RESEARCH ARTICLE

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Development of a Predictive Model for Therapy Response in Advanced-Stage Cervical Cancer Using Apparent Diffusion Coefficient (ADC) Value and Quantitative T2 Tumor on MRI: Correlation with Survivin Expression

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Abstract

Objective: The aims of this study are to optimize Magnetic Resonance Imaging (MRI) as a predictive modality for therapy response in advanced-stage cervical cancer and to identify predictors of this response in relation to survivin expression. **Methods:** This case-control study was conducted from January 2023 to May 2024, with total 35 subjects. The target population comprised patients with stages IIB to IIIC2 (FIGO 2018) cervical cancer. MR examination was performed three times: pre therapy, in the mid cycle of external radiation (20-30Gy), and 2 months after complete therapy. The study analyzed relations between age, tumor size, nodal metastasis, ADC and T2 parameters on MR, and survivin levels, with final therapeutic response. **Result:** The predictive model for final therapy response was developed using four variables: patient age, tumor size, nodal metastasis, and the T2 tumor-to-muscle ratio on MRI #2. The scoring system showed the minimum total score was 0 and the maximum total score was 6. The cut-off score on this predictive model is score 3 to differentiate between the prediction of good or poor response with the sensitivity of 92,86% and a specificity of 85,71%. **Conclusion:** This study found that T2 tumor-to-muscle ratio (T2 t/m ratio) on MR in the mid-cycle external radiation is a potential predictive factor of final therapy response on advanced-stage cervical cancer. A predictive model for assessing the final response could effectively incorporate clinical and MR parameters, including patient age, tumor size, nodal metastasis findings on MR, and Ratio T2 t/m on MR in the mid-cycle external radiation.

Keywords: Cervical cancer- magnetic resonance imaging- apparent diffusion coefficient- quantitative T2 tumor

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Introduction

Cervical cancer ranks as the second most common cancer among women in Indonesia and the fourth most common in Asia and worldwide. In 2020, there were 36,633 new cases reported in Indonesia, with a prevalence of 63,661 cases and an annual mortality rate of 18,000 [1, 2]. The diagnosis and staging of cervical cancer follow the FIGO 2018 guidelines, collaborate clinical, radiological, and pathological assessments. Magnetic Resonance Imaging (MRI) is the modality of choice for cervical cancer with a diagnostic accuracy up to 96% [2–4]. Treatment responses can vary among patients with the same FIGO stage, notably, studies show that approximately 30% of advanced-stage cervical cancer patients do not achieve a complete response to radiotherapy [5–7].

Research has increasingly focused on identifying additional predictors of radiotherapy response, including the analysis of molecular biomarkers like Survivin, an apoptosis inhibitor commonly expressed in cervical cancer. Despite its significance, molecular biomarker testing is not routinely conducted in Indonesia, particularly at our hospital [5, 8]. Multiparametric MRI plays a vital role in diagnosing and characterizing cervical cancer. It includes conventional imaging with T1-weighted (T1WI) and T2-weighted images (T2WI) sequences, and diffusion sequences with diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping. These sequences are essential for evaluating tumor cellularity and predicting radiotherapy response in advanced-stage

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cervical cancer [9–14].

The aims of this study are to optimize a non-contrast MR as a predictive modality for therapy response in advanced-stage cervical cancer and to identify predictors of this response in relation to survivin expression.

Materials and Methods

This case-control study was conducted from January 2023 to May 2024. The research focused on evaluating whether tumor ADC and quantitative T2 tumor values (tumor T2) and their ratio to-normal tissue: tumor-muscle ratio and tumor-urine ratio before therapy, as well as early changes in these parameters, could serve as predictors of the final therapeutic response in advanced-stage cervical cancer.

Study Subjects

The target population comprised patients with cervical cancer, they were recruited from the Installation of Radiology Service and Nuclear Medicine, referred by Gynecology Oncology Clinic in the Integrated Maternal and Child Health Service Unit, specifically those in stages IIB to IIIC2 according to FIGO 2018. Potential study subjects underwent an initial assessment, including a physical examination, abdominal MR (MRI #1), and cervical tissue biopsy for histopathological analysis and survivin level measurement.

MRI Protocol

MR examinations were performed three times: MRI #1 pra therapy, MRI #2 in the mid cycle of external radiation (20-30Gy), and MRI #3 at 2 months after complete therapy (Figure 1). MR preformed with Siemens Magnetom Avanto MR Machine and General Electric (GE) Optima MR Machine of 1,5 Tesla scanners. Conventional MRI sequences are T2-weighted imaging (WI) on sagittal and axial oblique images. The parameters for T2-weighted fast spin-echo imaging included a repetition time (TR) of 6188 ms, an echo time (TE) of 117 ms, a bandwidth of 20.83 kHz, an echo train length of 28 kHz, a slice thickness of 3 mm with a 1 mm gap, a field of view (FOV) of 24 cm, a matrix size of 256 × 256, two excitations, and a total acquisition time of 2 minutes. Conventional T2-weighted imaging was used to visualize the tumor, after which axial diffusion-weighted (DW) images were obtained with b-values set to 0 and 1000 s/mm². The DW imaging parameters comprised a TR of 6274 ms, a TE of 72 ms, a FOV of 24 cm, a bandwidth of 25 kHz, a slice thickness of 3 mm with no gap, six excitations, a matrix size of 128 × 128, and an acquisition time of 4 minutes. Single-shot spin-echo echoplanar imaging was used for diffusion imaging, which was carried out immediately after axial T2-weighted imaging and before intravenous contrast injection. The imaging was performed under free-breathing conditions, incorporating background body signal suppression through pre-saturation inversion recovery fat suppression. The parameters for this imaging were set as follows: TR/TE = 5238/64 ms, FOV = 240 × 240 mm, matrix size = 128 × 128, slice thickness = 4 mm, no intersection gap, parallel imaging with a sensitivity encoding factor of 2, and a receiver bandwidth of 62.5 Hz per pixel. B-values of 0 and 1000 s/mm² were captured in both the axial and sagittal planes, covering 20 slices to ensure the entire cervical cancer was included. Motion-probing gradients were applied along three orthogonal axes. The field of view, slice thickness, and intersection gap were adjusted to match those of the anatomical axial T2-weighted imaging, facilitating precise image overlay and co-registration (Table 1).

Image Analysis

MR images was interpreted by 2 radiologists with 30 and 10 years of experience. All images were analyzed using PACS (INFINITT Healthcare Co. Ltd., Seoul, South Korea). We evaluate these variables: tumor size, nodal metastasis findings, tumor ADC value (ADC Tumor), tumor quantitative T2 value (T2 Tumor), tumor ADC value-to-gluteus maximus muscle ratio (ADC t/m ratio), tumor ADC value-to-urine ratio (ADC t/u ratio), tumor T2 value-to-gluteus maximus muscle ratio (T2 t/m ratio), and tumor T2 value-to-urine ratio (T2 t/u ratio).

Tumor size is measured in 3 dimensional on antero-posterior (AP) x latero-lateral (LL) x cranio-caudal (CC) diameter on axial and sagittal T2 image. Tumor size is defined as the longest diameter between AP, LL, and CC

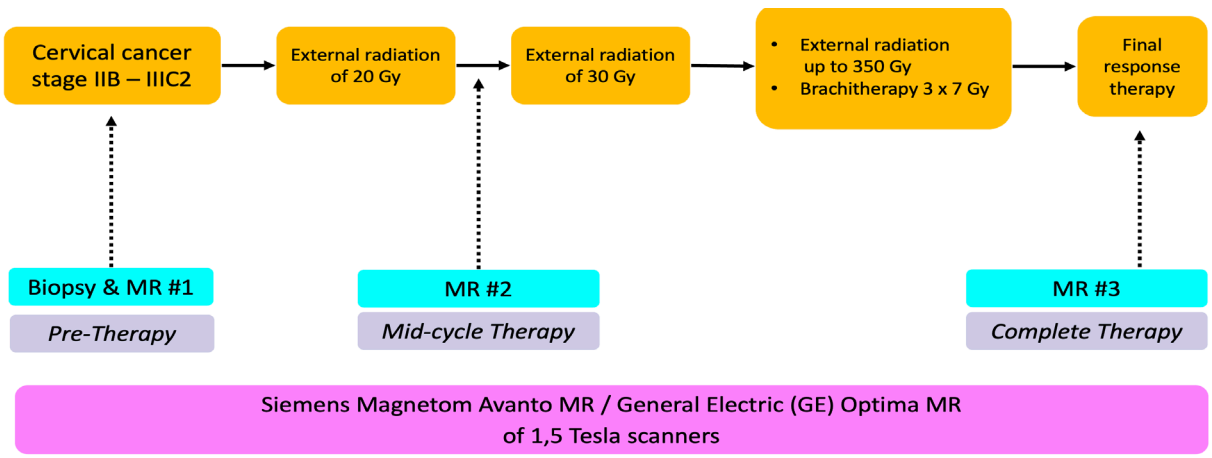

Figure 1. Research Diagram

Table 1. MR Protocol

Sequences	Acquisition parameters				
	TR / TE	Bandwith/ Echo train length	Slice thickness	FOV/ Matrix size	Total acquisition time
T2WI					
Sagittal	6188ms / 117ms	20.83kHz / 28kHz	3mm with a 1 mm gap	24 cm / 256 x 256	2 mins
Axial oblique	6188ms / 117ms	20.83kHz / 28kHz	3mm with a 1 mm gap	24 cm / 256 x 256	2 mins
T2FS					
Axial oblique	5238ms / 64ms	62.5 Hz	4 mm no intersection gap	24 cm / 128 x 128	4 mins
DWI b 0, 1.000 s/mm^2					
Axial	6274ms / 72ms	25 kHz	3 mm no gap	24cm / 128 x 128	4 mins

diameter. The ADC value and quantitative T2 value on the tumor, gluteus muscle, and urine were measured using by large ROI using freehand tools in the Infinitt PACS that covered more than 70% of tumor and tissue area.

Survivin Measurement

The tumor survivin levels were determined using ELISA analysis conducted at the Molecular Biology Proteomics Core Facilities Laboratory in Indonesian Medical Education and Research Institute. The median tumor survivin level was 17,9 pg/mg of total protein.

Data Analysis

The collected data included age, tumour size, histopathological tumour type, nodal metastasis findings, ADC and T2 tumour, survivin levels. These were tabulated and analysed using IBM Statistical Program for Social Science (SPSS) software version 20. The study employed the Shapiro-Wilk test to assess data normality, as this method is more suitable for sample sizes below 50. The relationships between subject characteristic (age, histopathology type, MR parameters) and therapy outcomes were examined using the Chi-Square test. This was followed by multivariate analysis using logistic regression, including only variables with a p-value of less than 0.25 from the bivariate analysis. The resulting models were evaluated for clinical and statistical quality (via calibration and discrimination) to select the best model, which was then converted into a scoring system. Calibration was assessed with the Hosmer-Lemeshow test, while discrimination was evaluated using the ROC curve and the area under the ROC curve (AUC). Sensitivity, and specificity were calculated at the end of the analysis.

Results

Data collection was conducted from January 2023 to May 2024, with a total of 134 subjects initially enrolled in the study (Figure 2). Ninety-nine participants were excluded due to the following reasons: 16 had histopathology results that were not cervical cancer, 5 had early-stage cervical cancer, 5 were diagnosed with stage IV cervical cancer, 3 underwent hysterectomies, 1 had recurrent cervical cancer, 9 passed away before the first MR, 15 did not attend the first MRI, 2 were referred to hospitals outside of RSCM, 2 passed away before the second MRI, 5 missed the second MRI, 13 had not completed therapy, and 15 refused to continue treatment.

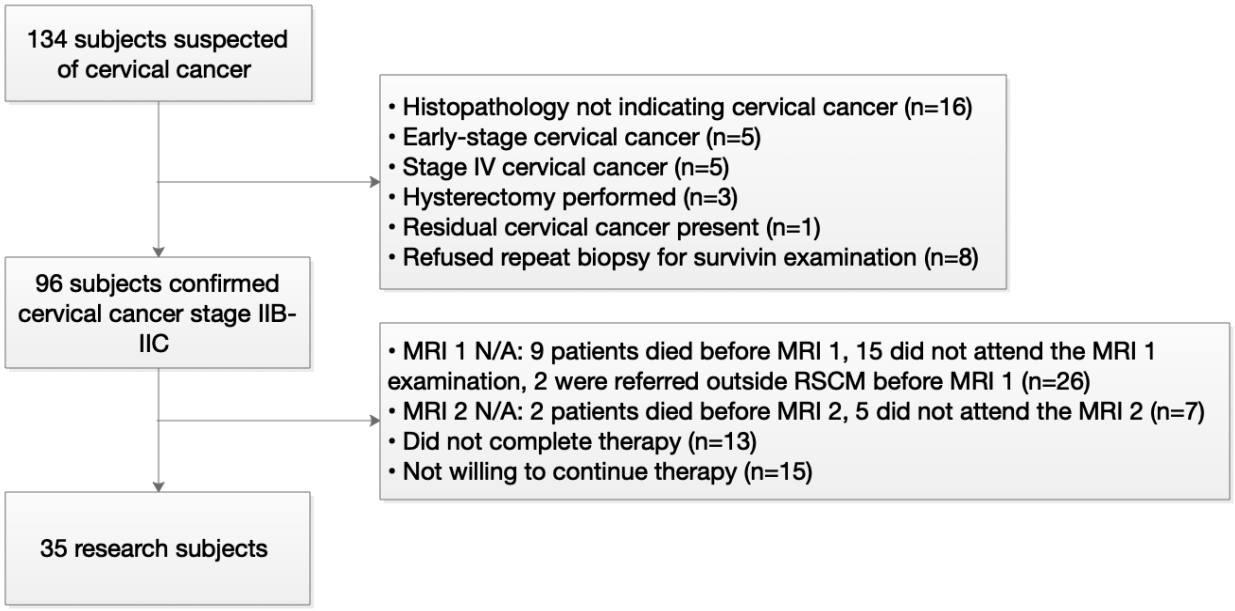

Figure 2. Diagram of Research Subject Enrollment

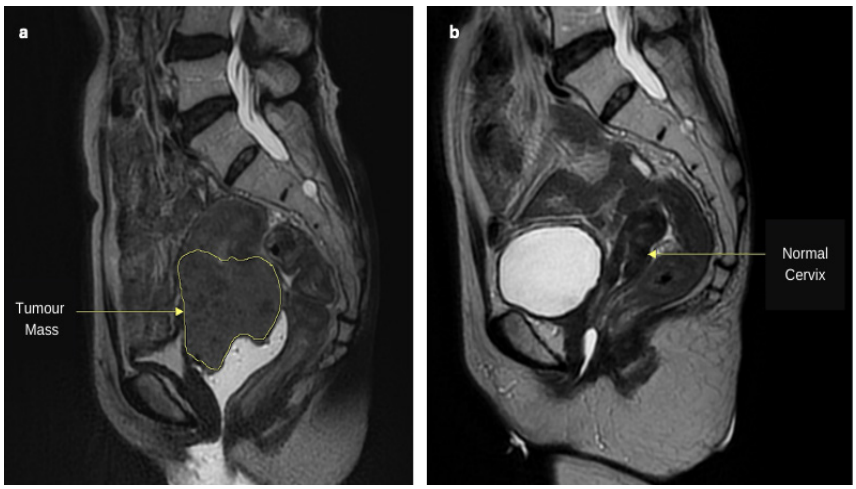

Figure 3. T2WI Sagittal MR Image in Subject with Complete Response. (a) Pre therapy MR showed cervical tumor, (b) Post therapy MR showed normal cervix without any residual mass

Table 2. Scoring System in Predictive Model

Variable	Score
Age	
≤ 52 years	2
> 52 years	0
Tumor Size	
> 60 mm	1
≤ 60 mm	0
Nodal Metastases	
Positive	1
Negative	0
T2 t/m Ratio MRI #2	
≤ 1.05	1
>1.05	0

Table 3. The Predictive Therapy Response in Research Subjects

Total Score	Final Therapy Response		Total	Probability
	Good	Poor		
0	9	0	9	0.01
1	2	0	2	0.04
2	7	1	8	0.21
3	1	6	7	0.57
4	2	4	6	0.87
5	0	3	3	0.97

Table 4. Probability of Subjects' Final Response to Therapy at Each Score

Total Score	Final Therapy Response		Total	Probability of Poor Final Response
	Good	Poor		
0-3	18	7	25	28,00%
4-6	2	7	9	77,78%

In the end, 35 subjects remained in the study.

Subjects Characteristics

Among the 35 subjects, the minimum age was 33 years, and the maximum age was 73 years. The average age of the subjects was 51.9 years. The most common histopathological type of cervical cancer was squamous cell carcinoma (n=29/35), followed by adenocarcinoma

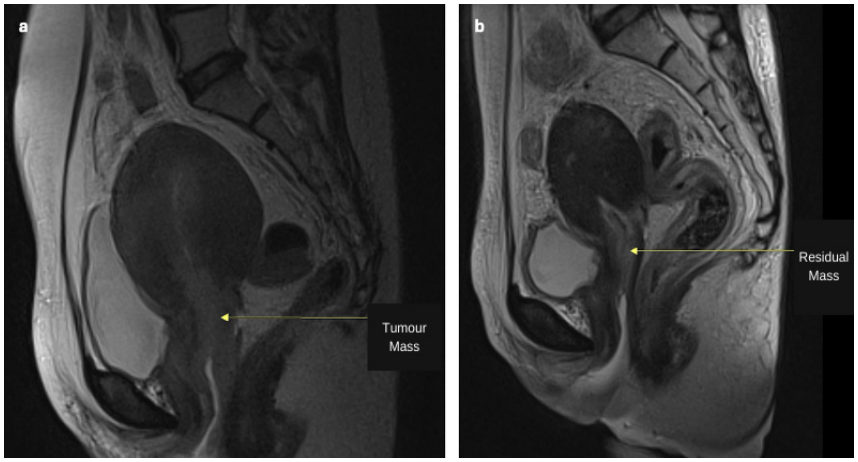

Figure 4. T2WI Sagittal MR Image in Subject with Partial Response. (a) Pre therapy MR showed cervical tumor, (b) Post therapy MR showed residual cervical mass

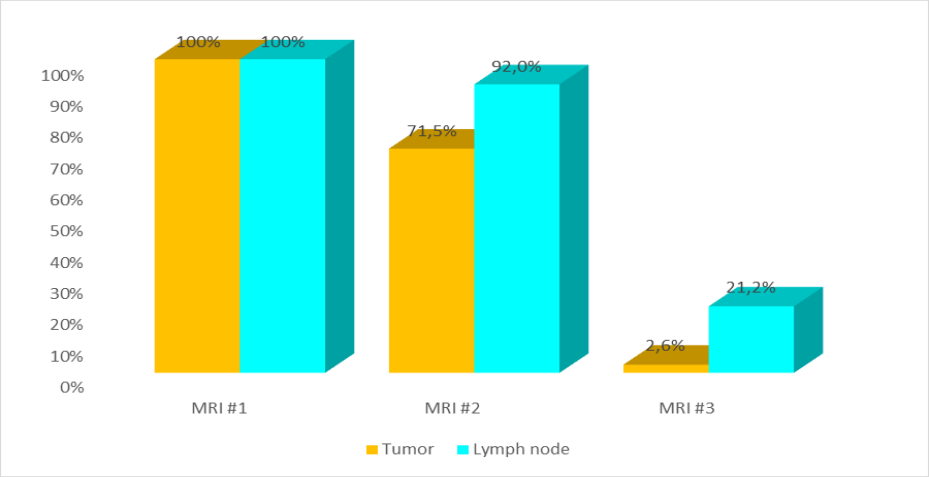

Figure 5. Diagram of Tumor and Lymph Node Size Observation on MR 1 – 2 – 3

Figure 6. Diagram of ADC Tumor Observation on MRI 1 – 2 – 3

(n=6/35 – 17.1%). The mean tumor size is 57,1 mm. Nodal metastasis findings are positive in 15 subjects. The median tumor ADC is 0,8 x 10-3 mm^2/s. The median tumor T2 is 596,3 ms. The median survivin level was 17.9 pg/mg of total protein.

Final Therapy Response

In this study, 21 subjects achieved a complete response (CR) (Figure 3), 7 had a partial response (PR) (Figure 4), and 7 experienced clinical deterioration or death.

Based on MR results from MRI #1, MRI #2, to MRI #3, there was a decrease in the mean tumor size and lymph

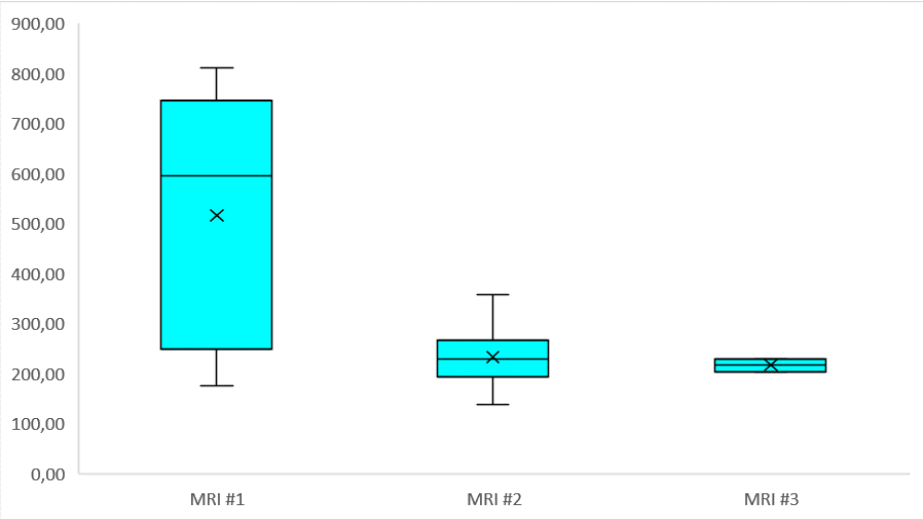

Figure 7. Diagram of T2 Tumor Observation on MRI 1 – 2 – 3

nodes (Figure 5), and increasing in tumor ADC values (Figure 6), and decreasing of tumor T2 (Figure 7).

Analysis of Subject Characteristics and MR Parameters with the Final Therapy Response

Bivariate and multivariate analysis was conducted on all variables to analyze their association with the final therapy response. This analysis resulting of 4 categorical variables that can be used in scoring system for predictive model. These variables are consisting of 1 clinical criterion: age and 3 MR parameters, they are tumor size, nodal metastasis findings, and the T2 t/m ratio on MRI #2. Each variable is categorized into two groups based on the cut-off point from the bivariate and multivariate analysis. Cut-off of age is 52 years, tumor size is 60 mm, nodal metastases findings is categorized on positive and negative, and T2 t/m ratio on MRI #2 cut-off is 1.05.

Therapy Response Predictive Model Scoring System

Two predictive models were generated, first model used only pre therapy variables and second model used pre- and mid-cycle therapy variables. Statical analysis of these two predictive models showed area under ROC curve is 0,825 on the first model and 0,931 on the second model. The final predictive model uses 4 variables consisting of pre- and mid-cycle therapy with total score 6 (Table 2).

The predictive model in this study showed that age younger than or equal to 52 years, tumor size greater than 60 mm, presence of positive nodal metastases on MR, and T2 t/m Ratio on MR in the mid-cycle therapy lower than or equal to 1.05 conferred a worse probability of the final therapy response. Based on the calculation of the scoring system that is implemented in our subjects, score 3 is identified as the optimal cut-off point (Table 3).

Subjects with a score of 0-3 had a 28.0% probability of poor final response, while subjects with a score of 4-6 had a 77.78% probability of poor final response.

Discussion

This study aimed to develop a predictive model for the final therapeutic response in advanced-stage cervical cancer by using clinical and MRI parameters, as well as by correlating these with tumor Survivin levels. The MRI parameters used were ADC and T2 values: tumor ADC value, the ratio of tumor ADC to normal tissue, tumor T2 value, and the ratio of tumor T2 to normal tissue. The normal tissues used for comparison were the gluteus muscle and the urine fluid in the urinary bladder, as visualized on MR. The study included 35 subjects with stage IIB to IIIC2 cervical cancer based on FIGO criteria, with proven histopathological biopsy. All subjects had their tumor Survivin levels assessed via biopsy, underwent pre-treatment MRI (MRI #1), and mid-cycle radiation therapy MRI (MRI #2). Twenty-eight subjects had post-therapy MRI (MRI #3), and seven did not due to clinical deterioration or death before the end of radiation therapy.

Age

The study analyzed the correlation between age and final therapeutic response, dividing participants into two age groups: ≤52 years and >52 years. A significant difference was found, with a p-value of 0.032, indicating that younger patients (≤52 years) had a poorer final therapeutic response. Epidemiological data show an increasing incidence of cervical cancer in younger age groups, with rates rising by about 10.3% for individuals aged 20-29 between 2000 and 2009 [15–17]. Patients are now being diagnosed 5-10 years earlier than before 2000, likely due to changes in sexual behavior related to HPV infections and a rise in smoking among younger people, leading to earlier abnormal cell changes HPV infections can cause precancerous lesions, which generally take around five years to develop into cervical cancer, though this process occurs more rapidly in younger patients, leading to higher cancer cell aggressiveness and quicker disease progression. This leads to a poorer prognosis for the therapeutic response obtained [15, 16].

Tumor Size

This study found no significant association ($p = 0.101$) between tumor size, using a cutoff of 60 mm, and the final therapeutic response in cervical tumor patients. Previous studies have commonly used a 40 mm cutoff to determine prognosis across all cancer stages. For instance, Miyasaka et al. [18] found that tumors larger than 40 mm were associated with poorer survival rates, while Lee et al. [19] noted that a minimum tumor size of 40 mm could serve as a prognostic factor for therapeutic success. Observational research by Pringgowibowo et al. [20] in 75 cervical tumor cases showed that patients with tumor diameters below 40 mm had a complete therapeutic response rate of 77.5%, compared to 54.6% in those with tumor diameters of at least 40 mm. The likelihood of achieving a complete therapeutic response was 2.86 times higher in patients with tumors smaller than 40 mm. Although the relationship was not statistically significant, tumor size (with a p-value < 0.25) was included in the multivariate analysis for the predictive model.

Nodal Metastases

This study found a significant difference between the presence of nodal metastases and the final therapeutic response in cervical tumor patients ($p=0.036$). Patients without nodal metastasis on MR had better therapeutic outcomes than those with nodal metastasis findings. Previous research by Hasan et al. [21] confirmed a significant impact of nodal metastasis on therapy response and prognosis, reporting a 5-year survival rate of 39-54% for patients with nodal metastasis compared to 67-92% for those without. Similarly, Kyung et al. [22] found that patients with nodal metastasis, detected via imaging, had a poorer prognosis than those without. Kilic et al. [23] noted that recurrence-free survival (RFS) declines with increasing numbers of nodal metastases, with a 5-year RFS rate of 77% in patients with up to 5 nodal metastases, 51% for those with 6 to 10, and 37% for those with at least 11 ($p=0.006$).

In this study, four of the seven subjects who experienced clinical deterioration or death, and thus did not undergo the MRI #3, had positive findings for nodal

metastasis on their MRI #1. Ho et al. [24] also found that, among 59 patients with positive nodal metastasis in the pelvic and paraaortic regions, those with paraaortic nodal metastasis had worse survival rates than those without. In the predictive model developed, nodal metastasis was included as a variable with a total score of 6 in the scoring system.

Histopathology

In this study, most subjects had squamous cell carcinoma (82.9%, n=29/35), while a smaller group had adenocarcinoma (17.1%, n=6/35). All subjects with adenocarcinoma showed a favorable therapeutic response, whereas among those with squamous cell carcinoma, 75.9% (n=22) had a good response, and 24.1% (n=7) had a poor response (p=0.178). This aligns with findings from Dashottar et al. [25] and Ho et al. [24], who observed that squamous cell carcinoma is the most common histopathological type in cervical tumors. Squamous cell carcinoma originates from the ectocervical cells, while adenocarcinoma arises from mucus-producing glandular cells in the endocervical area. Hasan et al. [21] reported that the mean ADC values for squamous cell carcinoma (0.88 x 10-3 mm^2/s) were statistically lower than those for adenocarcinoma (0.91 x 10-3 mm^2/s, $p<0.05$), indicating differences in cellular structure. Squamous cell carcinoma tends to be denser, while adenocarcinoma has tubular structures resembling glandular tissue, resulting in higher ADC values due to larger intercellular spaces.

Survivin

This study showed no significant difference between survivin levels and the final therapeutic response in tumors (p=0,544). However, Cheng et al. [26] conducted a meta-analysis of 11 studies, revealing a correlation between tumor survivin levels, histopathological findings in cervical cancer, and nodal metastasis. Their analysis indicated that survivin levels were not associated with FIGO stage or tumor size, but higher survivin expression was linked to poorer survival rates in cervical cancer patients. Additionally, Kusuma et al. [27] found that cervical cancer patients with squamous cell carcinoma at stage IIIB and survivin levels ≥932 pg/mL had a lower one-year survival rate. High survivin expression in tumors correlates with worse prognosis and increased therapy resistance.

MR Parameters and Response Therapy

This study utilized MR parameters, specifically the tumor quantitative T2 and ADC values, as well as the ratios of these values compared to normal tissues. The normal tissues selected for comparison were the gluteus maximus muscle and urine. The gluteus maximus was chosen as it is a representative soft tissue area less affected by acute radiation effects (fixed postmitotic tissue), while urine served as a physiological fluid representing normal structures. This approach provided two types of normal tissue consistency solid (muscle) and fluid (urine). Using these ratios minimizes measurement heterogeneity due to variations in MRI protocol implementation, resulting in a more homogeneous dataset of measurements [28].

In this study, no significant difference was found between the ADC parameters and the final therapeutic response. Previous research by Ghardon et al. [29] indicated that there are significant ADC value differences that can distinguish between stages 1, 2, and 3 of cervical cancer, with specific cutoff values for each stage. Notably, ADC values above 0.84 x 10-3 mm^2/s for stage 1 and 0.77 x 10-3 mm^2/s for stage 2 were associated with 100% accuracy and 57.8% accuracy, respectively. Additionally, Ho et al. [24] reported that smaller tumors with higher ADC values had better clinical outcomes. All ADC parameters measured in MRI #1 and MRI #2, including the delta values between the two MRIs, did not significantly correlate with the final therapeutic response, indicating they cannot be used as predictors of therapeutic success. However, there was an observed increase in tumor ADC values, along with higher ratios of tumor ADC to normal tissue, in most subjects after radiation doses of 20-30 Gy (n=32/35). This finding aligns with Dashottar et al., [25] who reported a significant increase in mean ADC values post-chemoradiotherapy (0,480 ± 0,134 x 10^{-3} mm^2/dt). They also noted that an ADC value below 0.799 x 10-3 mm^2/dt could predict residual lesions post-therapy with 100% sensitivity and 61.1% specificity. Ultimately, changes in ADC parameters after 20–30 Gy of therapy did not significantly relate to the final therapeutic response, showing no meaningful differences between the good and poor response groups [24,25,29].

In this study, a significant difference was observed in one T2 parameter related to the final therapeutic response: the Ratio T2 t/m MRI #2 ($p = 0.015$). There was a notable trend of decreasing quantitative T2 tumor values from MR #1 to MR #3. Previous studies have also indicated a correlation between quantitative T2 MR values and therapeutic response in various malignancies. For instance, Kim et al. 65 found that T2 values post-chemoradiotherapy in prostate cancer could predict complete pathological response with an AUC of 0.831 and a cutoff value of 649.6 mm3 (sensitivity of 0.850 and specificity of 0.725), while Souza et al. [30] demonstrated that T2 mapping values could serve as a biomarker for assessing treatment response in musculoskeletal tumors, showing results similar to this study, with a decrease in intratumoral quantitative T2 values following desmoid tumor therapy. Additionally, Liu et al. [12] reported that cervical cancer patients with good therapeutic responses showed a greater decrease in T2 signal intensity compared to those with poor responses, despite no significant differences in T2 values before treatment.

The findings in this research align with Liu et al.'s results, as a downward trend in quantitative T2 tumor values was noted post-radiation (20 Gy–30 Gy) until the completion of brachytherapy. Although parameters from MRI #1 and the delta values between MRI #2 did not significantly correlate with the final therapeutic response, the ratio T2 t/m MRI #2 emerged as a potential predictor, with a cutoff value of 1.05. Those with a ratio T2 t/m below 1.05 had a higher risk of poor response compared to those above this threshold. Overall, while ADC and quantitative T2 values from MRI #1 and their changes did not serve as predictors, the ratio T2 t/m MRI #2 proved to

be a more consistent metric. This suggests the importance of conducting MR midway through the radiation cycle to enhance predictive capabilities, as the ratio can be applied across different MR machines, minimizing variability in quantitative ADC and T2 values.

This study analyzed the relationship between MR parameters on the MRI #1 and tumor Survivin levels. Among the six MR parameters examined, none showed a significant correlation with Survivin levels. Survivin is a molecular biomarker expressed in various cancers, including cervical cancer, and is present in hypoxic cells and tumors with increased angiogenesis [31]. Survivin is an apoptosis inhibitor protein that plays a key role in regulating cell division and inhibiting apoptosis. This leads to changes in cellular conditions, reducing extracellular fluid diffusion, which correlates with lower ADC values. These cells contain higher fluid components, resulting in prolonged relaxation time (TR) and higher T2 values, making the tumor appear more hyperintense on MR [12, 32]. However, this study found no correlation between ADC and T2 parameters in MR and tumor Survivin levels, despite observing a trend of increased ADC and decreased T2 values post-radiation therapy in cervical cancer. This aligns with the theory that necrotic or scar tissue can enhance extracellular fluid diffusion, increasing ADC values and shortening T2 relaxation times, thereby reducing tumor intensity and quantitative T2 values following radiation therapy.

A limitation of this study is that it did not account for the possible role of other apoptosis inhibitor proteins, besides Survivin, in cervical cancer cells. Additionally, there were seven subjects with poor clinical outcomes or who had died, who were categorized under poor final response, making it impossible to carry out the MRI #3 scan to analyze ADC and quantitative T2 parameters. This study is the first in Indonesia to optimize the use of non-contrast MRI, not only for cervical cancer diagnosis but also to identify predictive factors from non-contrast MRI parameters for forecasting the final therapeutic response in advanced-stage cervical cancer. This research developed a new scoring system for predicting therapeutic outcomes in advanced-stage cervical cancer, incorporating both clinical and MR parameters.

In conclusion, this study found that T2 tumor-to-muscle ratio on the mid-cycle external radiation MRI could be used as one of the cervical cancer final therapy response predictive factors. This study generates an alternative new scoring system of predictive model for assessing the advanced stage cervical cancer final therapy response using patient age dan MR parameters: tumor size, nodal metastasis, and tumor T2-to-gluteus maximus muscle ratio on MR in the mid-cycle external radiation. This study needs to be conducted multicentered involving a larger sample size and various MR machine to increase external validity and ensure broader generalization of the results across populations.

Author Contribution Statement

Trifonia Pingkan Siregar: Conceptualized and developed the project, authored the manuscript, and was responsible for data collection and analysis. Septelia Inawati Wanandi: Contributed to refining the concept, provided biomolecular data, and conducted its analysis. Sawitri Darmiati: Offered valuable input and insights into the concept. Fitriyadi Kusuma: Contributed insights and provided data on cervical cancer cases. Sri Mutya Sekarutami: Provided input, insights, and data on cervical cancer therapy outcomes. Lisnawati: Contributed to the concept, supplied data, and performed histopathological analysis of cervical cancer cases. Joedo Prihartono: Offered input on the concept and carried out statistical data analysis. Muhammad Ilyas: Provided insights and reviewed the article. Ginva Amalia, Khalida Ikhlasiya Tajdar Gefariena Elfahmi, Nur Khofifah Aprilia, and Adila Salsabila: Collected data, created manuscript illustrations, conducted reference searches, performed translations, and assisted with editing and proofreading.

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General

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Conflict of Interest

The authors declare that there are no conflicts of interest in this study.

Ethical Declaration

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, University of Indonesia (No. LB.02.03/2.6.1/1065/2022; Ethical extension No. ND-567/UN2.F1/ETIK/PPM.00.02/2023), and Dr. Cipto Mangunkusumo Hospital (No. KET-996/UN2.F1/ETIK/PPM.00.02/2022).

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