

Research Article

The Proportion of Lymph Node Metastasis in Patients with Stage IIA 1and IIA2 Cervical Cancer who were Treated for Radical Hysterectomy and Pelvic Lymphadenectomy

Perbandingan Proporsi Metastasis Kelenjar Getah Bening pada Pasien Kanker Serviks Stadium IIA1 dan IIA2 yang Ditatalaksana Histerektomi Radikal dan Limfadenektomi Pelvis

Andrijono, Wahyu Ginealdy

Department of Obstetrics and Gynecology
Faculty of Medicine Universitas Indonesia
Dr. Cipto Mangunkusumo General Hospital
Jakarta

Abstract

Objective : This study was conducted to determine a difference in the prognosis of stage IIA1 cervical cancer compared to stage IIA2 based on the incidence of metastasis to pelvic lymph nodes by radical hysterectomy.

Methods: A cross-sectional study was conducted among 108 stage II cervical cancer patients who had undergone radical hysterectomy in the obstetric-gynecologic department of Dr. Cipto Mangunkusumo hospital since 2006-2016.

Results : Of 108 patients with cervical cancer stage IIA, 80 (74%) patients are stage IIA1 and the remaining 28 (26%) patients are stage IIA2. The average age of patients at stage IIA2 (47.79 years) younger than IIA1 (55.85 years) and also patient at stage IIA1 having a higher parity number which is four compared to stage IIA2 with the number of parity 2. The Involvement of lymph node metastasis in patients with stage IIA1 and IIA2 cervical cancer were 51 (63.75%) and 16 (57.14%) respectively.

Conclusions : Metastatic factor to lymph node in both stages have the same result. There was no difference in the proportion of lymph node metastasis occurring in both stage IIA cervical cancer stage which was corrected with radical hysterectomy and pelvic lymphadenectomy with $p = 0.535$. Changing staging did not seem to improve the prognosis.

Keywords : cervical cancer, lymph node metastatic, stage IIA

Abstrak

Tujuan : Membuktikan adanya perbedaan prognosis kanker serviks stadium IIA1 dibanding stadium IIA2 berdasarkan kejadian metastasis ke kelenjar getah bening pelvis yang dilakukan histerektomi radikal.

Metode : Dengan menggunakan metode potong lintang dilakukan pengambilan data 108 sampel pasien kanker serviks stadium IIA yang dilakukan pembedahan histerektomi radikal di Departemen Onkologi Ginekologi RSUP. Dr. Cipto Mangunkusumo Jakarta sejak tahun 2006 hingga tahun 2016.

Hasil : Pasien kanker serviks stadium IIA1 sebanyak 80 (74%) pasien dan stadium IIA2 sebanyak 28 (26 %) pasien. Pada stadium IIA2 (47.79 tahun) didapatkan rata-rata usia pasien lebih muda dibandingkan IIA1 (55.85 tahun). Pada stadium IIA1 juga didapatkan jumlah paritas yang lebih tinggi yaitu 4 sedangkan pada stadium IIA2 dengan jumlah paritas 2. Keterlibatan metastasis kelenjar getah bening pada pasien kanker serviks stadium IIA1 dan IIA2 berjumlah 51 (63.75%) dan 16 (57.14%) secara berurutan. Tidak terdapat perbedaan proporsi kejadian metastasis kelenjar getah bening pada kedua kelompok stadium kanker serviks pada stadium IIA dengan nilai $p = 0,535$.

Kesimpulan : Faktor metastasis kelenjar getah bening pada kedua stadium memiliki hasil yang serupa. Tidak terdapat perbedaan proporsi kejadian metastasis kelenjar getah bening pada kedua kelompok stadium kanker serviks stadium IIA1 dan IIA2 yang ditatalaksana dengan histerektomi radikal dan limfadenektomi pelvis. Perubahan penetapan stadium sepertinya tidak memperbaiki prognosis.

Kata kunci : faktor prognostik , kanker serviks, kelenjar getah bening, stage IIA.

INTRODUCTION

Cervical cancer is the fourth most common cancer in the world, but in women, cervical cancer was ranked second most after breast cancer.¹ Nowadays, cervical cancer is one of the main problems due to its high incidence and the leading cause of death, especially in developing country such as Indonesia.^{2,3} Data from thirteen anatomical pathologic centres in Indonesia showed that cervical cancer was ranked first among all of gynaecological cancer in women (31% from ten most common cancers in women) followed by ovarian cancer, endometrial cancer and vulvovaginal cancer.^{2,4}

These days, the staging of cervical cancer is based on the classification of The International Federation of Gynecology and Obstetrics (FIGO) which divides cervical cancer into four stages based on area and invasion. This classification was first used in 1928, until now has been done eight times revision, the last revision is in 2009 at stage 0 and IIA cervical cancer.⁵ FIGO has removed stage 0 because it is still considered as a pre-invasive lesion. While stage IIA changes were subdivided into two based on tumour size, ie IIA1 (Primary lesion size ≤ 4 cm) and IIA2 (Primary lesion size > 4 cm).⁵ This revision was performed after analysis of data, literature and cases found to date. This change was considered necessary after observing the previously revised IB stage in 1995, whereby there is a similar prognosis when stage IIA is also subdivided by tumour size.⁵ According to Jatupol study, it was found that the 5-year free of disease between stage IB1 and IB2 was 98, 1% and 82.8% with p value < 0.001 , another study conducted by Teresa also mentioned the number of 2 years free of disease between IB1 and IB2 stages was 92.5% and 74.3% with p value 0.012.^{6,7} Both studies showed that the division of stage IB into two categories showed different prognosis outcomes in stage IB1 had a better prognosis than IB2.⁷ Recommended treatment of cervical cancer patients stage IB to IIA is radical hysterectomy (type II-III) and pelvic lymphadenectomy (removal of pelvic lymph nodes).⁸ In general, proper treatment and therapy in the early stages will have a good prognosis. However, 10-17% of early-stage cervical cancers will remain residue even if they are recurrent before five years.⁸ Successful therapy and prognosis of the patient will be largely determined by the presence of

lymph node involvement in the pelvis. Jatupol research suggests that lymph nodes involvement reduces the 5-year recurrence rate.⁷ Other studies conducted by Kim also mention the same thing, patients with lymph nodes involvement have a higher recurrence rate than those who do not.⁹ Several factors can be used to predict Lymph nodes involvement such as, the size of the primary tumour, stage, histology, degree of differentiation and lymphovascular invasion.¹⁰

It is known that the 5-year survival rate of cervical cancer is better in earlier stages. The 5-year survival rate of women with stage I cervical cancer reaches 80-90%, and in stage II reaches 50-65%. While the 5-year survival rate of women with stage III cervical cancer reached 25-35% and cervical cancer stage IV less than 15%.⁸

There is a change in IB stage staging to IB1 and IB2 stage, as well as stage IIA. There is a stage IIA revision to stage IIA1 and stage IIA2. It is interesting to observe whether the change in staging determination improves the prognosis or is there a difference in the prognosis of stage IIA1 cervical cancer with stage IIA2 indirectly by looking at the metastatic factor of lymph nodes. As we know, the dominant prognosis factor in early-stage cervical cancer is a metastatic factor to the lymph nodes.

METHODS

This research used cross-sectional study design at Dr. Cipto Mangunkusumo general hospital, Jakarta in 2006 until 2016. The target population in this study was cervical cancer patients stage IIA1 and IIA2. The source population in this study was cervical cancer patients stage IIA1 and IIA2 who were treated for radical hysterectomy and pelvic lymphadenectomy in the Gynecology Oncology of RSCM Jakarta since 2006. Meanwhile, we also performed exclusions to stage IIA cervical cancer patients who received adjuvant chemotherapy and were accompanied by another kind of cancer disease.

The first step in this research working procedure is collecting primary data obtained from the Cancer Registration of RSCM Oncology Gynecology Division. According to this data, then conducted search on RSCM Medical Record section and anatomical pathology section, then

adjusted according to inclusion and exclusion criteria, so it will get the number patients that can be evaluated.

Results Data analysis for lymph node involvement is the number, percentage and P value. Bivariate analysis was performed to find the comparison of KGB proportion at stage IIA1 and IIA2 with chi-square analysis If the requirements for chi-square are met. If the conditions are not met, then the fisher test will be done. This research has received ethical approval from the ethical commission of Dr. RSUPN. Cipto Mangunkusumo / Faculty of Medicine University of Indonesia with number 962 / UN2.F1 / ETIK / 2016

larger-scale studies with 560 patients, the mean age of patients at stage IIA1 (49 years) while at stage IIA2 (54 years).¹² From these results, we can conclude that the mean age of patients with stage IIA2 lower in different parts of the world, with these lower results it will affect the survival rate of each stadium.

Those with IIA1 stage had a median parity of 4 (0-10) while those with IIA2 stage had a median parity of 2 (0-8). The Mann-Whitney test showed that there was a significant difference between the two stages of study based on parity with $p < 0.0005$. Although statistically different, it is known that parity did not affect the prognosis of

Table 1. Sociodemographic Characteristics and Comparison of Age and Parity Characteristics of Cervical Cancer Patients Stage IIA1 and IIA2

	Stage IIA1	Stage IIA2	P-value	OR	95% CI
Age (year)	55.85	47.79	< 0.0005	0.87	0.82 – 0.93
Mean (SD)	(7.98)	(7.38)			
Parity Median	4	2	<0.0005	0.55	0.41 – 0.74
	(0-10)	(0-8)			

RESULTS

A total of 108 subjects were recruited in this study. Eighty subjects were diagnosed with cervical cancer (74%) and patients with stage IIA2 of 28 cases (26%). Table 1 shows the sociodemographic characteristics and comparison of age and parity characteristics of both stages.

Table 1 shows that the mean age of stage IIA2 patients is younger than IIA1, whereas the mean age of patients in stage IIA1 and IIA2 are 55.85 years and 47.79 years respectively. Comparative

cervical cancer. In a study conducted by bjorge involving 2870 patients, it was found that parity did not affect the prognosis of cervical cancer.¹³

Histopathological characteristics can be seen in table 2. It is known that the most histopathologic type is epidermoid carcinoma with the number of 79 people (73.15%), the second is adenocarcinoma with 19 people (17.59%), and the third is adenosquamous carcinoma with ten people (9.26 %). This is consistent with previous research data conducted by Laila and Anggraeni, which obtained the highest percentage of

Table 2. Characteristics and Comparison of Histopathologic Types between Cervical Cancer Patients Stage IIA1 and IIA2

Histopathologic types	Stage IIA1 n (%)	Stage IIA2 n (%)	P-value	or	95% CI
Epidermoid Carcinoma	61 (76.25)	18 (62.29)			
Adenocarcinoma	11 (13.75)	8 (28.57)			
Adenosquamous Carcinoma	8 (10)	2 (7.14)	0.928	1.23	0.65 – 2.34
Clear Cell Carcinoma	0	0			

hypothesis testing using unpaired T-test showed that there were significant differences between the two age-based study groups with $p < 0.0005$. This is also in accordance with study conducted by Jery in Taiwan¹¹, in the study obtained the average age of patients in stage IIA1 and IIA2 that is 55.1 and 47.7 respectively. Garg also performed

histopathologic outcomes are squamous cell carcinoma of 71.6% and 70.2% respectively.^{3,14}

This result also corresponds with other studies in France, China and Japan which the results showed that the histopathology of squamous cell carcinoma was the most common.¹⁵⁻¹⁷

Table 3. Comparison of the Proportion of Lymph Node Metastasis between Cervical Cancer Patients Stage IIA1 and IIA2

Lymph node metastasis	Stadium IIA1 n (%)	Stadium IIA2 n (%)	P-value	or	95% CI
Yes	51 (63.75)	16 (57.14)	0.535	0.76	0.32 - 1.82
No	29 (36.25)	12 (48.26)			

The differences between the two groups can be seen by testing the Kolmogorov-Smirnov test hypothesis. From this test obtained p-value is 0,928 which means there is no relationship between histopathology type and stage of cervical cancer.

Table 3 illustrates the proportion of lymph node metastasis occurring in cervical cancer patients Stage IIA1 and IIA2. The result is 51 (63.75%) of patients with stage IIA1 have lymph node metastasis involved, whereas in stage IIA2 there

are 16 (57.14%) of patients. An analysis was conducted to assess the difference in the proportion of lymph node metastasis occurring in both cervical cancer stage groups. In this case, lymph node metastasis data can be tested with Chi-Square test. The results showed no difference in the proportion of lymph node metastasis occurrence in both cervical cancer stage groups between stage IIA1 and IIA2 treated with radical hysterectomy and pelvic lymphadenectomy with p-value 0.535. Similar results were also obtained in the study in Taiwan; this is because the number of patients in the study is also small that there are only 51 research patients.¹¹

The power of this study was only 53.55%, although it did not meet the number of samples, but we used using total sampling method to increase the power of this study. Therefore, the results of the analysis to see the possible difference in proportion in this study is not necessarily the same as that in the population. So it takes further research with more samples to get the result of analysis with the exact power.

Considering the results of this study on the revision of stage IIA issued by FIGO in 2009 that divides stage IIA into stage IIA1 and stage IIA2, it turns out that the staging revision does not affect the lymph node metastasis rate in both stages IIA. As we know lymph node metastasis factor is one of the dominant factors that affect the prognosis of cervical cancer, thus indirectly

the prognosis of patients stage IIA1 and IIA2 also not much different.

CONCLUSION

There was no difference in the proportion of lymph node metastasis occurring in both stage IIA1 and IIA2 cervical cancer stage which was correlated with radical hysterectomy and pelvic lymphadenectomy with p = 0.535. Changes in staging did not affect the rate of lymph node metastasis in both stage IIA.

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