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Survival of Cervical Cancer Patients Undergoing Neoadjuvant Chemotherapy (NACT) and Radical Hysterectomy at Dr. Saiful Anwar General Hospital Malang

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ABSTRACT

Introduction: Cervical cancer remains a significant health burden, particularly in developing countries where access to radiotherapy is limited. Neoadjuvant chemotherapy (NACT) followed by radical hysterectomy has emerged as an alternative treatment strategy for locally advanced cervical cancer. This study aims to evaluate the survival outcomes and histopathological characteristics of patients with stage IIB cervical cancer who underwent NACT followed by radical hysterectomy in Dr. Saiful Anwar General Hospital.

Material and Methods: This retrospective study analyzed medical records of patients with stage IIB cervical cancer who received NACT followed by radical hysterectomy at Dr. Saiful Anwar General Hospital from January 2021 to July 2022. Patients with incomplete medical records or loss to follow-up were excluded. Data analysis included descriptive survival outcomes and histopathological findings. Associations between histopathological variables and mortality were analyzed using Fisher's exact. A p-value ≤0.05 was considered significant.

Results: A total of 51 patients met the inclusion criteria. During the follow-up period, 39 patients (76.5%) were alive, while 12 patients (23.5%) had died. The estimated overall survival probability at 24 months was 76.5% (95% CI: 65.7–89.0). Fisher's exact test demonstrated no statistically significant association between histopathological subtype and mortality (p = 0.069). No statistically significant association was observed between histopathological subtype and mortality.

Conclusion: Survival outcomes of stage IIB cervical cancer treated with neoadjuvant chemotherapy followed by radical hysterectomy in a tertiary setting. Histopathological subtype and absence of residual tumor were associated with improved survival. Further comparative studies are required to evaluate the effectiveness relative to standard treatments.

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INTRODUCTION

Cervical cancer remains a leading cause of morbidity and mortality among women worldwide, with an estimated 662,044 new cases and 348,709 deaths in 2022. It ranks as the fourth leading cause of cancer-related mortality in women [1]. The majority of cases and deaths occur in China (23% and 16%, respectively) and India (19% and 23%, respectively). If the incidence rate remains consistent with 2022 data, the number of cervical cancer cases and deaths is projected to increase by 56.8% and 80.7%, respectively, by 2050 [2]. This rise is expected to be more pronounced in developing countries [3]. According to the 2021 Indonesian Health Profile,

cervical cancer ranks second after breast cancer in terms of incidence, with a total of 36,633 cases (17.2% of all cancers in women). Additionally, the mortality rate is substantial, reaching 21,003 deaths (19.1% of all cancer-related deaths). Data from GLOBOCAN 2020 indicate that Indonesia has a significantly higher cervical cancer incidence rate (24.4 per 100,000 population) compared to other developing countries such as Malaysia and India. This incidence rate remains high even when compared to developed countries like Singapore, a neighboring nation [4].

According to the FIGO 2009 guidelines, locally advanced cervical cancer (LACC), encompassing stages IB2 and IIA2–IVA, is recommended to undergo standard treatment consisting of brachytherapy following concurrent chemoradiotherapy (CCRT). Meta-analyses of randomized trials have demonstrated that this approach significantly improves both progression-free survival and overall survival compared to definitive radiotherapy alone [5,6]. However, in low- and middle-income countries such as Indonesia, limitations in infrastructure, technology, specialized personnel, patient access, and service volume often hinder the implementation of standard radiotherapy protocols. These barriers may lead to incomplete or prolonged treatment, negatively impacting therapeutic outcomes [7].

As an alternative, treatment strategies requiring less advanced radiation facilities have been developed, including neoadjuvant chemotherapy (NACT) followed by radical hysterectomy [8,9]. This approach is considered a promising option for a subset of patients with stage IB and II disease. Several studies have shown that NACT can reduce tumor size, facilitate surgical resection, decrease high-risk histopathological features, and lower the risk of distant metastases. Additionally, this method may help avoid toxic adjuvant therapy while preserving ovarian and vaginal function. Although NACT has demonstrated favorable outcomes in certain studies, the 2018 ESGO guidelines still regard it as controversial, as its prognostic benefits remain inconclusive [10,11].

As one of the leading tertiary referral hospitals in East Java, Dr. Saiful Anwar General Hospital treats a substantial number of cervical cancer patients. This study aims to evaluate the survival outcomes and histopathological characteristics of stage IIB cervical cancer patients treated with neoadjuvant chemotherapy followed by radical hysterectomy at Dr. Saiful Anwar General Hospital.

MATERIAL AND METHODS

This study is a retrospective analysis based on medical record data of patients diagnosed with locally advanced cervical cancer stage IIB who underwent neoadjuvant chemotherapy (NACT) followed by radical hysterectomy at Dr. Saiful Anwar General Hospital, Malang, between January 2021 and July 2022.

Inclusion and Exclusion Criteria

The study subjects included patients diagnosed with stage IIB cervical cancer who received NACT prior to radical hysterectomy. Patients were excluded if they had incomplete medical records, failed to attend postoperative follow-ups, or could not be contacted for health status confirmation.

Data Collection and Processing

Data were collected from both electronic and physical medical records available at the hospital. The primary variables analyzed included patient survival status, categorized as either alive or deceased within a 2- to 3-year follow-up period after surgery. Overall survival (OS) was defined as the time from the date of surgery to death from any cause or the last follow-up. Mortality rates were further classified based on histopathological tumor characteristics obtained from postoperative examinations.

Statistical Analysis

Descriptive statistical analysis was performed to characterize the study population, survival status, and histopathological findings. Due to the small number of events in several subgroups, Fisher's exact test was used to evaluate the association between histopathological characteristics and mortality. A p-value of ≤ 0.05 was considered statistically significant. All statistical analyses were conducted using R Studio and IBM SPSS Statistics version 21.

RESULTS

This study aimed to evaluate the outcomes of cervical cancer patients who underwent neoadjuvant chemotherapy (NACT) followed by radical hysterectomy at Dr. Saiful Anwar General Hospital, Malang, between January 2021 and July 2022. A total of 62 patients were initially included in the study, all diagnosed with stage IIB cervical cancer. After excluding cases with incomplete medical records and those lost to follow-up, 51 patients were included in the final descriptive analysis as summarized in Table 1.

The variables assessed included patient age and histopathological tumor subtype. Due to the retrospective nature of the study, several prognostic variables, such as tumor size, lymph node status, lymphovascular space invasion (LVSI), parametrial invasion, and surgical margin status, were not consistently documented in the medical records and were therefore excluded from the analysis.

Several prognostic variables, such as tumor size, lymph node status, lymphovascular space invasion (LVSI), parametrial invasion, and surgical margin status, were inconsistently documented in the medical records due to the study's retrospective design. The overall survival outcomes of the study population are summarized in Table 2. Among the 51 patients analyzed, 39 patients (76.50%) were still alive, while 12 patients (25.50%) had died.

Moreover, Kaplan–Meier survival analysis was performed to estimate overall survival among patients with stage IIB cervical cancer treated with neoadjuvant chemotherapy followed by radical hysterectomy. A total of 51 patients were included in the analysis. During the follow-up period, 39 patients (76.5%) were alive, while 12 patients (23.5%) had died. The estimated overall survival probability at 24 months was 76.5% (95% CI: 65.7–89.0). Kaplan–Meier survival analysis stratified by histopathological subtype demonstrated no statistically significant difference in overall survival between groups (log-rank p = 0.09), as shown in Figure 1. Subsequently, patients were categorized based on their histopathological findings, as summarized in Table 3.

An analysis of survival outcomes among cervical cancer patients who underwent neoadjuvant chemotherapy followed by radical hysterectomy revealed variations according to tumor histopathology. Among the 39 surviving patients, 15.4% had adenocarcinoma, 17.9% had keratinizing squamous cell carcinoma, 12.8% had non-keratinizing squamous cell carcinoma, 28.2% were categorized as other histological types, 12.8% demonstrated pathological complete response (no residual tumor), and 12.8% had unspecified squamous cell carcinoma.

Conversely, among the 12 patients who died, 25.0% had adenocarcinoma, 41.7% had non-keratinizing squamous cell carcinoma, 16.7% had other histological types, 8.3% had adenosquamous carcinoma, and 8.3% had unspecified squamous cell carcinoma. No mortality cases were observed among patients with keratinizing squamous cell carcinoma or those who achieved a pathological complete response. The association between histopathological subtype and mortality was evaluated using Fisher's exact test due to the small number of observations in several subgroups. The analysis showed no statistically significant association between histopathological subtype and patient mortality (p = 0.069), as summarized in Table 3.

DISCUSSION

Cervical cancer poses a higher risk in women aged 70 years and older. Radiotherapy and chemotherapy are the primary treatment options [12]. However, in developing countries, primary radical hysterectomy is often performed due to the high number of patients and limited radiotherapy facilities [13]. Previous studies have indicated no significant difference in mortality rates and survival outcomes between different treatment groups in stage IIA cervical cancer. Nonetheless, deaths were more frequently observed (n=4, 20%) within 7–8 months following neoadjuvant chemotherapy (NACT) and radical hysterectomy [14].

A study conducted in Italy evaluating the effects of NACT followed by radical hysterectomy in stage III cervical cancer reported a clinical response rate of 44%, with 77% achieving complete response and 36.5% experiencing partial response. This study recommended NACT followed by radical hysterectomy as a valid and

Table1. Baseline Characteristics

Variable	Value
Age (years)	
Mean ± SD	53.1 ± 7.39
Range	39–69
Histopathological subtype	
Keratinizing squamous cell carcinoma	14 (27.5%)
Non-keratinizing squamous cell carcinoma	8 (15.7%)
Adenocarcinoma	8 (15.7%)
Adenosquamous carcinoma	1 (2.0%)
No residual tumor (pathological complete response)	9 (17.6%)
Other/ unclear histology	11 (21.6%)
Tumor size	Not consistently available in medical records
Lymph node involvement	
Positive	1 (2.0%)
Negative	12 (23.5%)
Not reported	38 (74.5%)
Lymphovascular space invasion (LVSI)	
Present	2 (3.9%)
Absent	10 (19.6%)
Not reported	39 (76.5%)
Parametrial invasion	
Present	2 (3.9%)
Absent	14 (27.5%)
Not reported	35 (68.6%)
Surgical margin status (vaginal cuff)	
Positive	2 (3.9%)
Negative	15 (29.4%)
Not reported	34 (66.7%)
NACT regimen	
Carboplatin-based regimen (Carbofanco / similar)	46 (90.2%)
Other regimen	3 (5.9%)
Not clearly documented	2 (3.9%)

Table 2. Cervical Cancer IIB Patient Survival Rate after Two Years

Survival	N (%)	Estimated 24 months Survival Probability
Alive	39 (76.50)	0.765
Deceased	12 (25.50)	95% CI (0.657 – 0.890)
Total	51 (100)	

acceptable therapeutic approach, with overall survival (OS) rates of 56.4% at 3 years and 29.5% at 5 years [15]. These figures are lower than those reported in more recent research, which reported a 5-year OS of 80% [14]. However, the latter study focused on stage IIA cervical cancer.

A ten-year longitudinal study by Luvero revealed that adjuvant chemotherapy after surgery in patients who had previously undergone NACT did not correlate with lymph node involvement or survival rates. Lymph node involvement was identified as the primary determinant of OS, although it did not significantly impact disease-free survival (DFS). These findings suggest that chemotherapy may help reduce tumor invasion and lower lymph node involvement [16].

Consistent with previous studies, research has suggested that NACT followed by radical hysterectomy can serve as an alternative treatment when radiotherapy is unavailable. A retrospective one-year study in China involving 414 patients with stage IB2-IIB cervical cancer reported clinical response rates to chemotherapy as follows: 32.6% achieved complete response, 46.5% achieved partial response, and 90% had a response classified as satisfactory. The five-year survival rate was 81% among patients who received NACT prior to surgery [17].

NACT has been shown to mitigate intermediate-to-high-risk prognostic factors such as tumor size, lymphovascular space invasion, parametrial invasion, and deep stromal invasion, thereby reducing the necessity for postoperative radiotherapy [18]. Recent studies also indicate that 88.4% of patients with stage IIA and IIB cervical cancer successfully underwent surgery, while 11.6% could not proceed due to extensive metastases. In a cohort of 41 patients with a median follow-up of 34.4 months, the 3-year OS was 80.8%, with a recurrence rate of 20%. These findings suggest that NACT followed by radical hysterectomy remains a viable treatment alternative for advanced cervical cancer in regions with limited radiotherapy access [19].

A prior meta-analysis by Robova demonstrated that NACT followed by radical hysterectomy

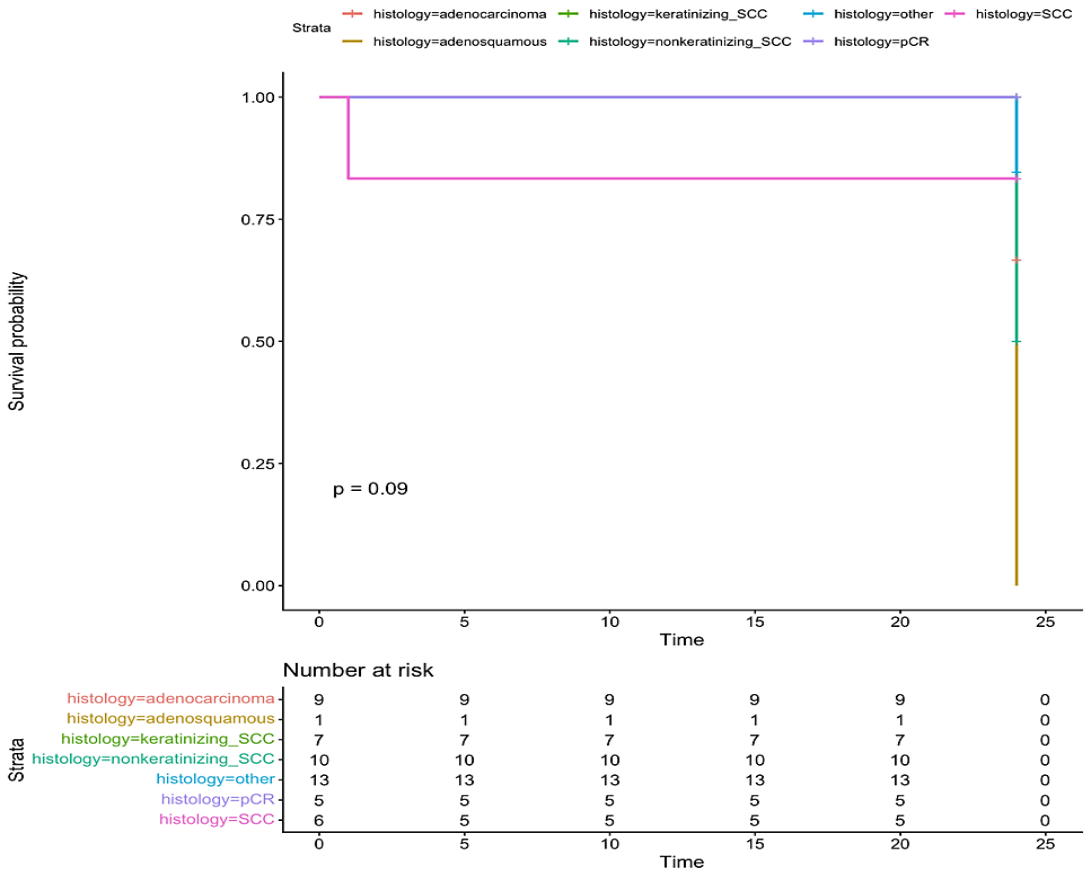


Figure 1. Kaplan–Meier Survival Analysis. The curve shows overall survival among patients with stage IIB cervical cancer treated with neoadjuvant chemotherapy followed by radical hysterectomy.

significantly improved survival rates in cases of aggressive cervical cancer, particularly in large tumors classified as stage IB [20]. Another study by Marchetti reported that over 70% of five-year OS outcomes were influenced by FIGO classification. Univariate analysis identified smoking, tumor size, lymphovascular space invasion (LVSI), parametrial invasion, and lymph node involvement as prognostic factors for OS, while multivariate analysis identified tumor size, histopathological grade, and parametrial invasion as significant factors [21]. Similarly, Benedetti-Panici's study demonstrated that NACT followed by radical hysterectomy significantly enhanced survival in patients with stage IB2-IIB cervical cancer [22].

Clinical trials on NACT followed by surgical intervention in cervical cancer have revealed that the TIP regimen (paclitaxel, ifosfamide, and cisplatin) achieved the highest rate of optimal pathological response but was associated with a higher incidence of grade 3–4 hematological toxicities, including neutropenia, thrombocytopenia, and anemia. Conversely, the dose-dense weekly PTX/CBCDA regimen developed by Salihi et al. demonstrated a comparable pathological response rate to the TIP regimen while exhibiting a more favorable hematological toxicity profile. These promising results may be attributed to the higher proportion of patients with early FIGO stage 1b1 disease (25%) and the increased number of weekly chemotherapy cycles administered prior to surgery [23,24].

In this study, Kaplan–Meier survival analysis demonstrated that patients with stage IIB cervical cancer who underwent neoadjuvant chemotherapy followed by radical hysterectomy had an estimated overall survival probability of 76.5% at 24 months. Although differences in survival distribution were observed among histopathological subtypes, statistical analysis using Fisher's exact test did not demonstrate a significant association between histopathology and mortality. These findings suggest that while histological subtype may influence clinical outcomes, the small sample size and heterogeneity of histopathological groups may limit the ability to detect statistically significant differences. Interestingly, no mortality cases were observed among patients with keratinizing squamous cell carcinoma or those who achieved a pathological complete response after treatment. Although these findings suggest a potentially favorable prognosis for these groups, the limited number of patients in each subgroup prevents definitive conclusions regarding their prognostic significance [14,25].

One of the primary limitations of our study was the relatively small number of patients available for follow-up after cervical cancer treatment. This was primarily due to socioeconomic constraints, as many patients faced financial difficulties and limited access to tertiary hospitals, making it challenging for them to attend scheduled follow-up visits.

The absence of statistically significant associations in this study should be interpreted cautiously. The relatively small sample size and

Table 3. Survival Rate Based on Histopathology Results.

Histopathology	**Alive (N=39; %)**	**Deceased (N=12; %)**
Adenocarcinoma	6 (66.7%)	3 (33.3%)
Adenosquamous	0 (0%)	1 (100%)
Keratinizing squamous cell carcinoma	7 (100%)	0 (0%)
Non-keratinizing squamous cell carcinoma	5 (50.0%)	5 (50.0%)
Other histology	11 (84.6%)	2 (15.4%)
Pathological complete response	5 (100%)	0 (0%)
Squamous cell carcinoma (unspecified)	5 (83.3%)	1 (16.7%)
Total	**39**	**12**
p-value	**0.069**	

In this study, "negative tumor" refers to the absence of residual tumor in the postoperative histopathological examination, which corresponds to a pathological complete response (pCR).

the distribution of patients across multiple histopathological subtypes may have reduced the statistical power to detect differences in survival outcomes. Future studies with larger cohorts are necessary to further clarify the prognostic role of histopathological subtype in patients receiving neoadjuvant chemotherapy followed by radical hysterectomy. Another limitation of this study is the absence of a comparator group, such as patients treated with concurrent chemoradiotherapy (CCRT). Therefore, the findings should be interpreted as descriptive observations rather than evidence of treatment superiority.

CONCLUSION

This study provides descriptive data on survival outcomes of stage IIB cervical cancer patients treated with neoadjuvant chemotherapy followed by radical hysterectomy in a tertiary referral hospital. No statistically significant association was observed between histopathological subtype and mortality, although certain subtypes such as keratinizing squamous cell carcinoma and pathological complete response showed favorable survival trends. Further prospective and comparative studies are required to confirm these findings.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this study.

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