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Original Research Article

Long-term treatment outcomes in cervical cancer patients aged 60 years and above: A comprehensive 12-year study in the Indian context

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ABSTRACT

Background: Cervical cancer remains a significant global health concern, with around 570,000 new cases and 310,000 deaths annually. Despite a decrease in incidence due to screening programs, rates among elderly women, typically aged 50 and above have remained steady. These demographic faces unique physiological and pathological factors, impacting treatment decisions and outcomes. Treatment of Cervical cancer is a multimodality approach which includes Surgery, concurrent chemo radiation, brachytherapy and in some cases Neoadjuvant chemotherapy determined by staging. However, the suitability of these treatments for elderly patients, considering their frailty, co morbidities, and age-related issues like malnutrition and cognitive decline, remains underexplored. There's a critical need to balance treatment benefits with risks, aiming to reduce mortality by individualizing care.

Materials and Methods: A retrospective study in India analyzed outcomes for elderly cervical cancer patients over 12 years. Out of 876 patients reviewed, 186 met inclusion criteria: aged 60 or older, with FIGO Stage IB to IVA and ECOG performance status I to III.

Results: The majority (61%) of patients were aged 60-65. Most had ECOG PS II status, and 96% had squamous cell carcinoma. Around 62.3% had locally advanced disease. Survival rates were highest in FIGO Stage IB, with overall survival statistically significant at 92.09 months, and disease-free interval at 103.24 months.

Conclusion: The study suggests age may not independently predict outcomes for elderly cervical cancer patients in India. Despite co morbidities necessitating treatment adjustments, radical management remains crucial, irrespective of age. Tailoring treatments to individual needs and improving survival prediction are essential for better outcomes in this population.

1. Introduction

Cervical cancer stands as one of the most commonly diagnosed malignancies afflicting women worldwide, with approximately 570,000 new cases emerging each year and an estimated 310,000 annual fatalities attributed to this disease.[1] While global efforts to implement various screening programs have brought about a decline in the incidence of cervical cancer, this decline has not been mirrored in the case of elderly females.[2] Disturbingly, statistics indicate that a substantial quarter of cervical cancer cases are diagnosed in the elderly age group.[3] A prior study has further substantiated these findings by revealing that the prevalence of cervical cancer is comparatively lower in women aged below 50 years, but as women surpass the age of 50, their risk of cervical cancer escalates by an annual 2% with each passing year.[4] Moreover, women aged 50 years and beyond typically find themselves in the perimenopausal or postmenopausal phase, leading to distinct disparities in their physiological and pathological characteristics when compared to women in their childbearing years.[5]

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In light of these factors, a discernible trend of heightened concern for elderly patients grappling with cervical cancer has gradually emerged over time. The spectrum of treatment options for cervical cancer encompasses surgical interventions, brachytherapy and concurrent radio-chemotherapy, with the selection contingent upon the well-established FIGO staging.[6] However, the pivotal aspect of this equation—the intricate balance between treatment benefits and risks, particularly in the context of the elderly population—remains a domain that has not received adequate scrutiny. Decision-making for older females presents a multifaceted challenge, primarily owing to their frailty and the burden of multiple comorbidities such as diabetes or cardiac ailments.[7] These comorbidities hasten the deterioration of their health in tandem with age-related setbacks, including malnutrition, functional dependency and cognitive decline. Consequently, these patients face an elevated risk of adverse treatment effects. For these reasons, the landscape of cervical carcinoma treatment remains far from standardized within the geriatric population. Additionally, prognostic factors with the capacity to predict survival in cervical cancer patients aged 60 and beyond remain an area of limited investigation.[8]

The imperative thus lies in our pursuit of reducing mortality rates among elderly patients. Achieving this goal necessitates the development of prognostic tools for predicting survival, the identification of pertinent prognostic factors, and the formulation of tailored treatment strategies in response to the distinctive challenges posed by cervical cancer in elderly individuals.

With this objective in mind, this retrospective single-institutional study undertakes a comprehensive exploration, scrutinizing the outcomes of elderly patients diagnosed with cervical cancer within the context of the Indian scenario.

2. Materials and Methods

2.1. Patient selection

Over a span of 12 years, from 2009 to 2021, a total of 876 patients were initially presented with cervical cancer in the outpatient department. Out of this cohort, 186 patients satisfied the defined inclusion criteria. A detailed representation of the patient selection process is depicted in Figure 1.

2.2. Inclusion criteria

Patients included in the study met the following criteria:

1. Diagnosis of cervical cancer
2. FIGO Stage IB to IVA
3. Age 60 years or older
4. ECOG performance status ranging from I to III

2.3. Exclusion criteria

Patients who fell under the following criteria were excluded from the study:

1. Age below 60 years
2. Metastatic cancer
3. FIGO Stage IVB

2.4. Demographic and clinico-pathological characteristics

Patient demographics and clinico-pathological characteristics were comprehensively documented and are presented in Table 1. These characteristics encompassed ECOG performance status (I-III), FIGO Staging (IB-IVA), histo-pathological features (e.g., adenocarcinoma, squamous carcinoma, or adenosquamous carcinoma), radiotherapy and brachytherapy doses, overall survival, disease-free survival, current patient status (alive or deceased), and the cause of death if applicable.

2.5. Radiation therapy

External beam radiation therapy, utilizing a 6 MV photon beam from a linear accelerator, was administered in varying doses, as illustrated in Figure 2. Following external beam radiation therapy, intracavitary brachytherapy to point A. Point A is defined as the point 2 cm above the distal end of the lowest source in the tandem and 2 cm lateral to the tandem A.

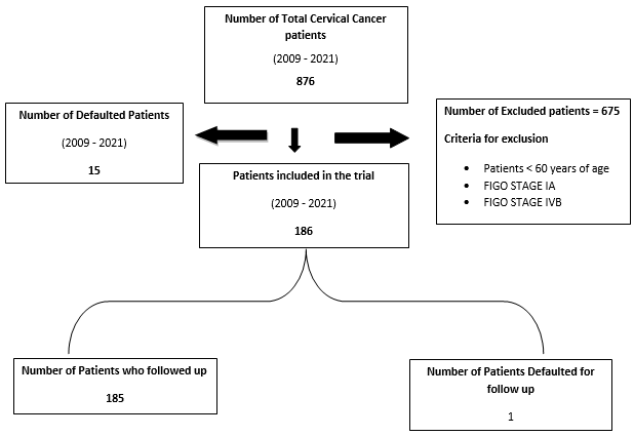


Figure 1: Patient selection flow chart

2.6. Statistical analysis

Categorical variables were expressed as counts and percentages. Overall survival and disease-free survival were analyzed in the study population using the Kaplan–Meier approach. A significance level of $p < 0.05$ was employed for all statistical analyses.

Table 1: Clinico-pathological characteristics of patients with cervical cancer between 2009 and 2021 in the study population (n=186)

Characteristics	Number of Patients	Percentage (%)
ECOG PS (n=186)		
• I	2	1.07
• II	167	89.78
• III	17	9.10
Histopathology (n=186)		
• Squamous cell	179	96.2
• Adenocarcinoma	6	3.2
• Adenosquamous	1	0.6
FIGO Stage (n=186)		
• IA	5	2.68
• IIA	19	10.21
• IIB	46	24.73
• IIIA	16	8.60
• IIIB	51	27.41
• IIIC	27	14.51
• IVA	22	11.86
Radiotherapy dose (n=186)		
46Gy/23#	72	38.70
• 45Gy/25#	4	2.15
• 50Gy/25#	89	47.89
• 50.5Gy/28#	6	3.22
• 40Gy/20#	3	1.61
• 30Gy/10#	8	4.30
• 20Gy/5#	2	1.07
• 20Gy/10#	1	0.53
• 6Gy/1#	1	0.53
Brachytherapy dose (n=186)		
• 9Gy	55	29.56
• 7Gy	74	39.78
• 9.5Gy	5	2.68
• 6Gy	5	2.68
• 5Gy	2	1.11
• Not Received	45	24.19
Boost Received (External Beam Radiotherapy)	34	
Response Assessment (n=185)*		
• Complete Response	126	67.74
• Disease Recurrence	28	15.05
• Residual Disease	27	14.51
• Disease Progression	4	2.15
Overall Survival (n=186)	**In months**	
• Average	63.3	
• Maximum	159	
• Minimum	2	
Overall Survival (Stage wise) (n=186)	**In months**	
• IB	82.2	
• IIA	75.9	
• IIB	72.5	
• IIIA	65	
• IIIB	53.5	
• IIIC	26.53	
• IVA	20.28	
Current Status (n=186)		
• Alive	94	50.53
• Death	92	49.47
Cause of Death (n=92)		
• Disease	41	44.56
• Other causes	51	55.44

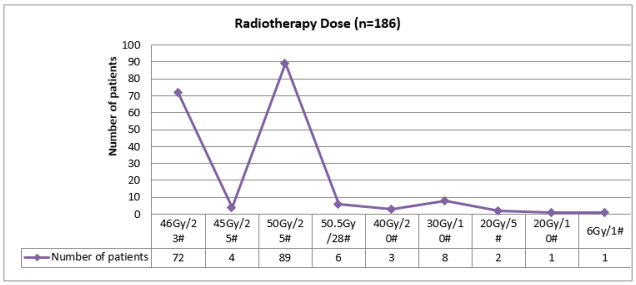


Figure 2: Conventional fractionation schedule in the study population(n=186)

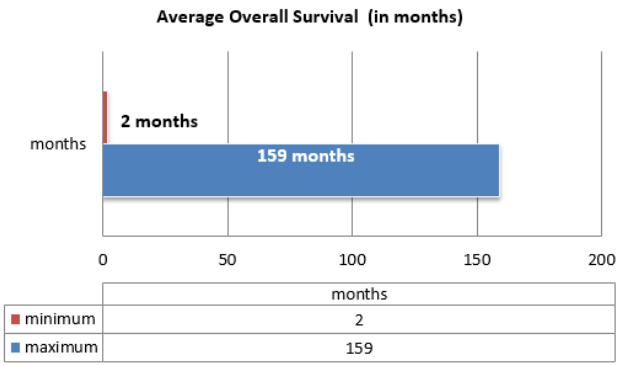


Figure 4: Average overall survival (in months) of the study population(n=186)

3. Results

3.1. Patient characteristics

Out of a total of 876 cervical cancer patients presenting over a 12-year period (2009-2021), 186 patients met the inclusion criteria. The patient selection process is visually outlined in Figure 1. Detailed clinicopathological characteristics of the study population are documented in Table 1. The study population was age-standardized, revealing that 61% of patients belonged to the 60–65 years age group (Figure 4). The ECOG performance status analysis indicated that the majority of patients were classified under ECOG PS II (Figure 5). Among the 186 patients, 179 (96%) were histologically diagnosed with squamous cell carcinoma, while other histological types, such as adenocarcinoma, adenosquamous carcinoma, etc., were also considered (Figure 6). Approximately 62.3% of the population belonged to locally advanced stages (Stage III-IVA).

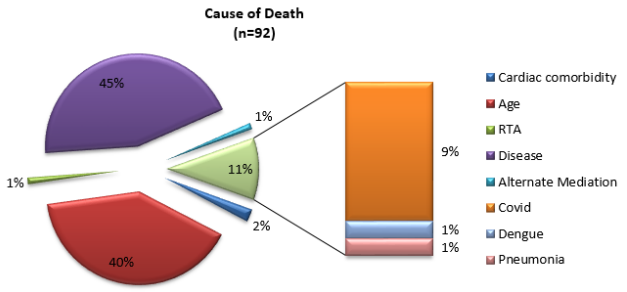


Figure 5: Analysis of the cause of death of the study population(n=92)

3.2. Response assessment

Response assessment was performed three months after the completion of chemo-radiotherapy followed by brachytherapy. The assessment utilized Recist 1.1 criteria.

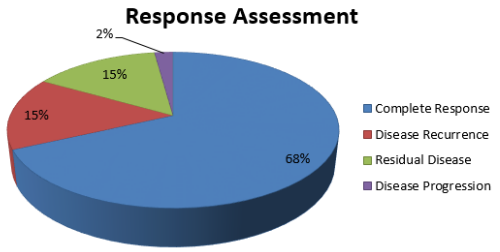


Figure 3: Response assessment using MRI Pelvis after completion of the primary treatment(n=186)

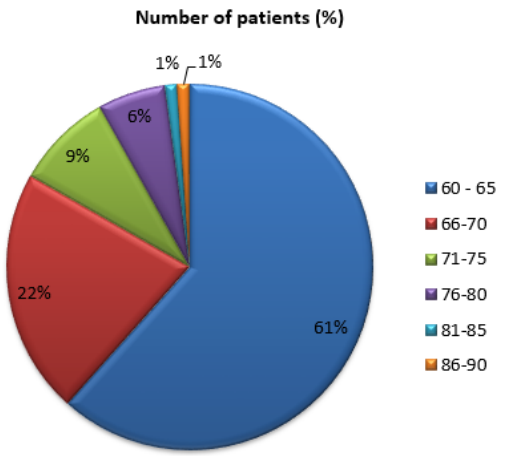
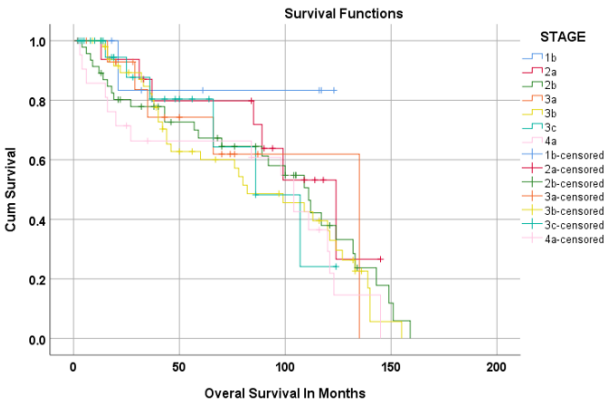


Figure 6: Age standard ization of the study population (n=186) study population(n=186)

3.3. Survival analysis

Kaplan–Meier survival analysis was employed to assess overall survival and disease-free survival across different clinico-pathological characteristics within the cervical cancer patient population (Graphs 1 and 2). The analysis showed that the maximum survival duration was 106.0 months in FIGO Stage IB patients compared to other stages. Overall survival was statistically significant at 92.09 months, with a 95% confidence interval ranging from 84.0 to 100.1 (Table 2). Similarly, the maximum disease-free interval was observed at 109.0 months in FIGO Stage IB, with an average disease-free interval of 103.24 months, significantly supported by a 95% confidence interval ranging from 85.42 to 122.08 (Table 3).

Table 2 is showing the Overall average Survival Time in month of the study population (n=186) . It is illustrated that the majority of survival was found 106.0 Months in FIGO IB as compared to other stages. The overall survival (in months) was 92.09months which was statistically significant with 95% Confidence Interval lower bound 84.0and upper bound 100.1in our study.

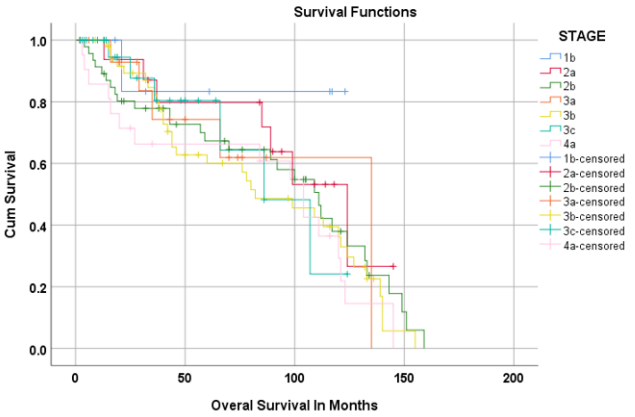


Graph 1: Show that he horizontal axis (x-axis) represents Overall survival (in months) and the vertical axis (y-axis) shows the probability of survival of patient.

Table 3 is showing the Disease free interval (in months) in the study population (n=186). It is illustrated that the maximum disease free interval was 109.0 month seen in FIGO Stage IB Stage, as compared to other stages and average disease free interval was 103.24 months which was significant with 95% Confidence Interval lower bound 85.42 and upper bound 122.08in our study.

4. Discussion

Cervical cancer is one of the most commonly diagnosed malignancies in women worldwide, with approximately 570,000 new cases diagnosed every year, leading to approximately 310,000 deaths annually.[1] In this study, which included 186 patients, 116 (62.3%) were diagnosed



Graph 2: Show that the horizontal axis (x-axis) represents Disease free survival (in months) and the vertical axis (y-axis) shows the probability of survival of patients in study population.

with stage III–IV disease. This indicates that a majority of older patients in our study presented with advanced-stage disease (62.3%) at the time of diagnosis. Notably, this percentage of patients with advanced-stage cervical cancer appears to be significantly higher than what is observed in large population studies.

While the global incidence of cervical cancer has been declining due to the implementation of various screening programs, the incidence among elderly females has remained unchanged.[9] The number of elderly patients being diagnosed with cervical cancer is on the rise worldwide, and elderly women now account for more than 40% of the deaths from cervical cancer.[10]

However, the impact of age on the survival of patients with cervical cancer remains uncertain. Some literature suggests that cervical cancer has a similar prognosis in both older and younger women.[11] Conversely, others have proposed that younger age is an unfavorable prognostic factor, particularly in more advanced stages of the disease.[12] In contrast, Wright et al. demonstrated that age is a poor prognostic factor for cervical cancer.[13] Furthermore, studies have indicated that younger patients may experience improved outcomes compared to older patients, and advanced age has been linked to decreased survival in various cancer types.[14]

Although large population-based studies have shown that survival for cervical cancer is inversely correlated with the stage of the disease, the survival among older women, regardless of the stage at diagnosis, has been reported to be worse than that of women in their 40s and 50s.[15] However, in our study, we did not observe a statistically significant difference in disease-free survival and overall survival. These findings align with a study conducted by Lindegaard et al., where age was not identified as a significant variable

Table 2: Stage wise overall average survival time (in month).

Treatment	Average Survival Time in Month (Disease Cases)			P-value
	Average	95% Confidence Interval		
		Lower Bound	Upper Bound	
1b	106.0	75.6	136.4	0.002
2a	101.54	78.4	124.7	
2b	99.42	76.1	108.7	
3a	98.82	66.8	130.9	
3b	86.33	71.8	100.9	
3c	85.30	64.0	106.6	
4a	82.13	59.0	105.3	
Overall	92.09	84.0	100.1	

Table 3: Disease free interval (inmonths) in the study population

Treatment	Average Survival Time in Month (Disease Free)			P-value
	Average	95% Confidence Interval		
		Lower Bound	Upper Bound	
1b	109.0	75.58	136.42	0.004
2a	106.24	65.72	122.76	
2b	104.76	61.21	132.32	
3a	98.55	61.95	121.15	
3b	95.63	65.45	105.82	
3c	91.07	61.61	106.54	
4a	83.25	49.78	96.71	
Overall	103.24	85.42	122.08	

in any of the investigated endpoints. This conclusion was reached after reviewing radiotherapy treatment data from 114 women with a median age of 75.5 years.[16] Our study suggests that outcomes in older women may not be independently correlated with age alone.

5. Limitation of the study

Firstly, it has a retrospective study design, which may introduce biases. Secondly, the analysis of the data is confined to a single institution, which may limit the generalizability of the results. Additionally, we cannot exclude the possibility that other factors not considered in this study may be correlated with survival in cervical cancer patients. Further research is needed to better understand the complex relationship between age and survival in cervical cancer.

6. Conclusion

The study concluded that age may not be an independent risk factor for defining the outcome in cervical cancer patients in Indian Scenario. Even though elderly females may present with multiple co- morbidities, which may need alteration in the standard treatment protocol. However, the management of cervical cancer must have a radical approach irrespective of the age of the patient.

7. Source of Funding

None.

8. Conflict of Interest

None.

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