients diagnosed at the National Cancer Institute cancer center were closest to the national median, with a time to treatment initiation of 47 days, while the safety net hospital patients experienced a median treatment initiation time of 61.5 days. The longest initiation times were patients diagnosed at an outside hospital and referred to the safety net hospital for treatment,

**Table 3** Multivariable analysis of significant variables from univariable analysis, showing relative risk for prolonged time to initiation of treatment

Variable	Cohort	RR (95% CI)	P value
Age at diagnosis (years)	≤50	Ref	-
	>50	1.13 (1.10 to 1.17)	<0.0001
Diagnosis institution	NCI CC	Ref	-
	SNH	1.26 (1.19 to 1.34)	<0.0001
	OSH	1.44 (1.36 to 1.52)	<0.0001
Treating institution	NCI CC	Ref	-
	SNH	0.98 (0.93 to 1.04)	0.594
Race/ethnicity	Non-Hispanic White	Ref	-
	Hispanic White	0.89 (0.84 to 0.95)	0.004
	African American	1.15 (1.09 to 1.22)	<0.0001
	Afro-Caribbean/Afro-Latina	0.83 (0.77 to 0.89)	<0.0001
Language	English	Ref	-
	Spanish	0.74 (0.70 to 0.77)	<0.0001
	Haitian Creole	1.24 (1.15 to 1.34)	<0.0001
	Other	1.37 (1.13 to 1.67)	0.001
Insurance status	Private	Ref	-
	Medicare/Medicaid	1.14 (1.09 to 1.18)	<0.0001
	County charity care	1.16 (1.10 to 1.22)	<0.0001
	Self-pay	1.59 (1.49 to 1.69)	<0.0001
Stage group	Group1: IA1-IB2	Ref	-
Language  Presurance status  Prestreatment PET  Prestreatment MRI pelvis  Prestreatment EUA	Group 2: IB3-IVA	0.77 (0.73 to 0.82)	<0.0001
	Group3: IVB	1.10 (1.01 to 1.21)	0.046
Pre-treatment PET	No	Ref	-
Language  Insurance status  Stage group  Pre-treatment PET  Pre-treatment MRI pelvis  Pre-treatment EUA  First treatment received	Yes	1.05 (1.01 to 1.09)	0.01
Pre-treatment MRI pelvis	No	Ref	-
	Yes	1.13 (1.09 to 1.17)	<0.0001
Pre-treatment EUA	No	Ref	-
	Yes	1.09 (1.05 to 1.12)	<0.0001
First treatment received	Chemoradiation	Ref	-
	Surgery	0.95 (0.89 to 1.01)	0.074
	Systemic chemotherapy	1.06 (0.99 to 1.12)	0.083
	Clinical trial	1.26 (1.19 to 1.33)	<0.0001
Moore	0	Ref	-
	1	0.63 (0.58 to 0.68)	<0.0001

EUA, exam under anesthesia; MRI, magnetic resonance imaging; NCI CC, National Cancer Institute designated cancer center; OSH, outside institution; Ref, reference; SNH, safety net hospital.

suggesting barriers to efficient initiation of care. Insurance type was a key factor in influencing initiation time, as any non-private insurance had a significantly longer treatment start time for any initial therapy. Of the non-private insurances, the government-based insurances of Medicare/Medicaid had the lowest risk of prolonged time to treatment, while self-pay carried the highest risk. Notably, in the subgroup analysis of patients initiating either chemoradiation therapy or surgery, self-pay patients were almost three times more likely and charity care patients were almost two times more likely

to have a prolonged time to treatment when receiving chemoradiation therapy than those with private insurance. The large variation in medical coverage by different insurance types may explain these findings, as those without private insurance often require longer approval processes than those with private insurance before initiating treatment. Additionally, chemoradiation requires two authorizations, while surgery typically requires only one. Charity care coverage was found to have the same median initiation time of 56 days as Medicare and Medicaid. As coverage provided by the

**Table 4** Multivariable analysis of factors affecting time to initiation of treatment in surgery and chemoradiation treatment cohorts

		Surgery		Chemoradiation	
Variable	Cohort	RR (95% CI)	P value	RR (95% CI)	P value
Age at diagnosis (years)	≤50	Ref	_	Ref	_
	>50	1.11 (1.05 to 1.18)	<0.0001	1.01 (0.95 to 1.06)	0.783
Diagnosis institution	NCI CC	Ref	_	Ref	_
	SNH	1.19 (1.08 to 1.31)	<0.0001	1.40 (1.25 to 1.57)	<0.0001
	OSH	1.36 (1.25 to 1.47)	<0.0001	1.55 (1.38 to 1.74)	<0.0001
Treating institution	NCI CC	Ref	_	Ref	_
	SNH	1.56 (1.43 to 1.70)	<0.0001	0.72 (0.65 to 0.79)	<0.0001
Race/ethnicity	Non-Hispanic White	Ref	_	Ref	_
	Hispanic White	0.66 (0.60 to 0.72)	<0.0001	0.74 (0.66 to 0.82)	<0.0001
	African American	0.98 (0.89 to 1.07)	0.626	0.84 (0.76 to 0.94)	0.002
	Afro-Caribbean/Afro-Latina	0.60 (0.52 to 0.70)	<0.0001	0.86 (0.77 to 0.96)	0.008
Language	English	Ref	_	Ref	_
	Spanish	0.94 (0.87 to 1.02)	0.014	0.78 (0.72 to 0.85)	<0.0001
	Haitian Creole	0.84 (0.69 to 1.03)	0.089	1.32 (1.20 to 1.46)	<0.0001
	Other	2.27 (1.83 to 2.80)	<0.0001	NE	NE
Insurance status	Private	Ref	_	Ref	_
	Medicare/Medicaid	0.94 (0.86 to 1.01)	0.102	1.64 (1.50 to 1.80)	<0.0001
	County charity care	0.86 (0.78 to 0.95)	0.003	1.95 (1.75 to 2.16)	<0.0001
	Self-pay	0.69 (0.61 to 0.78)	<0.0001	2.94 (2.65 to 3.26)	<0.0001
Stage group	Group1: IA1-IB2	Ref	_	Ref	_
	Group 2: IB3-IVA	0.54 (0.46 to 0.63)	<0.0001	1.00 (0.90 to 1.10)	0.93
	Group 3: IVB	NE	NE	0.25 (0.18 to 0.36)	<0.0001
Pre-treatment PET	No	Ref	-	Ref	_
	Yes	1.05 (0.99 to 1.12)	0.089	1.30 (1.21 to 1.40)	<0.0001
Pre-treatment MRI pelvis	No	Ref	_	Ref	_
	Yes	1.50 (1.41 to 1.59)	<0.0001	1.19 (1.12 to 1.27)	<0.0001
Pre-treatment EUA	No	Ref	_	Ref	_
	Yes	0.71 (0.67 to 0.76)	<0.0001	1.28 (1.21 to 1.35)	<0.0001
Moore	0	Ref	-	Ref	_
	1	0.67 (0.60 to 0.75)	<0.0001	0.99 (0.85 to 1.14)	0.845

EUA, exam under anesthesia; MRI, magnetic resonance imaging; NCI CC, National Cancer Institute designated cancer center; NE, not evaluable; OSH, outside institution; Ref, reference; SNH, safety net hospital.

hospital should not need additional approval, additional socioeconomic factors of those requiring charity care are likely influencing time to initial cervical cancer treatment.

Primary language also influenced initiation time. Our study identified Spanish-only speakers as having a lower risk of treatment delay, likely reflecting the unique ethnic and linguistic composition in Miami-Dade County. However, these findings can be generalizable to other locations in that they demonstrate the benefits to patient care when appropriate resources for navigating language barriers are in place. The two most common treatment modalities in our population, surgery and chemoradiation, demonstrated no significant difference in time to treatment (54 days vs 58 days, RR 1.01). However, patients treated with surgery at the safety net

hospital had a 1.5-fold increase in risk of prolonged initiation time compared with the cancer center. We speculate that limitations in operating room availability, difficulty in obtaining preoperative clearance, and surgeon availability could contribute to this discrepancy; however, there may be additional contributory factors.

## **Results in the Context of Published Literature**

The NCDB study by Ramey et al demonstrated the median time to initiate chemoradiation for cervical cancer patients was 44 days in 2014. Unlike that study, our study included patients initiating any treatment modality to determine factors influencing treatment initiation time in all newly diagnosed cervical cancer patients. The median time of 60 days within our entire cohort was 16 days longer

than the one reported in the NCDB study. <sup>10</sup> In contrast, our study found a decreased risk of delay in Hispanic White women compared with non-Hispanic White women. Prior studies have shown low English proficiency Latina women were more likely to experience treatment delays for cervical cancer. <sup>19</sup> Our population demonstrated a significantly lower risk of prolonged treatment initiation in Spanish speakers. Consistent with our findings, it has been shown that healthcare access is improved for minority patients in culturally diverse environments. <sup>20</sup>

Studies in other cancer types have demonstrated worse outcomes in patients with prolonged times to treatment. 13 14 In cervical cancer patients, results regarding prognosis are mixed. 10 15 16 Our data are consistent with prior studies showing no difference in overall or progression-free survival with increasing initiation time in cervical cancer. 10 21 This lack of effect has been demonstrated across treatment modalities. Patient satisfaction or anxiety associated with diagnosis and treatment have previously been shown to be negatively affected by delay in treatment.<sup>22 23</sup> Furthermore, perceived quality of care and confidence in the provider are both negatively impacted by long wait times.<sup>24</sup> Ensuring trust between the patient and care team is invaluable. In one study of surgeries of gynecologic malignancies, hospitals with higher Hospital Consumer Assessment of Healthcare Providers and Systems scores were associated with lower in-hospital mortality and surgical complications compared with those with lower scores. <sup>25</sup> Studies have also demonstrated an association between treatment delays and anxiety and depression in cancer patients.<sup>26</sup> <sup>27</sup>

## **Strengths and Weaknesses**

This study included multiple treatment modalities for cervical cancer. The examination of characteristics and outcomes within our unique hospital system is also a strength, as this information can be beneficial in designing specific interventions that will directly improve patient care. One limitation is that medical comorbidities, health literacy, family support, and access to transportation were not examined and they might have had an impact on initiating treatment. Furthermore, we did not examine the impact that delays in treatment had on our patients' confidence in their treatment, adherence to follow-up care, and psychological health. As in the NCDB study, our study showed that patients with more advanced disease had lower times to initiate treatment. The decreased time in metastatic disease could have affected the absence of demonstrable survival benefit by introducing selection bias. Additionally, analyzing the relationship between time to initiation of treatment and recurrence is an important and valuable exercise. The data we obtained did not allow us to perform this analysis in a meaningful way, as we include various treatment modalities depending on stage. However, this is an important question to investigate in future studies.

#### **Implications for Practice and Future Research**

Our study shows factors associated with prolonged treatment initiation include treatment modality, insurance status, language spoken, and institution of diagnosis. Potential barriers to treatment after diagnosis at an outside institution identified through our personal experiences include delay in obtaining outside records, language barriers, long interval in scheduling imaging studies due to availability, and difficulty in scheduling new patient visits with the financial assistance office. Efforts directed at pinpointing the

bottleneck areas and implementing changes may decrease the time to initiating treatment in a cohort at high risk for delay. Further investigation of specific barriers could better inform targeted solutions such as patient education, navigation, and support programs.

The differences in initiation time seen in our study for Hispanic-White patients compared with the NCDB study are likely due to demographic factors in our community that overcome traditional language and ethnic barriers to treatment initiation. In 2019, the population of Miami Dade County consisted of 69.4% of people who identify as Hispanic, making it one of the few counties within the USA with a majority Hispanic population. Further studies should examine whether similar outcomes are seen in counties with majority populations who are neither Caucasian nor Hispanic. Such studies should also examine the impact of physician and staff demographics, training, and language proficiency on time to treatment initiation.

#### **CONCLUSIONS**

Our study represents one of the first to assess treatment initiation time among multiple treatment modalities for cervical cancer within a multicultural community in the USA. Consistent with previous studies, our data demonstrated an overall increase in treatment time without a resultant negative impact on survival. While our study reflected some ethnic and racial disparities seen nationally and internationally, Hispanic White and Spanish-speaking patients had shorter initiation times, reflecting the regional demographic makeup. Expediting treatment by identifying modifiable barriers from diagnosis to transfer of care, pre-treatment workup, and scheduling primary treatment should remain a priority for obstetrician/gynecologists, gynecologic oncologists, and radiation oncologists who strive to minimize disparities in standard of care. The time between diagnosis and treatment initiation is stressful, impacting the patient's mental and emotional health and overall satisfaction, and may negatively influence the patient's confidence in their care. The knowledge of factors that may prolong this interval will assist providers in minimizing delays for their patients and initiating treatment expeditiously.

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